

THE YEAR IN HELICOBACTER – MALIGNANT DISEASES

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Abstract – The link between *Helicobacter pylori* (*H. pylori*) infection and gastric cancer is well established. Recent studies shed further light on the effects of an *H. pylori* screen-and-treat approach on primary prevention of gastric cancer. The residual risk following eradication highlights again the need to further define the ‘point of no return’ when the preventive effect of eradication is impaired. This also includes data on the impact of *H. pylori* eradication on the risk of metachronous and recurrent gastric cancer after endoscopic resection of early lesions. Further studies explored the relevance of *H. pylori* infection in the context of systemic gastric cancer treatment.

Recent research has offered new perspectives into clinical characteristics of gastric mucosa-associated lymphoid tissue lymphoma and the role of *H. pylori* eradication treatment in *H. pylori*-negative cases. The emerging issue of antibiotic resistance in the treatment of these patients was also addressed.

The risk between *H. pylori* infection and colorectal cancer and its premalignant lesions has also been explored with studies mainly focusing on causality, whilst additionally exploring potential modulatory effects of eradication therapy on these risks.

In this article, we have summarized the most noteworthy findings on the topic, focusing primarily on the studies with significant clinical implications published in the period between April 2024 and March 2025.

Keywords: *Helicobacter pylori*, Gastric cancer, Gastric adenocarcinoma, Gastric lymphoma, Colorectal cancer, Colorectal carcinoma.

INTRODUCTION

The association between *Helicobacter pylori* (*H. pylori*) and malignant disease is well known. Having been established as the main risk factor for gastric cancer, its role has also been described in the development of gastric mucosa-associated lymphoid tissue (MALT) lymphoma, and there is evolving data suggesting an association with colorectal cancer.

This review aims to provide an update on the major developments in the study of *H. pylori* and these malignancies between April 2024 and May 2025, focusing on publications with a clinical scope, such as those bringing novelties in screening, prevention, and therapeutic implications.



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METHODS

We searched PubMed for articles published in the above-mentioned period, applying only the search terms $\{[('Helicobacter pylori') \text{ AND } ('gastric cancer' \text{ OR } 'colorectal cancer' \text{ OR } 'lymphoma')]\}$. After filtering for articles published in English, the search revealed 831 articles. The abstracts of those papers were then screened. Reviews, commentaries, letters, and basic science publications were excluded, and finally, 31 of the most relevant manuscripts were selected.

GASTRIC CANCER

Whilst there is no debate about the relevance of *H. pylori* in gastric carcinogenesis, some issues still require further elucidation. These include the definitive effect of an *H. pylori* screen-and-treat approach for primary prevention, including the residual gastric cancer risk after eradication. Recent studies have provided important insights into these areas, and we summarize the most noteworthy findings.

Gastric Cancer Screening

A community-based cluster-randomized, controlled, superiority intervention trial by Pan et al¹ compared the incidence of gastric cancer between those receiving *H. pylori* eradication and those receiving symptom-alleviation treatment (single daily dose of omeprazole and bismuth citrate) in China. A total of 184,786 individuals were enrolled over 11.8 years of follow-up. Whilst the lowest incidence of gastric cancer was observed in *H. pylori*-negative individuals (Crude incidence rate, CR 0.31×10^{-3} person-years), the reduction in incidence between the eradication (CR 0.60×10^{-3} person-years) and symptom-alleviation (CR 0.68×10^{-3} person-years) groups was modest [hazard ratio (HR)=0.86, 95% CI= 0.74-0.99], with a number needed to treat (NNT) of 141. The authors suggested that the modest eradication success rate (72.9%), absence of endoscopic testing, and the anti-inflammatory effects of the symptom-alleviation treatment were key factors accounting for the limited preventive effect. Even so, the study supports the feasibility of large-scale, population-based eradication for primary gastric cancer prevention. Notably, eradication was particularly effective in individuals under the age of 45, lowering both gastric cancer incidence and mortality. Similarly, a large-scale Korean study by Jung et al² analyzed data from 916,438 individuals aged ≥ 20 years who received *H. pylori* eradication between 2009 and 2011, with follow-up until 2021. Compared with the general population, those who received eradication had significantly lower gastric cancer incidence and mortality across all age groups (except for individuals 20-29 years old), which reinforces the benefit of eradication across almost all ages, whilst emphasizing the greater benefit when administered at a younger age. Authors suggest that the lack of eradication benefit in reducing gastric cancer incidence and mortality in the 20-29 age group can likely be explained by the high proportion of *H. pylori*-negative individuals in the age-matched general population and the limited follow-up period.

