Richa *et al.*
Translational Medicine Communications (2022) 7:7
https://doi.org/10.1186/s41231-022-00111-x

Translational Medicine Communications

REVIEW

Open Access

Dietary factors associated with gastric cancer - a review

Richa[1], Neha Sharma[1] and Geetanjali Sageena[2*]

Abstract

Background: Cancer is considered one of the primary illnesses that cause morbidity and mortality in millions of people worldwide and due to its prevalence, there is undoubtedly an unmet need to discover novel anticancer drugs. As most of the target-specific anticancer drugs failed to achieve the expected result so far, new multi-targeted therapies using natural products have become significant. Natural products are readily applicable, inexpensive, accessible and acceptable therapeutic approaches with minimum cytotoxicity. This review explores the relationship between dietary factors and the probability of development of gastric cancer. Over the years, it has been proven that there are many natural products that have chemo-preventative effects such as vitamins, probiotics and prebiotics, green tea, and resveratrol on gastric cancer. Many investigations have looked into the links between dietary components and the risk of stomach cancer and a variety of protective and deleterious factors have been identified in our diet that is associated with gastric cancer. In this study, we have summarized the preventive and injurious components that affect the incidence of gastric cancer.

Conclusion: Based on the potential of natural products for the discovery of new compounds for the treatment of diseases, the purpose of the present review was to investigate the importance of dietary products mitigating the impacts due to the development of gastric cancer. The current analysis proves the protective as well as harmful roles of many elements which are found in our diet in the development of gastric cancer. Our findings can have significant public health implications in terms of gastric cancer prevention. There is an inherent need to offer an insight into benefits and risks, clinical trial designs future translational and cohort studies before effectively clinically translated.

Keywords: Gastric cancer, Diet, Alcohol in stomach cancer, Carcinogens in diet

Introduction

Gastric cancer is a major health concern throughout the world. Its incidence is highly variable by regions, most prevalent being in Eastern Asia. It is the 5th most frequent cancer in the world, accounting for 5.6% of all cancer diagnoses in 2020, and the 4th most deadly cancer, accounting for 7.7% of all cancer-related deaths globally [1]. Gastric cancer develops when cells in the stomach start to grow out of control. The most common type of gastric cancer is adenocarcinoma (about 90 of all gastric cancers) which can be of intestinal type or diffuse type. Other variants are squamous cell carcinomas, small cell carcinomas, gastrointestinal stromal tumors, neuroendocrine tumors, lymphomas and leiomyosarcomas. Gastric cancers are classified as cardia or non-cardia based on the structure of the stomach. Diet and *helicobacter pylori* infection play an important role in gastric cancer development. Other major etiological factors for gastric cancer include smoking, alcohol use, obesity, previous gastric surgery, pernicious anemia, adenomatous polyps, chronic atrophic gastritis and radiation exposure [2]. Gender, age, ethnicity and geography are also, important risk factors.

*Correspondence: geetanjalisageena@gmail.com
[2] Department of Environmental Studies, Keshav Mahavidyalaya, University of Delhi, New Delhi, India
Full list of author information is available at the end of the article

Diet is an important modifiable risk factor for gastric cancer. There is adequate epidemiological evidence which suggests links of some nutritional exposures and dietary components with gastric cancer. Adequate diet modification may play a key role in reducing the incidence of gastric cancers. This review updates and summarizes the existing data on diet related factors which are associated with increasing risk of gastric cancer or have role in gastric cancer prevention (Table 1).

Dietary factors associated with prevention of stomach cancer

Citrus fruit, flavonoids and vitamin C

Many studies have shown the positive effect of citrus fruit intake on prevention of gastric cancer. One- stage pooled analysis including 6340 cases and 14,490 controls from 15 case–control studies from the stomach cancer pooling (StoP) project consortium by Paola Bertuccio et al. has proved an inverse association between citrus fruits and gastric cancer. This association was similar for all gastric cancer sub-sites and histotypes [4]. Other hospital- and community- based case–control studies have also shown the similar effect with inclusion of citrus fruit in diet [5, 6]. This protective effect is due to flavanones (a type of flavonoids) which are present in citrus fruits and juices. These flavanones prevent human gastric cancer cell proliferation, migration and invasion. Hesperitin and naringenin are the two main protective compounds of flavanones due to their antioxidant potentials [7–9]. It was seen that by increasing the amount of fruit in the diet of Finnish women for 5 weeks, the mean plasma concentrations of hesperitin and naringenin were increased by more than 6 times and 20 times respectively [10]. Citrus fruits are also rich in vitamin C which reduces the risk of gastric cancer development [11]. A Korean case control study showed an inverse relationship between vitamin C and gastric cancer with a significant difference for the highestversus lowest intake categories. Also, it was seen that Vitamin C-contributing foods, including cabbage, strawberries, and bananas, were protective factors against the risk of gastric cancer [12]. Though some of the studies done in the \past failed to prove the preventive effect of vitamin C for gastric cancer [13, 14], but most other observational studies and meta-analysis proved its beneficial effects [15–17].

Phytochemicals display their anticancer movement through focusing on signaling pathways, advancing apoptosis, controlling cancer prevention agent status and detoxification. Individual flavonoids in food might apply distinctive chemoprotective activities against carcinogenesis and this can be one potential justification behind the conflicting discoveries of epidemiological learns about the relationship between absolute flavonoid intake and the risk of disease. The dietary sources flavonoids, hesperetin and naringenin have been reported as chemopreventive agents [18–20]. The benefits of the two flavanones exhibit antioxidant, anticancer and anti-inflammatory properties [21–24]. Recently, the citrus flavonoids naringenin (NAR) and hesperetin (HSP) have been accounted for to forestall senescence [25]. The likely chemoprotective impacts of flavonoids independently furthermore, later on, designated chemoprevention with explicit plant-determined polyphenolic mixtures could turn into the favored methodology for malignant growth anticipation [26]. At that, flavonoids don't act through a solitary natural system yet rather regulate molecular events and different intracellular signaling pathways for example, progression of cell cycle stage I and II metabolic enzymes [27, 28].

