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Current Perspectives on Gastric Cancer

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Synopsis

Gastric Cancer (GC) is 3rd leading cause of cancer related death worldwide; only 28.3% of are expected to survive >5 years. Although GC incidence has declined in the US during the last decade, an increase in the incidence of GC has been estimated for 2016. GC risk factors include, male gender, having >60 years, infectious agents such as *H. pylori*, GC family history, certain occupations, tobacco use, and diet, among others. Prognosis of GC is largely dependent on the tumor stage at diagnosis and classification as intestinal or diffuse type, which has worse prognosis. Although promising chemoprevention agents have been reported to decrease GC risk, none have been implemented into clinical practice to date. Risk assessment and surveillance guidelines have been implemented in Asian countries with high incidence of GC, whereas in the US, only the American Society for Gastrointestinal Endoscopy has recently published guidelines for the screening and management gastric lesions. Importance of diagnosis of GC at an early stage is imperative since 5 year survival rates can approximate 90% in this setting.

Keywords

Gastric Cancer; *Helicobacter pylori*; Atrophic gastritis; Intestinal metaplasia; Dysplasia

Global impact of Gastric Cancer

Despite the overall decrease in the incidence of gastric cancer (GC) since the 1930s, it is still a major cause of morbidity and mortality worldwide¹. As many as 952,000 new GC cases

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were estimated in 2012 alone; making it the 5th most common incident cancer in the world and the 3rd leading cause of cancer death in both sexes worldwide². Among patients diagnosed with GC, close to 75% die from this disease³. GC also is responsible for one of the highest cancer burdens as determined by disability-adjusted life years lost⁴.

Globally, GC incidence has been shown to be more common in men and to increase with age, with the majority of cases occurring after the age of 60². However, GC incidence rates vary dramatically across countries. The geographical distribution of GC has been mainly attributed to differences in dietary patterns, socioeconomic status, and the prevalence of *Helicobacter pylori* infections⁵. The highest GC incidence and mortality rates occur in Eastern Asia, Central, and Eastern Europe, and South America⁶. Mortality rates associated to GC, even in developed countries, are still very high; only 28.3% of newly diagnosed cases are expected to survive 5 years after diagnosis.

According to the Surveillance, Epidemiology, and End Results Program, approximately 22,220 new GC cases were diagnosed in the United States (US) in 2014. An increase in the incidence of GC in the US has been estimated for 2016; according to the American Cancer Society, approximately 26,370 individuals will be diagnosed with GC and 10,730 are expected to die due to this disease. Within the US, Hispanics, African Americans, and Native Americans are more frequently diagnosed with GC than non-Hispanic Whites (Figure 1)^{3, 7}.

Gastric Cancer Etiology and Risk Factors

Infectious Agents associated with Gastric Cancer

H. pylori—In 1994, the International Agency for Research on Cancer classified *H. pylori*, the first formally recognized bacterial carcinogen, as a class I human carcinogen for GC. *H. pylori* is involved in 90% of all gastric malignancies⁸. *H. pylori* incidence varies according age, ethnicity, and geographical location. In countries like Mexico, Argentina and Asia, the prevalence of *H. pylori* ranges from 30–70% by the age of 20 and 70–90% by the age of 60. In the US and France, the prevalence is approximately 20% and 40% for younger and older ages, respectively⁹.

H. pylori contributes to the development of gastric neoplasia by promoting inflammation in the gastric mucosa (gastritis), which leads to sequential histopathologic changes that may result in the development of GC (Figure 2)^{8, 10}. However, not every individual infected with *H. pylori* will develop GC. The exact pathophysiological mechanisms, as well as the contribution of environmental risk factors and host genetic susceptibility in the progression of gastric carcinogenesis, have yet to be fully elucidated. *H. pylori* virulence factors have been associated with a higher risk of GC. Infection with *H. pylori* strains with *vacAsI*-, *vacAmI*-, and *cagA*-positive genotypes are associated with an approximate 6-fold increase in GC risk¹². Increasing evidence supports that the extent of the inflammatory response to *H. pylori* is in large part determined by polymorphisms in host genes encoding cytokines and cytokine receptors. Individuals with pro-inflammatory IL-1 genotypes infected with *H. pylori* strains with *vacAsI*-, *vacAmI*-, and *cagA*-positive genotypes were reported to have up to an 87-fold higher risk of GC compared to *H. pylori*-infected individuals without pro-

inflammatory IL-1 polymorphisms¹³. Recently, GC stem cells were also proposed as a gastric carcinogenesis mechanism. Chronic infection with *H. pylori* induces recruitment of bone marrow-derived cells, which once recruited differentiate with local gastric epithelial cells, ultimately inducing stem cell properties leading to cell metaplasia, dysplasia, and adenocarcinoma¹⁴. Unfortunately, there are currently no robust biomarkers clinically available to reliably predict who will develop GC cancer after *H. pylori* infection.

Epstein-Barr Virus—Multiple studies in different parts of the world have found the prevalence of EBV in 5 to 16% of gastric carcinomas, which supports its possible role as an etiologic agent of GC¹⁵. In Asia, Europe, and the Americas, prevalence of EBV is close to 9% of all GC cases reported¹⁶. Male patients have been found to be twice as likely to have EBV-positive tumors compared to females. Tumors in the gastric cardia or corpus were found to be twice as likely to be EBV-positive compared to those in the antrum¹⁶. Although the role of EBV in gastric carcinogenesis is not yet clearly defined, EBV-positivity has been reported to be associated with favorable prognosis¹⁷.

Genetic predisposition: Familial Gastric Cancer

An estimated 20% of GC patients have a family history of GC¹⁸. According to the racial/ethnic group, family history was shown to confer 2- to 10-fold increased risk of GC¹⁹. While the majority of GCs are sporadic, 10% of the cases have familial clustering and 1–3% are hereditary²⁰. Hereditary GC includes syndromes such as hereditary diffuse GC (HDGC), gastric adenocarcinoma and proximal polyposis of the stomach (GAPPS), and familial intestinal GC (FIGC). HDGC is a rare, autosomal dominant disorder that is responsible for 1–3% of all familial GC cases²¹. About 40% of individuals with HDGC have germline mutations in the *CDH1* gene, which encodes E-cadherin²². In the presence of *CDH1* mutations, the lifetime risk of developing GC is 70–80%²¹. GC can also develop as part of familial cancer syndromes including: Lynch syndrome, familial adenomatous polyposis, Peutz-Jeghers syndrome, and Li-Fraumeni syndrome²³. GC is part of the Lynch syndrome tumor spectrum; GC risk is 2.9 times higher for subjects with germline *MLH1* mutations²⁴.