The matter of the cost-effectiveness of prevention strategies was also addressed. A systematic review by Lewis et al³ concluded that both primary and secondary gastric cancer prevention strategies are cost-effective in regions with high gastric cancer risk, particularly in Asian countries and their emigrants. However, the optimal age and screening modality still need to be defined.

A randomised controlled trial by Lee et al⁴ tested whether combining *H. pylori* stool antigen testing with faecal immunochemical testing (FIT) – as part of a bowel cancer screening program (for individuals aged 50-79) – has the potential to reduce gastric cancer incidence and mortality compared with FIT alone. Adjusted analyses accounting for participation rates and follow-up duration found a lower gastric cancer incidence in the combined-testing group [relative risk (RR) 0.79; 95% CI: 0.63-0.98], suggesting a benefit of integration of *H. pylori* testing into existing screening programs.

The need for early intervention was emphasized in a study by Mülder et al⁵, who developed a new simulation model comparing one-time screen-and-treat for *H. pylori* at ages 20-65 to no

screening. *H. pylori* screen – and – treat reduced the incidence of gastric cancer by 43% when performed at age 20, but only by 5% when performed at age 65. The NNT was also lowest at the youngest age (261), increasing to 448 at age 40 and 3,681 at age 65.

Early screening was also explored in a study by Okamura et al⁶, who incorporated *H. pylori* screening into school health check-ups among students aged 16-17 years old. Using urinary antibody tests (considered suitable for simplicity, sensitivity, and the fact that urine samples are routinely collected), the authors report a declining *H. pylori* prevalence from 4.7% in 2007-2011 to 2.8% in 2012-2017 ($p < 0.01$). Although only 56% of *H. pylori*-positive individuals underwent a follow-up endoscopy, atrophic gastritis was found in 66.7% (60/90), which is surprising for individuals of this young age. Against challenges, the high primary screening uptake (99.7%) suggests that school-based programs may serve as an effective strategy for reaching individuals at an early stage.

Novel research on the topic of gastric cancer screening in *H. pylori* naïve or low-prevalence populations was recently published by Ishibashi et al^{7,8}. In the first study⁷, the authors analyzed 519,368 endoscopies and 97 *H. pylori*-negative gastric neoplasms from 12 Japanese institutions, comparing them with a virtual cohort of 3,465,836 people to simulate occurrence, growth, and detection rates. Using a simulation model, they found that a 5-year interval strategy starting at 45 years had the lowest number needed-to-test, suggesting its potential in detecting *H. pylori* naïve neoplasms at earlier stages. The second study by the same group⁸ further explored the cost-effectiveness of endoscopic screening in countries with low *H. pylori* prevalence. The authors applied a simulation model constructed on the cohort data of 94,137 participants. They concluded that 4-yearly endoscopy starting at age 40 was the most cost-effective in low-*H. pylori* prevalence cohorts with the highest net monetary benefit of 97,401,578 ¥.

Korean national guidelines recommend biennial endoscopies for all Koreans aged 40-75 years⁹. However, recently published real-world data from Korea challenge this practice, suggesting a limited benefit for *H. pylori* naïve patients. Na et al¹⁰ analyzed data of individuals with endoscopies performed between 2010 and 2016. No gastric malignancies were detected in *H. pylori*-naïve participants ($p = 0.007$), whilst adenomas, adenocarcinomas, and neuroendocrine tumors were found in 1.9% and 2.5% of past- and currently infected individuals, respectively.

At last, the recently published third edition of the European MAPS guideline¹¹ on the management of epithelial precancerous conditions and early gastric neoplasia advocates population-based endoscopic screening in high (age standardized rate (ASR) >20/100,000 person-years) and intermediate-risk (ASR 10-20/100,000) regions. The latter, if cost-effectiveness is demonstrated locally. Screening is also recommended at age 45 for first-degree relatives of gastric cancer patients or 10 years before the relative's age at diagnosis. Non-invasive *H. pylori* testing and eradication between ages 20 and 30, and targeted endoscopic screening based on pepsinogen levels and *H. pylori* serology, are advised.

Gastric Cancer Risk Following *H. pylori* Eradication

Another area of interest remains the 'point of no return', i.e., at which stage of preneoplastic changes the *H. pylori* eradication loses its preventive effect. Fu et al¹² conducted a meta-analysis of 16 trials involving 15,026 patients, with 2.0 to 26.5 years of follow-up. Their analysis showed that eradication was associated with a 45% reduction in gastric cancer risk in patients with intestinal metaplasia or dysplasia compared to no treatment (RR: 0.55; 95% CI: 0.46-0.67; $p < 0.001$), underscoring the value of intervention even after precancerous changes have occurred.

