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ORIGINAL ARTICLE

Global and Regional Efforts in Preventing Gastric Cancer

EUROHELICAN—Accelerating Gastric Cancer Reduction Through *Helicobacter pylori* Eradication

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ABSTRACT

Background: Most gastric cancer cases are attributable to chronic *Helicobacter pylori (H. pylori)* infection and can theoretically be prevented. The objectives of the EUROHELICAN project were to assess the feasibility, acceptability, effectiveness, and adverse events of the *H. pylori* screen-and-treat program in younger adults aged 30 to 34 years, for the first time in Europe; to evaluate long-term effects of *H. pylori* eradication in middle-aged adults (starting from 45 years of age) previously enrolled for at least 5 years in the GISTAR study in Latvia, and to prepare the IARC expert Working Group Report on population-based *H. pylori* screen-and-treat strategies for gastric cancer prevention.

Methods: The study of *H. pylori* screen-and-treat in younger adults was conducted in the Community Healthcare Center Dr. Adolf Drolc Maribor following methodology prepared by the National Institute of Public Health of Slovenia. Assessment of possible effects of *H. pylori* screen-and-treat in the long term was conducted by following up on the long-running GISTAR study conducted by the Institute of Clinical and Preventive Medicine at the University of Latvia. A team of experts led by the Nantes University Hospital evaluated the study protocols and their progress at different stages. The IARC convened a Working Group of international experts to develop globally applicable guidance on best practices for implementing population-based *H. pylori* screen-and-treat strategies in adult populations to prevent gastric cancer.

Conclusions: Both studies received a positive evaluation at different stages of completion and were deemed appropriate for testing the feasibility of *H. pylori* screen-and-treat in a community health care setting and investigating possible adverse effects of the strategy in the long-term. The IARC expert group guidance report on the implementation of population-based *H. pylori* screen-and-treat strategies to prevent gastric cancer in adults will guide future primary gastric cancer prevention programs in Europe and beyond.

1 | Introduction

Gastric cancer is a disease with high morbidity and poor prognosis. It ranked as the fifth most diagnosed cancer and the fifth leading cause of cancer-related deaths worldwide in 2022 [1]. In absolute numbers, an estimated 969,000 new cases of gastric cancer (4.8% of all cancer cases) were diagnosed and 660,000 deaths from gastric cancer (6.8% of all cancer deaths) occurred in 2022. Eastern Europe ranks second after East Asia in the incidence of gastric cancer [2].

Gastric cancer incidence rates have been generally decreasing, but the absolute number of new gastric cancer cases is expected to increase because of demographic changes in populations (i.e., population growth and increasing longevity). Globally, the number of gastric cancer cases is predicted to increase by 87.5%, from an estimated 969,000 new cases in 2022 to 1.82 million in 2050, assuming current rates remain stable [3].

The World Health Organization's International Agency for Research on Cancer (IARC) classifies *H. pylori* as a Group 1 carcinogen, responsible for 89% of non-cardia gastric cancer [4, 5]. A recent review covering various time periods showed that the crude global prevalence of *H. pylori* infection between 2015 and 2022 was 44% in adults and 35% in children and adolescents [6]. The IARC estimated that 850,000 (4.3%) of all cancers diagnosed worldwide in 2020 were directly attributable to *H. pylori* infection. Of these *H. pylori*-attributable cancers, non-cardia gastric cancer (NCGC) accounted for 94%, cardia gastric cancer (CGC) for 4%, and gastric lymphoma for 2%. This cancer burden is higher than that of any other cancer caused by chronic infection, including human papillomavirus (730,000 attributable cases) and hepatitis B and C virus combined (550,000 attributable cases) [7]. The *H. pylori* strain, host genetic defined immune response, and some environmental factors (smoking, alcohol, and diet) define the pathway of active chronic gastritis to atrophy, intestinal metaplasia, and finally cancer, which can occur in up to 3% of those infected [8, 9].

We cannot predict which patients infected with *H. pylori* will remain at the stage of chronic gastritis (estimated at 80% of those infected) and which will develop peptic ulcer disease, gastric cancer, gastric MALT lymphoma, dyspepsia, or some extradigestive diseases such as idiopathic thrombocytopenic purpura (up to 20% of those infected) [10]. Several international and national guidelines advise eradicating *H. pylori* in all infected patients to prevent transmission and decrease the future incidence of *H. pylori*-induced disease, particularly gastric cancer [10–13]. The Kyoto global consensus on *H. pylori* gastritis supports the treatment of all patients with *H. pylori* infection, regardless of clinical symptoms [14].