Vegetables

Many studies have proved the benefit of vegetable intake in lowering the gastric cancer risk. The protective effect increases with portions per day [29, 30]. Cruciferous vegetables have anti-carcinogenic properties [31] and have been associated with reduced risk of various cancers, including stomach, lung, breast, bladder, gastric, colorectal, and prostate. Its cancer prevention properties may be due to vitamin C, folate, dietary fiber, phytoestrogens, selenium, and phytochemicals contained in it.

Table 1 Dietary factors associated with gastric cancer risk [3]

Dietary Factors	Decreased risk	Increased risk
	Green yellow vegetables	Salt and salty food
	Allium vegetables	Pickled foods
	Fruits: citrus fruits	Smoked foods
	Flavanoid	Nitrosamines and nitroso compounds
	Green tea	Alcohol (heavy intake)
		Red and processed meat (non cardia)
		Haem iron (from fresh meat)
		Grilled meat and fish

A study by Morrison et al. showed a strong inverse association between gastric cancer and cruciferous vegetable consumption [32]. Diets rich in vegetables and fruits and with low amounts of salty and starchy foods are recommendable for the prevention of gastric cancer [33].

Retinol

Vitamin A plays an important role in controlling cell proliferation and differentiation, hence influences carcinogenesis. A prospective cohort study consisted of 82,002 Swedish adults who were followed from 1997 to June 2005 with a mean follow up of 7.2 years showed that high intakes of vitamin A, retinol, dietary alpha-carotene and beta-carotene were associated with a lower risk of gastric cancer [34].There are other studies which have shown that higher plasma levels of retinol are associated with a reduction in risk of gastric cancer [35, 36].

Wine

Wine intake may decrease the chances of gastric cancer. A pooled database from three population studies conducted in 1964–1992 on a total of 15,236 men and 13,227 women which were followed for a total of 389,051 person-years, showed a significant association between glasses of wine drunk per day and gastric cancer [37].

There seems to be a negative association between wine intake and gastric cancer. The increase in wine intake decreases the risk of developing gastric cancer. The *Helicobacter pylori* disease has been demonstrated to be related with a twofold expansion in the danger of gastric malignant growth and quite a few studies have shown that wine obstructs the endurance of *Helicobacter pylori* in the stomach [38–40], however, the dynamic substances stay obscure. The connection between wine and gastric malignant growth in this study could likewise be ascribed to the substance of antioxidants in wine, which might have a defensive impact against malignant growth advancement. Resveratrol, a polyphenolic phytoalexin specialist in red wine has been implicated in cancer prevention [41–44]. These advantages ought to be accomplished by the influence of a therapeutic agent with numerous molecular mechanisms and biochemical pathways for the avoidance of chemoresistance while having little cytotoxic consequences for normal cells [45].

Mediterranean diet

The Mediterranean diet is based on the traditional foods that people used to eat in countries like Italy and Greece back in 1960 which mainly consists of vegetables, legumes and fish. The MD is thought to be protective against gastric cancer. An Italian case-control study with a total of 223 cases and 223 controls proved that higher adherence to MD is associated with a reduced risk of gastric cancer [46]. There are other evidence available in literature which showed similar results with adherence to MD [47, 48].

Dietary factors increasing the risk of gastric cancer

Salt and salty food

Gastric cancer is a common neoplasia, and dietary variables, such as salt consumption, are thought to have a role in its development. A number of experimental investigations found that salt had a co- carcinogenic effect when combined with *Helicobacter pylori* infection, as well as some independent effects like increased cell proliferation and endogenous mutations. A comprehensive meta-analysis of longitudinal studies found that overall salt intake and salt-rich foods have a strong negative influence on the incidence of stomach cancer in the general population [49].

Pickled foods

Consumption of pickled vegetables in East Asia has been linked to an increased incidence of stomach cancer in experimental investigations. A meta-analysis of epidemiologic observational studies which constituted a total of 60 studies, 50 case-control, and 10 prospective studies compared the risk of stomach cancer in pickled vegetable/food users to nonusers (11 studies) or to those in the lowest stated category of use (49studies). Thirty case-control studies revealed a substantial increase in risk, while one revealed a substantial decrease in risk. Two prospective trials revealed a significant increase in risk, while none revealed a substantial decrease. The findings imply that eating pickled vegetables/foods may increase the risk of stomach cancer by 50%, with larger connections in Korea and China [50].

Smoked foods

Smoking is a well-known source of carcinogenic polycyclic aromatic hydrocarbons-contaminated food. According to epidemiological studies, there is a statistical link between the frequent consumption of smoked foods and the increased risk of intestinal cancer [51]. Smoked meats contain heterocyclic amines which are both mutagens and carcinogenic. People who ate smoked-dried salted beef on a regular basis had a nearly three-fold elevated risk of stomach cancer [52].

Nitrosamines and nitroso compounds

Smoked preserved foods, cured meat products, salted preserved foods, and food dried by additions such as malt in the preparation of beer and whiskey all include preformed nitrosamine. Processed meats contain high levels of nitrates and nitrites. When nitrates and nitrites react with amino acids in the stomach, endogenous N-nitroso

compounds are formed. Endogenous synthesis of N-nitro compounds is triggered by haem iron in processed beef. By producing DNA damage and oxidative stress, haem iron accelerates the progression of pylori infection. Endogenously generated N-nitro compounds were reduced by ascorbic acid. By forming N-nitroso compounds, nitrates and nitrates, which are commonly used in processed foods, induce stomach cancer. N-nitroso compounds' reactive intermediates react with proteins and DNA in cells, causing cancer [53].

Alcohol

A meta-analysis by Ma et al. which included 10 studies implied that consuming alcohol raises the risk of stomach cancer. This could be due to the fact that alcohol can function as a solvent, making it easier for other toxic compounds to reach the cells lining the upper digestive tract. In order to determine the difference between moderate drinking and the risk of gastric cancer and heavy drinking and the risk of gastric cancer, they divided the study participants into three groups: control group (no drinking), moderate drinking group, and heavy drinking group. This meta-analysis confirmed that alcohol consumption can increase the risk of gastric cancer even at lower levels of alcohol consumption [54].