Wiklund et al¹³ presented a population-based cohort study including 659,592 individuals who received *H. pylori* eradication in the period from 1995 to 2019. The study focused on non-cardia gastric cancer and found an elevated standardized incidence ratio (SIR) in the treatment group compared to the general population (SIR 2.27; 95% CI: 2.10-2.44) within 1-5 years post-treatment. However, the most notable finding was a gradual decline in risk over time. The risk was comparable to the general population within 11 years after eradication (SIR 1.11; 95% CI, 0.98-1.27 for 11-24 years post-treatment).

Luo et al¹⁴ conducted a meta-analysis aiming to determine gastric cancer risk in patients with unsuccessful *H. pylori* eradication. The authors reviewed data from 7 studies involving 8,767 patients. Individuals who experienced reinfection or failed eradication had a significantly higher risk of developing gastric cancer compared to those with successful eradication (HR 1.86; 95% CI: 1.14-3.04; $p = 0.013$). The study emphasizes the importance of not only achieving *H. pylori* eradication but also suggests the need for long-term follow-up of treated individuals.

A challenge of identifying patients at risk after eradication was addressed in a study conducted at Oita University Hospital, Japan. Mizukami et al¹⁵ followed patients who underwent *H. pylori* eradication between 1997 and 2013 over a minimum period of three years. They found that patients who developed gastric cancer presented with more extensive mucosal atrophy (non-cancer group: 3.4 ± 1.4 vs. cancer group: 4.3 ± 1.4 ; $p = 0.037$) and a significantly lower serum pepsinogen I/II ratio (cancer group 2.6 ± 1.4 vs. non-cancer group 3.4 ± 1.43 , $p = 0.037$) at baseline.

In a systematic review and meta-analysis focusing on endoscopic features associated with gastric cancer following *H. pylori* eradication, Kodama et al¹⁶ provided evidence on risk stratification, highlighting the need for tailored surveillance even after successful eradication. The study identified several risk indicators, including severe gastric atrophy (RR 3.40; 95% CI: 1.98-5.84; $p < 0.001$), severe intestinal metaplasia (RR 5.38; 95% CI: 3.62-8.00), and the presence of gastric xanthomas (RR 2.75; 95% CI: 1.78-4.26). Additionally, map-like redness observed post-eradication was associated with increased cancer risk (RR 2.34; 95% CI: 1.16-4.68).

Risk of Metachronous and recurrent Gastric Cancer After Endoscopic Resection of Early Lesions

Kim et al¹⁷ aimed to identify risk factors for the development of metachronous neoplasia in a case-control study involving patients who underwent endoscopic resection for gastric dysplasia and early gastric cancer in the period 2010-2019. A total of 36 patients who developed metachronous neoplasia after *H. pylori* eradication and 36 matched controls were included. The study examined changes in mucosal immune markers before and after eradication. In the control group, eradication was associated with an increase in CD3 and CD8 expression ($p = 0.022$ and < 0.001), with significant changes in the CD4/CD3, CD8/CD4, and PD-L1/CD4 ratios. In contrast, patients who developed metachronous lesions showed no significant changes, suggesting that a subset of patients who do not achieve immune recovery after successful eradication remain at increased risk.

Lee et al¹⁸ retrospectively reviewed 747 patients who underwent curative endoscopic submucosal dissection for early gastric cancer and received successful *H. pylori* treatment in the period 2005-2018, with a minimum follow-up of 5 years. Regardless of adjusting for the severity of intestinal metaplasia, patients older than 60 years had a significantly increased risk of developing metachronous lesions [HR 4.40 (60-69); 95% CI, 1.03-18.84, HR 10.14 (>70); 95% CI, 2.31-44.57]. This study highlights age as one of the key factors of post-eradication outcomes, indicating the need for closer surveillance in patients above the age of 60.

In comparison, Liu et al¹⁹ developed a machine learning model to help predict gastric cancer recurrence. They evaluated 1,234 patients who underwent radical surgery for gastric cancer, with 117 of them experiencing recurrence. The XGBoost algorithm had the highest accuracy of 0.9129 in predicting recurrence in both the validation set (area under the curve, AUC=0.9478±0.0298) and the test set (AUC=0.9695). *H. pylori* infection was identified as the most significant predictor of recurrence, ahead of tumor invasion depth, lymph node metastasis, postoperative carcinoembryonic antigen levels, tumor size, and number.