In the latest meta-analysis [15], the relative risk of subsequent gastric cancer following eradication therapy compared to placebo or no eradication therapy was 0.64 (95% confidence interval (CI) 0.48–0.84). The number of patients needed to treat to prevent one case of gastric cancer was 228 (95% CI 158–514). *H. pylori* eradication was associated with a reduced risk of recurrent gastric adenocarcinoma in patients with *H. pylori* infection (relative risk 0.52; 95% CI 0.38–0.71). The number needed to treat was 18 (95% CI 14–30). This suggests that there is no "point of no return" for the prevention of gastric adenocarcinoma, provided that gastric adenocarcinoma has not already occurred before eradication therapy. There was no evidence that *H. pylori* eradication therapy increased the risk of esophageal cancer or reflux symptoms. The limitation of all the interventional studies is in the relatively short follow-up period. The longest follow-up of 26.5 years was in a study conducted by Yan et al. [16]. Participants receiving *H. pylori* treatment had a lower incidence of gastric cancer compared to their placebo counterparts (hazard ratio [HR] 0.57; 95% CI 0.33–0.98). More obvious risk reduction was observed among those young participants without premalignant gastric lesions at inclusion (HR 0.37; 95% CI 0.15–0.95).

Population-based *H. pylori*-screen-and-treat programs are being implemented in Japan through national insurance coverage of *H. pylori* treatment [17], as well as in Bhutan [18]. Population-based *H. pylori* screen-and-treat programs are also seen as important tools for gastric cancer prevention in the European Union, especially for countries with an intermediate and high burden of gastric cancer. These programs were endorsed in the recently announced Europe's Beating Cancer Plan and in subsequent recommendations on the prevention of gastric cancer from Science Advice for Policy by European Academies [19] and the European Council [20].

The EUROHELICAN project was launched in response to the calls for the need to establish gastric cancer prevention and screening programs in Europe and is co-funded by the EU. The objectives of the EUROHELICAN project were to: (1) assess the feasibility, acceptability, effectiveness, and adverse events of the *H. pylori* screen-and-treat program in younger adults aged 30 to 34 years, for the first time in Europe (Work package 4—WP 4); (2) evaluate long-term effects of *H. pylori* eradication in middle-aged adults (starting from 45 years of age) previously enrolled for at least 5 years in the GISTAR study in Latvia (WP 5); (3) evaluate the design, protocols, and progress of the studies team of experts led by the Nantes University Hospital, WP (3); and (4) prepare the IARC expert Working Group Report on population-based *H. pylori* screen-and-treat strategies for gastric cancer prevention (WP 6).

The following text will provide an overview of the project's structure, its work packages (dissemination, studies, evaluation, IARC guidance report), and a more detailed description of the design and methodology behind both studies.

2 | EUROHELICAN Project Design

The structure of the EUROHELICAN project is shown in Figure 1. Work packages (WP) 1, 2, and 4 were part of the *H. pylori* screen-and-treat implementation study conducted for the first time in Europe in younger adults aged 30 to 34 years in Slovenia. The study was coordinated by the Slovenian National Institute of Public Health (NIJZ), while the Community Health Center Dr. Adolf Drolc Maribor (CHC Maribor) was responsible for the practical implementation. Its objectives were to assess the feasibility, acceptance, effectiveness, and possible adverse consequences of a population-based *H. pylori* screen-and-treat strategy for gastric cancer prevention in Europe. WP2 was dedicated to raising public awareness on these topics. In WP 5, led by the Institute of Clinical and Preventive Medicine of the University of Latvia, the potential long-term effects of *H. pylori* test-and-treat were evaluated in middle-aged participants of the GISTAR study in Latvia, which is a cohort with a follow-up period reaching 10 years. Both field studies (WP 4 and 5) were evaluated by a group of experts from Nantes University Hospital (CHU-NANTES; WP 3) ensuring quality control and constructive feedback. Finally, in WP 6, the IARC organized an Expert Working Group to develop guidance for the implementation of

