Cancer Screening and Prevention **2024** vol. 3(4) | 227–229
DOI: 10.14218/CSP.2024.00007

Opinion

Eradication of *Helicobacter pylori* Reduces Gastric Cancer Risk by Preventing Gastric Mucosal Atrophy and Intestinal Metaplasia

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Received: November 13, 2024 | **Revised:** December 17, 2024 | **Accepted:** December 20, 2024 | **Published online:** December 30, 2024

The current situation of stomach cancer in China

Recent data from the global cancer database reveal that gastric cancer is the second most common malignant tumor in terms of both incidence and mortality in China.[1] Moreover, intestinal-type gastric cancer is the main type of gastric cancer reported in Chinese patients. Research suggests that the intestinal-type gastric cancer originates from the progression of atrophic gastritis, to intestinal metaplasia, and then dysplasia, with *Helicobacter pylori* (*H. pylori*) playing a crucial role in the process.[2] Approximately 4-5% of individuals infected with *H. pylori* in China ultimately develop gastric cancer.[3] Since the discovery of *H. pylori*, ongoing research has unveiled that intestinal-type gastric cancer is a preventable disease. Successful eradication of *H. pylori* is paramount in reducing the incidence of intestinal-type gastric cancer in China and globally. Early eradication of *H. pylori* has been shown to effectively lower the occurrence of intestinal-type gastric cancer.

In 1965, Pathologist Pekka Laurén from Finland categorized gastric cancer into two primary types based on histopathology: the intestinal type, characterized by differentiated adenocarcinoma prevalent in middle-aged and elderly individuals, and the diffuse type, which includes signet ring cell carcinoma or undifferentiated carcinoma more common in younger people.[4] Laurén's classification remains widely utilized in modern research.[4] Gastric cancer arises from a combination of factors, including *H. pylori* infection, genetic predisposition, and environmental influences.[5] *H. pylori* infection promotes the progression of gastritis to intestinal metaplasia, dysplasia, and eventually to intestinal-type gastric cancer.[2] Over the years, numerous studies have confirmed the efficacy of eradicating *H. pylori* in preventing gastric cancer.[6,7] Various domestic and international consensus guidelines underscore the critical role of *H. pylori* infection as a controllable risk factor in reducing the onset of gastric cancer.[8,9] This article will discuss the effectiveness of eradicating *H. pylori* in preventing the occurrence and development of gastric cancer.

The relationship between *H. pylori* infection and gastric cancer

In 1994, the World Health Organization classified *H. pylori* as a Type I carcinogen for gastric cancer, marking the first recognition of *H. pylori* infection as a causative factor in gastric cancer.[10] Multiple studies suggest that *H. pylori* infection plays a pivotal role in the Correa model of intestinal-type gastric cancer development, progressing from normal gastric mucosa through non-atrophic gastritis, atrophic gastritis, intestinal metaplasia, dysplasia, and finally to gastric cancer.[2] Epidemiological investigations demonstrate a positive correlation between *H. pylori* infection rates and gastric cancer incidence, with *H. pylori*-infected individuals facing a four- to six-fold increased risk of developing gastric cancer.[11,12]

The world's first meta-analysis on *H. pylori* eradication for gastric cancer prevention, published in 2014, revealed a 34% reduction in gastric cancer risk following eradication.[13] Building on this, the International Agency for Research on Cancer released the "Strategies to Combat Stomach Cancer" report, proposing *H. pylori* eradication as a preventive strategy against gastric cancer for the first time. However, the report emphasizes that implementing eradication strategies should be tailored to local conditions, considering factors such as disease burden, health resource priorities, cost-effectiveness, and potential adverse effects of large-scale eradication efforts.[14]

Japan has been at the forefront of gastric cancer prevention, initiating screening efforts 30 years ago and continuously refining screening methods.[15] In 2014, Japan introduced a roadmap to eradicate gastric cancer, designating *H. pylori* eradication as the primary defense against the disease, supplemented by screening and follow-up for high-risk groups as secondary defenses.[15] This comprehensive approach has significantly reduced gastric cancer incidence.[15] Moreover, a study in 2020 found that the probability of elderly individuals developing stomach cancer significantly decreases after eradicating *H. pylori*.[16]

Aligning with international consensus, China's consensus un-

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How to cite this article: Xu X, Hu Y, Lv N. Eradication of *Helicobacter pylori* Reduces Gastric Cancer Risk by Preventing Gastric Mucosal Atrophy and Intestinal Metaplasia. *Cancer Screen Prev* 2024;3(4):227–229. doi: 10.14218/CSP.2024.00007.

derscores *H. pylori* infection as a primary cause of gastric cancer in the country.[8,9] The consensus highlights that *H. pylori* eradication can decrease the risk of gastric cancer and serve as an effective prevention strategy.[8,9] In high-risk regions, *H. pylori* eradication also demonstrates significant cost-effectiveness.

