Table 1: Systematic reviews of garlic (Allium sativum) for cancer prevention

Source: Pilkington K, CAM Cancer Collaboration. <u>Garlic</u> (*Allium sativum*) [online document]. November 2023.

Study	Design and methods	Inclusion criteria	Included studies and	Included interventions	Main results/Conclusions	Comments
year (ref)			participants	and outcomes		
Chiavarini 2015	Systematic review and meta-analysis Search of 'multiple databases' including Web of Knowledge, MEDLINE and EMBASE databases in Sept 2014 Newcastle-Ottawa scale for quality assessment	 (i) the study (cohort or case–control) must have had garlic consumption assessed; (ii) it must have provided a risk estimate (HR/RR/OR plus 95% CI) for colorectal, colon or rectal cancer incidence (iii) it must have provided information on adjustment for confounding factors. 	14 studies (7 cohort and 7 case- control) Total number no reported	Various levels of garlic consumption (dietary intake and supplements) Risk of colorectal cancer (HR/OR/RR)	Garlic consumption was not associated with colorectal cancer risk (OR=0.93; 95 % CI 0.82, 1.06, P =0.281). Quality scores: 5 to 8 (median: 6) for case-control; 6 to 9 (median: 8) for cohort studies Preventive effect suggested by the case– control studies may be due to potential confounding factors and exposure misclassification	Search terms appropriate but databases unclear Full details of study selection process not provided but 2 reviewers involved Quality assessment process rigorous (≥7 out of total of 9 used to indicate a high quality study)
Guercio 2016	Meta-analysis Search of MEDLINE and reference lists of articles to May 2015 No quality appraisal	Case–control or cohort design. Intake of allium vegetables (i.e., garlic, onion, leeks, Chinese chives and others) Included estimates of risk or data for calculating risk of occurrence of cancers of the oral cavity, pharynx, larynx, and oesophagus	25 studies (21 case–control and 4 cohort) Total number 'more than 11,000'	Various levels of consumption of total allium, garlic, and onion Risk of cancer (RR)	RR for squamous cell carcinoma: 0.79 (95% CI 0.56–1.11) for total allium, 0.74 (95% CI 0.57–0.95) for garlic for highest versus lowest consumption. Association stronger for case-control studies, studies in China and oesophageal compared with head and neck cancers. No relation found between allium vegetable intake and adenocarcinoma of the oesophagus	Search limited to one database but strategy appropriate Limited to English Study selection and data extraction process rigorous No quality appraisal
Hu 2014	Meta-analysis Search of MEDLINE and references lists of articles to October 2013 Newcastle-Ottawa Scale used for quality assessment	 (1) prospective cohort studies (2) evaluated the association between garlic consumption and risk of colorectal cancer; (3) reported HR or RR with 95%CI, or data necessary to calculate them. 	5 cohort studies Total of 335,923 subjects	Raw and cooked (RC) garlic and garlic supplement intake Risk of colorectal cancer (RR)	No significant associations were found between consumption of RC garlic (RR: 1.06; 95%CI: 0.95-1.19) or garlic supplements (RR: 1.12; 95%CI: 0.96-1.31) and risk of colorectal cancer. All studies judged to be high quality	Search limited to one database but strategy appropriate Only included cohort studies Selection, extraction and appraisal processes rigorous (7+ assessed as high quality)