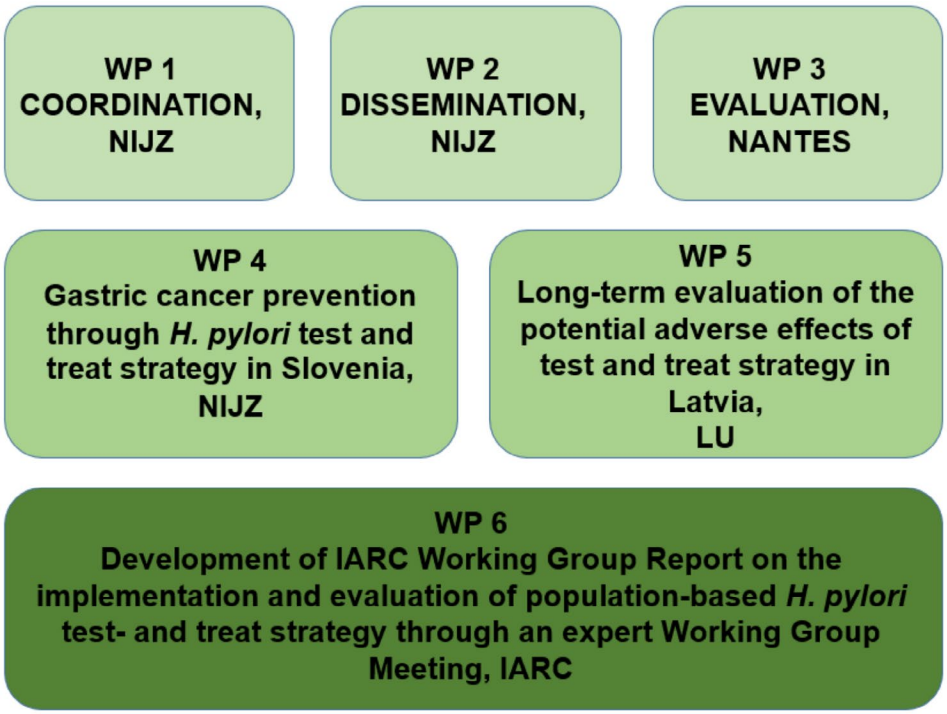

FIGURE 1 | Structure of the EUROHELICAN project.

population-based screen-and-treat strategies and the first ever recommendations for an impact evaluation strategy.

3 | Dissemination Strategies (WP2)

Raising public awareness about *H. pylori* infection, its relation to certain upper gastrointestinal diseases, and the possibility of preventing those diseases is of paramount importance. Without that and further education of the medical personnel and public, the success of screen-and-treat programs and studies is not possible. We used various media channels to reach the target group in Slovenia (30- to 34-year-olds). The NIJZ created graphics on social media websites and other digital channels for the purpose of communicating with different stakeholders and partners involved in dissemination. The primary channels were the NIJZ Facebook and Instagram accounts, as these modalities would reach a high number of individuals in the target age group. Paid campaigns were used to specifically target this group on TV and other media, as well as on city buses in Maribor. One of the stakeholders involved in dissemination activities was CHC Maribor, which disseminated the materials provided by the NIJZ (social media graphics, link to webpage with additional information, leaflets) through their channels and provided direct communication to their visitors and patients. CHC Maribor communicated with the target group on a local and regional level by using their social media accounts (Facebook), website and leaflets provided at their centers.

Additionally, NIJZ created press releases and articles that were published on the national level. The public, including potential participants, were able to access additional information about the project on the NIJZ and CHCM websites. Promotional materials and gifts for participants in Slovenia provided additional encouragement to participate and visibility for the project (e.g., pens, tote-bags).

The University of Latvia also used various channels to promote the project and increase awareness both among the public and medical professionals. Unlike the study in Slovenia, however, dissemination activities were not used to reach potential study participants, as participants recruited for the study conducted in Latvia were already part of an existing long-running study and so were contacted directly.

4 | Evaluation of the Studies (WP3)

The overall objective of the evaluation was to assess the project outputs and results with respect to the planned objectives and defined indicators. To fulfill this task, a dedicated consortium of experts representing the relevant project expertise and competences (gastroenterology, endoscopy, digestive oncology, microbiology, pathology, statistics, and methodology) was created, led by Nantes University Hospital (CHU-NANTES), and worked together with the coordinating teams of both studies. The evaluation was carried out at three levels: (1) the initial evaluation of both study protocols, including the assessment of the study design, its feasibility, as well as statistical and ethical aspects; (2) the interim evaluation of study progress, especially in terms of recruitment; and (3) the final evaluation report assessing the results of both studies, with respect to the predefined objectives.