Red and processed meat (non cardia)

There is a scarcity of prospective evidence on red and processed meat and the risk of esophageal and gastric cancer subtypes. In 1986, 120,852 people aged 55 to 69 were recruited, and their meat consumption was examined using a 150-item food frequency questionnaire. A case–cohort analysis was performed on 107 esophageal squamous cell carcinomas, 145 esophageal adenocarcinomas, 163 gastric cardia adenocarcinomas, 489 gastric non-cardia adenocarcinomas, and 3923 subcohort members after 16.3 years of follow-up. In men, both processed and red meat consumption were linked to esophageal squamous cell carcinoma [55].

Haem iron (from fresh meat)

Heme iron can catalyze the endogenous synthesis of N-nitroso compounds, which are strong carcinogens, causing oxidative stress and DNA damage. In animal studies, dietary iron increases the risk of esophageal cancer, and it has been discovered as a growth factor for *Helicobacter pylori*, a known risk factor for stomach cancer [56].

Chemoprevention with dietary supplements

Chemoprevention of gastric cancer appears to be the most promising approach in reducing the incidence and mortality related to this cancer. As there is enough evidence available now regarding the protective role of diet containing micronutrients such as ascorbic acid, beta-carotene and alpha-tocopherol which have antioxidant properties, these dietary supplements can be explored as chemopreventive measure for gastric cancer. A study from Linxian China which recruited about 30,000 individuals showed a lower incidence and risk of death from, gastric cancer in those receiving b-carotene, vitamin E and selenium [57]. In a prospective randomised study by Zullo et al., the administration of ascorbic acid following *H. pylori* eradication significantly helps to resolve intestinal metaplasia of the gastric mucosa [58]. A chinese interventional study of high dose folic acid in gastric carcinogenesis in beagles has proved an important role of folic acid as chemopreventive agent for gastric cancer with statistically significant difference between case and control arms [59]. Although there are many studies which have shown promising results for the role of dietary chemoprevention of gastric cancer, there are some studies which have failed to prove its benefit. A Colombian randomised control trial conducted on its high-risk population did not show significant benefit of vitamin C and b-carotene as chemopreventive agents for gastric cancer [60]. In another trial, supplementation with a combination of vitamin C, vitamin E, and selenium did not show any effect on the incidence of gastric cancer at 7 years [61].

The potential role of the various dietary supplements to be used for chemoprevention and in cancer patients need pharmacokinetic studies to determine the therapeutic concentration.

Effect of dietary factors on gastric cancer mortality

Along with effect of dietary changes on gastric cancer incidence, there are studies which have shown a significant effect of diet on gastric cancer mortality also. The Chinese study from Linxian mentioned above have also shown a significant difference in gastric cancer mortality in b-carotene, vitamin E and selenium group even after a longer follow up [57]. An epidemiological study conducted in 24 countries has shown that dietary salt intake is a dose-limiting factor for gastric cancer mortality while the effect of nitrates is mainly associated with high salt concentrations [62]. In a study by Ngoan et al. which enrolled more than 30,000 subjects, the dietary factors showed a significant difference included yellow and green vegetables, processed meat and frequent use of cooking oil. Other factors which were effective but failed to show statistical significances were fresh food, pickled food and traditional soups [63]. The correlation of dietary factors with incidence of gastric cancer is described below (Table 2).

Table 2 Correlation of dietary factors with incidence of gastric cancer

Study	Author/year	Participants	Follow up in years	Cases	Results
α-Tocopherol, ß-Carotene Cancer Prevention Study [64]	Nouraie et al. in 2005	29,133 male smokers (1985-1988)	13.7	243 incident gastric adenocarcinomas (64 Gastric cardia cancer (GCC) and 179 Gastric non cardia cancer (GNCC))	Benefit: it was reported For GCC, high dietary intake of retinol was protective. For GNCC, higher intakes of fruits, vitamin C, α-tocopherol, β tocopherol. Risk: For GCC, high intake of α-tocopherol and β-tocopherol increased risk.
Cancer Prevention Study II Nutrition Cohort [65]	Mccullough et al	60,041 participants	18	299 cases	PREVENTION: It was reported that high dietary intake of fruits and vegetables was protective RISK: For stomach cancer, obesity and hot beverages; coffee increased the risk.
Copenhagen Centre for Prospective Population Study [37]	Barstad et al	Three population studies conducted in 1964-1992, a total of 15,236 men and 13,227 women	389,051 person-years	122 cases	PREVENTION: protective effect of wine drinking on the risk of gastric cancer with a 40% decrease in risk of gastric cancer for each glass of wine per day attributed to antioxidant properties of wine, while no association between beer or spirits intake and gastric cancer.

Table 2 (continued)

Study	Author/year	Participants	Follow up in years	Cases	Results
European Prospective Investigation into Cancer and Nutrition (EPIC)	Buckland et al. [66]	485,044 subjects (144,577 men) aged 35-70 y from 10 European countries	8.9	449 validated incident GC cases	PREVENTION: Greater adherence to an rMED is associated with a significant reduction in the risk of incident GC.
	Duell et al. [67]			444 cases of first primary gastric adenocarcinoma	PREVENTION: Lower consumption of alcohol amounts (< 60 g/d) were not associated with increased risk to gastric cancer. RISK: Heavy (compared with very light) alcohol consumption (≥60 compared with 0.1-4.9 g/d) at baseline was positively associated with GC risk.
	Gonza'lez et al. 2006 [68]	521,457 men and women aged 35-70 years in 10 European countries	6.5	330 gastric adenocarcinoma	RISK: Gastric non-cardia cancer risk was statistically significantly associated with intakes of total meat, red meat, and processed meat.
	EPIC-EURGAST STUDY [69]	477,312	11	683 gastric adenocarcinoma	PREVENTION: They found an inverse association between total intake of vegetables and fruit and GC risk, between fresh fruit and risk of the diffuse type and an inverse association between citrus fruit and risk of cardia cancer. Fresh fruit and citrus fruit consumption may protect against diffuse and cardia GC, respectively.
	Jakszyn et al. [70], 2006	521,457 individuals	6.6	314 cases	dietary intake of nitrosodimethylamine (NDMA) and endogenous formation of nitroso compounds was significantly associated with non-cardia cancer risk but not with cardia cancer.
	Zamora-Ros et al. 2012 [71]	36,037 individuals from 10 European countries, aged 35-74 years			
Hisayama Study	Miyazaki et al. 2012 [72]	2467, age 40 years or more	14	93 cases	The age- and sex-adjusted incidence of gastric cancer rose progressively with increasing levels of dietary vitamin A