Kodali 2014	Meta-analysis Search of MEDLINE, PubMed, and EMBASE to June 2014 No quality assessment	 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; the risk point estimate was reported as OR plus CI or could be calculated 	17 studies (14 case control studies, 2 randomized controlled studies, and 1 cohort study) Meta-analysis of a total of 8,621 cases and 14,889 controls	Intake of garlic Risk of gastric cancer (OR)	High, low, and any garlic intake were all associated with reduced risk of gastric cancer. High intake had the most significant risk reduction, OR D 0.49 (95% CI: 0.38–0.62). Heterogeneity was low (I2 D 30.85, P D 0.17). A more modest risk reduction was associated with low intake, OR D 0.75 (95% CI: 0.58– 0.97). Half of the studies did not separate garlic intake into high or low amounts, only as consumption vs. non-consumption. Any amount of consumption still showed a risk reduction similar to low intake, OR D 0.77 (95% CI: 0.60– 1.00).	Searched several databases but search terms are limited. Few details of selection and extraction processes No quality assessment
Lee 2021	Systematic review Searches of three databases (MEDLINE, Embase, and Web of Science) to July or September 2018. Risk of bias assessment	RCTs and cohort studies	One medium-quality randomized controlled trial (RCT) and 13 cohort studies graded as high RoB were included	Effects of varying levels of garlic intake on cancer Mainly colorectal cancer; also lung, gastric, prostate, breast and haematological	AGE was effective in reducing the number and magnitude of colorectal adenomas in one RCT, but inconsistent results in cohort studies. No firm conclusion regarding the effects of garlic on cancer	Methods appear appropriate. All studies assessed as at moderate risk of bias. No meta-analysis due to hetereogeneity.
Li 2018	Systematic review and meta-analysis Searches of PubMed, Embase, MEDLINE, and Cochrane Library on April 2018. Cochrane risk of bias and Robins-I	(a) used a randomized controlled trial, cohort, or case-control design, (b) examined the association between garlic intake and gastric cancer occurrence, and (c) reported odds ratio (OR) or relative risk (RR) and their 95% confidence interval (CI) or provided sufficient information for OR/RR and 95% CI calculation.	18 studies with 142 921 subjects (5123 cases) (15 case-control studies (4573 cases), 1 case- cohort study (152 cases), 1 cohort study (292 cases), and 1 RCT (106 cases)	The majority of included studies examined garlic or garlic powder except for two studies using garlic supplement. Outcome: gastric cancer occurrence	High garlic consumption was associated with a reduced gastric cancer risk compared with low consumption (OR = 0.51, 95% CI = 0.44-0.57). Effect was nonsignificant effect if only derived from the prospective studies (OR = 0.95, 95% CI = 0.66-1.24).	Methods appear appropriate. The majority of these studies were judged to be poor quality with small sample size and high risk of bias.

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Turati 2014	Meta-analysis Search of MEDLINE and check of reference lists to April 2014 No quality assessment	 (i) Case-control or cohort study design, (ii) Outcome was colorectal (or colon, or rectal) cancer or colorectal adenomatous polyps incidence/death, (iii) examined the association with allium vegetables (including garlic, onions, leeks, and others), (iv) provided the RR with Cl or data necessary to calculate them 	16 studies (10 case-control and 6 cohort studies) Seven studies on garlic, six on onion, and four on total allium vegetables (13 333 cases)	Allium vegetables intake and risk of colorectal cancer and colorectal adenomatous polyps	RRs of colorectal cancer for the highest versus the lowest category of intake were 0.85 (95% CI 0.72–1.00) for garlic (0.76 for case-control, 0.99 for cohort studies), 0.85 (95% CI, 0.70–1.04) for onion (0.74 for case-control, 1.04 for cohort studies), and 0.78 (95% CI, 0.56–1.08) for total allium vegetables.	Search limited to one database but strategy appropriate Selection and extraction reasonably rigorous No quality assessment
Turati 2015	Case-control plus meta- analysis Search of MEDLINE and reference lists to December 2013 No quality assessment	(i) had a case-control or cohort study design, (ii) their outcome was gastric cancer occurrence, (iii) examined the association with allium vegetables (including garlic, onion, leek, Chinese chives, and others), (iv) provided the RR with Cls, or data necessary to calculate them	27 studies (23 case–control and 4 cohort studies) Total of 10,143 cases	Consumption of allium vegetables (including garlic, onion, leek, Chinese chives, and others) and risk of gastric cancer	Pooled RRs were 0.78 (95% CI, 0.67–0.91) for allium vegetables (ten case–control and four cohort studies—6227 cases), 0.60 (95% CI, 0.47–0.76) for garlic (12 case–control studies—3807 cases)	Search limited to one database but search strategy appropriate Few details of selection and extraction process No quality assessment
Wang 2022	Systematic review and meta-analysis Searches of Pubmed, Embase, and Cochrane Library to Sept 2021. Cochrane risk of bias assessment and Newcastle-Ottawa Scale	 i) randomized controlled trials, case- control trials, or with cohort design; ii) studies that include the evaluation of the association between garlic intake and gastric or colorectal cancers over nearly 30 years; iii) studies that provide odds ratio (OR) or relative risk (RR) and with 95% confidence interval (CI) or providing sufficient information for calculation; iv) studies published within the last 30 years 	20 studies (11 gastric cancer, 9 colorectal cancer) Gastric cancer: 3,299 patients and 133,801 controls from one RCT, 8 case-control studies, 2 cohort studies Colorectal cancer: 8,519 patients and 52,423 controls from 7 case-control studies, 2 cohort studies	Garlic intake and risk of gastric or colorectal cancer	Association between garlic intake and reduction in the risk of gastric cancer [odds ratio (OR)=0.65, 95% confidence interval (CI)=0.49-0.87, P<0.001] Association between garlic intake and reduced colorectal cancer risk (OR=0.75, 95% CI=0.65-0.87, P<0.001)	Search and appraisal methods appear appropriate. Results were highly heterogeneous although the effects of outlying studies were tested. All studies were judged to be of adequate quality or low bias.