Demographic, Environmental and lifestyle risk factors

In addition to infectious agents and family history, additional GC risk factors include: age, gender, certain occupations, tobacco use, diet, and being overweight, among others. The risk of developing GC is twice as higher in men than in women and it is usually diagnosed between the ages of 60–80 years. Individuals with certain occupations, such as those who work in the coal, metal, and rubber industries, have been reported to have an increased risk of GC²⁵. Tobacco smoking has been reported to cause a 60% and 20% increase in GC risk in men and women, respectively²⁶. It is estimated that 18% of GC cases are attributable to tobacco smoking²⁷. No association has been found between smokeless tobacco and GC²⁸. In contrast, alcohol consumption has not been consistently shown to be associated with gastric cancer; however, it has been identified as a risk factor for disease progression²⁹. A 5-fold increased risk in GC has been observed as a result of the combined effect of alcohol and smoking³⁰. A high intake of salted, pickled or smoked foods, and preserved foods rich in salt and nitrites have been reported to be associated with an increased risk of GC, whereas foods rich in fiber, vegetables, and fruit were found to be protective³¹. Individuals with

moderate and high salt intake had a 1.41 and 1.68 relative risk (RR) for GC, respectively, compared to those that consumed low levels of salt^{32, 33}. Additionally, in the presence of *H. pylori* infection, high salt intake further increases the risk of GC^{34, 35}. Significant associations were found between the consumption of processed meat (RR: 1.45 95% CI: 1.26–1.65) and GC risk³⁶. This association between processed meats and GC been described to be stronger in subjects infected with *H. pylori*³⁷. Although obesity has not been found to be associated to all gastric cancers, several meta-analysis have reported a positive association between increased BMI and risk of gastric cancer in the cardia³⁸.

Gastric Cancer Classification

GC is classified into two main groups: early and advanced stages. Prognosis is largely dependent on the tumor stage. The 5-year survival rate in patients with early GC is between 85–100%, whereas it is only 5–20% for advanced GC³⁹. The degree of invasion defines GC as early or advanced⁴⁰. Early gastric carcinoma is defined as malignancies limited to the mucosa or submucosa, regardless of lymph node invasion. Advanced GC is classified according to the extent of invasion and endoscopic appearance (polypoid lesions, ulcerated with well-defined border, ulcerated with ill-defined borders, or infiltrating diffuse without evidence of mass or ulcers).

Tumor location dictates the anatomic classification as cardia or non-cardia (distal from the cardia) (Figure 3). Cardia and non-cardia adenocarcinomas present with different clinical and epidemiological characteristics²¹. In contrast to cardia tumors, non-cardia tumors have decreased in the last decades. Cardia GC affects predominantly Caucasian populations and is more often associated with gastroesophageal reflux disease²¹. Cardia adenocarcinomas are aggressive and have a poor prognosis. Cardia tumors invade the gastric and esophageal walls and metastasize to local lymph nodes (Table 1). Due their aggressiveness, the American Joint Classification of Cancer (AJCC) decided to use the esophageal cancer staging system for all GC arising in the esophagogastric junction and any cancer arising in the proximal 5 cm of the stomach with involvement of the esophagogastric junction⁴¹. Non-cardia GC more likely associated with *H. pylori* and comprises more than 60% all GC cases worldwide⁴².

Histological Classification

The Lauren classification system⁴³, which classifies GC as intestinal (with intercellular junctions) and diffuse (without intercellular junctions), is the most frequently used system to classify GC (Table 1). Intestinal type adenocarcinomas form glands or tubules lined by epithelium resembling the intestinal mucosa. Although the incidence of intestinal type GC has decreased recently, it is still the most frequent type of GC found in high incidence populations²¹. This type of GC usually occurs in a 2:1 male-to-female ratio and in individuals between 55–80 years of age⁴⁴. The development of intestinal type GC is preceded by a sequence of histological lesions that may take years to develop (Figure 2)¹¹.

Diffuse type gastric adenocarcinomas are more aggressive and have a worse prognosis than the intestinal type. They do not have a gender bias and are generally diagnosed in younger patients (40–60 years of age). Diffuse GC cells lack cohesion, and invade tissues independently or in small clusters⁷. A variant of the diffuse histological type is the signet

ring cell gastric adenocarcinoma. Signet tumor cells contain abundant cytoplasmic mucin that displaces the nucleus toward the periphery^{7, 21}. While diffuse type GC can be associated with *H. pylori* infections, it is more frequently associated with loss of expression of E-cadherin (HDGC); no precancerous lesions have been defined to date⁴⁵.

Gastric Cancer Prevention

Lifestyle modification

Primary prevention aims to prevent the disease before it ever occurs by preventing exposures to hazards, changing unhealthy or unsafe behaviors, and increasing resistance to the disease. Recommended lifestyle changes to prevent GC include limiting exposure to tobacco and maintaining a healthy BMI. In terms of diet, consumption of fresh fruit and vegetables one or more days per week significantly reduces GC risk, as demonstrated in numerous prospective studies⁴⁶. Consumption of antioxidants has also been recommended for the prevention of GC; however, some clinical trials have conflicting results^{39, 47}.

Chemoprevention

Cyclooxygenase (COX)-2 overexpression is characteristic of non-cardia stomach cancers and also in well-differentiated stomach cancers⁴⁸, suggesting that suppression of COX-2 could be used as a chemopreventive strategy to prevent GC. Several cohort and observational studies have suggested that systematic use of non-aspirin non-steroid anti-inflammatory drugs (NSAIDs) and aspirin are protective factors, especially for non-cardia GC with *H. pylori* infection^{49, 50}. However, randomized controlled trials evaluating the role of non-aspirin NSAIDs for regression of IM after eradication of *H. pylori* failed to demonstrate a benefit compared to individuals without non-aspirin NSAID use^{51, 52}. The use of Celecoxib, a non-aspirin NSAID, has been shown to regress precancerous stomach mucosal conditions and/or lesions after *H. pylori* eradication⁵³. Statins are associated with a significant decrease in GC risk and have also been studied as potential GC chemopreventive agents⁵⁴.