Table 2 (continued)

Study	Author/year	Participants	Follow up in years	Cases	Results
Hisayama Study	Shikata et al. [73], 2006	2476 subjects aged 40 years or olde	14	93 cases	high dietary salt intake is a significant risk factor for gastric cancer; strong in the presence of *Helicobacter pylori* infection with atrophic gastritis.
Hokkaido Study	Khan et al. [74], 2004	1524 men and 1634 women separately aged 40 and over.	2.5	379 cases	For men, two dietary factors, miso soup and pickled vegetables were associated with lower risk for stomach and colorectal cancer respectively. For women, three factors, namely salty confectionery, black tea, and carbonated drink/juice appeared related to an elevated risk of stomach cancer.
Kaunas Rotterdam Intervention Study & Multifactorial Ischemic Heart Disease Prevention Study	Everatt et al. [75], 2012	7150 men in Kaunas, Lithuania	30	185 gastric cancer cases	Although an association with heavy wine consumption was observed, the effect of exposure to acetaldehyde on the development of gastric cancer in this cohort was not confirmed
Korean MultiCenter Cancer Cohort	Ko et al. [76], 2013	19,688	25 years	166 gastric cancer cases	inverse association between soybean/tofu intake and gastric cancer risk among women. Men with a high soybean/tofu intake had a lower risk of gastric cancer, but the reduction was not statistically significant
Miyako Study	Murata et al. [77] 2010	6830	8.9 years	87 gastric cancer	the HR for stomach cancer in males with high salt intake was 2.05 (95% CI:1.25 - 3.38), but not in women
Netherlands Cohort Study	Steevens et al. [78], 2011	120,852	16.3 years	156 GCA, 460 GNCA cases	Significant inverse associations were observed for Brassica vegetables and GCA risk. Citrus fruits were inversely associated with GCA risk

Table 2 (continued)

Study	Author/year	Participants	Follow up in years	Cases	Results
NIH-AARP Diet and Health Study	O'Doherty et al. [79], 2012	218,854 participants	40 years	191 gastric cardia adenocarcinomas and 125 gastric non-cardia adenocarcinomas	Overall obesity (BMI) was positively associated with gastric cardia adenocarcinoma risk (highest (≥35 kg/m(2)) vs referent (18.5- < 25 kg/m(2) Waist circumference was also positively associated with gastric cardia adenocarcinoma risk. In contrast, the majority of the anthropometric variables were not associated with adenocarcinomas of the gastric non-cardia.
Shanghai Cohort Study	Moy et al. [80], 2010	18,244	20 years	391 incident gastric cancer cases	Ever smokers experienced a statistically significant increased risk of gastric cancer. Heavy drinkers experienced a statistically significant increase in risk of gastric cancer (HR, 1.46; 95% CI, 1.05-2.04)
Shanghai Women's and Men's Health Studies	Epplein et al. [14], 2010	74,942 women aged 40–70 years 61,500 men aged 40–74	8 years	incident distal gastric cancers Shanghai Women's Health Study ($n = 206$) and the Shanghai Men's Health Study ($n = 132$)	For women, no associations were found between gastric cancer risk and the highest intake of fruits or vegetables. For men, increased fruit intake was associated with decreased risk of distal gastric cancer but no association was seen with increased intake of vegetables.

The anticancer activity of capsaicin is attained through several mechanisms including cell cycle arrest, activation of apoptosis, inhibition of metastasis and invasion and dysregulation of significant pathways involved in growth and metabolism. Thus, capsaicin has appeared to modify the outflow of a few qualities associated with malignancy cell survival, development capture, angiogenesis and metastasis [81]. Curcumin is also known to inhibit gastric cancer. Curcumin caused the induction of apoptosis and loss of MMP in SGC-7901 gastric cancer cell line via the inactivation of mito-KTAP. Curcumin is found to play important roles such as suppressing the transition of cells from G (1) to S phase to inhibit invasion and cell proliferation of gastric cancer cells. In addition to suppressing cell proliferation, it has been reported that curcumin is responsible for the down-regulation of mRNA and protein expression of cyclin D1 [22]. Formononetin isolated from red clover has many effects such as antioxidant, vasorelaxant, anti-inflammatory, neuroprotective and also possesses anticancer effects by regulating estrogen receptors and mitogen-activated protein kinase pathway [82]. Based on traditional Chinese Medicine, Jianpi Yangzheng Xiaozheng Decoction (JPYZXZ) is an empirical compound prescription. JPYZXZ, has been found to prolong and improve the quality of gastric cancer patients because it is "Qi-invigorating, spleen-strengthening and stasis-removing." Nevertheless, it is still unclear how the compound acts specifically as an antitumor agent [83].

Conclusion

The current decade has seen an expanding interest in the trajectory for prognosis of gastric cancer [84]. The inclusion of dietary regimens in cancer prevention for general well being is gaining attention. There is a plethora of literature on the role of diet and dietary habits in the occurrence of gastric cancer [85–87]. Recently studies have demonstrated the beneficiary role of dietary intake in prevention of gastric carcinogenesis [88–90].

