SOUNDING BOARD

Helicobacter pylori Screen-and-Treat Programs for Gastric Cancer Prevention — IARC Working Group Report

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Gastric cancer is the fifth leading cause of cancer-related death worldwide, and it will remain a major global public health problem for generations to come, despite its decreasing incidence, owing to the aging and growth of the world population.[1,2] The incidence of gastric cancer varies widely across world regions, with Asia, Europe, Latin America, and the Caribbean having the highest incidence (Fig. 1).[3] The largest relative increases in the absolute numbers of new cases of gastric cancer and corresponding deaths are projected to occur in countries with a low or medium Human Development Index level and in regions where the incidence of gastric cancer is currently low, which underscores the urgent need for greater global investment in gastric cancer prevention.[1]

In 1994, the World Health Organization's International Agency for Research on Cancer (IARC) Monographs program classified *Helicobacter pylori* infection as carcinogenic to humans[4] — more than a decade after the bacterium was discovered.[5] The classification established gastric cancer as largely an infection-caused disease, paving the way for prevention strategies that involve treating the infection.

In 2013, a working group was convened by the IARC to evaluate *H. pylori* eradication as a strategy for gastric cancer prevention.[6] The working group concluded that "[t]he continuing high global burden of gastric cancer and the feasibility of treating its principal cause thus make it a logical target for intervention" and called for increased public health investment in gastric cancer control. Although the working group acknowledged evidence from clinical trials that supports treating *H. pylori* infection as an effective preventive strategy, it also highlighted remaining uncertainties, particularly those regarding the generalizability of the results, cost-effectiveness, and possible adverse consequences of such programs.[6] It was therefore recommended that countries consider implementing population-based *H. pylori* screen-and-treat programs, accompanied by scientific assessment of their processes, feasibility, effectiveness, and potential harms.

Other international guidelines and consensus reports that emphasize patient-level management of *H. pylori* infection[7,8] also recommend eradication, ideally before the development of precancerous lesions, owing to the potential residual risk, especially in high-risk groups. Because *H. pylori* eradication substantially reduces but does not eliminate cancer risk, population-based screen-and-treat programs do not obviate the need for continued guideline-directed clinical management. Such programs are seen as key tools for gastric cancer prevention in European Union countries and have been endorsed in Europe's Beating Cancer Plan and in subsequent recommendations on the prevention of gastric cancer.[9,10]

However, despite the existence of these guidelines and recommendations, implementation has been met with hesitation and limited action. Only three population-level *H. pylori* treatment programs — in the Matsu Islands,[11] indirectly in Japan through national insurance coverage of *H. pylori* treatment,[12] and in Bhutan[13] — have been implemented. Countries such as China, Japan, and South Korea have continued to prioritize gastric cancer control through national or regional endoscopic screening programs. Although these programs

