Cancer Screening and Prevention **2025** vol. 4(1) | 61–63
DOI: 10.14218/CSP.2024.00008S

Letter to the Editor

Eradicating *Helicobacter pylori* Reduces Gastric Cancer Risk: New Evidence

Ye Chen[1*] and Bingyun Lu[2]

[1]*Integrative Microecology Clinical Center, Shenzhen Hospital, Southern Medical University, Shenzhen, Guangdong, China;* [2]*Department of Gastroenterology, Shenzhen Hospital, Southern Medical University, Shenzhen, Guangdong, China*

Received: December 10, 2024 | **Revised:** January 24, 2025 | **Accepted:** February 12, 2025 | **Published online:** March 03, 2025

Dear Editors,

Gastric cancer (GC) is a prevalent digestive tract tumor. The Global Cancer Statistics Report (GLOBOCAN 2020) reveals 1,089,103 new cases globally, ranking fifth in incidence and fourth in mortality, with a case fatality rate of nearly 0.7 (769,000/1,089,000).[1] If uncontrolled, GC could see 1.8 million new cases and 1.3 million deaths by 2040, significantly increasing the disease burden.[2] *Helicobacter pylori* (*H. pylori*) infection is a critical risk factor for GC, with strong evidence linking it to non-cardia gastric cancer.[3,4] However, its association with cardia gastric cancer remains inconsistent, particularly in Western populations where correlations are often absent or negative. In contrast, East Asian studies frequently show an increased cardia cancer risk with *H. pylori* infection.[5] Eradicating *H. pylori* is the most definitive and controllable factor in preventing gastric cancer, as shown by multiple clinical trials (Table 1),[4,6–11] and meta-analyses have confirmed this conclusion.[5,12–14] A meta-analysis of 10 global, randomized controlled trials observed that *H. pylori* eradication could decrease gastric cancer incidence (risk ratio = 0.54, 95% confidential interval (CI): 0.40–0.72) and mortality (risk ratio = 0.61, 95% CI: 0.40–0.92).[12] Another meta-analysis recruiting eight randomized controlled studies and 16 cohort studies reached a similar conclusion, indicating a 46% reduction in gastric cancer risk.[14] However, most studies included in these two meta-analyses come from East Asia, particularly China, where the baseline risk for healthy populations is relatively high. Additionally, many studies have an insufficient scale, leading to limited combined events.

A recently published article in Nature Medicine has provided new evidence. Pan *et al*.[8] designed a prospective, randomized, controlled study. Starting in 2011 in Linqu, Shandong, this study followed 180,284 individuals aged 25–54 for up to 11.8 years. Participants with positive C13 urea breath test results were randomly assigned to undergo a standard 10-day quadruple therapy for *H. pylori* eradication (with 20 mg omeprazole, 750 mg tetracycline, 400 mg metronidazole, and 300 mg bismuth citrate). The control group received symptom relief treatment once daily using omeprazole and bismuth citrate. Over the 11.8 years of follow-up, 1,035 new gastric cancer cases were recorded. An intention-to-treat analysis revealed a significant decline in gastric cancer incidence among individuals who received anti-*H. pylori* therapy (hazard ratio 0.86). There was a significant decrease in those who successfully eradicated *H. pylori* using the quadruple treatment (hazard ratio = 0.81). Subgroup analysis suggested that successfully eradicating *H. pylori* reduced the incidence (hazard ratio = 0.65) and mortality (hazard ratio = 0.57) of gastric cancer among individuals under 45. However, this reduction was only significant in the non-cardia gastric cancer subtype. For individuals aged 45 and above, the effect of *H. pylori* eradication treatment on the incidence and mortality of gastric cancer was insignificant. However, the cumulative incidence curves indicated that the group receiving anti-*H. pylori* treatment had lower incidence and mortality rates. Throughout the trial, the incidence of moderate adverse events within the anti-*H. pylori* treatment group was only 1.8%. No serious intolerance events were observed. This is the largest-scale follow-up interventional study on *H. pylori* to date. It confirms the importance of starting large-scale *H. pylori* screening and treatment within high-risk community settings immediately after reaching adulthood. These findings remain significantly consistent with the interventional trials undertaken in Changle, Fujian, with a 26.5-year follow-up,[10] which reported a 43% reduced risk of GC after *H. pylori* treatment.