Dietary products have been an unsurpassed source of cancer drugs in the modern era of drug discovery. These natural products, their derivatives and analogues based on these drugs constitute an arsenal against various types of neoplasms. They are capable of modulating cancer microenvironment and diverse cell signaling cascades; thus, playing a major role in combating cancer. These compounds are found to be effective against several signaling pathways, mainly cell death pathways (apoptosis and autophagy) and embryonic developmental pathways (Notch pathway, Wnt pathway and Hedgehog pathway). The historical record is strong, but what is the current impact of natural products in the discovery and development of cancer drugs, and importantly what are the prospects for natural products to be a valuable source of future agents is still a road less traveled. Yet there is a need to elucidate the potential efficacy of outlying mechanisms and other associations/cross-connections to discover amicable and sustainable methods for cancer prevention. However; we consider that a cautiously optimistic approach is required to assess the risk-benefit profile of this medication in the disease progression.

This analysis demonstrates that there are a multitude of potential risk factors and protective elements for stomach cancer that can be established in our diet. Our findings can have significant public health implications in terms of gastric cancer prevention, as well as offer insight into future cohort studies and clinical trial design.

Acknowledgements
None.

Authors' contributions
Dr. Richa: Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work. Drafting the work or revising it critically for important intellectual content. Final approval of the version to be published. Dr. Neha:Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work. Drafting the work or revising it critically for important intellectual content. Dr. Geetanjali Sageena: manuscript submission, peer review, and publication process. The author(s) read and approved the final manuscript.

Funding
No funding granted.

Availability of data and materials
Not applicable.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Author details
[1]Department of Radiation Oncology, Lady Hardinge Medical College and Smt. Sucheta Kriplani Hospital, New Delhi, India. [2]Department of Environmental Studies, Keshav Mahavidyalaya, University of Delhi, New Delhi, India.

Received: 27 August 2021 Accepted: 22 February 2022
Published online: 01 April 2022

References

1. Cancer today. Global Cancer Observatory. Available from: https://gco.iarc.fr/today/data/factsheets/cancers/7-Stomach-fact-sheet.
2. Stomach (gastric) cancer key statistics. American Cancer Society. Available from: http://www.cancer.org/cancer/stomachcancer/detailedguide/stomach-cancer-key-statistics.
3. Shah SK, et al. Dietary Risk Factors Associated with Development of Gastric Cancer in Nepal: a Hospital-Based Case-Control Study. Gastroenterol Res Pract. 2020;2020:1–8. https://doi.org/10.1155/2020/5202946.
4. Bertuccio P, Alicandro G, Rota M, Pelucchi C, Bonzi R, Galeone C, et al. Citrus fruit intake and gastric cancer: the stomach cancer pooling (StoP) project consortium. Int J Cancer. 2019;144(12):2936–44.

