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Meta-Analysis: Does Garlic Intake Reduce Risk of Gastric Cancer?

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In the past 2 decades, various epidemiological studies investigated whether garlic can positively modify the risk of gastric cancer. Garlic contains numerous sulfide compounds, including diallyl trisulfide, which have anticarcinogenic properties. We conducted a meta-analysis to determine if garlic intake reduces the risk of gastric cancer. An electronic search of MEDLINE, PubMed, and EMBASE to June 2014 was completed. There were 14 case control studies, 2 randomized controlled studies, and 1 cohort study that fulfilled our inclusion criteria. We used a random effects model to calculate pooled odds ratios (OR) and 95% confidence intervals (CIs) for risk of gastric cancer with garlic consumption. Meta-analysis of a total of 8,621 cases and 14,889 controls was conducted. Significant variability in duration of garlic intake and reference categories for amount of intake was noted. High, low, and any garlic intake were all associated with reduced risk of gastric cancer. High intake had the most significant risk reduction, OR = 0.49 (95% CI: 0.38–0.62). Heterogeneity was low (I^2 = 30.85, P = 0.17). A more modest risk reduction was associated with low intake, OR = 0.75 (95% CI: 0.58–0.97). Half of the studies did not separate garlic intake into high or low amounts, intake was only noted as consumption vs. non-consumption. Any amount of consumption still showed a risk reduction similar to low intake, OR = 0.77 (95% CI: 0.60–1.00). Low and any amount of consumption showed moderate heterogeneity (58% and 45%, respectively). Garlic intake appears to be associated with reduced risk of gastric cancer. Further high quality studies are required to confirm this finding and to assess the amount of garlic that needs to be consumed for protective effect.

INTRODUCTION

Gastric cancer is the fifth most common malignancy worldwide according to the International Agency for Research on Cancer (1). Global incidence was estimated to be around 952,000 in 2012 (1). Incidence in men is double that of cases in women (1–3). The majority of cases, more than 70%, occurred in developing countries (1). Around 42% of the new cases occurred in China (1). In the United States, there were 21,600 new cases of gastric cancer and 10,990 deaths from gastric cancer in 2013 (2). The global incidence of gastric cancer has significantly decreased in the past 4 decades (1), however it is still the third leading cause of cancer related death worldwide and contributes significantly to cancer related disability and morbidity (1,4).

Adenocarcinomas account for the vast majority of gastric cancers. Risk factors for gastric cancer include, atrophic gastritis (5), gastric metaplasia and dysplasia (6), and Helicobacter pylori infection (7). Smoking (8,9), high salt intake (10,11), and obesity are all also associated with increased risk of gastric cancer. High fruit and vegetable intake was found to be protective (13).

Epidemiological studies, as early as 2 decades ago, reported the positive effect of garlic on gastric cancer risk (14). Garlic contains numerous organosulfur compounds, including diallyl trisulfide, which have been shown to have anticarcinogenic properties in experimental animals (15). The exact mechanism is unclear, but it is hypothesized that the sulfur compounds reduce risk of cancer by enhancing DNA repair, detoxifying carcinogens and inducing apoptosis (15). Antibacterial properties of garlic may also be a protective factor (16).

METHOD

Search Protocol

A systematic search was performed on MEDLINE (from 1946), PubMed, and EMBASE (from 1974) looking at studies to June 2014. The search terms used were Garlic OR Garlic extract OR Allium OR diallyl trisulfide AND Stomach Cancer OR Stomach Neoplasm. Relevant articles from reference lists were also included. There were no restrictions placed on location, language, or age of study. Unpublished literature was not searched.

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Study Selection

Studies were included if 1) the study used a cohort, case control, or randomized control study design; 2) the study reported intake of garlic in gastric cancer cases and controls; 3) the risk point estimate was reported as odds ratio (OR) and had a 95% confidence interval (CI) or if both could be calculated from the data. There were no restrictions placed on minimum sample size. Nineteen studies met the above inclusion criteria. Two studies were excluded due to garlic not being separated from other allium vegetables for analysis (17,18). Seventeen studies were in the final analysis.