H. pylori eradication

Since only a very small proportion of *H. pylori*-infected subjects develop GC, the benefit of mass *H. pylori* eradication campaigns to prevent GC remains unsubstantiated⁵⁵. However, treatment and eradication of *H. pylori* infection is recommended in patients with gastritis. *H. pylori* eradication has been reported to restore gastric histology to normal in individuals with chronic gastritis and atrophic gastritis without IM⁵⁶. Atrophic gastritis has been reported to undergo regression within one or two years after successful eradication of *H. pylori*⁵⁷. The presence of IM in *H. pylori*-associated chronic gastritis suggests a less reversible stage compared to atrophic gastritis alone. Evidence suggests that eradication at the IM stage is less effective and that lesions are more likely to progress⁵⁸. In a randomized 6-year follow-up clinical trial examining the role of anti-*H. pylori* treatment and dietary antioxidant micronutrient supplementation in reducing the progression of precancerous lesions, use of anti-*H. pylori* treatment or antioxidants was associated with significant inhibition of precancerous lesions including IM³⁹. This reversion of gastric atrophy and IM was confirmed after twelve years⁵⁹. The eradication of *H. pylori* in GC patients with prior endoscopic resection reduces the incidence of new tumors and the extent of IM⁶⁰. There is

controversial data regarding the effect of *H. pylori* eradication on the development of gastric epithelial dysplasia⁶¹. At present, prophylactic *H. pylori* eradication is strongly recommended after endoscopic tumor resection in early GC (EGC) to prevent recurrence of malignancy⁶².

Screening and surveillance

Because GC can take decades to develop, the identification of precancerous lesions and endoscopic surveillance of patients at high risk may help to detect early-stage malignancies when they are still operable and have better prognosis. In a large scale 10 year follow-up study, progression rates to GC for patients with atrophic gastritis, intestinal metaplasia, low-grade dysplasia or high-grade dysplasia were estimated 0.8%, 1.8%, 4.0% and 33.0%, respectively⁶³. Therefore, there is insufficient evidence to conclude that it would be beneficial and cost-effective to implement population GC screening in regions not at high risk of GC. It has been suggested that the GC screening strategy should be based on GC incidence in the population and on the individual's risk.

Asian Countries (Japan, South Korea, Singapore and Taiwan), which have a high incidence of GC, have started national screening programs. The Korean National Cancer Screening Program (NCSP) provides regular 2-year interval GC screening by upper gastrointestinal X-ray or upper endoscopy for citizens aged ≥ 40 years⁶⁴. The current trend in GC mortality reduction, despite the stable age-standardized GC incidence during last decade, supports that the current screening program has a mortality-reducing effect in Korea⁶⁵. However, the current Korean NCSP does not recommend different screening intervals depending on pre-existing gastric lesions for risk stratification. In Japan, guidelines for GC screening recommend photofluorography (indirect X-ray using small films) for population-based and opportunistic screening⁶⁶. They do not recommend endoscopy as a screening tool in the general population due to the lack of sufficient evidence supporting a reduction of GC as a result of population endoscopy screening.

The European Society of Gastrointestinal Endoscopy, a group of European gastrological societies, recently published management (MAPS) guidelines for precancerous conditions and lesions in the stomach for high-risk groups (Table 2)⁶⁷. These guidelines emphasize the importance of GC risk stratification. The application of the Operative Links on Gastritis Assessment, to address the grade and extension of atrophy (OLGA) and IM (OLGIM), may be useful for identifying subgroups of patients with risk of progression to GC^{68, 69}. Both, OLGA and OLGIM have been validated in prospective studies^{70, 71}. In the US, only the American Society for Gastrointestinal Endoscopy (ASGE) has recently published guidelines for the screening and management gastric lesions based on MAPS (Table 2)⁷².

Studies suggest that individuals with GC family history do not necessarily need more frequent GC screening than the generally recommended 2-year interval in Korea¹⁸. Recommendations for management and surveillance of familial GC have only been made for individuals with HDGC⁷³. A prophylactic gastrectomy is recommended to those having a *CDH1* mutation at about 20 years of age, but annual endoscopic surveillance using a high-definition endoscope should be offered for those who do not have a gastrectomy⁷⁴. *H. pylori*

treatment is recommended by European and Chinese guidelines for the first-degree family members of GC patients⁷⁵; however, the 2008 version of the Japanese guidelines did not recommend treatment due to lack of direct evidence of GC prevention in family members⁷⁶.

Diagnostic Evaluation

Endoscopic diagnosis of GC is may be difficult because early gastric cancer (EGC) often only shows only minimal, subtle changes in the gastric mucosa. The first step in diagnosing GC endoscopically is to detect any suspicious lesions and to characterize them. Good reporting based on the Paris classification as the current standard is imperative⁷⁷. The European Society of Gastrointestinal Endoscopy recommends that for quality control, eight images should be taken to illustrate the examination of the stomach in its totality (complementary images should be taken in the case of a specific lesion)⁷⁸. Detection of subtle gastric mucosal changes during examination requires the use advanced endoscopic techniques, such as narrow-band imaging (NBI) with or without magnification (NBI-ME), which has high sensitivity and specificity^{78, 79}. NBI endoscopy may also help in assessing the extent of the lesions, and in improving safety margins and cure rates during endoscopic resection of EGC. Other techniques, including chromoendoscopy (CE), flexible spectral imaging color enhancement (FICE) endoscopy with or without magnification (FIME), and confocal laser endomicroscopy (CLE), have shown promising results^{80–82}. At present, NBI-ME is probably the most frequently used endoscopic technique and has the largest amount of technical data available.