Another objective of the evaluation process was to identify, at mid-term, the specific problems and challenges, with particular attention to the recruitment and study pathway of participants, in order to propose and discuss specific mitigation measures that could be put in place for implementation. Overall, the evaluation

was positive for both studies. The initial evaluation confirmed that the design of both studies adhered to the necessary standards. The mid-term analysis showed very good progress in the Latvian study, which was based on an existing study and so had a stronger foundation. As for the Slovenian study, although progressing well, insufficient recruitment was identified as an issue, which resulted in the introduction of several corrective measures. The final evaluation report concluded that both studies had reached their targets and fulfilled their objectives. The results of the studies provided important information about the conditions and challenges that should be anticipated when designing gastric cancer screening programs based on the *H. pylori* screen-and-treat strategy in the future.

5 | *H. pylori* Screen-And-Treat in Younger Adults (WP4)

The aim of the study was to assess the feasibility, acceptability, and effectiveness of implementing a *H. pylori* screen-and-treat strategy program in younger adults (aged 30–34 years) in Slovenia at the population level in a community health service setting. This is the first time that this type of assessment has been done in Europe. Other objectives of the study were: (1) to determine the profile of adverse events in treated participants and assess how this affects the results of *H. pylori* screen-and-treat; (2) to investigate the relationship between living conditions during childhood and the results of *H. pylori* screen-and-treat; and (3) to investigate the association between alcohol consumption and use of tobacco products and the results of the *H. pylori* screen-and-treat study.

The NIJZ designed the study (Figure 2) and created the questionnaires on risk factors in early childhood and harmful habits (alcohol consumption, tobacco use), developed the procedures for recruiting participants, and created invitation materials and set up the data entry system and platform that was used for quality assurance, monitoring, and evaluation. Local ethics approval (Slovenian Ethics approval 0120–12/2023/3) was obtained, and the study was registered internationally (EU PAS number of HMA-EMA RWD Catalogue: EUPAS107327, Study ID: 108428; ClinicalTrials.gov ID: NCT06216639, Protocol ID: EUROHELICAN01).

CHC Maribor compiled a list of registered patients who met the inclusion criteria. Randomization with the Monte Carlo method