Data Extraction

A standardized collection form was used to extract data such as publication year, study type (cohort, case control, randomized control), number of cases, number of controls, temporal direction, population derivation (population case control, hospital case control), country, continent, case control matching, adjusted variables, risk estimates or data used to calculate risk estimates. All studies had adjusted ratios, where more than 1 adjusted ratio was reported; the ratio with the highest number of adjusted variables was selected. Where multiple risk estimates were available in the same study for different amounts of garlic intake, they were included as separate risk estimates. For example, Munoz et al. (23), separated risk estimates by garlic eaten daily, garlic eaten several times a week, and garlic eaten less than once a week.

Statistical Analysis

Random effects model was used to calculate pooled odds ratios and 95% confidence intervals to determine the effect of garlic on gastric cancer risk. We tested heterogeneity with Cochran's Q statistic, with $P < 0.10$ indicating heterogeneity, and quantified the degree of heterogeneity using the I^2 statistic, which represents the percentage of the total variability across studies, which is due to heterogeneity. I^2 values of 25%, 50%, and 75% corresponded to low, moderate, and high degrees of heterogeneity respectively. We quantified publication bias using the Egger's regression model, with the effect of bias assessed using the fail-safe number method. The fail-safe number was the number of studies that we would need to have missed for our observed result to be nullified to statistical non-significance at the $P < 0.05$ level. Publication bias is generally regarded as a concern if the fail-safe number is less than $5n + 10$, with n being the number of studies included in the meta-analysis. All analyses were performed with Comprehensive Meta-analysis (version 2.0, Biostat, Englewood, NJ).

RESULTS

Study Characteristics

Our literature search identified 145 studies, of which 17 met inclusion criteria (Fig. 1). The vast majority of studies reported

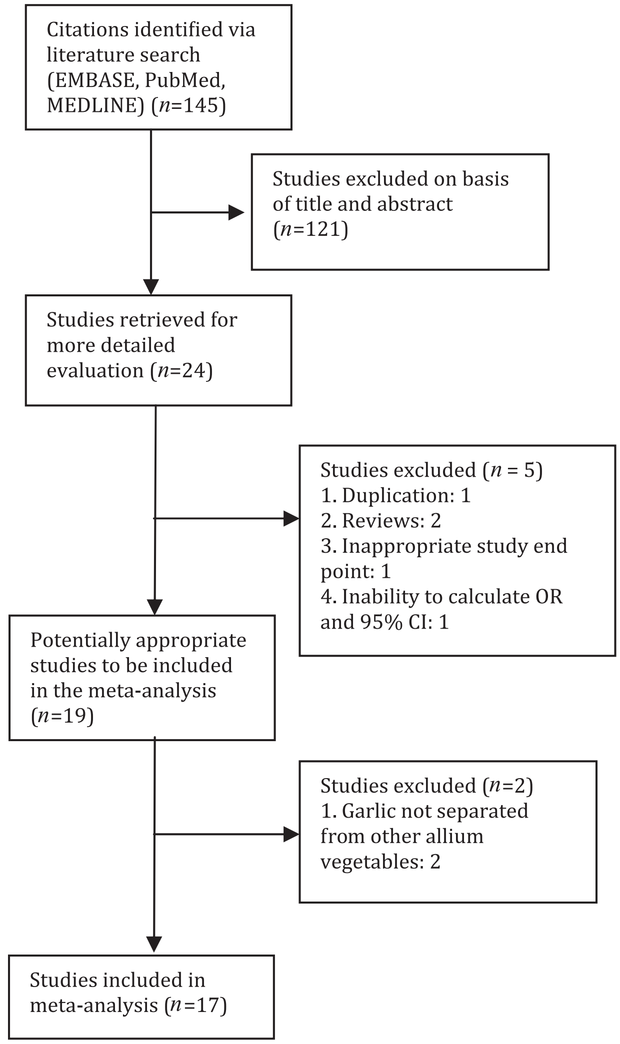

FIG. 1. Study selection flow sheet.