Finally, Omori et al²⁰ investigated the natural course of *H. pylori* infection following surgery by assessing the prevalence of 'spontaneous' eradication in patients undergoing distal or proximal partial gastrectomy. Among 1,247 patients whose *H. pylori* status was assessed at diagnosis, and in 541 of these patients reassessed one year after surgery, 52.7% showed "spontaneous" eradication. This was more common in men and patients over 70 years of age, regardless of the type of surgery. The authors recommend testing at the one-year postoperative follow-up to determine accurate infection status.

H. pylori Status and Cancer Treatment

There is an increasing number of studies focusing on the impact of *H. pylori* infection on the outcome of systemic gastric cancer treatment.

In a study including 307 gastric cancer patients, He et al²¹ found that *H. pylori* status significantly influences outcomes in those who underwent curative-intent gastrectomy following neoadjuvant chemotherapy. Specifically, in *H. pylori* positive patients who underwent radical gastrectomy after neoadjuvant chemotherapy postoperative adjuvant chemotherapy significantly improved overall survival (3-year overall survival (OS): 81.3% vs. 38.9%; $p < 0.001$; HR 0.23; 95% CI, 0.11-0.48), which was not confirmed in *H. pylori*-negative patients (3-year OS: 61.3% vs. 54.2%; $p = 0.880$; HR 0.95; 95% CI, 0.50-1.81). *H. pylori*-positive patients showed superior 3-year overall and disease-free survival (3-year OS: 75.9% vs. 60.2%; DFS: 70.2% vs. 52.3%; all $p < 0.001$). Despite being limited by its retrospective nature and sample size, the study suggests *H. pylori* status may affect the efficacy of chemotherapy and could potentially guide individualized treatment approaches.

Hu et al²² examined the relationship between *H. pylori* status and response to neoadjuvant immunotherapy in patients with advanced microsatellite stable (MSS) gastric and gastro-esophageal junction cancer. In this retrospective analysis of 201 patients treated between 2014 and 2024 across three institutions in China, *H. pylori*-positive patients showed a significantly higher response rate to neoadjuvant immunotherapy – 63.77% (95% CI, 51.98-74.11%) – compared to 47.73% (95% CI, 39.39-56.19%) in *H. pylori*-negative patients. The results imply that *H. pylori* positivity may serve as a favorable predictive marker for immunotherapy response in MSS gastric cancer.

Aquino de Morales et al²³ explored the impact of *H. pylori* status on outcomes of advanced gastric cancer patients treated with immune checkpoint inhibitors. This meta-analysis included three studies with a total of 928 patients (88.90% having stage IV cancer), 396 being *H. pylori* positive. Interestingly, the *H. pylori*-negative patients had significantly better outcomes after immunotherapy with longer overall survival (HR: 1.25; 95% CI: 1.05-1.50; $p = 0.012$) and a higher clinical response rate (OR: 0.40; 95% CI: 0.28-0.57; $p < 0.000001$) than *H. pylori*-positive patients. The authors speculate that this could be explained by the ability of the bacteria to modulate the cancer microenvironment and to induce PD-L1 expression and therefore suppress cytotoxic T-cell response. Nevertheless, further elucidation of these results is needed in the future.

The above-mentioned studies indicate that *H. pylori* status may serve as a biomarker in gastric cancer management, and its routine assessment could play a critical role in optimizing personalized treatment strategies.

Gastric Lymphoma

Gastric MALT lymphoma is a common indolent B-cell lymphoma, closely linked to *H. pylori* infection. Recent studies have brought new insights into predictors of treatment response, the role of eradication therapy in *H. pylori*-negative cases, and the growing challenge of antibiotic resistance.

Long-term outcomes of MALT lymphoma patients were retrospectively analyzed in a study by Sim et al²⁴. The authors report 5-year overall survival of 97.5% with aggressive disease being more likely in patients over 57 years of age [OR 2.50, 95% CI 1.15-5.74], males [OR 2.20, 95% CI 1.02-4.95], and those with at least stage II disease [OR 7.13, 95% CI 2.01-28.82]. *H. pylori* status and endoscopic findings showed no correlation with aggressiveness.

Focusing on *H. pylori*-negative disease, Lv et al²⁵ conducted a meta-analysis of 50 studies including 6,033 patients, with 20.5% being *H. pylori*-negative (95% CI: 17.0%-24.6%). They found *H. pylori*-negative patients more often to be males, presenting more often with proximal lesions, submucosal invasion, and advanced disease. Aiming to investigate the role of eradication in *H. pylori* negative cases, Laoruangroj et al²⁶ retrospectively reviewed all stage I MALT lymphoma cases in the period 2002-2022 (including 52 patients). Interestingly, only 13% of *H. pylori*-negative patients ($p = 0.033$) responded to eradication therapy, as opposed to 63% of *H. pylori*-positive patients. The results suggest a limited benefit of eradication in this patient group.