Endoscopic training and experience is essential, as well as good preparation for the endoscopic examination, for the diagnosis of GC. The most important process in the endoscopic diagnosis of GC lays in the scrutiny all gastric areas with targeted biopsies as histopathological examination remains the gold standard for the final diagnosis⁸³. Generally, the mass or abnormal mucosa is targeted for biopsy. In the case of a malignant gastric ulcer, at least seven biopsies of the heaped up edges of the ulcer and base should be performed⁸⁴. Diagnosis of linitis plastica can be more difficult due to reduction in the yield of mucosal biopsies. Large mucosal and submucosal biopsy samples may be taken with snare resection. Endoscopic Ultrasound with fine needle aspiration or core sampling may be necessary, but histopathology is still generally preferable to cytology for diagnosis⁷².

Clinical Management

Guidelines in both Europe⁸⁵ and the US⁸⁶ have been proposed for management of GC depending on location, stage, and surgical candidacy. GC screening in countries with high-risk populations is effective in identifying EGC, which can be treated endoscopically. Accurate pretreatment staging is critical in identifying EGC patients with disease that is limited to the mucosa and submucosa (stage T1) and who are candidates for endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD)⁸⁷. ESD permits en bloc resection of most lesions and is the preferred technique for resecting EGC in Asia⁸⁸, with a complete en bloc resection rate of 87.7% and low complication rates⁸⁹. ESD has been reported to outperform EMR for en bloc, complete and curative resection with lower recurrence rate⁹⁰. In the US, ESD is rarely performed outside referral centers with expertise

in this technique⁷². Depending on the size and location of the primary tumor, the preferred means of therapy is surgical resection with total or subtotal gastrectomy⁹¹.

While several targeted therapies have been studied, only two targeted GC treatments have been approved for use in the US. Inhibition of HER2 has been tested as a targeted therapy for several cancers, including GC. Trastuzumab is a monoclonal antibody that targets HER2 that inhibits HER2 mediated signaling, and thereby preventing the proliferation of HER2 dependent tumors⁹². The ToGA trial, a Phase III international study evaluating the efficacy of trastuzumab in combination with conventional therapy (cisplatin plus 5-FU or capecitabine), showed improvement in the overall survival (OS) compared with chemotherapy alone⁹³. Ramucirumab, a human monoclonal antibody against the vascular endothelial growth factor receptor 2 (an important signaling pathway in gastric and gastroesophageal cancer), is the first FDA approved biologic therapy used as a single agent that demonstrates survival benefit in patients with advanced GC or gastroesophageal cancer who have progressed after first-line treatment⁹⁴.

Prognosis and Survivorship

In the US, relative 5-year survival rates for GC increased from 15% to 29% during the period of 1975–2009⁹⁵. However, GC survival remains poor. Cardia GC and Diffuse type non-cardia GC present with the worst prognosis^{7, 96}. Compared to tumors in the pyloric antrum, cardia GC have lower 5-year survival and higher operative mortality⁹⁷. Overall, EGC can be associated with 5-year survival rates that approximate 90%. However, in both the US and Europe, few cancers are detected at early stages resulting in the low 5-year relative survival rates^{98, 99}. This emphasizes the importance of implementing public health measures that help identify individuals at high risk in order to increase early diagnosis and decrease GC mortality.

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References

1. Kelley JR, Duggan JM. Gastric cancer epidemiology and risk factors. *J Clin Epidemiol*. 2003; 56(1): 1–9. [PubMed: 12589864]
2. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*. 2015; 136(5):E359–86. [PubMed: 25220842]
3. Ferlay J, Shin HR, Bray F, et al. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer*. 2010; 127(12):2893–917. [PubMed: 21351269]
4. Soerjomataram I, Lortet-Tieulent J, Parkin DM, et al. Global burden of cancer in 2008: a systematic analysis of disability-adjusted life-years in 12 world regions. *Lancet*. 2012; 380(9856):1840–50. [PubMed: 23079588]