use of fresh garlic (14 of 17). Dorant et al. (19) reported daily garlic supplement use (components unknown), Li et al. (20) reported use of specific components of garlic: 200 mg of allitridium everyday and 100 mcg of selenium every other day and Ma et al. (21) reported garlic supplement use (mixture of garlic extract and steam-distilled garlic oil). There was great variability in duration of garlic and garlic supplement use, for example, Ma et al. (21) reported follow up after daily supplement use for 7 yr where as Li et al. (20) reported follow up after daily supplement intake for 1 mo a yr for 3 yr.

A special case was Setiwan et al. (22). This retrospective case control study attempted to compare risk of gastric cancer with garlic consumption between 2 areas in Qingdao, China and Shanghai, China. Data from this study was treated as 2 separate data sets, they are reported in our meta-analysis as Setiwan (2005a) and Setiwan (2005b) (22), respectively.

TABLE 1
Study characteristics

Author (Year)	Study type	Cases	Controls	Population derivation[1]	Country	Continent
You (1989)	Case control	562	1131	PCC	China	Asia
Hansson (1993)	Case control	338	669	PCC	Sweden	Europe
Dorant (1996)	Cohort	152	3340	PCC	Netherlands	Europe
Gao (1999)	Case control	153	234	PCC	China	Asia
Ekstrom (2000)	Case control	480	1067	PCC	Sweden	Europe
Takezaki (2001)	Case control	187	333	PCC	China	Asia
Munoz (2001)	Case control	292	477	PCC	Venezuela	South America
De Stefani (2001)	Case control	160	320	HCC	Uruguay	South America
Kim (2002)	Case control	136	136	HCC	Korea	Asia
Gao (2002)	Case control	91	169	PCC	China	Asia
Li (2004)	Randomized control trial	2526	2507	PCC	China	Asia
Setiawan (2005a)	Case control	128	128	PCC	China (Qingdao)	Asia
Setiawan (2005b)	Case control	750	750	PCC	China (Shanghai)	Asia
Zickute (2005)	Case control	379	1137	HCC	Lithuania	Europe
Pourfrazi (2009)	Case control	217	394	PCC	Iran	Asia
Pakseresht (2011)	Case control	286	304	PCC	Iran	Asia
Ma (2012)	Randomized control trial	1678	1687	PCC	China	Asia
Yassibas (2012)	Case control	106	106	HCC	Turkey	Asia–Europe

[1]HCC = hospital case control, PCC = population case control.

The studies were performed in various countries across 3 continents. Around 40% of the included studies ($n = 7$) were conducted in a Chinese population. There were 2 studies each in Swedish and Iranian populations. Uruguay, Netherlands, Venezula, Korea, Lithuania, and Turkey were the source of 1 study each. There were 14 case control studies, 2 randomized controlled studies, and 1 cohort study in our meta-analysis (Table 1). Sample size of controls ranged from 106 to 3340 and number of cases ranged from 91 to 2526 in the studies. A total of 8621 cases and 14,889 controls were analyzed (Table 3).

There was great variability in reference categories for amount of garlic intake (Table 2). Half of the studies compared high vs. low levels of intake, whereas the other half reported consumption (any) vs. nonconsumption. In those studies that separated high vs. low intake, all were found to use different categories for amount of intake. For example, high intake in the various studies was reported as: >1.5 kg/year, >1 time/wk, seldom to 1 time/day, everyday, "high," few times a month, every meal/every day, or >1 time/day. Low intake categories included: 0.1–1.5 kg/yr, 1–3 times/mo, 1–2 times/wk, several times/wk, "low," few times/wk, 1–3 times/mo. In the studies that reported any vs. nonconsumption, there was also great variability in amount of garlic consumed; for example, never vs. seldom to 1 time/day, 200 mg of allitridium every day and 100 mcg of selenium every other day, per 10 g of garlic, 0 servings per mo vs. >0 and <1 time/wk vs. less. There was no publication bias (Egger's regression: $P = 0.76$).