To investigate the impact of antibiotic resistance on the outcome of MALT lymphoma patients, Wang et al²⁷ conducted a meta-analysis involving 934 patients. They found resistance to clarithromycin and amoxicillin to be associated with worse outcomes, correlating with all-cause mortality (standard mean difference, SMD 5.13; 95% CI: 1.78-8.48; $p = 0.003$), tumor progression (SMD for clarithromycin: 7.09; 95% CI: 4.57-9.61; $p < 0.00001$; and for amoxicillin: 11.03; 95% CI: 5.81-16.25; $p < 0.00001$), and recurrence rates (SMD for clarithromycin: 9.31, 95% CIs: 6.16 to 12.47, $p < 0.00001$, and for amoxicillin: 13.81, 95% CIs: 2.78 to 24.85, $p = 0.01$). These findings support that antibiotic resistance is a global threat affecting patients' outcomes in all fields, including oncology.

Colorectal Cancer

The association between *H. pylori* and risk of colorectal carcinoma was reported previously. Recent studies have offered new insights into the causality of this relationship, the extent of *H. pylori* impact on the development of premalignant and malignant colonic lesions, and the role of eradication in modulating these risks.

Chen et al²⁸ retrospectively reviewed patients diagnosed with colorectal cancer (CRC) between 2015 and 2020 at a single US centre. Among 242 patients who underwent colonoscopy with polypectomy and gastric biopsy, 76.2% (16/21) of *H. pylori*-positive individuals had adenomatous polyps compared to 33.5% in the *H. pylori*-negative group ($p = 0.0001$). *H. pylori* was not identified within the actual polyp tissue. The authors performed *H. pylori* immunohistochemistry on 92 CRC samples from 2020, detecting *H. pylori* in 3 cases (2 patients <50 years). Further analysis of 52 CRC samples (2015-2022) revealed *H. pylori* in 13.5% of cases. Patients with *H. pylori*-positive CRC specimens had a mean age of 32.5 years, were all mismatch repair (MMR) proficient (vs. 88.2% MMR intact in *H. pylori*-negative cases, $p < 0.05$), and had predominantly left-sided tumors. These results support an association between *H. pylori* and sporadic CRC. The observed link between gastric *H. pylori* infection and a higher prevalence of colonic adenomatous polyps could have implications for future surveillance strategies.

To investigate the link between *H. pylori* and colorectal adenomas, Xu et al²⁹ conducted a meta-analysis of 15 studies. They found a significant difference in the prevalence of colorectal neoplastic polyps between *H. pylori*-positive and *H. pylori*-negative groups [OR = 1.80; 95% CI: 1.31-2.47; $p < .01$; $I^2 = 95\%$], suggesting that *H. pylori* infection may present a risk factor for colorectal polyps. Rias-Ordoñez et al³⁰ undertook a literature review to further explore the causality between *H. pylori* infection and CRC. The authors state that *H. pylori* meets Sir Bradford Hill's criteria for causality; however, future research is needed to explain the role of the bacteria in colorectal carcinogenesis.

Recent studies have explored whether *H. pylori* eradication can affect the risk of colorectal neoplasia. A retrospective cohort study by Liu et al³¹ analyzed adults with at least one eradication treatment between 2005 and 2012, comparing their CRC incidence to the general population. Whilst *H. pylori* infection was associated with increased CRC risk (SIR 1.27; 95% CI, 1.12-1.43), eradication did not result in a consistent risk reduction, particularly beyond six years (SIR 1.36; 95% CI, 0.78-2.21). However, the relatively short mean follow-up of 4.1 years may affect interpretation. Instead, a large-scale US study by Shah et al³² followed 812,736 veterans tested for *H. pylori* between 1999 and 2018. Over a 15-year period, those who received eradication had significantly lower CRC incidence and mortality, with an absolute risk reduction of 0.23-0.35%. Compared to treated individuals, those with untreated *H. pylori* infection had a 23% higher incidence (HR 1.23; 95% CI, 1.13-1.34) and 40% higher mortality from CRC (HR 1.40; 95% CI, 1.24-1.58). These findings underscore a possible protective role of eradication therapy against colorectal cancer in *H. pylori*-positive individuals.