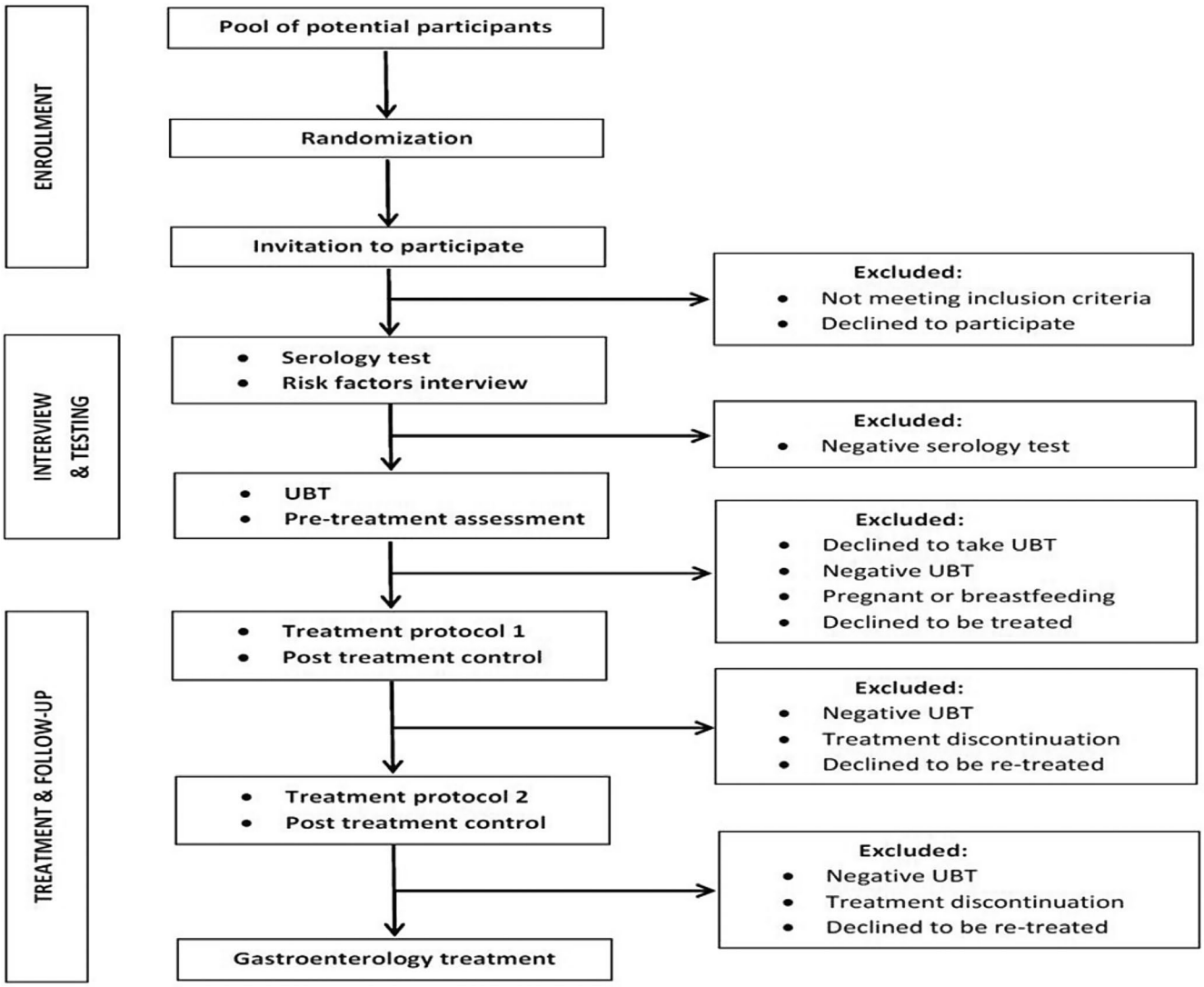

FIGURE 2 | EUROHELICAN study flowchart.

was used to prepare a protocol for inviting eligible persons. Based on the assumption of a 50% response rate, the initial list included 4000 individuals. Participants were excluded if they had a history of *H. pylori* treatment, partial or total resection of the stomach, as well as if they could not provide informed consent (e.g., cognitive disability). After the participant signed the informed consent form, a registered nurse interviewed the participant with predefined questions on family history of gastric cancer and other risk factors (smoking, alcohol), possible symptoms of infection with *H. pylori*, and medications used.

A two-step approach was used to determine *H. pylori* infection. First, locally validated IgG serology was used, and if positive, urea breath test (UBT) confirmation test was applied. If the UBT result was positive, the patient was referred to their family doctor for treatment in accordance with Slovenian and international recommendations. Patients received a high PPI 14-day bismuth-based regimen (Esomeprazole 40 mg BID, Amoxicillin 500 mg, Metronidazole 400 mg and Bismuth oxide 120 mg, all QID). If a person was allergic to penicillin, clarithromycin 500 mg BID was used instead. Patients were monitored for potential adverse effects during and after treatment by using a short questionnaire. One month after completion of the treatment, a second UBT was performed. In the case of a positive result, second-line treatment was prescribed. Participants who failed two rounds of treatment were referred to a gastroenterologist for susceptibility-based antibiotic therapy. Data on compliance with testing and treatment, treatment outcomes, adverse events, and reasons for withdrawal from the study were collected. The feasibility and sustainability of the *H. pylori* screen-and-treat strategy were evaluated using several key performance indicators that follow the structure of the five principal areas of feasibility.

6 | Evaluation of Potential Adverse Effects in the Long-Term (WP5)

The aim of the study was to investigate for potential adverse effects of the screen-and-treat strategy. Objectives of the study included investigating whether *H. pylori* screen-and-treat was associated with: (1) an increase in weight, body mass index (BMI) and waist-to-hip ratio; (2) an increase in the prevalence of gastroesophageal reflux disease (GERD) or worsening of existing GERD symptoms based on the validated GERDQ questionnaire [21]; (3) the incidence of major health events (myocardial infarction, stroke, cardiovascular stent placement), diabetes, and others; and (4) changes in blood parameters associated with metabolic and cardiovascular risk (including triglycerides, low- and high-density lipoprotein cholesterol, total cholesterol, insulin and glucose).