High vs. Low vs. Any Intake of Garlic

High, low, and any garlic intake were all associated with reduced risk of gastric cancer. High intake had the most significant risk reduction, OR = 0.49 (95% CI: 0.38–0.62) (Fig. 2). Heterogeneity was low ($I^2 = 30.85$, $P = 0.17$). A more modest risk reduction was associated with low intake, OR = 0.75 (95% CI: 0.58–0.97) (Fig. 3). Half of the studies did not separate garlic intake into high or low amounts, intake was only noted as consumption vs. nonconsumption. Any amount of consumption still showed a risk reduction similar to low intake, OR = 0.77 (95% CI: 0.60– 1.00) (Fig. 4). Low and any amount of consumption showed moderate heterogeneity (58% and 45%, respectively).

Regional Variation in High Garlic Intake Population

Regional analysis of the high garlic intake population was undertaken, comparing studies from Asia with Europe and South America. There were 11 studies in total from the Asian continent (22) was considered 2 separate data sets as detailed above), 2 from South America, and 4 from Europe. Yassibas et al. (24) was not included in the regional analysis due to a technicality (Turkey is considered part of both Asia and Europe).

Asian and South American studies showed similar amount of risk reduction associated with high garlic intake, OR = 0.54 (95% CI: 0.4–0.72) and OR = 0.53 (95% CI: 0.37–0.76)

TABLE 2
Study characteristics continued

Author (year)	Study type	Categories of amount of intake	Covariates in adjusted risk estimates	Method of data collection of garlic intake	Time period during which garlic was consumed prior to gastric cancer
You (1989)	Case control	0 kg/yr (reference) 0.1–1.5 kg/yr (low) >1.5 kg/yr (high)	Adjusted for sex, age, family income, intake of other allium vegetables.	Unavailable	Unavailable
Hansson (1993)	Case control	0 servings/mo (reference) > 0 servings/mo (any)	Adjusted for age, gender, and SES.	Unavailable	Unavailable
Dorant (1996)	Cohort	No supplements (reference) Exclusively garlic supplements (any)	Adjusted for age, alcohol intake, vitamin C intake, and b-carotene as continuous variables and sex, smoking status, education, history of stomach disorders, and family history of stomach cancer as categorical variables. Also adjusted for onion and leek consumption.	FFQ	Daily use of any garlic supplement for at least 1 yr in the 5-yr period before baseline. N.B. Analysis was restricted to cancer incidence in the first 3.3 yr of follow-up (from baseline in September 1986 to December 1989).
Gao (1999) 1–3 times/mo (low) >1 time/wk (high)	Case control	< 1 time/mo (reference)	Adjusted for age, sex, income, smoking, drinking, tea consumption, and intake of leftover gruel, pickled vegetables, meat, fruit, tomatoes, eggs and snap beans.	FFQ	Not stated
Ekstrom (2000)	Case control	Never (reference) Seldom–1 time/day (any)	Adjusted for age, sex, total caloric intake, tobacco use, BMI, geographic risk area, number of siblings, SES, number of meals/day, multivitamin supplements, table salt use, and urban environment.	FFQ	Dietary habits 20 yr prior to interview were assessed.