5. Foschi R, Pelucchi C, Maso LD, Rossi M, Levi F, Talamini R, et al. Citrus fruit and cancer risk in a network of case–control studies. Cancer Causes Control. 2009;21(2):237–42.
6. Bae J-M, Lee EJ, Guyatt G. Citrus fruit intake and stomach cancer risk: a quantitative systematic review. Gastric Cancer. 2008;11(2):127.
7. Zhang J, Wu D, Vikash, Song J, Wang J, Yi J, et al. Hesperetin induces the apoptosis of gastric Cancer cells via activating mitochondrial pathway by increasing reactive oxygen species. Dig Dis Sci. 2015;60(10):2985–95.
8. Bao L, Liu F, Guo H-B, Li Y, Tan B-B, Zhang W-X, et al. Naringenin inhibits proliferation, migration, and invasion as well as induces apoptosis of gastric cancer SGC7901 cell line by downregulation of AKT pathway. Tumor Biol. 2016;37(8):11365–74.
9. Kim M-J, Park HJ, Hong MS, Park H-J, Kim M-S, Leem K-H, et al. Citrus Reticulata Blanco induces apoptosis in human gastric cancer cells SNU-668. Nutr Cancer. 2005;51(1):78–82.
10. Erlund I, Silaste M, Alfthan G, Rantala M, Kesäniemi Y, Aro A. Plasma concentrations of the flavonoids hesperetin, naringenin and quercetin in human subjects following their habitual diets, and diets high or low in fruit and vegetables. Eur J Clin Nutr. 2002;56(9):891–8.
11. Jenab M, Riboli E, Ferrari P, Sabate J, Slimani N, Norat T, et al. Plasma and dietary vitamin C levels and risk of gastric cancer in the European prospective investigation into cancer and nutrition (EPIC-EURGAST). Carcinogenesis. 2006;27(11):2250–7.
12. Hoang BV, Lee J, Choi IJ, Kim Y-W, Ryu KW, Kim J. Effect of dietary vitamin C on gastric cancer risk in the Korean population. World J Gastroenterol. 2016;22(27):6257.
13. Pelucchi C, Tramacere I, Bertuccio P, Tavani A, Negri E, Vecchia CL. Dietary intake of selected micronutrients and gastric cancer risk: an Italian case-control study. Ann Oncol. 2009;20(1):160–5.
14. Epplein M, Shu XO, Xiang YB, Chow WH, Yang G, Li HL, et al. Fruit and vegetable consumption and risk of distal gastric cancer in the Shanghai women's and men's health studies. Am J Epidemiol. 2010;172:397–406.
15. Kong P, Cai Q, Geng Q, Wang J, Lan Y, Zhan Y, et al. Vitamin intake reduce the risk of gastric cancer: meta-analysis and systematic review of randomized and observational studies. PLoS One. 2014;9(12):e116060.
16. Kim HJ, Kim MK, Chang WK, Choi HS, Choi BY, Lee SS. Effect of nutrient intake and helicobacter pylori infection on gastric cancer in Korea: a case-control study. Nutr Cancer. 2005;52(2):138–46.
17. Botterweck AAM, Brandt PAVD, Goldbohm RA. Vitamins, carotenoids, dietary fiber, and the risk of gastric carcinoma. Cancer. 2000;88(4):737–48.
18. Kasote DM. Flaxseed phenolics as natural antioxidants. Int Food Res J. 2013;20(1):27.
19. Parhiz H, Roohbakhsh A, Soltani F, Rezaee R, Iranshahi M. Antioxidant and anti-inflammatory properties of the citrus flavonoids hesperidin and hesperetin: an updated review of their molecular mechanisms and experimental models. Phytother Res. 2015;29(3):323–31.
20. Paliwal R, Paliwal SR. Phytochemical bioactives in chemoprevention. In: Advances in nanochemoprevention. Singapore: Springer; 2020. p. 9–28.
21. Erlund I. Review of the flavonoids quercetin, hesperetin, and naringenin. Dietary sources, bioactivities, bioavailability, and epidemiology. Nutr Res. 2004;24(10):851–74.
22. Wang H, Zhang D, Ge M, Li Z, Jiang J, Li Y. Formononetin inhibits enterovirus 71 replication by regulating COX-2/PGE2 expression. Virol J. 2015;12(1):1–0.
23. Miler M, Živanović J, Ajdžanović V, Oreščanin-Dušić Z, Milenković D, Konić-Ristić A, et al. Citrus flavanones naringenin and hesperetin improve antioxidant status and membrane lipid compositions in the liver of old-aged Wistar rats. Exp Gerontol. 2016;84:49–60.
24. Ge S, Duo L, Wang J, Yang J, Li Z, Tu Y. A unique understanding of traditional medicine of pomegranate, Punica granatum L. and its current research status. J Ethnopharmacol. 2021;271:113877.
25. Testai L, Calderone V. Dietary polyphenols for active and healthy ageing. In: Nutrients and nutraceuticals for active & healthy ageing. Singapore: Springer; 2020. p. 147–66.
26. Scalbert A, Zamora-Ros R. Bridging evidence from observational and intervention studies to identify flavonoids most protective for human health. Am J Clin Nutr. 2015;101(5):897–8.
27. Hua X, Yu L, You R, Yang Y, Liao J, Chen D, et al. Association among dietary flavonoids, flavonoid subclasses and ovarian cancer risk: a meta-analysis. PLoS One. 2016;11(3):e0151134.
