



INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH AND BIO-SCIENCE

REVIEW: EPIDEMIOLOGY OF GASTRIC CANCER

AMAR P. PATIL, AJINKYA CHAVAN, TOHID ALIAS NAVAJ BAXU, SATYAJIT SATHE

Assistant Professor, Sant Gajanan Maharaj Rural Pharmacy College, Mahagaon M.S. India

Accepted Date: 31/12/2013; Published Date: 27/02/2014

Abstract: The prevalence and death of gastric cancer have fallen dramatically in India and elsewhere over the past several decades. Nevertheless, gastric cancer leftovers a major public health issue as the fourth most common cancer and the second leading cause of cancer death worldwide. Demographic trends differ by tumor location and histology. While there has been a marked decline in distal, intestinal type gastric cancers, the incidence of proximal, diffuse type adenocarcinomas of the gastric cardia has been increasing, particularly in the Western countries. Incidence by tumor sub-site also varies widely based on geographic location, race, and socio-economic status. Distal gastric cancer prevails in developing countries, in lower socio-economic groups, whereas proximal tumors are more common in developed countries, among whites, and in higher socio-economic classes. Diverging trends in the incidence of gastric cancer by tumor location suggest that they may represent two diseases with different etiologies. The main risk factors for distal gastric cancer include *Helicobacter pylori* infection and dietary factors; whereas gastroesophageal reflux disease and obesity play important roles in the development of proximal stomach cancer. The determination of this review is to study the epidemiology and risk factors of gastric cancer, and to discuss approaches for primary prevention.

Keywords: Epidemiology; Gastric cancer



PAPER-QR CODE

Corresponding Author: Mr. AMAR P. PATIL

Access Online On:

www.ijprbs.com

How to Cite This Article:

Amar P. Patil, IJPRBS, 2014; Volume 3(1): 65-92

INTRODUCTION

Generally, gastric cancer prevalence and mortality have dropped dramatically over the past 70 years^[1]. Despite its recent decline, gastric cancer is the fourth most common cancer and the second leading cause of cancer-related death worldwide^[2,3]. In 2000, about 880 000 people were diagnosed with gastric cancer and approximately 650 000 died of the disease^[4].

The two main tumor positions of gastric adenocarcinoma are proximal (cardia) and distal (noncardia). Despite a decline in distal gastric cancers, proximal tumors have been increasing in incidence since the 1970s, especially among males in the Western countries^[5,6]. These gastric tumor types lead in populations from different geographic locations, racial and socio-economic groups. They may also differ in genetic susceptibility, pathologic profile, clinical presentation, and prognosis. The observed differences between gastric cancers by anatomic site suggest that they are distinct diseases with different etiologies. Detailed epidemiological analyses of their demographic trends and risk factors will help monitor future cancer control strategies.

PATHOLOGIC REFLECTIONS

Around 90% of stomach cancers are adenocarcinomas, which are divided into two chief histologic forms: (1) well-differentiated or intestinal form, and (2) undifferentiated or diffuse form. The intestinal form is related to corpus-dominant gastritis with gastric atrophy and intestinal metaplasia, whereas the diffuse form usually originates in pangastritis lacking atrophy.

The intestinal form is more common in males, blacks, and older age groups, whereas the diffuse type has a more equal male-to-female ratio and is more frequent in younger individuals^[7,8]. Intestinal form tumors preponderate in high-risk geographic areas, such as East Asia, Eastern Europe, Central and South America, and account for much of the international variation of gastric cancer^[9]. Diffuse form adenocarcinomas of the stomach have a more uniform geographic scattering^[10]. A decrease in the prevalence of the intestinal form tumors in the corpus of the stomach accounts for most of the recent decrease in gastric cancer rates worldwide^[11]. In contrast, the incidence of diffuse type gastric carcinoma, particularly the signet ring type, has been increasing^[12].

DEMOGRAPHIC INCLINATIONS

Time inclinations

In the 1930s, gastric cancer was the most common cause of cancer death in US and Europe. During the past 70 years, mortality rates have fallen dramatically in all developed countries largely due to unplanned prevention. However, in the past 30 years, the incidence of gastric

cardia adenocarcinoma rose by five- to six-fold in developed countries^[13-19]. Gastric cardia tumors now account for nearly half of all stomach cancers among men from India, US and UK^[6,20]. There has also been a rising inclination in esophageal adenocarcinoma, in which obesity, gastroesophageal reflux disease (GERD), and Barrett's esophagus are major etiologic factors. Gastric cardia cancers share certain epidemiologic features with adenocarcinomas of the distal esophagus and gastroesophageal (GE) junction, signifying that they represent a similar disease entity.

GEOGRAPHIC VARIATION

Gastric cancer prevalence proportions vary by up to ten-fold throughout the world. Nearly two-thirds of stomach cancers occur in developing countries^[4]. Japan and Korea have the highest gastric cancer rates in the world^[21,22]. High-incidence areas for noncardia gastric adenocarcinoma include East Asia, Eastern Europe, and Central and South America^[20,23]. Low incidence rates are found in South Asia, North and East Africa, North America, Australia, and New Zealand (Figure 1A).

In Japan, gastric cancer remains the most common type of cancer among both men and women. Age-standardized incidence proportions in Japan are 69.2 per 100 000 in men and 28.6 per 100 000 in women^[3]. In distinction to the increasing prevalence of proximal tumors in the West, distal tumors endure to preponderate in Japan. On the other hand, even in Japan, the proportion of proximal stomach cancers has increased among men^[24].

Refugee populations from high-risk areas such as Japan show a marked reduction in risk when they move to low-incidence regions such as the US^[25]. Subsequent generations acquire risk levels approximating those of the host country^[20,23].

SEX, AGE, AND RACE DISTRIBUTION

Noncardia gastric cancer has a male-to-female ratio of approximately 2:1^[20,23]. Prevalence rates are significantly higher among blacks and lower socio-economic groups, and in developing countries^[20]. Prevalence rises progressively with age, with a peak occurrence between 50 and 70 years.

In distinction, for gastric cardia carcinomas, men are affected five times more than women and white twice as much as blacks^[26]. In addition, the incidence rates of proximal gastric cancers are relatively higher in the professional classes^[27]. Different rates of genetic polymorphisms according to tumor sub-site propose variation in predisposition to stomach cancer by tumor location^[28]. These findings suggest that noncardia and cardia adenocarcinomas are distinct biological entities.

SURVIVAL

For the past few decades, gastric cancer mortality has decreased markedly in most areas of the world^[29,30]. Though, gastric cancer remains a disease of poor prognosis and high mortality, second only to lung cancer as the leading cause of cancer-related death worldwide. In general, countries with higher incidence rates of gastric cancer show better survival rates than countries with lower incidence^[31]. This association is largely due to a difference in survival rates based on tumor location within the stomach. Tumors located in the gastric cardia have a much poorer prognosis compared to those in the pyloric antrum, with lower 5-year survival and higher operative mortality^[32].

In addition, the availability of screening for early detection in high-risk areas has led to a decrease in mortality. In Japan where mass screening programs are in place, mortality rates for gastric cancer in men have more than halved since the early 1970s^[33]. When disease is confined to the inner lining of the stomach wall, 5-year survival is on the order of 95%. In contrast, few gastric cancers are discovered at an early stage in US, leading to 5-year relative survival rates of less than 20%^[34]. Similarly in European countries, the 5-year relative survival rates for gastric cancer vary from 10% to 20%^[35,36]. Host-related factors may also affect prognosis, as a US study demonstrated that gastric cancers in persons of Asian descent had a better prognosis compared to non-Asians^[37].

RISK FACTORS

Gastric cancer is a multifactorial disease. The marked geographic deviation, time trends, and the migratory effect on gastric cancer incidence propose that environmental or lifestyle factors are major contributors to the etiology of this disease.

Helicobacter pylori infection

Helicobacter pylori (*H. pylori*) is a gram-negative bacillus that colonizes the stomach and may be the most common chronic bacterial infection worldwide^[38]. Countries with high gastric cancer proportions typically have a high prevalence of *H. pylori* infection, and the decline in *H. pylori* prevalence in developed countries parallels the decreasing incidence of gastric cancer^[39,40] (Figure 1B). In US, the prevalence of *H. pylori* infection is <20% at the age 20 years and 50% at 50 years^[41]. In Japan, it is also <20% at 20 years, but increases to 80% over the age of 40 years^[42] and in Korea, 90% of asymptomatic adults over the age of 20 years are infected by *H. pylori*^[43]. The increase in incidence with age is largely due to a birth cohort effect rather than late acquisition of infection. *H. pylori* infection is mainly acquired during early childhood, likely through oral ingestion, and infection persists throughout life^[44]. Incidence is closely linked to

socio-economic factors, such as low income and poor education, and living conditions during childhood, such as poor sanitation and overcrowding^[45-49].

The association between chronic *H. pylori* infection and the development of gastric cancer is well established^[50-53]. In 1994, the International Agency for Research on Cancer classified *H. pylori* as a type I (definite) carcinogen in human beings^[54]. In Correa's model of gastric carcinogenesis, *H. pylori* infection causes the progressive sequence of gastric lesions from chronic gastritis, gastric atrophy, intestinal metaplasia, dysplasia, and finally, gastric adenocarcinoma^[55]. Numerous case-control studies have shown important associations between *H. pylori* seropositivity and gastric cancer risk, with about a 2.1- to 16.7-fold greater risk compared to seronegative individuals^[56-62]. Prospective studies have also supported the association between *H. pylori* infection and gastric cancer risk^[50-52,63]. Perhaps the most compelling evidence for the link between *H. pylori* and gastric cancer comes from a prospective study of 1 526 Japanese participants in which gastric cancers developed in 2.9% of infected people and in none of the uninfected individuals^[64]. Interestingly, gastric carcinomas were detected in 4.7% of *H. pylori*-infected individuals with non-ulcer dyspepsia.