Takezaki (2001)	Case control	< 1 time/wk (reference) 1–2 times/wk (low) 3–5 times/wk (not included in meta-analysis) Everyday (high)	Adjusted for age (continuous), sex, and smoking (never, <20 cigarettes/day and ≥20 cigarettes/day, and 2–4 times/wk, everyday) habits.	FFQ	Not stated
Munoz (2001)	Case control	Less than once/wk (reference) Several times/wk (low) Every day (high)	Age, sex, SES	FFQ	Dietary habits during the year preceding the interview were assessed.
De Stefani (2001)	Case control	Single OR calculated per an increase of 25 g of garlic intake (specific categories not given in study)	Adjusted for age, sex, residence, urban/rural status, education, body mass index, and total energy intake.	FFQ	Not stated
Kim (2002)	Case control	For statistical analysis, the total amount of each food intake was divided into 3 groups (<25, 25–75, >75 percentiles) under the criterion of the control group <25th percentile (reference) 25–75th percentile (low) >75th percentile (high)	Adjusted for sex, age, socioeconomic status, family history and refrigerator use.	FFQ	Dietary habits over 12-mo period, 3 yr prior to the interview.
Gao (2002)	Case control	<1 time/wk (reference) ≥1 time/wk (any)	Adjusted for age (continuous), sex, smoking and drinking habits, and consumption of meat, pickled vegetables, raw vegetables.	FFQ	Dietary habits "before the onset of disease" were assessed.
Li (2004)	Randomized control trial	200 mg of synthetic allitridum daily and 100 mcg of selenium every alternative day for 1 mo each year vs placebo	Adjusted for age, family history of cancer, smoking, alcohol use and history of stomach illness.	Not applicable	Dietary supplements and placebo were given for 2 yr (November 1989 to December 1991). Study participants were followed up for 5 yr postintervention.

(*Continued on next page*)

TABLE 2
Study characteristics continued *(Continued)*

Author (year)	Study type	Categories of amount of intake	Covariates in adjusted risk estimates	Method of data collection of garlic intake	Time period during which garlic was consumed prior to gastric cancer
Setiawan (2005a)	Case control	Never (reference) Occasional—few times/wk (low) Often—few times/mo (high)	Adjusted for matching variables (age, gender), education, BMI, pack-years of smoking, alcohol drinking, salt intake, and vegetable and fruit intake.	FFQ	Dietary habits approximately 10 yr before diagnosis for cases.
Setiawan (2005b)	Case control	Never (reference) Occasional—few times/wk (low) Often—few times/mo (high)	Adjusted for matching variables (age, gender), education, BMI, pack-years of smoking, alcohol drinking, salt intake, and vegetable and fruit intake.	FFQ	Dietary habits approximately 10 yr before diagnosis for cases.
Zickute (2005)	Case control	Never (reference) 1–3 times/mo (low) 1–6 times/wk (not included in meta-analysis) ≥1 times/day (high)	Adjusted for other food items (vegetables, fruits, different types of meat, processed meat and fish, dairy and starchy products, coffee, green tea) that were related to outcome, smoking, alcohol use, family history on cancer, education level, and residence.	Unavailable	Unavailable
Pourfrazi (2009)	Case control	Never or infrequently (reference) 1–2 times/wk (low) > 3 times/wk (high)	Adjusted for gender, age group, education, family history of gastric cancer, citrus fruits, onion, red meat, fish, dairy products, strength and warmth of tea, preference for salt intake and H. pylori.	FFQ	Not stated

Pakseresht (2011)	Case control	Single odds ratio calculated per an increase of 10 g of garlic intake (specific categories not given in study)	Adjusted for age, sex, education, living area, smoking, gastric symptoms, income, owning refrigerator, duration of using refrigerator, seeds preparing method, frying, H. pylori infection, and total energy intake.	FFQ	Dietary habits over the last year prior to interview (for cases at 1 yr prior to date of diagnosis).
Ma (2012)	Randomized control trial	Randomly assigned in a 2 × 2 × 2 (H.pylori treatment, garlic supplements or vitamins) factorial design to the 3 treatments or their placebos (for those who were Helicobacter seropositive) or in a 2 × 2 (garlic supplements or vitamins) factorial design to the 2 treatments or their placebos (for those who were Helicobacter seronegative)	Adjusted for baseline histology, age (<40, 40–44, 45–54, ≥55 years), sex, history of ever using alcohol, and history of ever smoking.	Not applicable	Supplements (garlic, vitamins, placebo) were given for 7 yr then ceased, subjects were then followed for a further 7.3 yr.
Yassibas (2012)	Case control	<1 time/ mo or none (reference) 1–2 times/mo (low) 1–2 times/wk (not included in meta-analysis) 3–4 times/wk (not included in meta-analysis) Every meal every day or ≥1 time/day (high)	Adjusted for gender, residence, education, smoking, alcohol consumption, and familial history of cancer or gastric cancer.	FFQ	Not stated