5. Jemal A, Bray F, Center MM, et al. Global cancer statistics. *CA Cancer J Clin.* 2011; 61(2):69–90. [PubMed: 21296855]
6. Ferlay, JSI.; Ervik, M.; Dikshit, R.; Eser, S.; Mathers, C.; Rebelo, M.; Parkin, DM.; Forman, D.; Bray, F. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: <http://globocan.iarc.fr> [Accessed on October 11, 2014]
7. Correa P. Gastric cancer: overview. *Gastroenterol Clin North Am.* 2013; 42(2):211–7. [PubMed: 23639637]
8. Noto JM, Peek RM Jr. *Helicobacter pylori*: an overview. *Methods Mol Biol.* 2012; 921:7–10. [PubMed: 23015485]
9. Pounder RE, Ng D. The prevalence of *Helicobacter pylori* infection in different countries. *Aliment Pharmacol Ther.* 1995; 9(Suppl 2):33–9. [PubMed: 8547526]
10. Correa P, Cuello C, Duque E. Carcinoma and intestinal metaplasia of the stomach in Colombian migrants. *J Natl Cancer Inst.* 1970; 44(2):297–306. [PubMed: 11515071]
11. Correa P, Cuello C, Duque E, et al. Gastric cancer in Colombia. III. Natural history of precursor lesions. *J Natl Cancer Inst.* 1976; 57(5):1027–35. [PubMed: 1003539]
12. An international association between *Helicobacter pylori* infection and gastric cancer. The EUROGA Study Group. *Lancet.* 1993; 341(8857):1359–62. [PubMed: 8098787]
13. Figueiredo C, Machado JC, Pharoah P, et al. *Helicobacter pylori* and interleukin 1 genotyping: an opportunity to identify high-risk individuals for gastric carcinoma. *J Natl Cancer Inst.* 2002; 94(22):1680–7. [PubMed: 12441323]
14. Bessede E, Dubus P, Megraud F, et al. *Helicobacter pylori* infection and stem cells at the origin of gastric cancer. *Oncogene.* 2015; 34(20):2547–55. [PubMed: 25043305]
15. Chen XZ, Chen H, Castro FA, et al. Epstein-barr virus infection and gastric cancer: a systematic review. *Medicine (Baltimore).* 2015; 94(20):e792. [PubMed: 25997049]
16. Murphy G, Pfeiffer R, Camargo MC, et al. Meta-analysis shows that prevalence of Epstein-Barr virus-positive gastric cancer differs based on sex and anatomic location. *Gastroenterology.* 2009; 137(3):824–33. [PubMed: 19445939]
17. Camargo MC, Kim WH, Chiaravalli AM, et al. Improved survival of gastric cancer with tumour Epstein-Barr virus positivity: an international pooled analysis. *Gut.* 2014; 63(2):236–43. [PubMed: 23580779]
18. Han MA, Oh MG, Choi IJ, et al. Association of family history with cancer recurrence and survival in patients with gastric cancer. *J Clin Oncol.* 2012; 30(7):701–8. [PubMed: 22271486]
19. Yaghoobi M, Bijarchi R, Narod SA. Family history and the risk of gastric cancer. *Br J Cancer.* 2010; 102(2):237–42. [PubMed: 19888225]
20. Figueiredo C, Costa S, Karameris A, et al. Pathogenesis of Gastric Cancer. *Helicobacter.* 2015; 20(Suppl 1):30–5. [PubMed: 26372822]
21. Piazuelo MB, Correa P. Gastric cancer: Overview. *Colomb Med (Cali).* 2013; 44(3):192–201. [PubMed: 24892619]
22. Oliveira C, Pinheiro H, Figueiredo J, et al. Familial gastric cancer: genetic susceptibility, pathology, and implications for management. *Lancet Oncol.* 2015; 16(2):e60–70. [PubMed: 25638682]
23. Oliveira C, Seruca R, Carneiro F. Genetics, pathology, and clinics of familial gastric cancer. *Int J Surg Pathol.* 2006; 14(1):21–33. [PubMed: 16501831]
24. Capelle LG, Van Grieken NC, Lingsma HF, et al. Risk and epidemiological time trends of gastric cancer in Lynch syndrome carriers in the Netherlands. *Gastroenterology.* 2010; 138(2):487–92. [PubMed: 19900449]
25. Raj A, Mayberry JF, Podas T. Occupation and gastric cancer. *Postgrad Med J.* 2003; 79(931):252–8. [PubMed: 12782770]
26. Ladeiras-Lopes R, Pereira AK, Nogueira A, et al. Smoking and gastric cancer: systematic review and meta-analysis of cohort studies. *Cancer Causes Control.* 2008; 19(7):689–701. [PubMed: 18293090]

27. Gonzalez CA, Pera G, Agudo A, et al. Smoking and the risk of gastric cancer in the European Prospective Investigation Into Cancer and Nutrition (EPIC). *Int J Cancer*. 2003; 107(4):629–34. [PubMed: 14520702]
28. Sinha DN, Abdulkader RS, Gupta PC. Smokeless tobacco-associated cancers: A systematic review and meta-analysis of Indian studies. *Int J Cancer*. 2016; 138(6):1368–79. [PubMed: 26443187]
29. Leung WK, Lin SR, Ching JY, et al. Factors predicting progression of gastric intestinal metaplasia: results of a randomised trial on *Helicobacter pylori* eradication. *Gut*. 2004; 53(9):1244–9. [PubMed: 15306578]
30. Sjødahl K, Lu Y, Nilsen TI, et al. Smoking and alcohol drinking in relation to risk of gastric cancer: a population-based, prospective cohort study. *Int J Cancer*. 2007; 120(1):128–32. [PubMed: 17036324]
31. Abnet CC, Corley DA, Freedman ND, et al. Diet and upper gastrointestinal malignancies. *Gastroenterology*. 2015; 148(6):1234–1243 e4. [PubMed: 25680671]
32. D'Elia L, Rossi G, Ippolito R, et al. Habitual salt intake and risk of gastric cancer: a meta-analysis of prospective studies. *Clin Nutr*. 2012; 31(4):489–98. [PubMed: 22296873]
33. Ge S, Feng X, Shen L, et al. Association between Habitual Dietary Salt Intake and Risk of Gastric Cancer: A Systematic Review of Observational Studies. *Gastroenterol Res Pract*. 2012; 2012:808120. [PubMed: 23125851]
34. de Martel C, Forman D, Plummer M. Gastric cancer: epidemiology and risk factors. *Gastroenterol Clin North Am*. 2013; 42(2):219–40. [PubMed: 23639638]
35. Peleteiro B, Lopes C, Figueiredo C, et al. Salt intake and gastric cancer risk according to *Helicobacter pylori* infection, smoking, tumour site and histological type. *Br J Cancer*. 2011; 104(1):198–207. [PubMed: 21081930]
36. Zhu H, Yang X, Zhang C, et al. Red and processed meat intake is associated with higher gastric cancer risk: a meta-analysis of epidemiological observational studies. *PLoS One*. 2013; 8(8):e70955. [PubMed: 23967140]
37. Gonzalez CA, Agudo A. Carcinogenesis, prevention and early detection of gastric cancer: where we are and where we should go. *Int J Cancer*. 2012; 130(4):745–53. [PubMed: 21918974]
38. Chen Y, Liu L, Wang X, et al. Body mass index and risk of gastric cancer: a meta-analysis of a population with more than ten million from 24 prospective studies. *Cancer Epidemiol Biomarkers Prev*. 2013; 22(8):1395–408. [PubMed: 23697611]
39. Correa P, Fontham ET, Bravo JC, et al. Chemoprevention of gastric dysplasia: randomized trial of antioxidant supplements and anti-*helicobacter pylori* therapy. *J Natl Cancer Inst*. 2000; 92(23):1881–8. [PubMed: 11106679]
40. Japanese classification of gastric carcinoma: 3rd English edition. *Gastric Cancer*. 2011; 14(2):101–12. [PubMed: 21573743]
41. Washington K. 7th edition of the AJCC cancer staging manual: stomach. *Ann Surg Oncol*. 2010; 17(12):3077–9. [PubMed: 20882416]
42. Colquhoun A, Arnold M, Ferlay J, et al. Global patterns of cardia and non-cardia gastric cancer incidence in 2012. *Gut*. 2015
43. Lauren P. 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. [PubMed: 14320675]
44. Henson DE, Dittus C, Younes M, et al. 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(7):765–70. [PubMed: 15214826]
45. Barber M, Murrell A, Ito Y, et al. Mechanisms and sequelae of E-cadherin silencing in hereditary diffuse gastric cancer. *J Pathol*. 2008; 216(3):295–306. [PubMed: 18788075]
46. Kobayashi M, Tsubono Y, Sasazuki S, et al. 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(1):39–44. [PubMed: 12353232]
47. Plummer M, Vivas J, Lopez G, et al. Chemoprevention of precancerous gastric lesions with antioxidant vitamin supplementation: a randomized trial in a high-risk population. *J Natl Cancer Inst*. 2007; 99(2):137–46. [PubMed: 17227997]