28. Zhou Y, Zheng J, Li Y, Xu DP, Li S, Chen YM, et al. Natural polyphenols for prevention and treatment of cancer. Nutrients. 2016;8(8):515.
29. Ferro A, Costa AR, Morais S, Bertuccio P, Rota M, Pelucchi C, et al. Fruits and vegetables intake and gastric cancer risk: a pooled analysis within the stomach cancer pooling project. Int J Cancer. 2020;147(11):3090–101.
30. Lunet N, Lacerda-Vieira A, Barros H. Fruit and vegetables consumption and gastric cancer: a systematic review and Meta-analysis of cohort studies. Nutr Cancer. 2005;53(1):1–10.
31. Gupta P, Wright SE, Kim S-H, Srivastava SK. Phenethyl isothiocyanate: a comprehensive review of anti-cancer mechanisms. Biochim Biophys Acta. 2014;1846(2):405–24.
32. Morrison MEW, Joseph JM, Mccann SE, Tang L, Almohanna HM, Moysich KB. Cruciferous vegetable consumption and stomach cancer: a case-control study. Nutr Cancer. 2019;72(1):52–61.
33. Stefani ED, Correa P, Boffetta P, Deneo-Pellegrini H, Ronco AL, Mendilaharsu MA. Dietary patterns and risk of gastric cancer: a case-control study in Uruguay. Gastric Cancer. 2004;7(4):211–20.
34. Larsson SC, Bergkvist L, Näslund I, Rutegård J, Wolk A. Vitamin a, retinol, and carotenoids and the risk of gastric cancer: a prospective cohort study. Am J Clin Nutr. 2007;85(2):497–503.
35. Jenab M, Riboli E, Ferrari P, Friesen M, Sabate J, Norat T, et al. Plasma and dietary carotenoid, retinol and tocopherol levels and the risk of gastric adenocarcinomas in the European prospective investigation into cancer and nutrition. Br J Cancer. 2006;95(3):406–15.
36. Persson C, Sasazuki S, Inoue M, Kurahashi N, Iwasaki M, Miura T, et al. Plasma levels of carotenoids, retinol and tocopherol and the risk of gastric cancer in Japan: a nested case–control study. Carcinogenesis. 2008;29(5):1042–8.
37. Barstad B, Sørensen TIA, Tjønneland A, Johansen D, Becker U, Andersen IB, et al. Intake of wine, beer and spirits and risk of gastric cancer. Eur J Cancer Prev. 2005;14(3):239–43.
38. Brenner H, Rothenbacher D, Bode G, Adler G. Inverse graded relation between alcohol consumption and active infection with Hellcobacter pylori. Am J Epidemiol. 1999;149(6):571–6.
39. Uemura N, Okamoto S, Yamamoto S, Matsumura N, Yamaguchi S, Yamakido M, et al. Helicobacter pylori infection and the development of gastric cancer. N Engl J Med. 2001;345(11):784–9.
40. Polk DB, Peek RM. Helicobacter pylori: gastric cancer and beyond. Nat Rev Cancer. 2010;10(6):403–14.
41. Damianaki A, Bakogeorgou E, Kampa M, Notas G, Hatzoglou A, Panagiotou S, et al. Potent inhibitory action of red wine polyphenols on human breast cancer cells. J Cell Biochem. 2000;78(3):429–41.
42. Sgambato A, Ardito R, Faraglia B, Boninsegna A, Wolf FI, Cittadini A. Resveratrol, a natural phenolic compound, inhibits cell proliferation and prevents oxidative DNA damage. Mutat Res. 2001;496(1-2):171–80.
43. He S, Sun C, Pan Y. Red wine polyphenols for cancer prevention. Int J Mol Sci. 2008;9(5):842–53.
44. Kraft TE, Parisotto D, Schempp C, Efferth T. Fighting cancer with red wine? Molecular mechanisms of resveratrol. Crit Rev Food Sci Nutr. 2009;49(9):782–99.
45. Yance DR Jr, Sagar SM. Targeting angiogenesis with integrative cancer therapies. Integr Cancer Ther. 2006;5(1):9–29.
46. Stojanovic J, Giraldi L, Arzani D, Pastorino R, Biondi A, Persiani R, et al. Adherence to Mediterranean diet and risk of gastric cancer: results of a case–control study in Italy. Eur J Cancer Prev. 2017;26(6):491–6.
47. Praud D, Bertuccio P, Bosetti C, Turati F, Ferraroni M, Vecchia CL. Adherence to the Mediterranean diet and gastric cancer risk in Italy. Int J Cancer. 2013;134(12):2935–41.
48. González CA, Buckland G. The Mediterranean diet and gastric cancer. In: The Mediterranean diet; 2015. p. 417–25.
49. D'Elia L, et al. Dietary salt intake and risk of gastric cancer. In: Zappia V, et al., editors. Advances in nutrition and cancer, vol. 159. Berlin Heidelberg: Springer; 2014. p. 83–95. https://doi.org/10.1007/978-3-642-38007-5_6.
50. Ren J-S, et al. Pickled food and risk of gastric cancer—a systematic review and meta-analysis of English and Chinese literature. Cancer Epidemiol Biomarkers Prev. 2012;21(6):905–15. https://doi.org/10.1158/1055-9965.EPI-12-0202.
51. Fritz W, Soós K. Smoked food and cancer. In: Forum of nutrition foreign substances and nutrition; 1980. p. 57–64.