FFQ = food frequency questionnaire; BMI = body mass index; SES = socioeconomic status.

TABLE 3
Regional breakdown of cases and controls

Region	Cases (% of total)	Controls (% of total)
Europe	1349 (15.9)	6213 (42.1)
Asia	6586 (77.5)	7645 (51.8)
South America	452 (5.3)	797 (5.4)
Turkey (excluded from regional analysis)	106 (1.2)	106 (0.7)
Total	8493	14,761

(Fig. 5), respectively. The Asian studies were moderate heterogeneous with $I^2 = 60.32$, $P = 0.005$, the South American studies had no heterogeneity ($I^2 = 0.00$, $P = 0.73$). European studies also showed a positive effect on gastric cancer risk reduction from high garlic intake but significantly less than the Asian and South American studies, OR = 0.88 (95% CI: 0.69–1.13). There was low heterogeneity ($I^2 = 6.86$, $P = 0.36$) in the European studies.

DISCUSSION

Our meta-analysis shows a reduction of gastric cancer risk with garlic consumption. Risk reduction was greater with relatively higher levels of intake but any level of intake also showed reasonable benefit. Regional analysis showed gastric cancer risk reduction was greater in Asian and South American populations than the European population.

It is important to recognize several limitations when considering the above findings. Recall bias is a concern as 14 of the 17 studies in our meta-analysis were case controls that relied on dietary histories, some from the quite distant past. For example, in Ekstrom et al. (25), dietary habits 20 yr prior to the interview were assessed, and the food-frequency questionnaire included 45 items of foods and beverages, which would add a further degree of difficulty. Though imperfect, this type of retrospective dietary history appears more accurate than using current diet to approximate previous intake (26,27).

Another confounding factor is the significant variability in the duration of garlic intake in the studies. For example, Li et al. (20) conducted a randomized controlled trial using garlic and selenium supplementation given every alternative day for 1 mo each yr for 3 yr vs. placebo given at the same intervals. In contrast, in the randomized trial by Ma et al. (21), the treatment arm received standardized amounts of garlic extract and garlic oil daily for 7 yr vs. placebo given at the same intervals. The rest of the studies fall somewhere in between these 2 extremes. Our meta-analysis did not adjust for duration of supplementation, and this remains a question for future investigation.

As mentioned previously in Results, there was significant variability in the reference categories for amount of intake. For example, high intake in the various studies was reported as: >1.5 kg/year, >1 time/wk, seldom to 1 time/day, every day, "high," few times a mo, every meal/every day, or > 1 time/day. Low intake categories included 0.1–1.5kg/year, 1–3 times/m, 1–2 times/wk, several times/wk, "low," few times/

Study name	Odds ratio	Lower limit	Upper limit	*p*-Value
		Statistics for each study		
You (1989)	0.70	0.49	1.00	0.05
Gao (1999)	0.31	0.22	0.44	0.00
Takezaki (2001)	0.37	0.20	0.68	0.00
Munoz (2001)	0.50	0.31	0.82	0.01
Kim (2002)	0.53	0.27	1.03	0.06
Setiawan (2005)	0.45	0.16	1.30	0.14
Setiawan (2005) a	0.68	0.37	1.25	0.22
Pourfrazi (2009)	0.35	0.03	3.98	0.40
Yassibas (2012)	0.80	0.16	3.90	0.78
Zickute (2005)	0.49	0.22	1.09	0.08
	0.49	0.38	0.62	0.00