The study by Pan *et al*.[8] has clarified the effectiveness and feasibility of *H. pylori* eradication for gastric cancer prevention in large-scale community populations and supports the implementation of *H. pylori* screening and treatment from early adulthood as an important public health policy in high-incidence areas of GC. The current research was conducted in high-incidence gastric cancer populations within China, and it is not appropriate to apply these findings to Western populations with lower gastric cancer incidence rates. A cohort study in the South American region found that *H. pylori* therapy was not associated with a reduction in GC risk, possibly because of the minimal number of outcome events.[6] However, the risk of disease progression after *H. pylori* treatment was reduced by 41% in individuals who had precancerous gastric lesions at baseline. Recently, a large retrospective study from the United States evaluated the impact of *H. pylori* eradication

[*]**Correspondence to:** Ye Chen, Integrative Microecology Clinical Center, Shenzhen Hospital, Southern Medical University, Shenzhen, Guangdong 518000, China. ORCID: https://orcid.org/0000-0002-7964-7899. Tel: +86-0755-23360950, E-mail: yechen@smu.edu.cn

How to cite this article: Chen Y, Lu B. Eradicating *Helicobacter pylori* Reduces Gastric Cancer Risk: New Evidence. *Cancer Screen Prev* 2025;4(1):61–63. doi: 10.14218/CSP.2024.00008S.

Table 1. Clinical studies on *Helicobacter pylori* eradication for GC prevention

Authors	Study type	Region	Sample size	Intervention	Follow-up (years)	Primary endpoint	Results
Li *et al*,[9] 2019	Blinded randomized placebo controlled trial	China	3,365	*Helicobacter pylori* treatment; vitamin supplementation; garlic supplementation	22.3	GC incidence; GC mortality	The risk of GC incidence was reduced by 52% and the risk of gastric cancer mortality was reduced by 38%.
Kumar *et al*,[11] 2020	Retrospective cohort study	United States	371,813	*Helicobacter pylori* treatment	20	Gastric cancer incidence	The risk of GC was reduced among patients with confirmed eradication of *Helicobacter pylori* (sHR: 0.24, 95% CI: 0.15–0.41, $p < 0.001$)
Chiang *et al*,[7] 2020	Long-term cohort study	Taiwan, China	6,512	*Helicobacter pylori* treatment	14	GC incidence; GC mortality	The incidence of GC was reduced by 53% (95% CI: 30–69%, $p < 0.001$) and the mortality rate was reduced by 25% (95% CI: −14–51%, $p = 0.18$)
Piazuelo *et al*,[6] 2021	Prospective cohort study	United States	356	*Helicobacter pylori* treatment; placebo treatment	20	GC incidence	The GC risk was not reduced. Progression of the Correa score was reduced (OR: 0.59, 95% CI: 0.38–0.93)
Yan *et al*,[10] 2022	Randomized controlled trial	China	/	*Helicobacter pylori* treatment; placebo treatment	26.5	GC incidence; GC mortality	The incidence of GC was reduced (HR: 0.57, 95% CI: 0.33–0.98)
Li *et al*,[4] 2023	retrospective cohort study	United States	29,543	*Helicobacter pylori* treatment	21	NCGA incidence	The incidence of NCGA was reduced after a follow-up of ≥eight years (sHR: 0.37, 95% CI: 0.14-0.97).
Pan *et al*,[8] 2024	Cluster-randomized controlled trial	China	180,284	*Helicobacter pylori* treatment; Symptom alleviation treatment	11.8	GC incidence	The incidence of GCr was reduced (HR: 0.86, 95% CI: 0.74–0.99)

CI, confidential interval; GC, gastric cancer; HR, hazard ratio; sHR, sub-hazard ratio.

treatment on the incidence of non-cardia gastric adenocarcinoma (NCGA).[4] Compared to untreated *H. pylori*-positive individuals, treated individuals had a significantly decreased adjusted sub-distribution hazard ratio for NCGA after eight years (0.37, 95% CI: 0.14–0.97). Therefore, *H. pylori* eradication treatment has a sustained protective effect on NCGA. This study provides a scientific basis for implementing *H. pylori* screening and treatment strategies in regions with low incidence of gastric cancer, like the United States.