The huge majority of *H. pylori*-infected individuals remain asymptomatic without any clinical sequelae. Cofactors, which determine that *H. pylori*-infected people are at particular risk for gastric cancer, include bacterial virulence factors and proinflammatory host factors. Gastric cancer risk is enhanced by infection with a more virulent strain of *H. pylori* carrying the cytotoxic-associated gene A (*cagA*)^[65,66]. Compared to *cagA*- strains, infection by *H. pylori cagA*+ strains was associated with an increased risk of severe atrophic gastritis and distal gastric cancer^[67-70]. In the Western countries, about 60% of *H. pylori* isolates are *cagA*+^[71], whereas in Japan, nearly 100% of the strains possess functional *cagA*^[72,73]. Host factors associated with an increased risk of gastric cancer include genetic polymorphisms which lead to high-level of expression of the proinflammatory cytokine, interleukin-1^[74,75].

The effects of *H. pylori* on gastric tumor growth may vary by anatomical site. The falling incidence of *H. pylori* infection and noncardia gastric cancer in developed countries has been diametrically opposed to the rapid increase in the prevalence of gastric cardia adenocarcinoma^[76]. Based on a meta-analysis of potential cohort studies, *H. pylori* infection was associated with the risk of noncardia gastric cancer, but not cardia cancer^[77]. Other studies revealed a significant inverse association between *H. pylori* infection, particularly *cagA*+ strains, and the development of gastric cardia and esophageal adenocarcinomas^[78,79]. In the Western countries, where the prevalence of *H. pylori* infection is falling, GERD and its sequelae are increasing. Studies have shown that severe atrophic gastritis and reduced acid production associated with *H. pylori* infection significantly reduced the risk of GERD^[80-83]. However, current studies have found conflicting results on whether *H. pylori* eradication therapy increases the

risk of esophagitis and gastric cardia adenocarcinoma^[84-91]. Thus, the protective effect of *H. pylori* against cardia tumors remains controversial.

Dietary factors

It is questionable that *H. pylori* infection alone is responsible for the development of gastric cancer. Rather, *H. pylori* may produce an environment conducive to carcinogenesis and interact with other lifestyle and environmental exposures. There is evidence that consumption of salty foods and N-nitroso compounds and low intake of fresh fruits and vegetables increases the risk of gastric cancer. *H. pylori* gastritis facilitates the growth of nitrosating bacteria, which catalyze the production of carcinogenic N-nitroso compounds^[92]. In addition, *H. pylori* infection is known to inhibit gastric secretion of ascorbic acid, which is an important scavenger of N-nitroso compounds and oxygen free radicals^[93].

Salt-preserved foods and dietary nitrite found in preserved meats are actually carcinogenic. Intake of salted food may increase the risk of *H. pylori* infection and act synergistically to promote the development of gastric cancer. In animal models, ingestion of salt is known to cause gastritis and enhance the effects of gastric carcinogens^[94,95]. Mucosal damage induced by salt may increase the possibility of persistent infection with *H. pylori*^[96]. Several case-control studies have shown that a high intake of salt and salt-preserved food was associated with gastric cancer risk^[97-103], but evidence from prospective studies is inconsistent^[104-107]. N-nitroso compounds are carcinogenic in animal models and are formed in the human stomach from dietary nitrite. However, case-control studies have revealed a weak, nonsignificant increased risk of gastric cancer for high vs low nitrite intake^[97,108-110]. Potential studies have reported significant reductions in gastric cancer risk arising from fruit and vegetable consumption^[111-114]. The worldwide decline in gastric cancer incidence may be attributable to the advent of refrigeration, which led to decreased consumption of preserved foods and increased intake of fresh fruits and vegetables.

Animal studies have revealed that polyphenols in green tea have antitumor and anti-inflammatory effects. In preclinical studies, polyphenols have antioxidant activities and the ability to inhibit nitrosation, which have been implicated as etiologic factors of gastric cancer^[115-117]. Although various case-control studies have shown a reduced risk of gastric cancer in relation to green tea consumption^[118-121], recent prospective cohort studies found no protective effect of green tea on gastric cancer risk^[122-125].

Tobacco

Potential studies have established a significant dose-dependent relationship between smoking and gastric cancer risk^[126,127]. The effect of smoking was more noticeable for distal gastric

cancer, with adjusted rate ratios of 2.0 (95% CI, 1.1-3.7) and 2.1 (95% CI, 1.2-3.6) for past and current smokers, respectively^[128]. There is little support for an association between alcohol and gastric cancer^[129].

Obesity

Obesity is one of the chief risk factors for gastric cardia adenocarcinoma^[130,131]. Obesity can support GE reflux disease which influences to Barrett's esophagus, a metaplastic precursor state for adenocarcinoma of the esophagus and GE junction^[132,133]. A Swedish study found that the heaviest quarter of the population had a 2.3-fold increased risk for gastric cardia adenocarcinoma compared to the lightest quartile of the population^[134]. A recent prospective study from US found that body mass index was significantly associated with higher rates of stomach cancer mortality among men^[135]. Thus, risk factors positively associated with adenocarcinoma of the esophagus and gastric cardia include obesity, GE reflux, and the presence of Barrett's esophagus. A summary of the main differences between cardia and noncardia gastric cancer can be found in Table 1.

Other

Fewer common risk factors for gastric cancer include radiation^[136], pernicious anemia^[137], blood type A^[138], prior gastric surgery for benign conditions^[139], and Epstein-Barr virus^[140-142]. In addition, a positive family history is an important risk factor, particularly with genetic syndromes such as hereditary nonpolyposis colon cancer and Li-Fraumeni syndrome^[143-145].

PREVENTION OF GASTRIC CANCER

Lifestyle modifications

Since, gastric cancer is often linked with a poor prognosis; the main policy for improving clinical outcomes is through primary prevention. Decrease in gastric cancer mortality is mainly due to unplanned prevention. The widespread introduction of refrigeration has led to a decrease in the intake of chemically preserved foods and increased consumption of fresh fruits and vegetables^[98,146]. A decline in the prevalence of *H. pylori* infection may be due to improvements in sanitary and housing conditions, as well as the use of eradication therapy^[54]. In addition, reduced tobacco smoking at least in males may have contributed to the decline in gastric cancer incidence^[147]. Therefore, changeable risk factors, such as high salt and nitrite consumption, low fruit and vegetable intake, cigarette smoking, and *H. pylori* infection, may be directed for prevention.

H. pylori eradication

Public health measures to develop sanitation and housing surroundings are the key factors in reducing the worldwide prevalence of *H. pylori* infection. *H. pylori* abolition therapy is another potential strategy for gastric cancer chemoprevention. A 7 to 14 day course of two antibiotics and an antisecretory agent has a cure rate of about 80% with durable responses^[148]. However, higher reinfection rates are seen in developing countries after people have had effective eradication therapy^[149]. In Japanese patients treated for early gastric cancer, *H. pylori* abolition therapy resulted in a significantly lower rate of gastric cancer reappearance^[150]. A randomized controlled chemoprevention trial showed that antimicrobial therapy directed against *H. pylori* or dietary supplementation with antioxidants improved the reversion rate of gastric atrophy and intestinal metaplasia compared to placebo^[151]. In a randomized, placebo-controlled primary prevention trial conducted in a high-risk region of China, 1 630 healthy carriers of *H. pylori* infection were randomized to a 2-wk course of eradication treatment or placebo^[152]. Although the prevalence of gastric cancer was similar in both groups after 7.5 years of follow-up, post hoc analysis of a subgroup of *H. pylori* carriers without precancerous lesions at baseline showed a significant decrease in the development of gastric cancer with abolition therapy.

Numerous comprehensive chemoprevention trials of *H. pylori* abolition therapy with gastric cancer endpoints are continuing. Potential disadvantages of widespread abolition therapy in asymptomatic carriers include developing antibiotic-resistant strains of *H. pylori* and perhaps increasing the risk of GERD and adenocarcinoma of the esophagus and gastric cardia.

Antioxidants

High consumption of antioxidants, such as vitamins C and E and β -carotene, may have a protective influence on the risk of gastric cancer. High serum levels of β -carotene, α -carotene, lycopene, and vitamin C were significantly associated with reduced risk of gastric cancer in a cohort from Shanghai, China^[153]. A randomized trial in Linxian, China showed a reduced risk of both cardia and noncardia gastric cancers in individuals supplemented with a combination of selenium, β -carotene, and α -tocopherol^[154]. However, a randomized trial from Finland showed no association between α -tocopherol or β -carotene supplementation and the prevalence of gastric cancer in elderly men with atrophic gastritis^[155]. Another prospective study from the US Cancer Prevention Study II cohort found that vitamin supplementation did not significantly reduce the risk of stomach cancer mortality^[156]. Therefore, dietary supplementation may only play a preventive role in populations with high rates of gastric cancer and small intake of micronutrients.

COX-2 inhibitors

Cyclooxygenase-2 (COX-2) plays a role in cell proliferation, apoptosis, and angiogenesis, and may be involved in gastric carcinogenesis^[157,158]. Increasing levels of COX-2 are present in the progression from atrophic gastritis to intestinal metaplasia and adenocarcinoma of the stomach^[159]. Exposure to cigarette smoke, acidic conditions, and *H. pylori* infection all induce COX-2 expression^[160-162]. Furthermore, McCarthy *et al.* showed that COX-2 expression in the antral mucosa was reduced in the epithelium after successful eradication of *H. pylori*^[163].

Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) are supposed to inhibit cancer cell growth primarily through the inhibition of COX-2, and evidence is mounting that COX-2 inhibitors may be beneficial in preventing upper gastrointestinal malignancies. Compared to colorectal cancer, the link between NSAID use and the development of gastric cancer has been studied less comprehensively^[164-166]. A recent meta-analysis showed that NSAID use was associated with a reduced risk of noncardia gastric adenocarcinoma^[167]. Thus, COX-2 inhibitors may provide a chemopreventive strategy against gastric carcinogenesis.