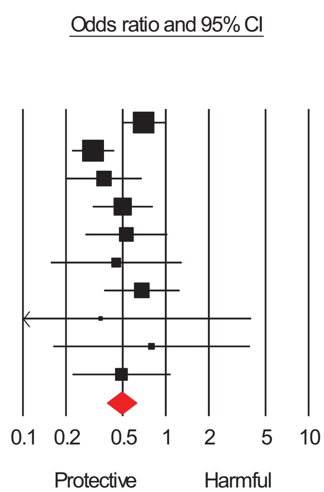

FIG. 2. Gastric cancer risk with high intake of garlic.

Study name	Odds ratio	Lower limit	Upper limit	*p*-Value
	Statistics for each study			
You (1989)	0.80	0.53	1.20	0.28
Gao (1999)	0.40	0.21	0.76	0.01
Takezaki (2001)	1.49	0.86	2.59	0.16
Munoz (2001)	0.70	0.49	1.00	0.05
Kim (2002)	0.50	0.27	0.92	0.03
Setiawan (2005)	0.71	0.27	1.87	0.49
Setiawan (2005) a	1.11	0.87	1.41	0.40
Pourfrazi (2009)	0.48	0.25	0.92	0.03
Yassibas (2012)	0.94	0.12	7.28	0.95
Zickute (2005)	0.75	0.44	1.27	0.29
	0.75	0.58	0.97	0.03

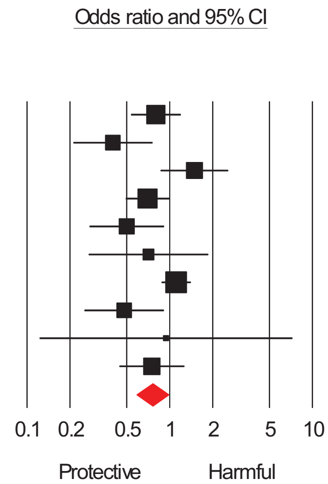

FIG. 3. Gastric cancer risk with low intake of garlic.

Study name	Odds ratio	Lower limit	Upper limit	*p*-Value
	Statistics for each study			
Dorant (1996)	1.27	0.65	2.50	0.49
Ekstrom (2000)	0.90	0.59	1.37	0.63
Li (2004)	0.48	0.21	1.08	0.08
Pakseresht (2011)	0.28	0.12	0.64	0.00
Ma (2012)	0.80	0.53	1.20	0.28
De Stefani (2001)	0.57	0.33	0.98	0.04
Gao (2002)	1.18	0.60	2.34	0.63
Hansson (1993)	0.89	0.64	1.24	0.49
	0.77	0.60	1.00	0.05

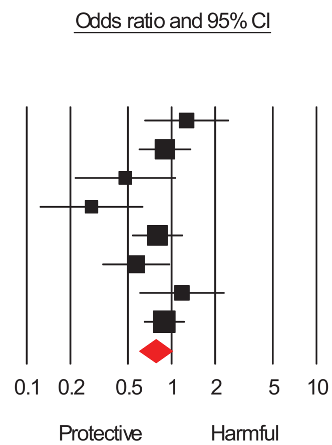

FIG. 4. Gastric cancer risk with any intake of garlic.