Eradicating *H. pylori* to prevent gastric cancer

Research on the relationship between *H. pylori* and gastric cancer continues to grow, with increasing evidence supporting the effectiveness of *H. pylori* eradication in preventing gastric cancer. The latest meta-analysis of randomized controlled trials on *H. pylori* eradication reveals promising results: asymptomatic "healthy individuals" who undergo *H. pylori* eradication can reduce their risk of developing gastric cancer by 46%, while eradication among patients following endoscopic submucosal dissection lowers the risk of metachronous gastric cancer by 51%.[6]

A study from Hong Kong tracked 73,237 individuals who underwent *H. pylori* eradication for an average of 7.6 years, showing a significant reduction in gastric cancer risk, particularly among those aged 60 and above, with a more than 50% decrease in incidence ten years after eradication.[17] Additionally, a report from South Korea found that individuals with a family history of gastric cancer who received *H. pylori* treatment had a 55% lower risk of developing gastric cancer compared to the placebo group. Further analysis demonstrated a 73% decrease in gastric cancer risk in the eradication group compared to the persistent infection group.[18] Korean scholars also found that *H. pylori*-positive early gastric cancer patients who underwent eradication after endoscopic submucosal dissection (median follow-up of 5.9 years) experienced approximately a 50% reduction in the risk of metachronous gastric cancer.[19] These studies indicate the substantial preventive effect of *H. pylori* eradication in high-risk populations for gastric cancer.

The duration of follow-up is crucial in assessing the preventive impact of *H. pylori* eradication on gastric cancer incidence. Studies have shown a positive correlation between eradication and length of follow-up, with risk reductions of 29%, 39%, and 52% observed after eight, 15, and 22 years, respectively.[20] Projections indicate a potential 65% decrease in gastric cancer risk after 30 years of follow-up.

The midterm report from a large-scale intervention study conducted on Mazu Island, Taiwan, published in 2020, corroborates these findings. The report revealed that after five years of *H. pylori* eradication, the population's risk of gastric cancer decreased by approximately 25%; after a 12-year follow-up, the risk decreased by 53%; and projections estimate that by 2025, with a 21-year follow-up, the risk of gastric cancer could decrease by 68%.[21] By implementing *H. pylori* eradication as a primary preventive measure, the risk of developing gastric cancer can be reduced by two-thirds. When combined with other primary prevention measures (e.g., reducing salt intake, quitting smoking, increasing consumption of fresh vegetables and fruits) and secondary prevention measures, it is estimated that 70%–80% of gastric cancer cases can be prevented.[21]

The importance of widespread screening and *H. pylori* eradication is clear in reducing gastric cancer incidence. Early and comprehensive eradication efforts could make this cancer a rare occurrence, significantly lowering associated mortality and achieving the goal of eliminating the threat posed by gastric cancer.

In summary, approximately 90% of gastric cancers worldwide are linked to *H. pylori* infection, underscoring the significance of *H. pylori* eradication in preventing gastric cancer.[8] Previous reports suggested that *H. pylori* infection might be negatively correlated with certain diseases, including gastroesophageal reflux disease, inflammatory bowel disease, and asthma.[22–24] This raised concerns among some scholars that eradicating *H. pylori* could eliminate its "protective effect" against these conditions. However, recent research has clarified that *H. pylori* eradication does not increase the risk of gastroesophageal reflux disease, metabolic syndrome, or autoimmune diseases such as asthma and inflammatory bowel disease. The concept of *H. pylori*'s "protective effect" has been largely refuted.[8] Furthermore, chronic inflammation of the gastric mucosa caused by *H. pylori* infection can lead to imbalances in the gastric microbiota. Eradication of *H. pylori* has been shown to restore the gastric microbial composition to a state similar to that of uninfected individuals. While *H. pylori* eradication may temporarily disrupt intestinal microbiota diversity, studies indicate that intestinal microbiota diversity typically returns to normal within two to six months post-eradication.[8] Therefore, the overall benefits of eradicating *H. pylori* far outweigh any potential drawbacks.

By prioritizing *H. pylori* eradication as a critical primary preventive measure against gastric cancer, China can address its high incidence rates of both gastric cancer and *H. pylori* infection. Comprehensive prevention strategies, including lifestyle adjustments, antioxidant supplementation, and targeted screening and monitoring of high-risk individuals, can significantly reduce these risks. This proactive approach effectively combats intestinal-type gastric cancer and contributes to improved public health outcomes.

Acknowledgments

None.

Funding

This work was supported by the National Science and Technology Award Reserve Cultivation Project (20192AEI91008), the First Affiliated Hospital of Nanchang University Clinical Research and Cultivation Project (YFYLCYJPY202002), the Key Laboratory Project of Digestive Diseases in Jiangxi Province (2024SSY06101), and the Jiangxi Clinical Research Center for Gastroenterology (20223BCG74011).

Conflict of interest

One of the authors, NL, has been an editorial board member of *Cancer Screening and Prevention* since March 2022. The authors have no other conflict of interest to note.

Author contributions

Manuscript writing (XX, YH) and revision (NL). All authors have approved the final version and publication of the manuscript.

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