Endoscopic screening and surveillance

Since, the high risk of gastric cancer in Japan, there has been a national endoscopic surveillance program within the commercial workforce. Annual screening with a double-contrast barium technique and endoscopy is suggested for persons over the age of 40 years^[168]. With mass screening, about half of gastric tumors are being detected at an early stage in asymptomatic individuals and the mortality rate from gastric cancer has more than halved since the early 1970s^[33]. An intervention study in China is underway which involves a comprehensive approach to gastric cancer prevention, including *H. pylori* eradication, nutritional supplements, and aggressive screening with double contrast X-ray and endoscopic examination. In the first four years after involvement, the relative risk of overall mortality with this intervention for a high-risk group was 0.51 (95% CI, 0.35-0.74)^[169]. This study recommends that targeting high-risk populations for aggressive screening and prevention may fall gastric cancer mortality.

SUMMARY & CONCLUSION

In summary, cardia and noncardia gastric cancers showsingle epidemiologic features characterized by marked geographic variation, diverging time trends, and differences based on race, sex, and socio-economic status. *H. pylori* infection and dietary factors appear to be the main causative agents for distal gastric cancer, whereas GERD and obesity play a primary role in proximal gastric cancer. Future guidelines in primary prevention should target changeable risk factors in high-risk populations. In the planning and evaluation of gastric cancer control

activities, detailed demographic investigates will inform future selection and interference studies.

ACKNOWLEDGMENTS

The authors are grateful to Mr. Ansar M. Patel Sant Gajanan Maharaj Rural Pharmacy, College for providing the full research articles for compilation of this review.

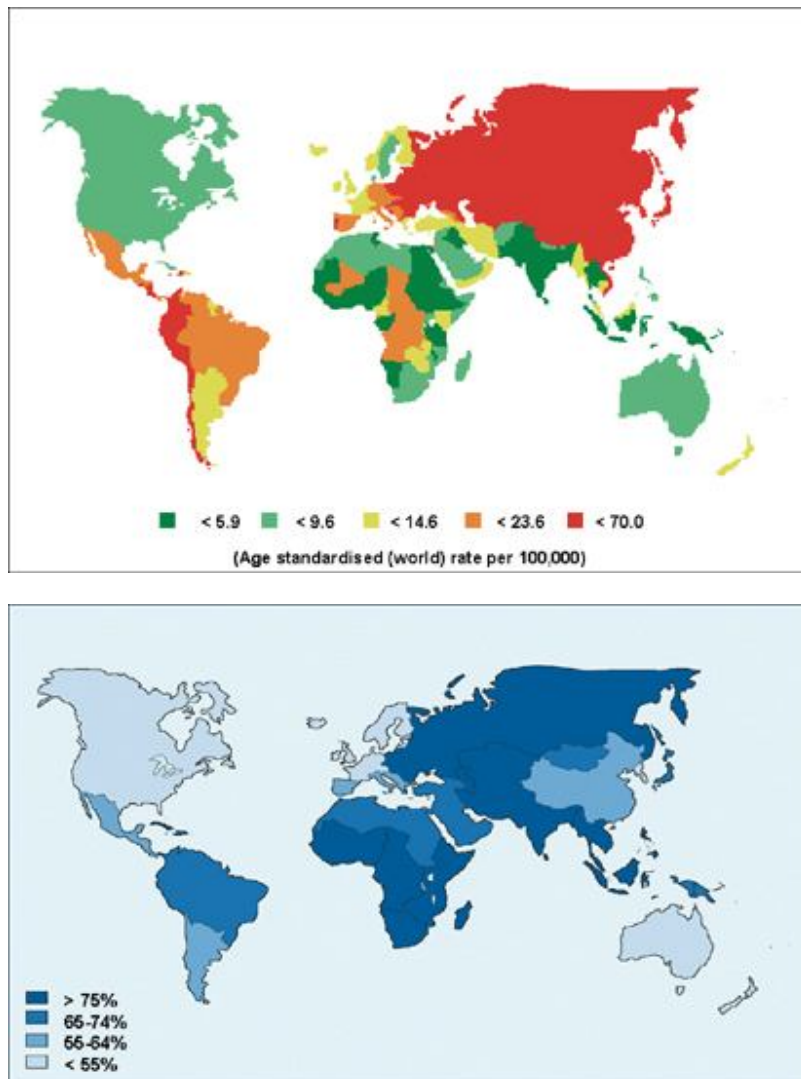


Figure 1 Gastric cancer and *Helicobacter pylori* infection prevalence in the world. (A) Incidence of stomach cancer in males; (B) Prevalence of *Helicobacter pylori* infection in asymptomatic adults. (Data adapted from Parkinet *al*^[3].)

Table 1 Epidemiologic differences between cardia and noncardia gastric cancer

Particulars	Cardia	Noncardia
Incidence	Increasing	Decreasing
Geographic location		
Western countries	+	-
East Asia	-	+
Developing countries	-	+ ++
Age	++	+
Male gender	++	-
Caucasian race	+	+
Low socioeconomic status	-	+
<i>H. pylori</i> infection	?	+
Diet		
Preserved foods	+	-
Fruits/vegetables	-	?
Obesity	+	+
Tobacco	+	

NOTE: ++, strong positive association; +, positive association; -, negative association; ?, ambiguous studies.

REFERENCES

1. Parkin D.M, Pisani P, Ferlay J; "Estimates of the worldwide incidence of eighteen major cancers in 1985". *Int J Cancer* 1993, 54: 594-606. [doi:10.1002/ijc.2910540413](https://doi.org/10.1002/ijc.2910540413)
2. Parkin D.M, Bray F.I, Devesa S.S; "Cancer burden in the year 2000. The global picture". *Eur J Cancer* 2001; 37 (8): S4-S66. [doi:10.1016/S0959-8049\(01\)00267-2](https://doi.org/10.1016/S0959-8049(01)00267-2)
3. Parkin D.M; " International variation". *Oncogene* 2004, 23: 6329-6340. [doi:10.1038/sj.onc.1207726](https://doi.org/10.1038/sj.onc.1207726)
4. Stewart B.W, Kleihues P; "World Cancer Report". Lyon: *IARC Press*, 2003.
5. Blot W.J, Devesa S.S, Kneller R.W, Fraumeni J.F; "Rising incidence of adenocarcinoma of the esophagus and gastric cardia". *JAMA* 1991, 265: 1287-1289. [doi:10.1001/jama.265.10.1287](https://doi.org/10.1001/jama.265.10.1287)
6. Brown L.M, Devesa S.S; "Epidemiologic trends in esophageal and gastric cancer in the United States". *Surg Oncol Clin N Am* 2002, 11: 235-256. [doi:10.1016/S1055-3207\(02\)00002-9](https://doi.org/10.1016/S1055-3207(02)00002-9)
7. Lauren P *et al*; "The two histological main types of gastric carcinoma: Diffuse and so-called intestinal-type carcinoma. An attempt at a histo-clinical classification". *Acta Pathol Microbiol Scand* 1965, 64: 31-49.
8. Correa P, Sasano N, Stemmermann G.N, Haenszel W; "Pathology of gastric carcinoma in Japanese populations: comparisons between Miyagi prefecture, Japan, and Hawaii". *J Natl Cancer Inst* 1973, 51: 1449-1459.
9. Munoz N. Gastric Carcinogenesis. In: Reed P.I, Hill M.J, eds. Gastric carcinogenesis: proceedings of the 6th Annual Symposium of the European Organization for Cooperation in Cancer Prevention Studies (ECP). Amsterdam: *Elsevier Science*, 1988, 51-69.
10. Munoz N, Correa P, Cuello C, Duque E; "Histologic types of gastric carcinoma in high- and low-risk areas". *Int J Cancer* 1968, 3: 809-818 [doi:10.1002/ijc.2910030614](https://doi.org/10.1002/ijc.2910030614)
11. Kaneko S, Yoshimura T; "Time trend analysis of gastric cancer incidence in Japan by histological types". 1975-1989. *Br J Cancer* 2001, 84: 400-405 [doi:10.1054/bjoc.2000.1602](https://doi.org/10.1054/bjoc.2000.1602)
12. Henson D.E, Dittus C, Younes M, Nguyen H, Albores-Saavedra J. "Differential trends in the intestinal and diffuse types of gastric carcinoma in the United States" 1973-2000: increase in the signet ring cell type. *Arch Pathol Lab Med* 2004, 128: 765-770.

13. Pera M, Cameron A.J, Trastek V.F, Carpenter H.A, Zinsmeister A.R; "Increasing incidence of adenocarcinoma of the esophagus and esophagogastric junction". *Gastroenterology* 1993,104: 510-513.
14. Hansen S, Wiig J.N, Giercksky K.E, Tretli S; "Esophageal and gastric carcinoma in Norway 1958-1992: incidence time trend variability according to morphological subtypes and organ subsites". *Int J Cancer* 1997, 71: 340-344 [doi:10.1002/\(SICI\)1097-0215\(19970502\)71:3<340::AID-IJC5>3.0.CO;2-Y](https://doi.org/10.1002/(SICI)1097-0215(19970502)71:3<340::AID-IJC5>3.0.CO;2-Y)
15. Moller H. "Incidence of cancer of oesophagus, cardia and stomach in Denmark". *Eur J Cancer Prev*1992, 1: 159-164.
16. Harrison S.L, Goldacre M.J, Seagroatt V; Trends in registered incidence of oesophageal and stomach cancer in the Oxford region, 1974-88. *Eur J Cancer Prev* 1992, 1: 271-274. [doi:10.1097/00008469-199204000-00009](https://doi.org/10.1097/00008469-199204000-00009)
17. Levi F, La Vecchia C, Te V.C;"Descriptive epidemiology of adenocarcinomas of the cardia and distal stomach in the Swiss Canton of Vaud". *Tumori*1990, 76: 167-171.
18. Armstrong R.W, Borman B;"Trends in incidence rates of adenocarcinoma of the oesophagus and gastric cardia in New Zealand, 1978-1992". *Int J Epidemiol* 1996, 25: 941-947. [doi:10.1093/ije/25.5.941](https://doi.org/10.1093/ije/25.5.941)
19. Thomas R.J, Lade S, Giles G.G, Thursfield V; "Incidence trends in oesophageal and proximal gastric carcinoma in Victoria". *Aust N Z J Surg* 1996, 66: 271-275. [doi:10.1111/j.1445-2197.1996.tb01183.x](https://doi.org/10.1111/j.1445-2197.1996.tb01183.x)
20. Parkin D.M, Whelan S.L, Ferlay J; "Cancer Incidence in Five Continents, vol VII. Lyon, France". *International Agency for Research on Cancer*1997, 822-823.
21. Yamamoto S; " Stomach cancer incidence in the world". *Jpn J ClinOncol* 2001, 31: 471. [doi:10.1093/jjco/31.9.471](https://doi.org/10.1093/jjco/31.9.471) PMID:11689605
22. Ahn Y.O, Park B.J, Yoo K.Y, Kim N.K, Heo D.S, Lee J.K, Ahn H.S, Kang D.H, Kim H, Lee M.S; " Incidence estimation of stomach cancer among Koreans". *J Korean Med Sci*1991, 6: 7-14.
23. Nomura A;"Stomach Cancer. In: Schottenfeld D, Fraumeni JF, eds. *Cancer Epidemiology and Prevention*". New York, NY: Oxford University Press, 1996, 707-724.