CONCLUSIONS

Altogether, these studies further highlight the role of *H. pylori* eradication in the prevention of gastric neoplasia. However, older patients and those with persistent immune dysfunction remain at risk despite successful eradication. Advances in predictive tools and insights into

‘spontaneous’ eradication call for tailored approaches to postoperative care after gastric cancer surgery. Reflecting this, the recent MAPS guidelines recommend eradication for all patients with gastric neoplasia following endoscopic or surgical therapy. In patients with MALT lymphoma, new research is needed to further elucidate the role of eradication in *H. pylori*-negative patients, as well as to address the global threat of antibiotic resistance. Recent studies suggest the causality between *H. pylori* infection and colorectal cancer; however, there remains the need to explain the exact role of the infection as well as the effects of eradication on colorectal carcinogenesis.

Conflict of Interests

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Authors’ Contributions

JB screened the recently published literature and selected relevant articles. He supervised the writing of the article and critically reviewed the manuscript. MC performed the final selection of articles for inclusion, critically analyzed them, and wrote the original draft of the manuscript. Both authors approved the final version of the manuscript.

Data Availability Statement

All data supporting the findings of this study are included within the article and/or its supplementary materials.

Use of Artificial intelligence (AI)

No generative AI or AI-assisted technologies were used during the writing or development of this manuscript.

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REFERENCES

1. Pan KF, Li WQ, Zhang L, Liu WD, Ma JL, Zhang Y, Ulm K, Wang JX, Zhang L, Bajbouj M, Zhang LF, Li M, Vieth M, Quante M, Wang LH, Suchanek S, Mejías-Luque R, Xu HM, Fan XH, Han X, Liu ZC, Zhou T, Guan WX, Schmid RM, Gerhard M, Classen M, You WC. Gastric cancer prevention by community eradication of *Helicobacter pylori*: a cluster-randomized controlled trial. *Nat Med* 2024; 30: 3250-3260.
2. Jung YS, Tran MTX, Park B, Moon CM. Preventive Effect of *Helicobacter pylori* Treatment on Gastric Cancer Incidence and Mortality: A Korean Population Study. *Gastroenterology* 2025; S0016-5085(25)00607-9.
3. Lewis D, Jimenez L, Mansour MH, Horton S, Wong WWL. A Systematic Review of Cost-Effectiveness Studies on Gastric Cancer Screening. *Cancers (Basel)* 2024; 16: 2353.
4. Lee YC, Chiang TH, Chiu HM, Su WW, Chou KC, Chen SL, Yen AM, Fann JC, Chiu SY, Chuang SL, Chen YR, Chen SD, Hu TH, Fang YJ, Wu MS, Chen TH, Yeh YP; Collaborators of Taiwan Community-based Integrated Screening Group. Screening for *Helicobacter pylori* to Prevent Gastric Cancer: A Pragmatic Randomized Clinical Trial. *JAMA* 2024; 332: 1642-1651.
5. Mulder DT, O’Mahony JF, Sun D, van Duuren LA, van den Puttelaar R, Harlass M, Han W, Huang RJ, Spaander MCW, Ladabaum U, Lansdorp-Vogelaar I. The Optimal Age of *Helicobacter pylori* Screen-and-Treat for Gastric Cancer Prevention in the United States. *Helicobacter* 2025; 30: e70039.
6. Okamura T, Ito A, Iwaya Y, Nagaya T, Hirayama A, Ota H, Akamatsu T. Long-term evaluation of *Helicobacter pylori* screening in school health checkups: an 11-year study in Japan. *J Gastroenterol* 2025; 60: 696-704.
7. Ishibashi F, Okusa K, Tokai Y, Hirasawa T, Kawakami T, Mochida K, Yanai Y, Yokoi C, Hayashi Y, Ozawa SI, Uraushihara K, Minato Y, Nakanishi H, Ueyama H, Kataoka M, Toyama Y, Mizokami Y, Suzuki S. A mathematical simulation