Group by Region	Study name	Odds ratio	Lower limit	Upper limit	*p*-Value
		Statistics for each study			
Asia	You (1989)	0.70	0.49	1.00	0.05
Asia	Gao (1999)	0.31	0.22	0.44	0.00
Asia	Takezaki (2001)	0.37	0.20	0.68	0.00
Asia	Kim (2002)	0.53	0.27	1.03	0.06
Asia	Li (2004)	0.48	0.21	1.08	0.08
Asia	Setiawan (2005)	0.45	0.16	1.30	0.14
Asia	Setiawan (2005) a	0.68	0.37	1.25	0.22
Asia	Pourfrazi (2009)	0.35	0.03	3.98	0.40
Asia	Pakseresht (2011)	0.28	0.12	0.64	0.00
Asia	Ma (2012)	0.80	0.53	1.20	0.28
Asia	Gao (2002)	1.18	0.60	2.34	0.63
Asia		0.54	0.40	0.72	0.00
Europe	Dorant (1996)	1.27	0.65	2.50	0.49
Europe	Ekstrom (2000)	0.90	0.59	1.37	0.63
Europe	Hansson (1993)	0.89	0.64	1.24	0.49
Europe	Zickute (2005)	0.49	0.22	1.09	0.08
Europe		0.88	0.69	1.13	0.33
South America	Munoz (2001)	0.50	0.31	0.82	0.01
South America	De Stefani (2001)	0.57	0.33	0.98	0.04
South America		0.53	0.37	0.76	0.00

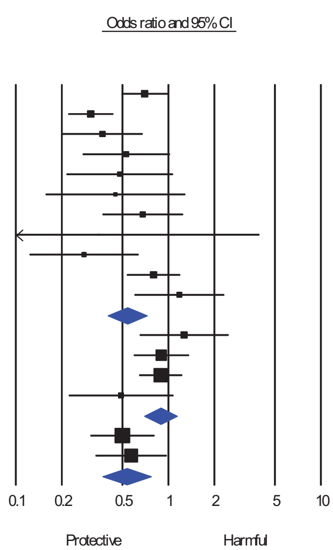

FIG. 5. Gastric cancer risk by region (high intake population).

wk, 1–3 times/mo. As there is no standardized value for high garlic intake between the studies, a definite recommendation cannot to be made as to the amount of garlic that needs to be consumed for greatest benefit.

It should also be noted that the type of garlic product consumed (e.g., fresh garlic, garlic extract, garlic oil) was not documented in most of these studies. It is unknown whether the state of garlic (fresh vs. processed) affects the bioavailability or efficacy of the protective organosulfur compounds.

Our study had a number of strengths. Our search protocol was broad and covered 3 major reference databases, and a review of relevant references was also completed. No restriction was placed on date of publication or language to increase yield. Analysis of a statistically significant number of controls and cases was undertaken, a total of 8621 cases and 14,889 controls were included in the study. Regional analysis of the studies showed that the risk reduction with garlic intake was consistent across in different patient population, though with varying degrees of benefit.

There was no publication bias (Egger's regression: $P = 0.76$). Meta-Analysis of Observational Studies in Epidemiology (MOOSE) recommendations for reporting meta-analysis of observational studies were followed where possible (29).

The case control studies were generally uniform in their use of trained interviewers for obtaining a dietary history. For example, Ekstrom et al. (25) used professional interviewers from Statistics Sweden who conducted face-to-face interviews using a structured questionnaire and Gao et al. (28) conducted interviews by rural physicians or medical administrators who were trained as interviewers. Dorant et al. (19) used self-administered questionnaires on their study participants but recall of garlic supplement use was evaluated by comparing questionnaire data with information from 3 personal interviews as reference.

In conclusion, our meta-analysis supports garlic intake for gastric cancer protection. Gastric cancer is one of the leading causes of cancer-related death and morbidity. Garlic consumption is relatively cheap; the product is freely available and easy to incorporate into a daily diet in a palatable manner. There are no real safety concerns with regards to side effects or overdosing. There appears to be a dose-dependent effect, with higher amount of garlic consumption conferring a greater degree of protection. The results also appear consistent across various racial groups, with the Asian and South American populations receiving the greatest benefit. More studies are required, preferably cohort or randomized control trials, to mitigate recall bias with the observational studies and to clearly establish if there is dose-dependency and an optimal dose.

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