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Zhang 2021	Systematic review and meta-analysis. Search of Medline, Embase, and Web of Science to May 2021. Newcastle-Ottawa Scale used for quality assessment.	Cohort, case-cohort, or intervention studies; if they investigated the relationship between allium vegetables or garlic supplements and malignancy risk; and if they provided or allowed for the calculation	22 prospective studies on allium vegetables involving 13,677 patients and 10 studies on garlic supplements involving 6,555 patients (cohort or case-cohort studies except for one intervention study)	Intake of allium vegetables or garlic supplements and cancer risk (all types)	High consumption of allium vegetables showed no significant association with cancer risk (relative risk [RR] = 0.97, 95% CI 0.92–1.03) Garlic supplements were not found to be significantly associated with an increased risk of cancer (RR = 0.97, 95% CI 0.84–1.12	Search and appraisal methods appear appropriate. Results for garlic were heterogeneous. All studies were assessed as lower risk of bias and better quality (NOS 7+).
Zhang 2022	Systematic review and meta-analysis. PubMed, Web of Knowledge, Scopus and Chinese National Knowledge Infrastructure (CNKI) were searched up to June 2021. Newcastle-Ottawa Scale used for quality assessment.	1) cohort, nested case-control study, or case-control study design; 2) the exposure of interest was allium vegetables (including garlic, onion, leek, Chinese chives, and others); 3) the outcome of interest was breast cancer; (4) reported risk estimate and its 95% confidence interval (CI). The exclusion criteria were as follows: 1) experimental study; 2) letters or case reports; 3) articles that provided insufficient data or only information for cancer mortality	3 prospective studies and 14 case-control studies (comprising a total of 4675 cases)	Intake of allium vegetables (including garlic, onion, leek, Chinese chives, and others) and breast cancer risk	Combined risk estimate breast cancer for the highest vs lowest category of total allium vegetables and garlic intake was 0.70 (95% CI: 0.49–0.91, P < 0.001), 0.77 (95% CI: 0.61–0.93, P = 0.016)	Search and appraisal methods appear appropriate but numbers of garlic studies were inconsistent (9 listed in Table 1; 7 stated in results). Results were heterogenous. Scores for quality ranged between 5 and 8 (4 were scored 7+)
Zhou 2011	Meta-analysis Search of MEDLINE from 1966 to 2010 Checking reference lists No quality assessment	(1) used a case-control or cohort study design; (2) had data of gastric cancer occurrence; (3) presented the consumption of Allium vegetables (including garlic, onion, leek, scallion, garlic stalk, onion leaves, Welsh onion, and Chinese chives); and (4) provided OR or RR plus CI or data necessary to calculate them.	21 studies (19 case-control studies, 2 cohort studies) 543,220 subjects	Consumption of Allium vegetables (highest and lowest consumption) and risk of gastric cancer occurrence	High versus low consumptions of Allium vegetables reduced the risk for gastric cancer (OR 0.54; 95% Cl 0.43–0.65). OR for an increment of 20 g/day of Allium vegetables consumed (approximately 1 garlic bulb) was 0.91 (95% Cl 0.88–0.94), Consumption of large amounts of Allium vegetables reduces risk for gastric cancer	Search limited to one database but search strategy appropriate Few details of selection process Extraction process appropriate No quality assessment