48. Song J, Su H, Zhou YY, et al. Cyclooxygenase-2 expression is associated with poor overall survival of patients with gastric cancer: a meta-analysis. *Dig Dis Sci*. 2014; 59(2):436–45. [PubMed: 24178897]
49. Wu CY, Wu MS, Kuo KN, et al. Effective reduction of gastric cancer risk with regular use of nonsteroidal anti-inflammatory drugs in *Helicobacter pylori*-infected patients. *J Clin Oncol*. 2010; 28(18):2952–7. [PubMed: 20479409]
50. Tian W, Zhao Y, Liu S, et al. Meta-analysis on the relationship between nonsteroidal anti-inflammatory drug use and gastric cancer. *Eur J Cancer Prev*. 2010; 19(4):288–98. [PubMed: 20386312]
51. Leung WK, Ng EK, Chan FK, et al. Effects of long-term rofecoxib on gastric intestinal metaplasia: results of a randomized controlled trial. *Clin Cancer Res*. 2006; 12(15):4766–72. [PubMed: 16899628]
52. Yanaoka K, Oka M, Yoshimura N, et al. Preventive effects of etodolac, a selective cyclooxygenase-2 inhibitor, on cancer development in extensive metaplastic gastritis, a *Helicobacter pylori*-negative precancerous lesion. *Int J Cancer*. 2010; 126(6):1467–73. [PubMed: 19711347]
53. Hung KH, Yang HB, Cheng HC, et al. Short-term celecoxib to regress long-term persistent gastric intestinal metaplasia after *Helicobacter pylori* eradication. *J Gastroenterol Hepatol*. 2010; 25(1): 48–53. [PubMed: 19793174]
54. Singh PP, Singh S. Statins are associated with reduced risk of gastric cancer: a systematic review and meta-analysis. *Ann Oncol*. 2013; 24(7):1721–30. [PubMed: 23599253]
55. Compare D, Rocco A, Nardone G. Screening for and surveillance of gastric cancer. *World J Gastroenterol*. 2014; 20(38):13681–91. [PubMed: 25320506]
56. Rokkas T, Pistiolas D, Sechopoulos P, et al. The long-term impact of *Helicobacter pylori* eradication on gastric histology: a systematic review and meta-analysis. *Helicobacter*. 2007; 12(Suppl 2):32–8. [PubMed: 17991174]
57. De Vries AC, Kuipers EJ. Review article: *Helicobacter pylori* eradication for the prevention of gastric cancer. *Aliment Pharmacol Ther*. 2007; 26(Suppl 2):25–35. [PubMed: 18081646]
58. Wang J, Xu L, Shi R, et al. Gastric atrophy and intestinal metaplasia before and after *Helicobacter pylori* eradication: a meta-analysis. *Digestion*. 2011; 83(4):253–60. [PubMed: 21282951]
59. Mera R, Fontham ET, Bravo LE, et al. Long term follow up of patients treated for *Helicobacter pylori* infection. *Gut*. 2005; 54(11):1536–40. [PubMed: 15985559]
60. Uemura N, Mukai T, Okamoto S, et al. Effect of *Helicobacter pylori* eradication on subsequent development of cancer after endoscopic resection of early gastric cancer. *Cancer Epidemiol Biomarkers Prev*. 1997; 6(8):639–42. [PubMed: 9264278]
61. You WC, Brown LM, Zhang L, 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. [PubMed: 16849680]
62. Fukase K, Kato M, Kikuchi S, et al. Effect of eradication of *Helicobacter pylori* on incidence of metachronous gastric carcinoma after endoscopic resection of early gastric cancer: an open-label, randomised controlled trial. *Lancet*. 2008; 372(9636):392–7. [PubMed: 18675689]
63. de Vries AC, van Grieken NC, Looman CW, et al. Gastric cancer risk in patients with premalignant gastric lesions: a nationwide cohort study in the Netherlands. *Gastroenterology*. 2008; 134(4):945–52. [PubMed: 18395075]
64. Lee KS, Oh DK, Han MA, et al. Gastric cancer screening in Korea: report on the national cancer screening program in 2008. *Cancer Res Treat*. 2011; 43(2):83–8. [PubMed: 21811423]
65. Jung KW, Won YJ, Kong HJ, et al. Cancer statistics in Korea: incidence, mortality, survival, and prevalence in 2011. *Cancer Res Treat*. 2014; 46(2):109–23. [PubMed: 24851102]
66. Hamashima C, Shibuya D, Yamazaki H, et al. The Japanese guidelines for gastric cancer screening. *Jpn J Clin Oncol*. 2008; 38(4):259–67. [PubMed: 18344316]
67. Dinis-Ribeiro M, Areia M, de Vries AC, et al. Management of precancerous conditions and lesions in the stomach (MAPS): guideline from the European Society of Gastrointestinal Endoscopy (ESGE), European *Helicobacter* Study Group (EHSg), European Society of Pathology (ESP), and