- model to determine the optimal endoscopic screening strategy for detection of *H. pylori*-naïve gastric neoplasms. *Gastric Cancer* 2024; 27: 1078-1087.
8. Ishibashi F, Suzuki S, Kobayashi K, Tanaka R, Kawakami T, Mochida K, Nagai M, Ishibashi Y, Morishita T. Cost-effective endoscopic screening for gastric cancer in a cohort with low *Helicobacter pylori* prevalence. *J Gastroenterol Hepatol* 2024; 39: 2424-2431.
 9. Kim IH, Kang SJ, Choi W, Seo AN, Eom BW, Kang B, Kim BJ, Min BH, Tae CH, Choi CI, Lee CK, An HJ, Byun HK, Im HS, Kim HD, Cho JH, Pak K, Kim JJ, Bae JS, Yu JI, Lee JW, Choi J, Kim JH, Choi M, Jung MR, Seo N, Eom SS, Ahn S, Kim SJ, Lee SH, Lim SH, Kim TH, Han HS; Development Working Group for the Korean Practice Guideline for Gastric Cancer 2024 Task Force Team. Korean Practice Guidelines for Gastric Cancer 2024: An Evidence-based, Multidisciplinary Approach (Update of 2022 Guideline). *J Gastric Cancer* 2025; 25: 5-114.
 10. Na JH, Lee SY, Kim JH, Sung IK, Park HS. *Helicobacter pylori* Infection Status and Gastric Tumor Incidence According to the Year of Birth. *Gut Liver* 2024; 18: 457-464.
 11. Dinis-Ribeiro M, Libânio D, Uchima H, Spaander MCW, Bornschein J, Matysiak-Budnik T, Tziatzios G, Santos-Antunes J, Areia M, Chapelle N, Esposito G, Fernandez-Esparrach G, Kunovsky L, Garrido M, Tachei I, Link A, Marcos P, Marcos-Pinto R, Moreira L, Pereira AC, Pimentel-Nunes P, Romanczyk M, Fontes F, Hassan C, Bisschops R, Feakins R, Schulz C, Triantafyllou K, Carneiro F, Kuipers EJ. Management of epithelial precancerous conditions and early neoplasia of the stomach (MAPS III): European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter and Microbiota Study Group (EHMSG) and European Society of Pathology (ESP) Guideline update 2025. *Endoscopy* 2025; 57: 504-554.
 12. Fu Q, Yu H, Liu M, Chen L, Chen W, Wang Z, Li W. Effect of *Helicobacter pylori* eradication on gastric cancer risk in patients with intestinal metaplasia or dysplasia: a meta-analysis of randomized controlled trials. *Front Microbiol* 2025; 16: 1530549.
 13. Wiklund AK, Santoni G, Yan J, Radkiewicz C, Xie S, Birgisson H, Ness-Jensen E, von Euler-Chelpin M, Kauppila JH, Lagergren J. Risk of Gastric Adenocarcinoma After Eradication of *Helicobacter pylori*. *Gastroenterology* 2025; 169: 244-250.e1.
 14. Luo X, Qi S, Chen M, Gan T, Lv X, Yang J, Deng K. Maintaining *H. pylori* Negativity After Eradication Can Consolidate Its Benefit in Gastric Cancer Prevention: A Meta-Analysis. *Clin Transl Gastroenterol* 2024; 15: e00742.
 15. Mizukami K, Kodama M, Hirashita Y, Fukuda M, Ozaka S, Tsutsumi K, Sagami R, Fukuda K, Ogawa R, Murakami K. Predictors of the Development of Gastric Cancer in Post-*Helicobacter pylori* Eradication Patients Followed Up for More than 10 Years: A Histological, Serological, and Endoscopic Study. *Cancers (Basel)* 2025; 17: 552.
 16. Kodama M, Handa O, Sugimoto M, Kotachi T, Kobayashi M, Take S, Hoteya S, Mabe K, Murao T, Namikawa K, Kawai T, Murakami K; Research committee for the Establishment of Risk Evaluation of Gastric Cancer after *H. pylori* Eradication in Endoscopic Findings, The Japanese Society for Helicobacter Research, Japan. Endoscopic risk factors to inform early detection of gastric cancer after *Helicobacter pylori* eradication: Meta-analysis and systematic review. *DEN Open* 2025; 5: e70086.
 17. Kim MJ, Je Y, Chun J, Youn YH, Park H, Nahm JH, Kim JH. *Helicobacter pylori* Eradication Is Associated with a Reduced Risk of Metachronous Gastric Neoplasia by Restoring Immune Function in the Gastric Mucosa. *Helicobacter* 2025; 30: e70030.
 18. Lee S, Cho SJ, Chung H, Kim B, Oh MJ, Na YS, Lee JH, Kim J, Kim SG. Risk Assessment of Metachronous Gastric Neoplasm after Endoscopic Resection for Early Gastric Cancer According to Age at *Helicobacter pylori* Eradication. *Gut Liver* 2024; 18: 992-1001.
 19. Liu Y, Shang X, Du W, Shen W, Zhu Y. *Helicobacter Pylori* Infection as the Predominant High-Risk Factor for Gastric Cancer Recurrence Post-Gastrectomy: An 8-Year Multicenter Retrospective Study. *Int J Gen Med* 2024; 17: 4999-5014.
 20. Omori T, Takahashi T, Kurokawa Y, Masuzawa T, Akamaru Y, Motoori M, Saito T, Yamamoto K, Nishikawa K, Imamura H, Takeno A, Kawabata R, Fujiwara Y, Eguchi H, Doki Y. *Helicobacter pylori* prevalence and its spontaneous eradication rate after distal or proximal gastrectomy for gastric cancer: A multicenter prospective cohort study. *Ann Gastroenterol Surg* 2024; 9: 244-250.
 21. He QC, Huang ZN, Lv CB, Wu YH, Qiu WW, Ma YB, Wu J, Zheng CY, Lin GS, Li P, Wang JB, Lin JX, Lin M, Tu RH, Zheng CH, Huang CM, Cao LL, Xie JW. Effect of *Helicobacter pylori* infection on survival outcomes of patients undergoing radical gastrectomy after neoadjuvant chemotherapy: a multicenter study in China. *BMC Cancer* 2025; 25: 460.
 22. Hu C, Liu H, Hong B, Wang L, Wu Z, Xie W, Luo B, Cao D, Zhong Y, Liu Y, Gong W. *Helicobacter pylori* reversing the landscape of neoadjuvant immunotherapy for microsatellite stable gastric cancer: a multicenter cohort study. *BMC Med* 2025; 23: 230.
 23. Moraes FCA, Sobreira LER, Kelly FA, Rodríguez Burbano RM. Impact of *helicobacter pylori* infection status on outcomes among patients with gastric cancer treated with immune checkpoint inhibitors: A systematic review and meta-analysis. *Microb Pathog* 2025; 202: 107407.
 24. Sim JY, Chung HS, Kim SG, Cho SJ, Kim BK, Hong JS, Kim IH. Long-term Outcomes and Prognostic Factors of Gastric MALT Lymphoma. *J Gastric Cancer* 2024; 24: 406-419.
 25. Lv XH, Lu Q, Liu JH, Xia BH, Wang ZJ, Wang Z, Yang JL. Proportion and Characteristics of *Helicobacter Pylori* -Negative Gastric Mucosa-Associated Lymphoid Tissue Lymphoma: A Systematic Review and Meta-Analysis. *Clin Transl Gastroenterol* 2025; 16: e00781.
 26. Laoruangroj C, Habermann TM, Wang Y, King RL, Lester SC, Thompson CA, Witzig TE. Should All Patients With Stage IE Gastric Mucosa-Associated Lymphoid Tissue Lymphoma Receive Antibiotic Eradication Therapy for *Helicobacter pylori*? *JCO Oncol Pract* 2024; 20: 1103-1108.
 27. Wang P, Wang N, Han J, Ma H. Impact of *Helicobacter pylori* Antibiotic Resistance on Treatment Outcomes in Gastrointestinal Lymphomas: A Meta-Analysis. *Br J Hosp Med (Lond)* 2025; 86: 1-14.