Zhou 2013	Meta-analysis Search of PubMed, EMBASE, Scopus, Web of Science, Cochrane register, and Chinese National Knowledge Infrastructure (CNKI) databases to May 2013 No quality assessment	(a) evaluation of the Allium vegetables intake and prostate cancer risk, (b) had a case control or cohort design, (c) reported the OR or RR and 95% CI.	9 studies (6 case-control and 3 cohort studies)	Allium vegetable intake and risk of prostate cancer	Significantly decreased risk of prostate cancer for intake of allium vegetables (OR = 0.82, 95% CI 0.70, 0.97). Subgroup analysis showed significant association with garlic intake (OR = 0.77, 95% CI 0.64- 0.91) Allium vegetables, especially garlic intake, are related to decreased risk of prostate cancer.	Search comprehensive Selection and extraction appear appropriate No quality assessment
Zhou 2020	Systematic review and meta-analysis. Cochrane Database of Systematic Reviews, PubMed, and EMBASE, were searched to May 2019. Study quality was evaluated using Newcastle–Ottawa scale (NOS)	 (1) cohort or case-control studies; (2) studies evaluating the relationship of garlic consumption with CRC risk; (3) studies reporting the relative risk (RR) or odds ratio (OR) and 95% CI or the essential data for calculation. excluded garlic supplementation 	11 studies (involving 12,558 cases)	Dietary garlic intake and the risk of colorectal cancer	Integrated relative risk (RR) of CRC was 0.80 (95% confidence interval [CI], 0.69– 0.91) for the highest versus the lowest garlic consumption categories	Search and appraisal methods appear appropriate. All studies scored 7+ (high quality) Significant heterogeneity was seen across all enrolled studies

Zhu 2014	Meta-analysis	(1) the design of the study was	13 studies	Consumption of allium	No association between higher intake of	Search of two databases
	Search of MEDLINE and	prospective such as a cohort or case-	(8 studies of the effects	vegetables or garlic	allium vegetables and CRC risk (RR 1.06;	but strategy not fully
	EMBASE databases	cohort study; (2) the study	of allium vegetables	supplements and	95% CI 0.96–1.17; P 0.26). Intake of	reported
	from inception to 2013	investigated the relationship of	(5458 patients with	colorectal cancer (CRC)	allium vegetables did not correspond to	English-language only
	Checking reference lists	allium vegetables or garlic	CRC) and 5 studies of	risk	CRC risk.	Some details of selection
	and reviews	supplements and colorectal cancer	the effects of garlic		Higher consumption of allium vegetables	process reported
	No quality assessment	(CRC) risk; and (3) the study provided	supplements (2685		was associated marginally with increased	Extraction process
		or allowed the calculation of RR with	patients with CRC)		risk of colon cancer	appropriate
		95% CI			among women (RR, 1.23; 95% Cl, 1.01–	No quality assessment
					1.50; P [.05). Use of garlic supplements	
					was associated	
					significantly with an increased risk of CRC	
					(RR, 1.18; 95% Cl, 1.02–1.36; P [.03).	
					"We found no evidence that higher	1
					intake of allium vegetables reduced the	
					risk for CRC. We observed that garlic	
					supplements increased the risk for CRC	1
					but this finding requires external	
					validation"	

Abbreviations: CI – confidence interval; HR – hazard ratio; NHMRC - National Health and Medical Research Council, Australia; OR – odds ratio; RR – risk ratio