The study was conducted by the Institute of Clinical and Preventive Medicine at the University of Latvia and was based on the follow-up of a GISTAR study participant cohort [22]. The GISTAR study began in 2013 and enrolled generally healthy individuals aged 40 to 64 years. Upon signing the informed consent, participants were randomly assigned to either the intervention or control group within the GISTAR study. The GISTAR intervention consisted of testing for *H. pylori* infection and serum pepsinogens, with *H. pylori* eradication offered to *H. pylori* positives and upper endoscopy to those with serologic evidence of atrophic gastritis. At entry into the intervention group, *H. pylori* infection was determined initially by serology, but for most of the participants UBT was later used as the main form of testing at baseline. Infected participants received clarithromycin-based triple therapy (amoxicillin 1000 mg, clarithromycin 500 mg, esomeprazole 40 mg BID) for 14 days. Participants of the GISTAR control group were not tested for *H. pylori* as part of GISTAR and followed their usual healthcare in Latvia.

For the EUROHELICAN project, a comprehensive questionnaire compatible with the original GISTAR questionnaire was designed, the GISTAR data entry system and standard operating procedures were updated, and new ethics approvals were obtained (refer to ethics statement).

Regional study centers were established and opened sequentially in cities where GISTAR centers had been opened (Ludza, Alūksne, Cēsis, Saldus, and Rēzekne). For each of the centers, new medical personnel had to be employed (nurses, nursing assistants, paramedics); local infrastructure was set up, and the new employees were trained to perform the necessary tasks.

Participants already enrolled in the GISTAR study for at least 4 years were invited for follow up by phone call. Participants that were not reached by phone were sent text messages or e-mails with an invitation to participate in follow-up. Participants who agreed to come for follow up at the study centers signed a repeat informed consent form.

Similarly to the original GISTAR study design, the following was carried out by study personnel in each of the study centers: participants questioned according to the questionnaire designed for follow-up (including medical history, lifestyle, harmful habits, family history, use of medication, GERD symptoms), measuring of anthropometric parameters (including weight, height, BMI, waist-to-hip ratio), collection of relevant documentation (endoscopy results and discharge papers) dated since intervention, and the collection and processing of blood samples. Participants that had been *H. pylori* positive when first enrolled in the GISTAR study were tested by UBT.

To best interpret the character of the associations that may be found during analysis, the design anticipated the creation of study groups to be compared at several levels, listed here in decreasing order of participant count: (1) original GISTAR intervention group versus control group (the largest groups by count); (2) *H. pylori* positive versus *H. pylori* negative at baseline when enrolled in GISTAR; (3) received eradication treatment versus did not receive eradication during GISTAR; and (4) successfully eradicated versus not eradicated (the smallest groups by count).

7 | Population-Based *H. pylori* Screen-And-Treat Strategies for Gastric Cancer Prevention: Guidance on Implementation (WP6)

The IARC convened a Working Group of 35 international, interdisciplinary experts from 20 countries in early 2025 to discuss best practices in the implementation of population-based *H. pylori* screen-and-treat strategies for gastric cancer prevention in adult populations. As the Working Group Meeting involved

worldwide experts, the scope of the Working Group Report was not limited to Europe but covered all world regions, including various levels of the Human Development Index and background burdens of disease, thus ensuring that the guidance is globally applicable.

The Working Group Report describes the global epidemiology of gastric cancer and *H. pylori* infection and provides summaries of the scientific evidence on the effect of population-based *H. pylori* screen-and-treat strategies for gastric cancer prevention and the currently available guidelines and recommendations on the strategies. The report presents various gastric cancer prevention efforts for each World Health Organization (WHO) region, highlights the gaps in knowledge and the future efforts that are needed, and details programmatic aspects of the strategies for implementation at the population level. The report also covers a range of key considerations for implementation of the strategies, including needs and readiness assessments, choosing screening methods and treatment regimens, antibiotic stewardship, process and outcome measures for improving quality and equity, and the cost–benefits of the strategies [23].

8 | Conclusions

The EUROHELICAN project is a much-needed initiative bringing together researchers in Europe to address unanswered questions regarding *H. pylori* screen-and-treat. The study on *H. pylori* screen-and-treat in Slovenia is a unique study, assessing, for the first time, the feasibility of implementing the strategy in younger adults aged 30 to 34 years. The study on assessing *H. pylori* screen-and-treat in the long-term is based on follow-up with a cohort of the largest prospective study of its kind in Europe—the GISTAR study. Both studies carried out as part of the project have received positive evaluations at several stages throughout their duration, showing that they are well-suited in reaching the proposed objectives and that the collected data is valid. Finally, the IARC expert group guidance report on the implementation of population-based *H. pylori* screen-and-treat strategies in adult populations to prevent gastric cancer will guide future primary gastric cancer prevention programs in Europe and beyond.