24. Liu Y, Kaneko S, Sobue T; "Trends in reported incidences of gastric cancer by tumour location, from 1975 to 1989 in Japan". *Int J Epidemiol* 2004, 33: 808-815. [doi:10.1093/ije/dyh053](https://doi.org/10.1093/ije/dyh053) PMID:15020567
25. McMichael A.J, McCall M.G, Hartshorne J.M, Woodings T.L; "Patterns of gastro-intestinal cancer in European migrants to Australia: the role of dietary change". *Int J Cancer* 1980, 25:431-437. [doi:10.1002/ijc.2910250402](https://doi.org/10.1002/ijc.2910250402)
26. El-Serag H.B, Mason A.C, Petersen N, Key C.R; "Epidemiological differences between adenocarcinoma of the oesophagus and adenocarcinoma of the gastric cardia in the USA". *Gut* 2002,50:368-372 [doi:10.1136/gut.50.3.368](https://doi.org/10.1136/gut.50.3.368) PMID:11839716
27. Powell J, McConkey C.C; "The rising trend in oesophageal adenocarcinoma and gastric cardia". *Eur J Cancer Prev* 1992, 1: 265-269. [doi:10.1097/00008469-199204000-00008](https://doi.org/10.1097/00008469-199204000-00008)
28. Shen H, Xu Y, Qian Y, Yu R, Qin Y, Zhou L, Wang X, Spitz MR, Wei Q; " Polymorphisms of the DNA repair gene XRCC1 and risk of gastric cancer in a Chinese population". *Int J Cancer* 2000, 88: 601-606. [doi: 10.1002/1097-0215\(20001115\)88:4<601::AID](https://doi.org/10.1002/1097-0215(20001115)88:4<601::AID)
29. Jemal A, Thomas A, Murray T, Thun M; "Cancer statistics, 2002". *CA Cancer J Clin* 2002, 52: 23-47.
30. Ries L.A, Kosary C.L, Hankey B.F; "SEER Cancer Statistics Review 1973-1995. Bethesda: U.S. Dept. of Health and Human Services, Public Health Service, National Institutes of Health, National Cancer Institute". 1998.
31. Verdecchia A, Corazziari I, Gatta G, Lisi D, Faivre J, Forman D; " Explaining gastric cancer survival differences among European countries". *Int J Cancer* 2004, 109: 737-741. [doi:10.1002/ijc.20047](https://doi.org/10.1002/ijc.20047)
32. Fielding J.W.L, Powell J, Allum W,H; "Cancer of the Stomach. London", The Macmillan Press, 1989.
33. IARC Unit of Descriptive Epidemiology: WHO cancer mortality databank. *Cancer Mondial*, 2001; Available from [URL:www-dep.iarc.fr/ataava/globocan/who.htm](http://www-dep.iarc.fr/ataava/globocan/who.htm)
34. Ries L.A.G, Kosary C.L, Hankey B.F, Miller B.A, HARRAS A, Edwards B.K; "SEER Cancer Statistics Review 1973-1994, National Cancer Institute NIH Publication No". 97-2789. Bethesda: Department of Health and Human Services, 1997.

35. Faivre J, Forman D, Esteve J, Gatta G; "Survival of patients with oesophageal and gastric cancers in Europe". *Eur J Cancer* 1998, 34: 2167-2175. [doi:10.1016/S0959-8049\(98\)00329-3](https://doi.org/10.1016/S0959-8049(98)00329-3) PMID: 10773522
36. Berrino F, Capocaccia R, Esteve J; "Survival of Cancer Patients in Europe: The EURO CARE-2 Study". *IARC Scientific Publications No. 151*. Lyon: IARC, 1999.
37. Theuer C.P, Kurosaki T, Ziogas A, Butler J, Anton-Culver H. "Asian patients with gastric carcinoma in the United States exhibit unique clinical features and superior overall and cancer specific survival rates". *Cancer* 2000, 89: 1883-1892. [doi:10.1002/1097-0142\(20001101\)89:9<1883::AID-CNCR3>3.3.CO;2-8](https://doi.org/10.1002/1097-0142(20001101)89:9<1883::AID-CNCR3>3.3.CO;2-8) PMID:11064344
38. Marshall B.J, Warren J.R. "Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration". *Lancet* 1984, 1:1311-1315. [doi:10.1016/S0140-6736\(84\)91816-6](https://doi.org/10.1016/S0140-6736(84)91816-6)
39. Parsonnet J. "The incidence of Helicobacter pylori infection". *Aliment Pharmacol Ther* 1995, 9 (2): 45-51.
40. Howson C.P, Hiyama T, Wynder E.L; "The decline in gastric cancer: epidemiology of an unplanned triumph". *Epidemiol Rev* 1986, 8: 1-27.
41. Dooley C.P, Cohen H, Fitzgibbons P.L, Bauer M, Appleman M.D, Perez-Perez G.I, Blaser M.J; "Prevalence of Helicobacter pylori infection and histologic gastritis in asymptomatic persons". *N Engl J Med* 1989, 321: 1562-1566.
42. Asaka M, Kimura T, Kudo M, Takeda H, Mitani S, Miyazaki T, Miki K, Graham D.Y; "Relationship of Helicobacter pylori to serum pepsinogens in an asymptomatic Japanese population. *Gastroenterology*". 1992, 102: 760-766.
43. Youn H.S, Ko G.H, Chung M.H, Lee W.K, Cho M.J, Rhee K.H; " Pathogenesis and prevention of stomach cancer". *J Korean Med Sci* 1996, 11: 373-385.
44. Feldman R.A; "Epidemiologic observations and open questions about disease and infection caused by Helicobacter pylori. In: Achtman M, Serbaum S. *Helicobacter pylori: Molecular and Cellular Biology*". *Wymondham: Horizon Scientific*. 2001, 29-51.
45. Buckley M.J, O'Shea J, Grace A, English L, Keane C, Hourihan D, O'Morain C.A; " A community-based study of the epidemiology of Helicobacter pylori infection and associated asymptomatic gastroduodenal pathology". *Eur J GastroenterolHepatol* 1998, 10: 375-379. [doi:10.1097/00042737-199805000-00004](https://doi.org/10.1097/00042737-199805000-00004)

46. Webb P.M, Knight T, Greaves S, Wilson A, Newell D.G, Elder J, Forman D; "Relation between infection with *Helicobacter pylori* and living conditions in childhood: evidence for person to person transmission in early life". *BMJ* 1994, 308: 750-753.
47. Kurosawa M, Kikuchi S, Inaba Y, Ishibashi T, Kobayashi F; "Helicobacter pylori infection among Japanese children". *J GastroenterolHepatol* 2000, 15: 1382-1385. [doi:10.1046/j.1440-1746.2000.02360.x](https://doi.org/10.1046/j.1440-1746.2000.02360.x) PMID:11197047
48. Olmos J.A, Rios H, Higa R. "Prevalence of *Helicobacter pylori* infection in Argentina: results of a nationwide epidemiologic study. Argentinean Hp Epidemiologic Study Group". *J ClinGastroenterol* 2000, 31: 33-37. [doi:10.1097/00004836-200007000-00008](https://doi.org/10.1097/00004836-200007000-00008) PMID:10914773
49. Goodman K.J, Correa P; "Transmission of *Helicobacter pylori* among siblings". *Lancet* 2000, 355: 358-362. [doi:10.1016/S0140-6736\(99\)05273-3](https://doi.org/10.1016/S0140-6736(99)05273-3)
50. Parsonnet J, Friedman G.D, Vandersteen D.P, Chang Y, Vogelman J.H, Orentreich N, Sibley R.K. *Helicobacter pylori* infection and the risk of gastric carcinoma". *N Engl J Med* 1991, 325: 1127-1131.
51. Forman D, Newell D.G, Fullerton F, Yarnell J.W, Stacey A.R, Wald N, Sitas F; "Association between infection with *Helicobacter pylori* and risk of gastric cancer: evidence from a prospective investigation". *BMJ* 1991, 302: 1302-1305.
52. Nomura A, Stemmermann G.N, Chyou P.H, Kato I, Perez-Perez G.I, Blaser M.J; "Helicobacter pylori infection and gastric carcinoma among Japanese Americans in Hawaii". *NEngl J Med* 1991, 325: 1132-1136.
53. "An international association between *Helicobacter pylori* infection and gastric cancer. The EUROGAST Study Group". *Lancet* 1993, 341: 1359-1362. [doi:10.1016/0140-6736\(93\)90938-D](https://doi.org/10.1016/0140-6736(93)90938-D)
54. "International Agency for Research on Cancer Working Group on the Evaluation of Carcinogenic Risks to Humans. Schistosomes, Liver Flukes, and *Helicobacter pylori*". *Lyon: International Agency for Research on Cancer*, 1994: 177-240.
55. Correa P; " Helicobacter pylori and gastric cancer: state of the art". *Cancer Epidemiol Biomarkers Prev* 1996, 5: 477-481.
56. Sipponen P, Kosunen T.U, Valle J, Riihela M, Seppala K; "Helicobacter pylori infection and chronic gastritis in gastric cancer". *J ClinPathol* 1992, 45: 319-323. [doi:10.1136/jcp.45.4.319](https://doi.org/10.1136/jcp.45.4.319) PMID:1577969