Moreover, *H. pylori* eradication in high-incidence areas of gastric cancer demonstrates significant cost-effectiveness. Wang *et al*.[15] compared various strategies for GC prevention and found that *H. pylori* eradication therapy is a cost-effective strategy to reduce the gastric cancer burden in the long run. In this research, annual endoscopic screening was the most effective for the general population, but it was less cost-effective compared to *H. pylori* eradication, with costs exceeding 70,000 yuan per gained quality-adjusted life year. Similarly, European SAPEA (Science Advice for Policy by European Academies) experts do not recommend annual gastroscopy for gastric cancer screening. Instead, they regard *H. pylori* eradication as the most viable solution for reducing GC incidence in Europe.[16] Although nationwide endoscopic screening does not provide a cost-effective advantage, combining *H. pylori* eradication therapy with screening for risk subgroups may improve the balance between cost and effectiveness. In summary, we recommend implementing a "screen and treat" strategy for *H. pylori* in populations from high-incidence areas of GC, while adopting a "test and treat" strategy in low-incidence areas. In addition to *H. pylori* screening, improving the rate of *H. pylori* eradication is also an important strategy for gastric cancer prevention and control. *H. pylori* infection has a familial clustering tendency and can be transmitted among family members. Therefore, we emphasize the management of *H. pylori* at the family level to reduce the risk of reinfection.[17] Future studies aimed at comparing the *H. pylori* eradication benefits in various gastric cancer risk populations can improve the precise prevention of gastric cancer. Meanwhile, better screening models for accurately differentiating the high-risk levels of gastric cancer populations will globally advance screening efforts.

Acknowledgments

None.

Funding

This research was supported by The Science and Technology Project of Shenzhen under Grant No. KCXFZ20211020163558024.

Conflict of interest

Prof. Ye Chen has been an editorial board member of *Cancer Screening and Prevention* since March 2022. The authors declare that they have no other conflict of interests.

Author contributions

Article design, writing (YC), and literature review (BL). All authors have read and approved the final manuscript.

References

[1] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, *et al*. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021;71(3):209–249. doi:10.3322/caac.21660, PMID: 33538338.

[2] Morgan E, Arnold M, Camargo MC, Gini A, Kunzmann AT, Matsuda T, *et al*. The current and future incidence and mortality of gastric cancer in 185 countries, 2020-40: A population-based modelling study. EClinicalMedicine 2022;47:101404. doi:10.1016/j.eclinm.2022.101404, PMID:35497064.

[3] de Martel C, Georges D, Bray F, Ferlay J, Clifford GM. Global burden of cancer attributable to infections in 2018: a worldwide incidence analysis. Lancet Glob Health 2020;8(2):e180–e190. doi:10.1016/S2214-109X(19)30488-7, PMID:31862245.

[4] Li D, Jiang SF, Lei NY, Shah SC, Corley DA. Effect of Helicobacter pylori Eradication Therapy on the Incidence of Noncardia Gastric Adenocarcinoma in a Large Diverse Population in the United States. Gastroenterology 2023;165(2):391–401.e2. doi:10.1053/j.gastro.2023.04.026, PMID:37142201.

[5] Yang L, Kartsonaki C, Yao P, de Martel C, Plummer M, Chapman D, *et al*. The relative and attributable risks of cardia and non-cardia gastric cancer associated with Helicobacter pylori infection in China: a case-cohort study. Lancet Public Health 2021;6(12):e888–e896. doi:10.1016/S2468-2667(21)00164-X, PMID:34838195.