28. Chen T, Han B, Cochran E, Chen G. *Helicobacter pylori* infection is associated with the development of sporadic colorectal carcinoma and colorectal adenomatous polyps. *Pathol Res Pract* 2024; 260: 155368.
29. Xu H, Zhang Y, Guo Y, Chen Y, Ju X, Guan X. Meta-analysis of the Correlation between *Helicobacter Pylori* Infection and the risk of Colorectal Neoplasia. *Altern Ther Health Med* 2024; 30: 92-97.
30. Frías-Ordoñez JS, Riquelme A, Marulanda-Fernandez H, Otero-Parra L, Urrego JA, Otero-Ramos E, Portillo-Miño JD, Regino WO. *Helicobacter pylori* and Colorectal Cancer: Meeting Sir Austin Bradford Hill's Causality Criteria. *Helicobacter* 2025; 30: e70024.
31. Liu Q, Sadr-Azodi O, Engstrand L, Fall K, Brusselaers N. *Helicobacter pylori* Eradication Therapy and the Risk of Colorectal Cancer: A Population-Based Nationwide Cohort Study in Sweden. *Helicobacter* 2024; 29: e70001.
32. Shah SC, Camargo MC, Lamm M, Bustamante R, Roumie CL, Wilson O, Halvorson AE, Greevy R, Liu L, Gupta S, Demb J. Impact of *Helicobacter pylori* Infection and Treatment on Colorectal Cancer in a Large, Nationwide Cohort. *J Clin Oncol* 2024; 42: 1881-1889.