Author Contributions

Bojan Tepes was the scientific coordinator for the EUROHELICAN project; he was responsible for the final protocol for the Slovenia study; supervised the monitoring and quality check; assisted with the analysis, interpretation, and synthesis of data for Slovenia (WP 4); wrote the first draft; and approved the submitted manuscript. Tatjana Kofol Bric participated in the preparation of the methodology and study protocol, as well as obtained the results for the Slovenia study (WP 4); supervised the monitoring and quality check; critically reviewed the manuscript's drafts and approved the final submitted manuscript. Jernej Završnik coordinated the study at CHC Maribor (WP 4) and approved the final submitted manuscript. Mārcis Leja participated in creating the design and supervised the carrying out of the Latvia study (WP 5); supervised the monitoring and quality check; critically reviewed the manuscript's drafts, and approved the final submitted manuscript. Danute Ražuka-Ebela prepared the study protocol and all other documentation for the Latvia study, coordinated the scientific activities and collection of data for the Latvia study (WP 5); participated in writing the draft, critically reviewed the manuscript's drafts, and approved the final submitted manuscript. Viktoria Knaze participated in creating the study design for the Latvia study (WP 5) and co-coordinated WP 6, critically reviewed the manuscript's drafts, and approved the submitted manuscript. Jin Young Park led WP 6; participated in creating the study design for the Latvia study (WP 5); critically reviewed the manuscript's drafts and approved the submitted manuscript. Tamara Matyasiak Budnik led the external evaluation process of the study (WP 3); critically reviewed the manuscript's drafts and approved the submitted manuscript.

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Disclosure

The views and opinions expressed are however those of the author (s) only and do not necessarily reflect those of the European Union or the European Health and Digital Executive Agency (HaDEA). Neither the European Union nor HaDEA can be held responsible for them. Where authors are identified as personnel of the IARC/WHO, the authors alone are responsible for the views expressed in this article, and they do not necessarily represent the decisions, policies, or views of the IARC/WHO.

Ethics Statement

The study in Slovenia (WP 4) was approved by the National Medical Ethics Committee of the Republic of Slovenia on February 27, 2023, no. 0120–12/2023/3. The study in Latvia (WP 5) was approved by the Riga East Clinical University Support Foundation's Medical and Biomedical Research Ethics Committee on February 14, 2023, no. 5-A/23, and revised on August 29, 2024, no. 13.1-A/24. The IARC Ethics Committee (IEC) gave ethics approval on July 3, 2023 to the study in WP 4 (IEC 23–22 project) with Ref. IEC meeting 2023–04, and to the study in WP 5 (IEC 12–36-A2 project) with Ref. IEC meeting 2023–03. The study was registered internationally. EU PAS number: EUPAS107327, Study ID: 108428. ClinicalTrials.gov ID: NCT06216639, Protocol ID: EUROHELICAN01.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

1. F. Bray, M. Laversanne, H. Sung, et al., "Global Cancer Statistics 2022: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries," *CA: A Cancer Journal for Clinicians* 74, no. 3 (2024): 229–263, https://doi.org/10.3322/caac.21834.

2. J. Ferlay, M. Ervik, F. Lam, et al., *Global Cancer Observatory: Cancer Today (Version 1.1)* (International Agency for Research on Cancer, 2024), https://gco.iarc.who.int/today.

3. J. Ferlay, M. Laversanne, M. Ervik, et al., *Global Cancer Observatory: Cancer Tomorrow (Version 1.1)* (International Agency for Research on Cancer, 2024), https://gco.iarc.who.int/tomorrow.

4. International Agency for Research on Cancer, "Infection With Helicobacter Pylori," in *IARC Monogr Eval Carcinog Risks Hum*, vol. 61 (World Health Organization (WHO), 1994), 177–240.

5. IARC Helicobacter pylori Working Group, *Helicobacter Pylori Eradication as a Strategy for Preventing Gastric Cancer*, vol. 2014 (International Agency for Research on Cancer IARC Working Group Reports, 2014), 1–181.