57. Hansson L.E, Engstrand L, Nyren O, Evans D.J , Lindgren A, Bergstrom R, Andersson B, Athlin L, Bendtsen O, Tracz P; "Helicobacter pylori infection: independent risk indicator of gastric adenocarcinoma". *Gastroenterology* 1993, 105: 1098-1103.
58. Hu P.J, Mitchell H.M, Li Y.Y, Zhou M.H, Hazell S.L;"Association of Helicobacter pylori with gastric cancer and observations on the detection of this bacterium in gastric cancer cases". *Am J Gastroenterol* 1994, 89: 1806-1810.
59. Kikuchi S, Wada O, Nakajima T, Nishi T, Kobayashi O, Konishi T, Inaba Y;"Serum anti-Helicobacter pylori antibody and gastric carcinoma among young adults". *Cancer* 1995, 75: 2789-2793. [doi:10.1002/1097-0142\(19950615\)75:12<2789::AID-CNCR2820751202>3.0.CO;2-4](https://doi.org/10.1002/1097-0142(19950615)75:12<2789::AID-CNCR2820751202>3.0.CO;2-4) PMID:7773928
60. Kokkola A, Valle J, Haapiainen R, Sipponen P, Kivilaakso E, Puolakkainen P; "Helicobacter pylori infection in young patients with gastric carcinoma". *Scand J Gastroenterol* 1996, 31: 643-647. [doi:10.3109/00365529609009143](https://doi.org/10.3109/00365529609009143) PMID:8819211
61. Barreto-Zuniga R, Maruyama M, Kato Y, Aizu K, Ohta H, Takekoshi T, Bernal SF. Significance of Helicobacter pylori infection as a risk factor in gastric cancer: serological and histological studies. *J Gastroenterol* 1997; 32: 289-294 [doi:10.1007/BF02934482](https://doi.org/10.1007/BF02934482) PMID:9213239
62. Miehlik S, Hackelsberger A, Meining A, von Arnim U, Muller P, Ochsenkuhn T, Lehn N, Malferttheiner P, Stolte M, Bayerdorffer E. Histological diagnosis of Helicobacter pylori gastritis is predictive of a high risk of gastric carcinoma. *Int J Cancer* 1997; 73: 837-839 [doi:10.1002/\(SICI\)1097-0215\(19971210\)73:6<837::AID-IJC12>3.0.CO;2-1](https://doi.org/10.1002/(SICI)1097-0215(19971210)73:6<837::AID-IJC12>3.0.CO;2-1)
63. Nomura AM, Stemmermann GN, Chyou PH. Gastric cancer among the Japanese in Hawaii. *Jpn J Cancer Res* 1995; 86: 916-923
64. Uemura N, Okamoto S, Yamamoto S, Matsumura N, Yamaguchi S, Yamakido M, Taniyama K, Sasaki N, Schlemper RJ. Helicobacter pylori infection and the development of gastric cancer. *N Engl J Med* 2001; 345: 784-789 [doi:10.1056/NEJMoa001999](https://doi.org/10.1056/NEJMoa001999) PMID:11556297
65. Tomb JF, White O, Kerlavage AR, Clayton RA, Sutton GG, Fleischmann RD, Ketchum KA, Klenk HP, Gill S, Dougherty BA, Nelson K, Quackenbush J, Zhou L, Kirkness EF, Peterson S, Loftus B, Richardson D, Dodson R, Khalak HG, Glodek A, McKenney K, Fitzegerald LM, Lee N, Adams MD, Hickey EK, Berg DE, Gocayne JD, Utterback TR, Peterson JD, Kelley JM, Cotton MD, Weidman JM, Fujii C, Bowman C, Watthey L, Wallin E, Hayes WS, Borodovsky M, Karp PD, Smith HO, Fraser CM, Venter JC. The complete genome sequence of the gastric pathogen Helicobacter pylori. *Nature* 1997; 388: 539-547 [doi:10.1038/41483](https://doi.org/10.1038/41483) PMID:9252185

66. Alm RA, Ling LS, Moir DT, King BL, Brown ED, Doig PC, Smith DR, Noonan B, Guild BC, deJonge BL, Carmel G, Tummino PJ, Caruso A, Uria-Nickelsen M, Mills DM, Ives C, Gibson R, Merberg D, Mills SD, Jiang Q, Taylor DE, Vovis GF, Trust TJ. Genomic-sequence comparison of two unrelated isolates of the human gastric pathogen *Helicobacter pylori*. *Nature* 1999; 397: 176-180 [doi:10.1038/16495](https://doi.org/10.1038/16495) PMID:9923682
67. Kuipers EJ, Perez-Perez GI, Meuwissen SG, Blaser MJ. *Helicobacter pylori* and atrophic gastritis: importance of the *cagA* status. *J Natl Cancer Inst* 1995; 87: 1777-1780 [doi:10.1093/jnci/87.23.1777](https://doi.org/10.1093/jnci/87.23.1777) PMID:7473834
68. Blaser MJ, Perez-Perez GI, Kleanthous H, Cover TL, Peek RM, Chyou PH, Stemmermann GN, Nomura A. Infection with *Helicobacter pylori* strains possessing *cagA* is associated with an increased risk of developing adenocarcinoma of the stomach. *Cancer Res* 1995; 55: 2111-2115
69. Parsonnet J, Friedman GD, Orentreich N, Vogelman H. Risk for gastric cancer in people with *CagA* positive or *CagA* negative *Helicobacter pylori* infection. *Gut* 1997; 40: 297-301
70. Huang JQ, Zheng GF, Sumanac K, Irvine EJ, Hunt RH. Meta-analysis of the relationship between *cagA* seropositivity and gastric cancer. *Gastroenterology* 2003; 125: 1636-1644 [doi:10.1053/j.gastro.2003.08.033](https://doi.org/10.1053/j.gastro.2003.08.033) PMID:14724815
71. Vicari JJ, Peek RM, Falk GW, Goldblum JR, Easley KA, Schnell J, Perez-Perez GI, Halter SA, Rice TW, Blaser MJ, Richter JE. The seroprevalence of *cagA*-positive *Helicobacter pylori* strains in the spectrum of gastroesophageal reflux disease. *Gastroenterology* 1998; 115: 50-57 [doi:10.1016/S0016-5085\(98\)70364-6](https://doi.org/10.1016/S0016-5085(98)70364-6) PMID:9649458
72. Ito Y, Azuma T, Ito S, Miyaji H, Hirai M, Yamazaki Y, Sato F, Kato T, Kohli Y, Kuriyama M. Analysis and typing of the *vacA* gene from *cagA*-positive strains of *Helicobacter pylori* isolated in Japan. *J Clin Microbiol* 1997; 35: 1710-1714
73. Azuma T, Yamakawa A, Yamazaki S, Fukuta K, Ohtani M, Ito Y, Dojo M, Yamazaki Y, Kuriyama M. Correlation between variation of the 3' region of the *cagA* gene in *Helicobacter pylori* and disease outcome in Japan. *J Infect Dis* 2002; 186: 1621-1630 [doi:10.1086/345374](https://doi.org/10.1086/345374) PMID:12447739
74. El-Omar EM, Carrington M, Chow WH, McColl KE, Bream JH, Young HA, Herrera J, Lissowska J, Yuan CC, Rothman N, Lanyon G, Martin M, Fraumeni JF Jr, Rabkin CS. Interleukin-1 polymorphisms associated with increased risk of gastric cancer. *Nature* 2000; 404: 398-402 [doi:10.1038/35006081](https://doi.org/10.1038/35006081) PMID:10746728

75. El-Omar EM, Rabkin CS, Gammon MD, Vaughan TL, Risch HA, Schoenberg JB, Stanford JL, Mayne ST, Goedert J, Blot WJ, Fraumeni JF Jr, Chow WH. Increased risk of noncardia gastric cancer associated with proinflammatory cytokine gene polymorphisms. *Gastroenterology* 2003; 124: 1193-1201 [doi:10.1016/S0016-5085\(03\)00157-4](https://doi.org/10.1016/S0016-5085(03)00157-4) PMID:12730860
76. Blaser MJ. Hypothesis: the changing relationships of *Helicobacter pylori* and humans: implications for health and disease. *J Infect Dis* 1999; 179: 1523-1530 [doi:10.1086/314785](https://doi.org/10.1086/314785) PMID:10228075
77. Gastric cancer and *Helicobacter pylori*: a combined analysis of 12 case control studies nested within prospective cohorts. *Gut* 2001; 49: 347-353 [doi:10.1136/gut.49.3.347](https://doi.org/10.1136/gut.49.3.347) PMID:11511555
78. Hansen S, Melby KK, Aase S, Jellum E, Vollset SE. *Helicobacter pylori* infection and risk of cardia cancer and non-cardia gastric cancer. A nested case-control study. *Scand J Gastroenterol* 1999; 34: 353-360 [doi:10.1080/003655299750026353](https://doi.org/10.1080/003655299750026353) PMID:10365894
79. Chow WH, Blaser MJ, Blot WJ, Gammon MD, Vaughan TL, Risch HA, Perez-Perez GI, Schoenberg JB, Stanford JL, Rotterdam H, West AB, Fraumeni JF Jr. An inverse relation between *cagA*⁺ strains of *Helicobacter pylori* infection and risk of esophageal and gastric cardia adenocarcinoma. *Cancer Res* 1998; 58: 588-590
80. Warburton-Timms VJ, Charlett A, Valori RM, Uff JS, Shepherd NA, Barr H, McNulty CA. The significance of *cagA*(+) *Helicobacter pylori* in reflux oesophagitis. *Gut* 2001; 49: 341-346 [doi:10.1136/gut.49.3.341](https://doi.org/10.1136/gut.49.3.341) PMID:11511554
81. El-Serag HB, Sonnenberg A, Jamal MM, Inadomi JM, Crooks LA, Feddersen RM. Corpus gastritis is protective against reflux oesophagitis. *Gut* 1999; 45: 181-185
82. Koike T, Ohara S, Sekine H, Iijima K, Abe Y, Kato K, Toyota T, Shimosegawa T. *Helicobacter pylori* infection prevents erosive reflux oesophagitis by decreasing gastric acid secretion. *Gut* 2001; 49: 330-334 [doi:10.1136/gut.49.3.330](https://doi.org/10.1136/gut.49.3.330) PMID:11511552
83. Raghunath A, Hungin AP, Wooff D, Childs S. Prevalence of *Helicobacter pylori* in patients with gastro-oesophageal reflux disease: systematic review. *BMJ* 2003; 326: 737 [doi:10.1136/bmj.326.7392.737](https://doi.org/10.1136/bmj.326.7392.737) PMID:12676842
84. Labenz J, Malfertheiner P. *Helicobacter pylori* in gastro-oesophageal reflux disease: causal agent, independent or protective factor? *Gut* 1997; 41: 277-280