- the Sociedade Portuguesa de Endoscopia Digestiva (SPED). *Endoscopy*. 2012; 44(1):74–94. [PubMed: 22198778]
68. Rugge M, Genta RM. Staging gastritis: an international proposal. *Gastroenterology*. 2005; 129(5): 1807–8. [PubMed: 16285989]
 69. Capelle LG, de Vries AC, Haringsma J, et al. The staging of gastritis with the OLGA system by using intestinal metaplasia as an accurate alternative for atrophic gastritis. *Gastrointest Endosc*. 2010; 71(7):1150–8. [PubMed: 20381801]
 70. Satoh K, Osawa H, Yoshizawa M, et al. Assessment of atrophic gastritis using the OLGA system. *Helicobacter*. 2008; 13(3):225–9. [PubMed: 18466398]
 71. Rugge M, de Boni M, Pennelli G, et al. Gastritis OLGA-staging and gastric cancer risk: a twelve-year clinico-pathological follow-up study. *Aliment Pharmacol Ther*. 2010; 31(10):1104–11. [PubMed: 20180784]
 72. Evans JA, Chandrasekhara V, et al. Committee, A.S.o.P. The role of endoscopy in the management of premalignant and malignant conditions of the stomach. *Gastrointest Endosc*. 2015; 82(1):1–8. [PubMed: 25935705]
 73. Choi JJ. Endoscopic gastric cancer screening and surveillance in high-risk groups. *Clin Endosc*. 2014; 47(6):497–503. [PubMed: 25505714]
 74. Kluij I, Sijmons RH, Hoogerbrugge N, et al. Familial gastric cancer: guidelines for diagnosis, treatment and periodic surveillance. *Fam Cancer*. 2012; 11(3):363–9. [PubMed: 22388873]
 75. Liu WZ, Xie Y, Cheng H, et al. Fourth Chinese National Consensus Report on the management of *Helicobacter pylori* infection. *J Dig Dis*. 2013; 14(5):211–21. [PubMed: 23302262]
 76. Asaka M, Kato M, Takahashi S, et al. Guidelines for the management of *Helicobacter pylori* infection in Japan: 2009 revised edition. *Helicobacter*. 2010; 15(1):1–20. [PubMed: 20302585]
 77. The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon: November 30 to December 1, 2002. *Gastrointest Endosc*. 2003; 58(6 Suppl):S3–43. [PubMed: 14652541]
 78. Rey JF, Lambert R. ESGE recommendations for quality control in gastrointestinal endoscopy: guidelines for image documentation in upper and lower GI endoscopy. *Endoscopy*. 2001; 33(10): 901–3. [PubMed: 11605605]
 79. Omori T, Kamiya Y, Tahara T, et al. Correlation between magnifying narrow band imaging and histopathology in gastric protruding/or polypoid lesions: a pilot feasibility trial. *BMC Gastroenterol*. 2012; 12:17. [PubMed: 22356674]
 80. Tanioka Y, Yanai H, Sakaguchi E. Ultraslim endoscopy with flexible spectral imaging color enhancement for upper gastrointestinal neoplasms. *World J Gastrointest Endosc*. 2011; 3(1):11–5. [PubMed: 21258601]
 81. Mouri R, Yoshida S, Tanaka S, et al. Evaluation and validation of computed virtual chromoendoscopy in early gastric cancer. *Gastrointest Endosc*. 2009; 69(6):1052–8. [PubMed: 19152892]
 82. Jung SW, Lim KS, Lim JU, et al. Flexible spectral imaging color enhancement (FICE) is useful to discriminate among non-neoplastic lesion, adenoma, and cancer of stomach. *Dig Dis Sci*. 2011; 56(10):2879–86. [PubMed: 21800158]
 83. Pasechnikov V, Chukov S, Fedorov E, et al. Gastric cancer: prevention, screening and early diagnosis. *World J Gastroenterol*. 2014; 20(38):13842–62. [PubMed: 25320521]
 84. Graham DY, Schwartz JT, Cain GD, et al. Prospective evaluation of biopsy number in the diagnosis of esophageal and gastric carcinoma. *Gastroenterology*. 1982; 82(2):228–31. [PubMed: 7054024]
 85. Waddell T, Verheij M, Allum W, et al. Gastric cancer: ESMO-ESSO-ESTRO clinical practice guidelines for diagnosis, treatment and follow-up. *Eur J Surg Oncol*. 2014; 40(5):584–91. [PubMed: 24685156]
 86. Gastric Cancer NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines). National Comprehensive Cancer Network, Inc; 2015. Version 3.2015
 87. Kantsevoy SV, Adler DG, Conway JD, et al. Endoscopic mucosal resection and endoscopic submucosal dissection. *Gastrointest Endosc*. 2008; 68(1):11–8. [PubMed: 18577472]
 88. Kim SG. Endoscopic treatment for early gastric cancer. *J Gastric Cancer*. 2011; 11(3):146–54. [PubMed: 22076219]

89. Chung IK, Lee JH, Lee SH, et al. Therapeutic outcomes in 1000 cases of endoscopic submucosal dissection for early gastric neoplasms: Korean ESD Study Group multicenter study. *Gastrointest Endosc.* 2009; 69(7):1228–35. [PubMed: 19249769]
90. Park YM, Cho E, Kang HY, et al. The effectiveness and safety of endoscopic submucosal dissection compared with endoscopic mucosal resection for early gastric cancer: a systematic review and metaanalysis. *Surg Endosc.* 2011; 25(8):2666–77. [PubMed: 21424201]
91. Blakely AM, Miner TJ. Surgical considerations in the treatment of gastric cancer. *Gastroenterol Clin North Am.* 2013; 42(2):337–57. [PubMed: 23639644]
92. Hudis CA. Trastuzumab--mechanism of action and use in clinical practice. *N Engl J Med.* 2007; 357(1):39–51. [PubMed: 17611206]
93. Bang YJ, Van Cutsem E, Feyereislova A, et al. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastrooesophageal junction cancer (ToGA): a phase 3, open-label, randomised controlled trial. *Lancet.* 2010; 376(9742):687–97. [PubMed: 20728210]
94. Fuchs CS, Tomasek J, Yong CJ, et al. Ramucirumab monotherapy for previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (REGARD): an international, randomised, multicentre, placebo-controlled, phase 3 trial. *Lancet.* 2014; 383(9911):31–9. [PubMed: 24094768]
95. Siegel R, Ma J, Zou Z, et al. Cancer statistics, 2014. *CA Cancer J Clin.* 2014; 64(1):9–29. [PubMed: 24399786]
96. Botterweck AA, Schouten LJ, Volovics A, et al. Trends in incidence of adenocarcinoma of the oesophagus and gastric cardia in ten European countries. *Int J Epidemiol.* 2000; 29(4):645–54. [PubMed: 10922340]
97. Crew KD, Neugut AI. Epidemiology of gastric cancer. *World J Gastroenterol.* 2006; 12(3):354–62. [PubMed: 16489633]
98. Surveillance, Epidemiology, and End Results (SEER) Program. Research Data (1973–2010). National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch; (www.seer.cancer.gov) released April 2013, based on the November 2012 submission
99. Dassen AE V, Lemmens E, van de Poll-Franse LV, et al. Trends in incidence, treatment and survival of gastric adenocarcinoma between 1990 and 2007: a population-based study in the Netherlands. *Eur J Cancer.* 2010; 46(6):1101–10. [PubMed: 20219351]