52. Phukan RK, Narain K, Zomawia E, Hazarika NC, Mahanta J. Dietary habits and stomach cancer in Mizoram. India J Gastroenterol. 2006;41(5):418–24.
53. Iqbal A. Effect of food on causation and prevention of gastric cancer. J Cancer Prev Curr Res. 2017;8(5). https://doi.org/10.15406/jcpcr.2017.08.00289.
54. Ma K, Baloch Z, He T-T, Xia X. Alcohol consumption and gastric cancer risk: a meta-analysis. Med Sci Monit. 2017;23:238–46.
55. Keszei A, Schouten L, Goldbohm R, Brandt PVD. Red and processed meat consumption and the risk of esophageal and gastric cancer subtypes in the Netherlands cohort study. Ann Oncol. 2012;23(9):2319–26.
56. Ward MH, Cross AJ, Abnet CC, Sinha R, Markin RS, Weisenburger DD. Heme iron from meat and risk of adenocarcinoma of the esophagus and stomach. Eur J Cancer Prev. 2012;21(2):134–8.
57. Qiao Y-L, Dawsey SM, Kamangar F, Fan J-H, Abnet CC, Sun X-D, et al. Total and Cancer mortality after supplementation with vitamins and minerals: follow-up of the Linxian general population nutrition intervention trial. J Natl Cancer Inst. 2009;101(7):507–18.
58. Zullo A, Rinaldi V, Hassan C, Diana F, Winn S, Castagna G, et al. Ascorbic acid and intestinal metaplasia in the stomach: a prospective, randomized study. Aliment Pharmacol Ther. 2000;14(10):1303–9.
59. Xiao SD, et al. Interventional Study of High Dose Folic Acid in Gastric Carcinogenesis in Beagles. Gut. 2002;50(1):61–4. https://doi.org/10.1136/gut.50.1.61.
60. Correa P, Fontham ETH, Bravo JC, Bravo LE, Ruiz B, Zarama G, et al. RESPONSE: re: chemoprevention of gastric dysplasia: randomized trial of antioxidant supplements and anti-helicobacter pylori therapy. J Natl Cancer Inst. 2001;93(7):559–60.
61. You W-C, Brown LM, Zhang L, Li J-Y, Jin M-L, Chang Y-S, et al. Randomized double-blind factorial trial of three treatments to reduce the prevalence of precancerous gastric lesions. J Natl Cancer Inst. 2006;98(14):974–83.
62. Joossens JV, Hill MJ, Elliott P, Stamler R, Stamler J, Lesaffre E, et al. Dietary salt, nitrate and stomach cancer mortality in 24 countries. Int J Epidemiol. 1996;25(3):494–504.
63. Ngoan LT, Mizoue T, Fujino Y, Tokui N, Yoshimura T. Dietary factors and stomach cancer mortality. Br J Cancer. 2002;87(1):37–42.
64. Nouraie M. Fruits, vegetables, and antioxidants and risk of gastric cancer among male smokers. Cancer Epidemiol Biomark Prev. 2005;14(9):2087–92.
65. Mccullough ML, Giovannucci EL. Diet and cancer prevention. Oncogene. 2004;23(38):6349–64.
66. Buckland G, Agudo A, Luján L, Jakszyn P, Bueno-De-Mesquita HB, Palli D, et al. Adherence to a Mediterranean diet and risk of gastric adenocarcinoma within the European prospective investigation into cancer and nutrition (EPIC) cohort study. Am J Clin Nutr. 2009;91(2):381–90.
67. Duell EJ, Travier N, Lujan-Barroso L, Clavel-Chapelon F, Boutron-Ruault M-C, Morois S, et al. Alcohol consumption and gastric cancer risk in the European prospective investigation into cancer and nutrition (EPIC) cohort. Am J Clin Nutr. 2011;94(5):1266–75.
68. González CA, Jakszyn P, Pera G, Agudo A, Bingham S, Palli D, et al. Meat intake and risk of stomach and esophageal adenocarcinoma within the European prospective investigation into cancer and nutrition (EPIC). J Natl Cancer Inst. 2006;98(5):345–54.
69. Gonzalez CA, Lujan-Barroso L, Bueno-De-Mesquita HB, Jenab M, Duell EJ, Agudo A, et al. Fruit and vegetable intake and the risk of gastric adenocarcinoma: a reanalysis of the european prospective investigation into cancer and nutrition (EPIC-EURGAST) study after a longer follow-up. Int J Cancer. 2012;131(12):2910–9.
70. Jakszyn P, Bingham S, Pera G, Agudo A, Luben R, Welch A, et al. Endogenous versus exogenous exposure to N -nitroso compounds and gastric cancer risk in the European prospective investigation into cancer and nutrition (EPIC-EURGAST) study. Carcinogenesis. 2006;27(7):1497–501.
71. Zamora-Ros R, Knaze V, Luján-Barroso L, Kuhnle GGC, Mulligan AA, Touillaud M, et al. Dietary intakes and food sources of phytoestrogens in the European prospective investigation into cancer and nutrition (EPIC) 24-hour dietary recall cohort. Eur J Clin Nutr. 2012;66(8):932–41.
72. Miyazaki M, Doi Y, Ikeda F, Ninomiya T, Hata J, Uchida K, et al. Dietary vitamin a intake and incidence of gastric cancer in a general Japanese population: the Hisayama study. Gastric Cancer. 2012;15(2):162–9. https://doi.org/10.1007/s10120-011-0092-7 Epub 2011 Sep 23. PMID: 21948483.
73. Shikata K, Kiyohara Y, Kubo M, Yonemoto K, Ninomiya T, Shirota T, et al. A prospective study of dietary salt intake and gastric cancer incidence in a defined Japanese population: the Hisayama study. Int J Cancer. 2006;119(1):196–201. https://doi.org/10.1002/ijc.21822 PMID: 16450397.
74. Khan MM, Goto R, Kobayashi K, Suzumura S, Nagata Y, Sonoda T, et al. Dietary habits and cancer mortality among middle aged and older Japanese living in Hokkaido, Japan by cancer site and sex. Asian Pac J Cancer Prev. 2004;5(1):58–65 PMID: 15075007.
75. Everatt R, Tamosiunas A, Kuzmickiene I, Virviciute D, Radisauskas R, Reklaitiene R, et al. Alcohol consumption and risk of gastric cancer: a cohort study of men in Kaunas, Lithuania, with up to 30 years follow-up. BMC Cancer. 2012;12. https://doi.org/10.1186/1471-2407-12-475.
76. Ko K-P, Park SK, Yang JJ, Ma SH, Gwack J, Shin A, et al. Intake of soy products and other foods and gastric cancer risk: a prospective study. J Epidemiol. 2013;23:337–43. https://doi.org/10.2188/jea.je20120232.
77. Murata A, Fujino Y, Pham TM, Kubo T, Mizoue T, Tokui N, et al. Prospective cohort study evaluating the relationship between salted food intake and gastrointestinal tract cancer mortality in Japan. Asia Pac J Clin Nutr. 2010;19(4):564–71 PMID: 21147719.
78. Steevens J, Schouten LJ, Goldbohm RA, van den Brandt PA. Vegetables and fruits consumption and risk of esophageal and gastric cancer subtypes in the Netherlands cohort study. Int J Cancer. 2011;129(11):2681–93. https://doi.org/10.1002/ijc.25928 Epub 2011 Aug 24. PMID: 21960262.
79. O'Doherty MG, Freedman ND, Hollenbeck AR, Schatzkin A, Abnet CC. A prospective cohort study of obesity and risk of oesophageal and gastric adenocarcinoma in the NIH-AARP Diet and Health Study. Gut. 2012;61(9):1261–8. https://doi.org/10.1136/gutjnl-2011-300551 Epub 2011 Dec 15. PMID: 22174193; PMCID: PMC3504700.
80. Moy KA, Fan Y, Wang R, Gao YT, Yu MC, Yuan JM. Alcohol and tobacco use in relation to gastric cancer: a prospective study of men in Shanghai, China. Cancer Epidemiol Biomarkers Prev. 2010;19(9):2287–97. https://doi.org/10.1158/1055-9965.EPI-10-0362 Epub 2010 Aug 10. PMID: 20699372; PMCID: PMC2936659.
81. Yu T, Tong L, Ao Y, Zhang G, Liu Y, Zhang H. Novel design of NIR-triggered plasmonic nanodots capped mesoporous silica nanoparticles loaded with natural capsaicin to inhibition of metastasis of human papillary thyroid carcinoma B-CPAP cells in thyroid cancer chemo-photothermal therapy. J Photochem Photobiol B Biol. 2019;197:111534.
82. Liu X, Sun K, Chen H, Song A, Zhang X, Zhang X, et al. Curcumin inhibits proliferation of gastric cancer cells by impairing ATP-sensitive potassium channel opening. World J Surg Oncol. 2014;12(1):1–8.
83. Wu J, Zhang XX, Zou X, Wang M, Wang HX, Wang YH, et al. The effect of Jianpi Yangzheng Xiaozheng decoction and its components on gastric cancer. J Ethnopharmacol. 2019;235:56–64.
84. Zhang Y, Yu C. Bibliometric evaluation of publications (2000-2020) on the prognosis of gastric cancer. Inquiry. 2021;58:00469580211056015.
85. Daniyal M, Ahmad S, Ahmad M, Asif HM, Akram M, Rehman SU, et al. Risk factors and epidemiology of gastric cancer in Pakistan. Asian Pac J Cancer Prev. 2015;16(12):4821–4.
86. Compare D, Rocco A, Nardone G. Risk factors in gastric cancer. Eur Rev Med Pharmacol Sci. 2010;14(4):302–8.
87. Shen X, Zhang J, Yan Y, Yang Y, Fu G, Pu Y. Analysis and estimates of the attributable risk for environmental and genetic risk factors in gastric cancer in a Chinese population. J Toxic Environ Health A. 2009;72(11-12):759–66.
88. Yusefi AR, Lankarani KB, Bastani P, Radinmanesh M, Kavosi Z. Risk factors for gastric cancer: a systematic review. Asian Pac J Cancer Prev. 2018;19(3):591.
89. McNamara KM, Gobert AP, Wilson KT. The role of polyamines in gastric cancer. Oncogene. 2021;40(26):4399–412.
90. Vahid F, Davoodi SH. Nutritional factors involved in the etiology of gastric cancer: a systematic review. Nutr Cancer. 2021;73(3):376–90.

Publisher's Note