85. Bytzer P, Aalykke C, Rune S, Weywadt L, Gjorup T, Eriksen J, Bonnevie O, Bekker C, Kromann-Andersen H, Kjaergaard J, Rask-Madsen J, Vilien M, Hansen J, Justesen T, Vyberg M, Teglbjaerg PS. Eradication of *Helicobacter pylori* compared with long-term acid suppression in duodenal ulcer disease. A randomized trial with 2-year follow-up. The Danish Ulcer Study Group. *Scand J Gastroenterol* 2000; 35: 1023-1032 [doi:10.1080/003655200451135](https://doi.org/10.1080/003655200451135) PMID:11099054
86. Vakil N, Hahn B, McSorley D. Recurrent symptoms and gastro-oesophageal reflux disease in patients with duodenal ulcer treated for *Helicobacter pylori* infection. *Aliment Pharmacol Ther* 2000; 14: 45-51 [doi:10.1046/j.1365-2036.2000.00677.x](https://doi.org/10.1046/j.1365-2036.2000.00677.x)
87. McColl KE, Dickson A, El-Nujumi A, El-Omar E, Kelman A. Symptomatic benefit 1-3 years after *H. pylori* eradication in ulcer patients: impact of gastroesophageal reflux disease. *Am J Gastroenterol* 2000; 95: 101-105
88. Manes G, Mosca S, De Nucci C, Lombardi G, Lioniello M, Balzano A. High prevalence of reflux symptoms in duodenal ulcer patients who develop gastro-oesophageal reflux disease after curing *Helicobacter pylori* infection. *Dig Liver Dis* 2001; 33: 665-670 [doi:10.1016/S1590-8658\(01\)80042-6](https://doi.org/10.1016/S1590-8658(01)80042-6) PMID:11785711
89. Befrits R, Sjostedt S, Odman B, Sorngard H, Lindberg G. Curing *Helicobacter pylori* infection in patients with duodenal ulcer does not provoke gastroesophageal reflux disease. *Helicobacter* 2000; 5: 202-205 [doi:10.1046/j.1523-5378.2000.00031.x](https://doi.org/10.1046/j.1523-5378.2000.00031.x) PMID:11179984
90. Sasaki A, Haruma K, Manabe N, Tanaka S, Yoshihara M, Chayama K. Long-term observation of reflux oesophagitis developing after *Helicobacter pylori* eradication therapy. *Aliment Pharmacol Ther* 2003; 17: 1529-1534 [doi:10.1046/j.1365-2036.2003.01643.x](https://doi.org/10.1046/j.1365-2036.2003.01643.x)
91. Laine L, Sugg J. Effect of *Helicobacter pylori* eradication on development of erosive esophagitis and gastroesophageal reflux disease symptoms: a post hoc analysis of eight double blind prospective studies. *Am J Gastroenterol* 2002; 97: 2992-2997 [doi:10.1111/j.1572-0241.2002.07116.x](https://doi.org/10.1111/j.1572-0241.2002.07116.x) PMID:12492181
92. Sanduleanu S, Jonkers D, De Bruine A, Hameeteman W, Stockbrugger RW. Non-*Helicobacter pylori* bacterial flora during acid-suppressive therapy: differential findings in gastric juice and gastric mucosa. *Aliment Pharmacol Ther* 2001; 15: 379-388 [doi:10.1046/j.1365-2036.2001.00888.x](https://doi.org/10.1046/j.1365-2036.2001.00888.x)
93. O'Connor HJ, Schorah CJ, Habibzedah N, Axon AT, Cockel R. Vitamin C in the human stomach: relation to gastric pH, gastroduodenal disease, and possible sources. *Gut* 1989; 30:

436-442

[doi:10.1136/gut.30.4.436](https://doi.org/10.1136/gut.30.4.436) PMID:2714677

94. Tatematsu M, Takahashi M, Fukushima S, Hananouchi M, Shirai T. Effects in rats of sodium chloride on experimental gastric cancers induced by N-methyl-N-nitro-N-nitrosoguanidine or 4-nitroquinoline-1-oxide. *J Natl Cancer Inst* 1975; 55: 101-106

95. Takahashi M, Hasegawa R. Enhancing effects of dietary salt on both initiation and promotion stages of rat gastric carcinogenesis. *Princess Takamatsu Symp* 1985; 16: 169-182

96. Fox JG, Dangler CA, Taylor NS, King A, Koh TJ, Wang TC. High-salt diet induces gastric epithelial hyperplasia and parietal cell loss, and enhances *Helicobacter pylori* colonization in C57BL/6 mice. *Cancer Res* 1999; 59: 4823-4828

97. Kono S, Hirohata T. Nutrition and stomach cancer. *Cancer Causes Control* 1996; 7: 41-55
[doi:10.1007/BF00115637](https://doi.org/10.1007/BF00115637) PMID:8850434

98. World Cancer Research Fund, American Institute for Cancer Research. *Food, Nutrition and the Prevention of Cancer: a Global Perspective*. Washington, D.C.: American Institute for Cancer Research, 1997

99. Ward MH, Lopez-Carrillo L. Dietary factors and the risk of gastric cancer in Mexico City. *Am J Epidemiol* 1999; 149: 925-932

100. Kim HJ, Chang WK, Kim MK, Lee SS, Choi BY. Dietary factors and gastric cancer in Korea: a case-control study. *Int J Cancer* 2002; 97: 531-535 [doi:10.1002/ijc.10111](https://doi.org/10.1002/ijc.10111)

101. Lee SA, Kang D, Shim KN, Choe JW, Hong WS, Choi H. Effect of diet and *Helicobacter pylori* infection to the risk of early gastric cancer. *J Epidemiol* 2003; 13: 162-168

102. Joossens JV, Hill MJ, Elliott P, Stamler R, Lesaffre E, Dyer A, Nichols R, Kesteloot H. Dietary salt, nitrate and stomach cancer mortality in 24 countries. *European Cancer Prevention (ECP) and the INTERSALT Cooperative Research Group. Int J Epidemiol* 1996; 25: 494-504
[doi:10.1093/ije/25.3.494](https://doi.org/10.1093/ije/25.3.494) PMID:8671549

103. Tsugane S, Tsuda M, Gey F, Watanabe S. Cross-sectional study with multiple measurements of biological markers for assessing stomach cancer risks at the population level. *Environ Health Perspect* 1992; 98: 207-210 [doi:10.2307/3431272](https://doi.org/10.2307/3431272) PMID:1486851

104. Kato I, Tominaga S, Matsumoto K. A prospective study of stomach cancer among a rural Japanese population: a 6-year survey. *Jpn J Cancer Res* 1992; 83: 568-575

105. Kneller RW, McLaughlin JK, Bjelke E, Schuman LM, Blot WJ, Wacholder S, Gridley G, CoChien HT, Fraumeni JF Jr. A cohort study of stomach cancer in a high-risk American population. *Cancer* 1991; 68: 672-678 [doi:10.1002/1097-0142\(19910801\)68:3<672::AID-CNCR2820680339>3.0.CO;2-T](https://doi.org/10.1002/1097-0142(19910801)68:3<672::AID-CNCR2820680339>3.0.CO;2-T) PMID:2065291
106. Nomura A, Grove JS, Stemmermann GN, Severson RK. A prospective study of stomach cancer and its relation to diet, cigarettes, and alcohol consumption. *Cancer Res* 1990; 50: 627-631
107. Tsugane S, Sasazuki S, Kobayashi M, Sasaki S. Salt and salted food intake and subsequent risk of gastric cancer among middle-aged Japanese men and women. *Br J Cancer* 2004; 90: 128-134 [doi:10.1038/sj.bjc.6601511](https://doi.org/10.1038/sj.bjc.6601511) PMID:14710219
108. Buiatti E, Palli D, Decarli A, Amadori D, Avellini C, Bianchi S, Bonaguri C, Cipriani F, Cocco P, Giacosa A. A case-control study of gastric cancer and diet in Italy: II. Association with nutrients. *Int J Cancer* 1990; 45: 896-901 [doi:10.1002/ijc.2910450520](https://doi.org/10.1002/ijc.2910450520)
109. La Vecchia C, Ferraroni M, D'Avanzo B, Decarli A, Franceschi S. Selected micronutrient intake and the risk of gastric cancer. *Cancer Epidemiol Biomarkers Prev* 1994; 3: 393-398
110. Hansson LE, Nyren O, Bergstrom R, Wolk A, Lindgren A, Baron J, Adami HO. Nutrients and gastric cancer risk. A population-based case-control study in Sweden. *Int J Cancer* 1994; 57: 638-644 [doi:10.1002/ijc.2910570505](https://doi.org/10.1002/ijc.2910570505)
111. McCullough ML, Robertson AS, Jacobs EJ, Chao A, Calle EE, Thun MJ. A prospective study of diet and stomach cancer mortality in United States men and women. *Cancer Epidemiol Biomarkers Prev* 2001; 10: 1201-1205
112. Hirayama T. A large scale cohort study on cancer risk by diet-with special reference to the risk reducing effects of green-yellow vegetable consumption. In: Hayashi Y, Nagao M, Sugimura T. Diet, nutrition and cancer: proceedings of the 16th International Symposium of the Princess Takamatsu Cancer Research Fund. Utrecht: Tokyo/VNU Science, 1986: 41-53
113. Hertog MG, Bueno-de-Mesquita HB, Fehily AM, Sweetnam PM, Elwood PC, Kromhout D. Fruit and vegetable consumption and cancer mortality in the Caerphilly Study. *Cancer Epidemiol Biomarkers Prev* 1996; 5: 673-677
114. Kobayashi M, Tsubono Y, Sasazuki S, Sasaki S, Tsugane S. Vegetables, fruit and risk of gastric cancer in Japan: a 10-year follow-up of the JPHC Study Cohort I. *Int J Cancer* 2002; 102: 39-44 [doi:10.1002/ijc.10659](https://doi.org/10.1002/ijc.10659)