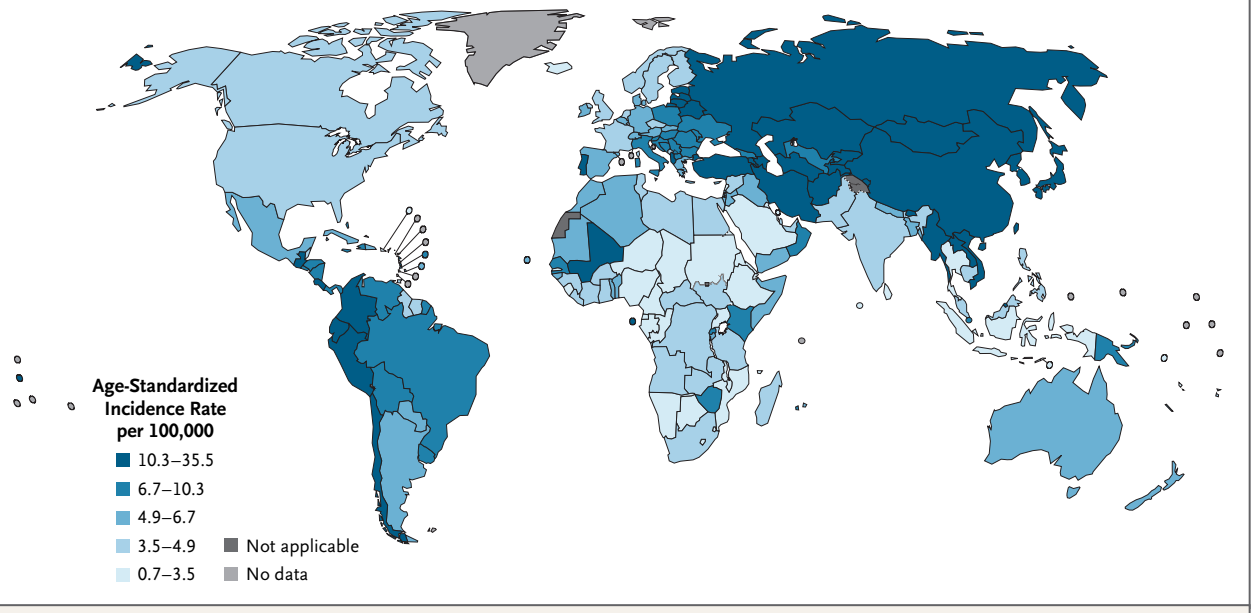

Figure 1. Age-Standardized Incidence Rates of Gastric Cancer among Men and Women in 2022 According to Country.
Adapted from Ferlay et al.[3]

have shown mortality benefits and strong public acceptance, their high cost and infrastructure demands limit broader applicability. By contrast, *H. pylori* screen-and-treat strategies offer a more scalable, cost-effective, alternative approach for wider implementation. The inaction and slow progress in global gastric cancer prevention may be attributable to a lack of guidance on implementation of such programs, both at the population-level and in pilot approaches, in regions with various levels of disease burden and resources.

2025 IARC WORKING GROUP REPORT

In December 2023, the IARC set up a working group comprising an international, interdisciplinary panel of experts with the aim of developing globally applicable guidance on best practices for implementing population-based *H. pylori* screen-and-treat strategies in adult populations to prevent gastric cancer. In total, 35 experts and two ad hoc contributors from 20 countries and territories across six continents contributed to the 2025 IARC Working Group meeting and report.[14]

The IARC Working Group report was structured to address the key aspects that need to be incorporated when designing *H. pylori* screen-and-treat strategies as a gastric cancer prevention program. To make the guidance globally applicable, the scope of the report covered all the regions of the world that have varying Human Development Index levels and background burdens of the disease.

The report includes chapters on the global epidemiologic characteristics of gastric cancer and *H. pylori* infection and the scientific evidence on the effect of the strategies for gastric cancer prevention, as well as a summary of currently available guidelines on the strategies. The report also provides a comprehensive map covering ongoing gastric cancer prevention efforts worldwide and highlights progress, gaps, and future priorities.[15] Subsequent chapters detail the programmatic aspects of the strategies, including assessment of needs and readiness, the selection of appropriate *H. pylori* screening methods and treatment regimens for a population-based program, and adherence to the principles of organized screening programs for effective and equitable outcomes. One of the most notable features of the report is the chapter outlining how to follow antibiotic stewardship principles and monitor antibiotic use and resistance for such programs. Finally, the report also summarizes approaches

to maximize the benefits against the costs of these programs.

2025 IARC WORKING GROUP MEETING

In February 2025, the working group convened at the IARC in Lyon, France, to refine the key summary elements of each chapter for inclusion in the report as the final consensus version. The working group first emphasized the importance of global action to implement resource-appropriate prevention strategies, given the expected demographic-driven rise in gastric cancer burden in low-resource settings. The meeting continued with a discussion of the results from a systematic review of randomized trials showing that eradication of *H. pylori* infection in otherwise healthy persons reduced the incidence of gastric cancer by 36% and mortality by 22%, with numbers needed to treat of 228 and 812, respectively.[16] The corresponding numbers needed to screen were estimated to be 456 and 1624 to prevent one case of gastric cancer and one gastric cancer–related death, respectively, in high-risk populations.