Key Points

- Although GC incidence has declined in the US during the last decade, an increase in the incidence of GC has been estimated for 2016.
- GC prognosis is very poor. Only 28.3% of newly discovered GC are expected to survive >5 years after diagnosis.
- Prognosis of GC is largely dependent on the tumor stage at diagnosis and classification as intestinal or diffuse type.
- Although NSAID, aspirin, and statins use, although reported to decrease GC risk, these have not been implemented for GC chemoprevention in clinical practice.
- Risk assessment and surveillance guidelines have been implemented in Asian countries with high incidence of GC. In the US, only the ASGE has recently published guidelines for the screening and management gastric lesion.

Figure 1. Age-standardized gastric cancer incidence rates, both sexes for 2012

From Ferlay J, Ervik M, Dikshit R, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available at: <http://globocan.iarc.fr>. Accessed on October 11, 2014; with permission.

Figure 2. The precancerous cascade

Prolonged gastric inflammation resulting from chronic *H. pylori* infection causes epithelial damage that leads to gastric atrophy, characterized by loss of parietal cells and chief cells and glandular atrophy. The gastric epithelium is then replaced by intestinal metaplasia, followed by foci of low-grade dysplasia, which can later develop to high-grade dysplasia that can later become adenocarcinomas.

Figure 3. Tumor location dictates the anatomic classification and histopathological characteristics

A. GC classification according to anatomic locations. B. Hematoxylin and Eosin stained Intestinal Type Non-Cardia Gastric Cancer. C. Hematoxylin and Eosin stained Diffuse Type Non-Cardia Gastric Cancer.

Table 1

Gastric cancer characteristics according to location and classification.

Cardia Gastric Cancer		Non-Cardia Gastric Cancer			
		Intestinal Type	Diffuse Type		
•	Incidence is increasing ⁹⁶	•	Incidence is decreasing ^{21, 44} .	•	Incidence is increasing ⁷
•	Associated with Gastro esophageal Reflux	•	Associated with <i>H. pylori</i> ²¹ .	•	Can be associated with <i>H. pylori</i> ; strongly associated with loss of expression of <i>E-cadherin</i> ⁴⁵ .
•	Resembles esophageal adenocarcinoma ⁹⁶	•	Presents with precancerous lesions ⁴⁵ .	•	No precancerous lesions ⁴⁵
•	More aggressive and worse prognosis than non-Cardia ⁹⁶	•	Histological characteristics include: malignant epithelial cells, and hyper chromatic irregular and angulated glands that show cohesiveness and glandular differentiation infiltrating the stroma.	•	Histological characteristics include: cells lacking cohesion invading tissues independently or in small clusters.
•	Associated with Caucasian population and strong male predominance (6:1) ⁹⁶	•	May present in three scenarios: Polypoid lesion attached on a wide base; an ulcerated carcinoma with sharp and raised margins; and an ulcerated carcinoma without definite limits ²¹ .	•	Lesions are non-ulcerated, diffusely infiltrating carcinomas
		•	Diagnosed in individuals with ages ranging from 55–80 years ⁴⁴ .	•	Signet ring adenocarcinoma: are a variant of the diffuse histological type with abundant cytoplasmic mucin that displaces the nucleus to the periphery ^{7, 21} .
		•	Male to female ratio 2:1 ⁴⁴ .	•	Diagnosed in younger patients with ages ranging 40–60 years ^{7, 21} .
				•	Male to female ratio 1:1 ⁴⁴ .
				•	Worst prognosis than Intestinal Type GC ⁷ .
				•	HDGC autosomal dominant pattern of inheritance ⁴⁵ .

GC = Gastric Cancer; histology images courtesy of Dr. Carmen Gonzalez Keelan

Table 2

Surveillance guidelines for precancerous conditions and lesions in the stomach

Premalignant Lesion	European Society of Gastrointestinal Endoscopy (MAPS) guidelines ⁶⁷	American Society for Gastrointestinal Endoscopy guidelines ⁷²
Atrophic Gastritis/IM	<ul style="list-style-type: none"> At least 4 non-target biopsies from two topographic sites should be taken s for adequate staging and grading of the premalignant condition Patients with extensive atrophy and/or IM should be offered endoscopic surveillance A 3-year follow-up after diagnosis is recommended for patients with extensive atrophy and/or IM Surveillance endoscopy is not recommended for patients with mild to moderate atrophy and/or intestinal metaplasia restricted to stomach antrum 	<ul style="list-style-type: none"> A surveillance endoscopy for patients with GIM who are at increased risk of GC (Asian ethnicity or family History of GC) Surveillance intervals should be individualized
Low Grade Dysplasia	<ul style="list-style-type: none"> In the absence of an endoscopically defined lesion, should receive follow-up within 1 year after diagnosis In the presence of endoscopically define lesion, endoscopic resection should be considered to obtain a more accurate histological diagnosis 	<ul style="list-style-type: none"> A follow-up EGD within 1 year with a topographic mapping biopsy strategy is indicated
High Grade Dysplasia	<ul style="list-style-type: none"> In the absence of endoscopically defined lesions, immediate endoscopic reassessment with extensive biopsy sampling and surveillance at 6-month to 1–year intervals is indicated 	<ul style="list-style-type: none"> Endoscopic resection and surveillance endoscopy is recommended