115. Wang ZY, Cheng SJ, Zhou ZC, Athar M, Khan WA, Bickers DR, Mukhtar H. Antimutagenic activity of green tea polyphenols. *Mutat Res* 1989; 223: 273-285 [doi:10.1016/0165-1218\(89\)90120-1](https://doi.org/10.1016/0165-1218(89)90120-1)
116. Wang ZY, Hong JY, Huang MT, Reuhl KR, Conney AH, Yang CS. Inhibition of N-nitrosodiethylamine- and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone-induced tumorigenesis in A/J mice by green tea and black tea. *Cancer Res* 1992; 52: 1943-1947
117. Xu Y, Ho CT, Amin SG, Han C, Chung FL. Inhibition of tobacco-specific nitrosamine-induced lung tumorigenesis in A/J mice by green tea and its major polyphenol as antioxidants. *Cancer Res* 1992; 52: 3875-3879
118. Setiawan VW, Zhang ZF, Yu GP, Lu QY, Li YL, Lu ML, Wang MR, Guo CH, Yu SZ, Kurtz RC, Hsieh CC. Protective effect of green tea on the risks of chronic gastritis and stomach cancer. *Int J Cancer* 2001; 92: 600-604 [doi:10.1002/ijc.1231](https://doi.org/10.1002/ijc.1231)
119. Yu GP, Hsieh CC, Wang LY, Yu SZ, Li XL, Jin TH. Green-tea consumption and risk of stomach cancer: a population-based case-control study in Shanghai, China. *Cancer Causes Control* 1995; 6: 532-538 [doi:10.1007/BF00054162](https://doi.org/10.1007/BF00054162) PMID:8580302
120. Ji BT, Chow WH, Yang G, McLaughlin JK, Gao RN, Zheng W, Shu XO, Jin F, Fraumeni JF Jr, Gao YT. The influence of cigarette smoking, alcohol, and green tea consumption on the risk of carcinoma of the cardia and distal stomach in Shanghai, China. *Cancer* 1996; 77: 2449-2457 [doi:10.1002/\(SICI\)1097-0142\(19960615\)77:12<2449::AID-CNCR6>3.0.CO;2-H](https://doi.org/10.1002/(SICI)1097-0142(19960615)77:12<2449::AID-CNCR6>3.0.CO;2-H) PMID:8640692
121. Inoue M, Tajima K, Hirose K, Hamajima N, Takezaki T, Kuroishi T, Tominaga S. Tea and coffee consumption and the risk of digestive tract cancers: data from a comparative case-referent study in Japan. *Cancer Causes Control* 1998; 9: 209-216 [doi:10.1023/A:1008890529261](https://doi.org/10.1023/A:1008890529261)
122. Tsubono Y, Nishino Y, Komatsu S, Hsieh CC, Kanemura S, Tsuji I, Nakatsuka H, Fukao A, Satoh H, Hisamichi S. Green tea and the risk of gastric cancer in Japan. *N Engl J Med* 2001; 344: 632-636 [doi:10.1056/NEJM200103013440903](https://doi.org/10.1056/NEJM200103013440903)
123. Hoshiyama Y, Kawaguchi T, Miura Y, Mizoue T, Tokui N, Yatsuya H, Sakata K, Kondo T, Kikuchi S, Toyoshima H, Hayakawa N, Tamakoshi A, Ohno Y, Yoshimura T. A prospective study of stomach cancer death in relation to green tea consumption in Japan. *Br J Cancer* 2002; 87: 309-313 [doi:10.1038/sj.bjc.6600487](https://doi.org/10.1038/sj.bjc.6600487)

124. Nagano J, Kono S, Preston DL, Mabuchi K. A prospective study of green tea consumption and cancer incidence, Hiroshima and Nagasaki (Japan). *Cancer Causes Control* 2001; 12: 501-508 [doi:10.1023/A:1011297326696](https://doi.org/10.1023/A:1011297326696)
125. Galanis DJ, Kolonel LN, Lee J, Nomura A. Intakes of selected foods and beverages and the incidence of gastric cancer among the Japanese residents of Hawaii: a prospective study. *Int J Epidemiol* 1998; 27: 173-180 [doi:10.1093/ije/27.2.173](https://doi.org/10.1093/ije/27.2.173)
126. Koizumi Y, Tsubono Y, Nakaya N, Kuriyama S, Shibuya D, Matsuoka H, Tsuji I. Cigarette smoking and the risk of gastric cancer: a pooled analysis of two prospective studies in Japan. *Int J Cancer* 2004; 112: 1049-1055 [doi:10.1002/ijc.20518](https://doi.org/10.1002/ijc.20518)
127. Gonzalez CA, Pera G, Agudo A, Palli D, Krogh V, Vineis P, Tumino R, Panico S, Berglund G, Siman H, Nyren O, Agren A, Martinez C, Dorronsoro M, Barricarte A, Tormo MJ, Quiros JR, Allen N, Bingham S, Day N, Miller A, Nagel G, Boeing H, Overvad K, Tjonneland A, Bueno-De-Mesquita HB, Boshuizen HC, Peeters P, Numans M, Clavel-Chapelon F, Helen I, Agapitos E, Lund E, Fahey M, Saracci R, Kaaks R, Riboli E. Smoking and the risk of gastric cancer in the European Prospective Investigation Into Cancer and Nutrition (EPIC). *Int J Cancer* 2003; 107: 629-634 [doi:10.1002/ijc.11426](https://doi.org/10.1002/ijc.11426)
128. Chao A, Thun MJ, Henley SJ, Jacobs EJ, McCullough ML, Calle EE. Cigarette smoking, use of other tobacco products and stomach cancer mortality in US adults: The Cancer Prevention Study II. *Int J Cancer* 2002; 101: 380-389 [doi:10.1002/ijc.10614](https://doi.org/10.1002/ijc.10614)
129. Franceschi S, La Vecchia C. Alcohol and the risk of cancers of the stomach and colon-rectum. *Dig Dis* 1994; 12: 276-289
130. Chow WH, Blot WJ, Vaughan TL, Risch HA, Gammon MD, Stanford JL, Dubrow R, Schoenberg JB, Mayne ST, Farrow DC, Ahsan H, West AB, Rotterdam H, Niwa S, Fraumeni JF Jr. Body mass index and risk of adenocarcinomas of the esophagus and gastric cardia. *J Natl Cancer Inst* 1998; 90: 150-155 [doi:10.1093/jnci/90.2.150](https://doi.org/10.1093/jnci/90.2.150)
131. Vaughan TL, Davis S, Kristal A, Thomas DB. Obesity, alcohol, and tobacco as risk factors for cancers of the esophagus and gastric cardia: adenocarcinoma versus squamous cell carcinoma. *Cancer Epidemiol Biomarkers Prev* 1995; 4: 85-92
132. Clark GW, Smyrk TC, Burdiles P, Hoeft SF, Peters JH, Kiyabu M, Hinder RA, Bremner CG, DeMeester TR. Is Barrett's metaplasia the source of adenocarcinomas of the cardia? *Arch Surg* 1994; 129: 609-614

133. Ishaq S, Jankowski JA. Barrett's metaplasia: clinical implications. *World J Gastroenterol* 2001; 7: 563-565
134. Lagergren J, Bergstrom R, Nyren O. Association between body mass and adenocarcinoma of the esophagus and gastric cardia. *Ann Intern Med* 1999; 130: 883-890
135. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. *N Engl J Med* 2003; 348: 1625-1638
[doi:10.1056/NEJMoa021423](https://doi.org/10.1056/NEJMoa021423)
136. Thompson DE, Mabuchi K, Ron E, Soda M, Tokunaga M, Ochiai S, Sugimoto S, Ikeda T, Terasaki M, Izumi S. Cancer incidence in atomic bomb survivors. Part II: Solid tumors, 1958-1987. *Radiat Res* 1994; 137: S17-S67 [doi:10.2307/3578892](https://doi.org/10.2307/3578892)
137. Hsing AW, Hansson LE, McLaughlin JK, Nyren O, Blot WJ, Ekblom A, Fraumeni JF Jr. Pernicious anemia and subsequent cancer. A population-based cohort study. *Cancer* 1993; 71: 745-750 [doi:10.1002/1097-0142\(19930201\)71:3<745::AID-CNCR2820710316>3.0.CO;2-1](https://doi.org/10.1002/1097-0142(19930201)71:3<745::AID-CNCR2820710316>3.0.CO;2-1)
138. AIRD I, BENTALL HH, ROBERTS JA. A relationship between cancer of stomach and the ABO blood groups. *Br Med J* 1953; 1: 799-801
139. Stalnikowicz R, Benbassat J. Risk of gastric cancer after gastric surgery for benign disorders. *Arch Intern Med* 1990; 150: 2022-2026
[doi:10.1001/archinte.150.10.2022](https://doi.org/10.1001/archinte.150.10.2022)
140. Levine PH, Stemmermann G, Lennette ET, Hildesheim A, Shibata D, Nomura A. Elevated antibody titers to Epstein-Barr virus prior to the diagnosis of Epstein-Barr-virus-associated gastric adenocarcinoma. *Int J Cancer* 1995; 60: 642-644 [doi:10.1002/ijc.2910600513](https://doi.org/10.1002/ijc.2910600513)
141. Uemura Y, Tokunaga M, Arikawa J, Yamamoto N, Hamasaki Y, Tanaka S, Sato E, Land CE. A unique morphology of Epstein-Barr virus-related early gastric carcinoma. *Cancer Epidemiol Biomarkers Prev* 1994; 3: 607-611
142. Shousha S, Luqmani YA. Epstein-Barr virus in gastric carcinoma and adjacent normal gastric and duodenal mucosa. *J Clin Pathol* 1994; 47: 695-698 [doi:10.1136/jcp.47.8.695](https://doi.org/10.1136/jcp.47.8.695) PMID:7962618
143. Palli D, Galli M, Caporaso NE, Cipriani F, Decarli A, Saieva C, Fraumeni JF Jr, Buiatti E. Family history and risk of stomach cancer in Italy. *Cancer Epidemiol Biomarkers Prev* 1994; 3: 15-18