The available clinical-trial evidence also indicated that *H. pylori* eradication reduced the incidence of dyspepsia and health care costs by a mean of U.S.$117 over the course of 10 years.[17] In addition, three large long-term trials showed no increase in the risk of esophageal cancer.[18] The balance of evidence suggests that *H. pylori* eradication does not increase the risk of gastroesophageal reflux disease.[18]

A major session was dedicated to showcasing ongoing and planned regional efforts of gastric cancer prevention according to world region. The need for preparatory steps before the implementation of an *H. pylori* screen-and-treat program was emphasized. These steps include setting up registries to collect local information on *H. pylori* burden, efficacy of various treatment options, and antibiotic resistance. Other topics included the importance of population-based communication and awareness campaigns to increase adherence to *H. pylori* screen-and-treat programs and the value of international expert support in the design and implementation of local programs. The session also showed that it is possible to implement an *H. pylori* screen-and-treat approach that leads to highly successful outcomes.

IARC WORKING GROUP RECOMMENDATIONS

The members of the IARC Working Group collectively endorsed recommendations on best practices for implementing population-based *H. pylori* screen-and-treat strategies to prevent gastric cancer. These recommendations are summarized here and in Table 1.

NEEDS AND READINESS ASSESSMENT

An assessment of the needs and readiness for an *H. pylori* screen-and-treat program is critical before it is implemented. The working group recommended making the implementation of a population-based *H. pylori* screen-and-treat program a public health priority in intermediate-to-high-risk areas (age-standardized incidence rate of gastric cancer, ≥10 cases per 100,000 person-years). Even in low-incidence areas (age-standardized incidence rate, <10 cases per 100,000 person-years), there are populations at risk that will benefit from *H. pylori* screen-and-treat programs. For successful implementation, sustainable funding, governance, and leadership, as well as additional infrastructure to support the overall implementation of the program, are required. Pilot projects need to be carried out before a full program is implemented, since they provide the best evidence for the local level of readiness.

CONSIDERATIONS FOR THE CHOICE OF *H. PYLORI* DETECTION METHOD

For population-based *H. pylori* screen-and-treat programs, noninvasive tests, including the ^{13}C-labeled urea breath test (^{13}C-UBT), the stool antigen test, and the serologic test, should be used. Considerations for the choice of testing include test performance and the prevalence of *H. pylori* infection in the target population as priorities, and the predictive value should be estimated when the results are interpreted in clinical practice. For population-wide implementation, additional considerations may include the availability of support systems for testing (such as cold-chain transportation of stool antigen test), participants' preferences regarding the test type, and economic factors. If the serologic test is chosen for screening, it should be validated locally to ensure that sensitivity and specificity exceed 90%, and a confirmatory ^{13}C-UBT or stool antigen test may be

Table 1. IARC Working Group Recommendations on Best Practices for Implementing Population-Based *Helicobacter pylori* Screen-and-Treat Strategies for Gastric Cancer Prevention.*

Key Areas	Recommendations
Needs and readiness assessment	Assessment of needs and readiness is critical before the implementation of an *H. pylori* screen-and-treat program. Sustainable funding, governance, and leadership are required for *H. pylori* screen-and-treat programs for gastric cancer prevention, and additional infrastructure will be required.
H. pylori screening methods	A population-based *H. pylori* screening program should use one or more of the three methods for *H. pylori* detection: ^{13}C-labeled urea breath test, the stool antigen test, and the serologic test. Considerations for the choice of screening test include the validation of test performance, the prevalence of *H. pylori* in the target population, and other factors, such as infrastructure, participants' preferences, and costs. Confirmation of the success of *H. pylori* eradication, if undertaken, should be based on the ^{13}C-labeled urea breath test or the stool antigen test given at least 4 (ideally 6) weeks after completion of anti–*H. pylori* therapy.
H. pylori treatment regimens	Participants with a positive screening result should receive information and counseling about the anticipated, generally mild adverse events and the importance of completing the full course of the treatment as prescribed. Participants with a positive screening result should be treated with appropriate *H. pylori* eradication regimens, as informed by local antibiotic resistance data and level of successful local *H. pylori* eradication. Bismuth-based quadruple therapy is recommended as first-line therapy because it is unaffected by clarithromycin resistance and can overcome metronidazole resistance.
Antibiotic stewardship	A population-based *H. pylori* screen-and-treat program for gastric cancer prevention should follow antibiotic stewardship principles and include a multidisciplinary group that monitors antibiotic use and resistance. The effect of increased exposure to antibiotics on the human microbiome, including the resistome, is not yet fully understood and warrants continued awareness, monitoring, and research. A vaccine against *H. pylori* would be the ideal solution to the problems associated with antibiotic use in the *H. pylori* screen-and-treat programs, although candidate vaccines are still in the preclinical stage of development. Further investment is needed to develop highly effective anti–*H. pylori* therapies.
Monitoring process and outcome measures	A population-based *H. pylori* screen-and-treat program for gastric cancer prevention should adhere to the principles of an organized screening program for effective and equitable outcomes across groups. The program must be supported by an information system for data collection and the generation of quality indicators. Quality indicators must be monitored to ensure and improve program effectiveness, equity, safety, and cost-effectiveness. To ensure equity, at-risk communities should be involved in the design and governance of the *H. pylori* screen-and-treat program.
Improving the cost–benefit performance	*H. pylori* screen-and-treat programs are cost-effective (and may be cost-saving) in high-risk populations and is likely to be cost-effective even in low-risk populations. Cost-effectiveness improves with higher risk of gastric cancer and other *H. pylori*–related diseases. The appropriateness of strategies (with respect to the target population, *H. pylori* detection methods, age of the participants, confirmatory tests, and choice of treatment) depends on the local context. Decision modeling should be considered when making recommendations for the context-appropriate strategy on the basis of the information collected from the pilot projects. Long-term follow-up data are needed to incorporate ancillary benefits and potential harms into decision modeling; these data may play an important role in finding the right balance of benefits, harms, and costs of *H. pylori* screen-and-treat programs.