[6] Piazuelo MB, Bravo LE, Mera RM, Camargo MC, Bravo JC, Delgado AG, *et al*. The Colombian Chemoprevention Trial: 20-Year Follow-Up of a Cohort of Patients With Gastric Precancerous Lesions. Gastroenterology 2021;160(4):1106–1117.e3. doi:10.1053/j.gastro.2020.11.017, PMID:33220252.

[7] Chiang TH, Chang WJ, Chen SL, Yen AM, Fann JC, Chiu SY, *et al*. Mass eradication of *Helicobacter pylori* to reduce gastric cancer incidence and mortality: a long-term cohort study on Matsu Islands. Gut 2021;70(2):243–250. doi:10.1136/gutjnl-2020-322200, PMID:32792335.

[8] Pan KF, Li WQ, Zhang L, Liu WD, Ma JL, Zhang Y, *et al*. Gastric cancer prevention by community eradication of Helicobacter pylori: a cluster-randomized controlled trial. Nat Med 2024;30(11):3250–3260. doi:10.1038/s41591-024-03153-w, PMID:39079993.

[9] Li WQ, Zhang JY, Ma JL, Li ZX, Zhang L, Zhang Y, *et al*. Effects of Helicobacter pylori treatment and vitamin and garlic supplementation on gastric cancer incidence and mortality: follow-up of a randomized intervention trial. BMJ 2019;366:l5016. doi:10.1136/bmj.l5016, PMID:31511230.

[10] Yan L, Chen Y, Chen F, Tao T, Hu Z, Wang J, *et al*. Effect of Helicobacter pylori Eradication on Gastric Cancer Prevention: Updated Report From a Randomized Controlled Trial With 26.5 Years of Follow-up. Gastroenterology 2022;163(1):154–162.e3. doi:10.1053/j.gastro.2022.03.039, PMID:35364066.

[11] Kumar S, Metz DC, Ellenberg S, Kaplan DE, Goldberg DS. Risk Factors and Incidence of Gastric Cancer After Detection of Helicobacter pylori Infection: A Large Cohort Study. Gastroenterology 2020;158(3):527–536.e7. doi:10.1053/j.gastro.2019.10.019, PMID:31654635.

[12] Ford AC, Yuan Y, Moayyedi P. Helicobacter pylori eradication therapy to prevent gastric cancer: systematic review and meta-analysis. Gut 2020;69(12):2113–2121. doi:10.1136/gutjnl-2020-320839, PMID:32205420.

[13] Lei WY, Lee JY, Chuang SL, Bair MJ, Chen CL, Wu JY, *et al*. Eradicating Helicobacter pylori via (13)C-urea breath screening to prevent gastric cancer in indigenous communities: a population-based study and development of a family index-case method. Gut 2023;72:2231–2240. doi:10.1136/gutjnl-2023-329871, PMID:37197905.

[14] Lee YC, Chiang TH, Chou CK, Tu YK, Liao WC, Wu MS, *et al*. Association Between Helicobacter pylori Eradication and Gastric Cancer Incidence: A Systematic Review and Meta-analysis. Gastroenterology 2016;150(5):1113–1124.e5. doi:10.1053/j.gastro.2016.01.028, PMID:26836587.

[15] Wang Z, Han W, Xue F, Zhao Y, Wu P, Chen Y, *et al*. Nationwide gastric cancer prevention in China, 2021-2035: a decision analysis on effect, affordability and cost-effectiveness optimisation. Gut 2022;71(12):2391–2400. doi:10.1136/gutjnl-2021-325948, PMID:35902213.

[16] Leja M. Where are we with gastric cancer screening in Europe in 2024? Gut 2024;73(12):2074–2082. doi:10.1136/gutjnl-2024-332705, PMID:39237127.

[17] Zhou XZ, Lyu NH, Zhu HY, Cai QC, Kong XY, Xie P, *et al*. Large-scale, national, family-based epidemiological study on Helicobacter pylori infection in China: the time to change practice for related disease prevention. Gut 2023;72(5):855–869. doi:10.1136/gutjnl-2022-328965, PMID:36690433.