144. La Vecchia C, Negri E, Franceschi S, Gentile A. Family history and the risk of stomach and colorectal cancer. *Cancer* 1992; 70: 50-55 [doi:10.1002/1097-0142\(19920701\)70:1<50::AID-CNCR2820700109>3.0.CO;2-I](https://doi.org/10.1002/1097-0142(19920701)70:1<50::AID-CNCR2820700109>3.0.CO;2-I) PMID:1606546
145. Lissowska J, Groves FD, Sobin LH, Fraumeni JF Jr, Nasierowska-Guttmejer A, Radziszewski J, Regula J, Hsing AW, Zatonski W, Blot WJ, Chow WH. Family history and risk of stomach cancer in Warsaw, Poland. *Eur J Cancer Prev* 1999; 8: 223-227
146. La Vecchia C, Negri E, D'Avanzo B, Franceschi S. Electric refrigerator use and gastric cancer risk. *Br J Cancer* 1990; 62: 136-137
147. Tredaniel J, Boffetta P, Buiatti E, Saracci R, Hirsch A. Tobacco smoking and gastric cancer: review and meta-analysis. *Int J Cancer* 1997; 72: 565-573 [doi:10.1002/\(SICI\)1097-0215\(19970807\)72:4<565::AID-IJC3>3.0.CO;2-O](https://doi.org/10.1002/(SICI)1097-0215(19970807)72:4<565::AID-IJC3>3.0.CO;2-O)
148. Suerbaum S, Michetti P. Helicobacter pylori infection. *N Engl J Med* 2002; 347: 1175-1186 [doi:10.1056/NEJMra020542](https://doi.org/10.1056/NEJMra020542) PMID:12374879
149. Coelho LG, Passos MC, Chausson Y, Costa EL, Maia AF, Brandao MJ, Rodrigues DC, Castro LP. Duodenal ulcer and eradication of Helicobacter pylori in a developing country. An 18-month follow-up study. *Scand J Gastroenterol* 1992; 27: 362-366 [doi:10.3109/00365529209000088](https://doi.org/10.3109/00365529209000088) PMID:1529269
150. Uemura N, Mukai T, Okamoto S, Yamaguchi S, Mashiba H, Taniyama K, Sasaki N, Haruma K, Sumii K, Kajiyama G. Effect of Helicobacter pylori eradication on subsequent development of cancer after endoscopic resection of early gastric cancer. *Cancer Epidemiol Biomarkers Prev* 1997; 6: 639-642
151. Correa P, Fontham ET, Bravo JC, Bravo LE, Ruiz B, Zarama G, Realpe JL, Malcom GT, Li D, Johnson WD, Mera R. Chemoprevention of gastric dysplasia: randomized trial of antioxidant supplements and anti-Helicobacter pylori therapy. *J Natl Cancer Inst* 2000; 92: 1881-1888 [doi:10.1093/jnci/92.23.1881](https://doi.org/10.1093/jnci/92.23.1881) PMID:11106679
152. Wong BC, Lam SK, Wong WM, Chen JS, Zheng TT, Feng RE, Lai KC, Hu WH, Yuen ST, Leung SY, Fong DY, Ho J, Ching CK, Chen JS. Helicobacter pylori eradication to prevent gastric cancer in a high-risk region of China: a randomized controlled trial. *JAMA* 2004; 291: 187-194 [doi:10.1001/jama.291.2.187](https://doi.org/10.1001/jama.291.2.187) PMID:14722144

153. Yuan JM, Ross RK, Gao YT, Qu YH, Chu XD, Yu MC. Prediagnostic levels of serum micronutrients in relation to risk of gastric cancer in Shanghai, China. *Cancer Epidemiol Biomarkers Prev* 2004; 13: 1772-1780
154. Blot WJ, Li JY, Taylor PR, Guo W, Dawsey S, Wang GQ, Yang CS, Zheng SF, Gail M, Li GY. Nutrition intervention trials in Linxian, China: supplementation with specific vitamin/mineral combinations, cancer incidence, and disease-specific mortality in the general population. *J Natl Cancer Inst* 1993; 85: 1483-1492 [doi:10.1093/jnci/85.18.1483](https://doi.org/10.1093/jnci/85.18.1483) PMID:8360931
155. Varis K, Taylor PR, Sipponen P, Samloff IM, Heinonen OP, Albanes D, Harkonen M, Huttunen JK, Laxen F, Virtamo J. Gastric cancer and premalignant lesions in atrophic gastritis: a controlled trial on the effect of supplementation with alpha-tocopherol and beta-carotene. The Helsinki Gastritis Study Group. *Scand J Gastroenterol* 1998; 33: 294-300 [doi:10.1080/00365529850170892](https://doi.org/10.1080/00365529850170892) PMID:9548624
156. Jacobs EJ, Connell CJ, McCullough ML, Chao A, Jonas CR, Rodriguez C, Calle EE, Thun MJ. Vitamin C, vitamin E, and multivitamin supplement use and stomach cancer mortality in the Cancer Prevention Study II cohort. *Cancer Epidemiol Biomarkers Prev* 2002; 11: 35-41
157. Wong BC, Zhu GH, Lam SK. Aspirin induced apoptosis in gastric cancer cells. *Biomed Pharmacother* 1999; 53: 315-318 [doi:10.1016/S0753-3322\(00\)88503-0](https://doi.org/10.1016/S0753-3322(00)88503-0)
158. Sawaoka H, Tsuji S, Tsujii M, Gunawan ES, Sasaki Y, Kawano S, Hori M. Cyclooxygenase inhibitors suppress angiogenesis and reduce tumor growth in vivo. *Lab Invest* 1999; 79: 1469-1477
159. Ristimaki A, Honkanen N, Jankala H, Sipponen P, Harkonen M. Expression of cyclooxygenase-2 in human gastric carcinoma. *Cancer Res* 1997; 57: 1276-1280
160. Kelley DJ, Mestre JR, Subbaramaiah K, Sacks PG, Schantz SP, Tanabe T, Inoue H, Ramonetti JT, Dannenberg AJ. Benzo[a]pyrene up-regulates cyclooxygenase-2 gene expression in oral epithelial cells. *Carcinogenesis* 1997; 18: 795-799 [doi:10.1093/carcin/18.4.795](https://doi.org/10.1093/carcin/18.4.795) PMID:9111217
161. Shirvani VN, Ouatu-Lascar R, Kaur BS, Omary MB, Triadafilopoulos G. Cyclooxygenase 2 expression in Barrett's esophagus and adenocarcinoma: Ex vivo induction by bile salts and acid exposure. *Gastroenterology* 2000; 118: 487-496 [doi:10.1016/S0016-5085\(00\)70254-X](https://doi.org/10.1016/S0016-5085(00)70254-X) PMID:10702199
162. Fu S, Ramanujam KS, Wong A, Fantry GT, Drachenberg CB, James SP, Meltzer SJ, Wilson KT. Increased expression and cellular localization of inducible nitric oxide synthase and

cyclooxygenase 2 in Helicobacter pylori gastritis. *Gastroenterology* 1999; 116: 1319-1329
[doi:10.1016/S0016-5085\(99\)70496-8](https://doi.org/10.1016/S0016-5085(99)70496-8) PMID:10348815

163. McCarthy CJ, Crofford LJ, Greenson J, Scheiman JM. Cyclooxygenase-2 expression in gastric antral mucosa before and after eradication of Helicobacter pylori infection. *Am J Gastroenterol* 1999; 94: 1218-1223 [doi:10.1111/j.1572-0241.1999.01070.x](https://doi.org/10.1111/j.1572-0241.1999.01070.x) PMID:10235197

164. Farrow DC, Vaughan TL, Hansten PD, Stanford JL, Risch HA, Gammon MD, Chow WH, Dubrow R, Ahsan H, Mayne ST, Schoenberg JB, West AB, Rotterdam H, Fraumeni JF Jr, Blot WJ. Use of aspirin and other nonsteroidal anti-inflammatory drugs and risk of esophageal and gastric cancer. *Cancer Epidemiol Biomarkers Prev* 1998; 7: 97-102

165. Akre K, Ekstrom AM, Signorello LB, Hansson LE, Nyren O. Aspirin and risk for gastric cancer: a population-based case-control study in Sweden. *Br J Cancer* 2001; 84: 965-968
[doi:10.1054/bjoc.2001.1702](https://doi.org/10.1054/bjoc.2001.1702) PMID:11286478

166. Coogan PF, Rosenberg L, Palmer JR, Strom BL, Zauber AG, Stolley PD, Shapiro S. Nonsteroidal anti-inflammatory drugs and risk of digestive cancers at sites other than the large bowel. *Cancer Epidemiol Biomarkers Prev* 2000; 9: 119-123

167. Wang WH, Huang JQ, Zheng GF, Lam SK, Karlberg J, Wong BC. Non-steroidal anti-inflammatory drug use and the risk of gastric cancer: a systematic review and meta-analysis. *J Natl Cancer Inst* 2003; 95: 1784-1791

168. Kakizoe T. *Cancer Statistics in Japan*. Tokyo: Foundation for Promotion of Cancer Research, 1999

169. Guo HQ, Guan P, Shi HL, Zhang X, Zhou BS, Yuan Y. Prospective cohort study of comprehensive prevention to gastric cancer. *World J Gastroenterol* 2003; 9: 432-436.