* IARC denotes International Agency for Research on Cancer.

needed to distinguish current from past infections before treatment. To verify the success of eradication, the ^{13}C-UBT or stool antigen test is recommended at least 4 (ideally 6) weeks after completion of anti–*H. pylori* therapy to avoid potential false negative results.

CONSIDERATIONS FOR THE CHOICE OF TREATMENT REGIMEN

H. pylori infection is an infectious disease; therefore, the use of treatment regimens should be informed by local population-based surveillance data and national treatment guidelines to minimize the risk of antibiotic resistance. Participants should be informed about potential, generally mild adverse events; the importance of completing the full course of therapy as prescribed; and the fact that treatment is not uniformly effective in eradicating *H. pylori* infection or preventing gastric cancer. They should also be advised that participation in the program does not replace routine medical care. For an organized program, the primary goal should be to select a locally validated regimen with a proven eradication level exceeding 90%, for which bismuth-based quadruple therapy stands as a powerful option because it is unaffected by clarithromycin resistance and can overcome metronidazole resistance.

ANTIBIOTIC STEWARDSHIP

The results of a modeling exercise that was conducted by the working group using a best-case scenario were reassuring in that the proportional increase in antibiotic prescribing due to implementation of the program was relatively modest in most countries. However, if implemented without efforts to minimize antibiotic exposure, programs risk increasing antimicrobial resistance. Therefore, every effort should be made to maximize the chances of eradicating *H. pylori* infection and minimize antibiotic exposure, and the focus should be on providing the greatest benefit per dose of antibiotics used. The working group highlighted the importance of establishing an antibiotic stewardship program in advance, with oversight by a multidisciplinary group that monitors antibiotic use and resistance (Table S1 in the Supplementary Appendix). When a program is implemented, a priori metrics for treatment success should be established. *H. pylori* eradication levels should be assessed through systematic follow-up testing of a subgroup of treated participants to monitor treatment success. *H. pylori* strains from a subgroup of participants should be tested for antibiotic resistance before and after program implementation. Noting the limited evidence on the effect of increased antibiotic exposure on the human microbiome, including the resistome, as well as on the environment, the working group recommended continued awareness, monitoring, and research. Although the working group acknowledged the need for further investment in vaccine development, it placed equal emphasis on the importance of developing highly effective anti–*H. pylori* therapies that minimize ineffective antibiotic exposure.

PROCESS AND OUTCOME MEASURES FOR IMPROVING QUALITY AND EQUITY

Ensuring the quality and equity of *H. pylori* screen-and-treat programs across risk groups is a key consideration. The working group recommended applying the principles of organized screening programs and proposed a set of quality indicators, as outlined in Table S2, to monitor processes and outcomes of the programs. These indicators need to be collected and monitored through an information system at various stages of the program over time to improve effectiveness, equity, safety, and cost-effectiveness. An *H. pylori* screen-and-treat program has the greatest chance of being equitable if persons at the highest risk of *H. pylori* infection participate and are successfully treated.

HOW TO IMPROVE THE COST–BENEFIT PERFORMANCE

The working group concluded that population-based *H. pylori* screen-and-treat programs are cost-effective (and may be cost-saving) in high-risk populations and probably cost-effective even in low-risk populations (Fig. 2). Given that the effectiveness of strategies depends on the local context, the collection of information by means of pilot projects for decision modeling is essential for making context-appropriate strategies. In addition, decision modeling can be improved by incorporating long-term data on the proven ancillary benefits of reducing the risk of other important clinical conditions (e.g., peptic ulcer disease and its complications and dyspepsia) and on the potential harms related to antimicrobial resistance in order to balance the benefits and harms of *H. pylori* screen-and-treat programs.

CONCLUSIONS

The 2025 IARC Working Group report represents a comprehensive global effort to provide guidance on implementing population-based *H. pylori*

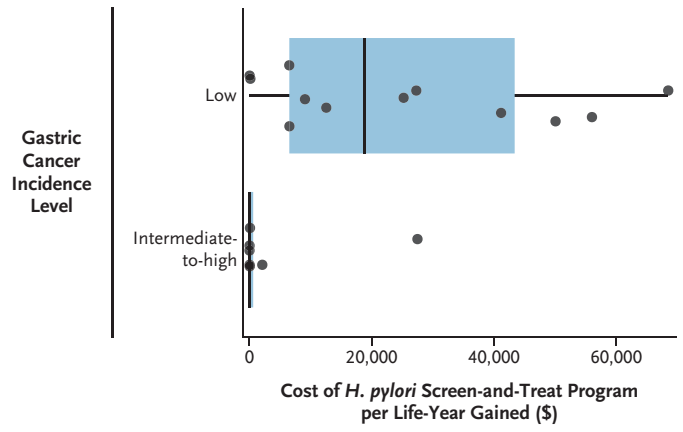

Figure 2. Costs of *H. pylori* Screen-and-Treat Programs per Life-Year Gained, Stratified According to Gastric Cancer Incidence Level.

Data are from cost-effectiveness analyses, as reviewed in individual studies.[19-22] An intermediate-to-high incidence rate was defined by an age-standardized incidence rate of at least 10 cases per 100,000 person-years, and a low incidence rate by an age-standardized incidence rate lower than 10 cases per 100,000 person-years. Studies showing cost savings are set at 0. The vertical lines indicate the median, the blue shading the interquartile range, and the solid circles the individual studies. The horizontal lines (whiskers) extend to the lowest and highest values within 1.5 times the interquartile range. Because the data for the intermediate-to-high-rate category are clustered, the whiskers are not visible. Adapted from the 2025 IARC Working Group report (chapter 9).[23]

screen-and-treat strategies as an organized program for gastric cancer prevention at the population level. Considering the growing global burden of gastric cancer, driven by shifting demographics and epidemiologic trends, the working group unanimously agreed that prevention remains the most effective and resource-appropriate strategy for reducing this burden globally. Implementation of *H. pylori* screen-and-treat strategies provides a key opportunity to address health inequalities, even in populations residing in areas traditionally considered to be at low risk for gastric cancer. Coordinated global efforts and sustainable investment, such as initiatives for the elimination of cervical cancer and viral hepatitis, are urgently needed to curb the anticipated growing burden of gastric cancer.

The views expressed by the authors who are affiliated with the International Agency for Research on Cancer (IARC) of the World Health Organization (WHO) are theirs alone, and they do not necessarily represent the decisions, policies, or views of the IARC, WHO, or European Union. The contributions of the authors who are affiliated with the National Institutes of Health (NIH) are considered works of the U.S. government; however, the findings and conclusions presented in this article are those of the authors and do not necessarily reflect the views of the NIH or the U.S. Department of Health and Human Services.

Supported in part by an intramural grant from the IARC and in part by the European Union under the EU4Health Program as part of the EUROHELICAN project.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank Ms. Viktoria Knaze (IARC) for project coordination and Dr. Beatrice Lauby-Secretan (IARC) for scientific advice.

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DOI: 10.1056/NEJMsb2515372