6. Y. C. Chen, P. Malfertheiner, H. T. Yu, et al., "Global Prevalence of *Helicobacter pylori* Infection and Incidence of Gastric Cancer Between 1980 and 2022," *Gastroenterology* 166, no. 4 (2024): 605–619, https://doi.org/10.1053/j.gastro.2023.12.022.

7. C. de Martel, D. Georges, F. Bray, J. Ferlay, and G. M. Clifford, "Global Burden of Cancer Attributable to Infections in 2018: A Worldwide Incidence Analysis," *Lancet Global Health* 8, no. 2 (2020): e180–e190, https://doi.org/10.1016/S2214-109X(19)30488-7.

8. S. Mocellin, D. Verdi, K. A. Pooley, and D. Nitti, "Genetic Variation and Gastric Cancer Risk: A Field Synopsis and Meta-Analysis," *Gut* 64 (2015): 1209–1219.

9. H. Li, W. Li, S. Liu, et al., "Dnmt1, Dnmt3a and Dnmt3b Polymorphisms Associated With Gastric Cancer Risk: A Systematic Review and Meta-Analysis," *eBioMedicine* 13 (2016): 125–131.

10. P. Malfertheiner, F. Megraud, T. Rokkas, et al., "Management of Helicobacter Pylori Infection: The Maastricht VI/Florence Consensus Report," *Gut* 71 (2022): 327745.

11. W. D. Chey, C. W. Howden, S. F. Moss, et al., "ACG Clinical Guideline: Treatment of *Helicobacter Pylori* Infection," *American Journal of Gastroenterology* 119, no. 9 (2024): 1730–1753, https://doi.org/10.14309/ajg.0000000000002968.

12. M. Asaka, M. Kato, S. Takahashi, et al., "Guidelines for the Management of *Helicobacter Pylori* Infection in Japan: 2009 Revised Edition," *Helicobacter* 15 (2010): 1–20.

13. B. Tepeš and B. Štabuc, "A Position Statement of the Slovenian Association for Gastroenterology and Hepatology on the Management of Patients Infected With *Helicobacter Pylori*," *Zdravstveni Vestnik* 87 (2018): 2615.

14. K. Sugano, J. Tack, E. J. Kuipers, et al., "Kyoto Global Consensus Report on Helicobacter Pylori Gastritis," *Gut* 64 (2015): 1353–1367.

15. A. C. Ford, Y. Yuan, J. Y. Park, D. Forman, and P. Moayyedi, "Eradication Therapy to Prevent Gastric Cancer in *Helicobacter Pylori*-Positive Individuals: Systematic Review and Meta-Analysis of Randomized Controlled Trials and Observational Studies," *Gastroenterology* 169, no. 2 (2025): 033, https://doi.org/10.1053/j.gastro.2024.12.033.

16. L. Yan, Y. Chen, F. Chen, 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* 163, no. 1 (2022): 154–162.e3, https://doi.org/10.1053/j.gastro.2022.03.039.

17. M. Asaka and K. Mabe, "Strategies for Eliminating Death From Gastric Cancer in Japan," *Proceedings of the Japan Academy. Series B, Physical and Biological Sciences* 90, no. 7 (2014): 251–258, https://doi.org/10.2183/pjab.90.251.

18. T. Dorji, S. Wangmo, S. Dargay, et al., "Population-Level Cancer Screening and Cancer Care in Bhutan, 2020–2023: A Review," *Lancet Regional Health - Southeast Asia* 24 (2024): 100370, https://doi.org/10.1016/j.lansea.2024.100370.

19. SAPEA, *Improving Cancer Screening in the European Union* (Science Advice for Policy by European Academies, 2022), https://doi.org/10.26356/cancerscreening.

20. Council of the European Union, "Council Recommendation on Strengthening Prevention Through Early Detection: A New EU Approach on Cancer Screening, Replacing Council Recommendation 2003/878/EC," (2022), https://data.consilium.europa.eu/doc/document/ST-14770-2022-INIT/en/pdf.

21. C. Jonasson, B. Wernersson, D. A. Hoff, and J. G. Hatlebakk, "Validation of the GerdQ Questionnaire for the Diagnosis of Gastro-Oesophageal Reflux Disease," *Alimentary Pharmacology & Therapeutics* 37, no. 5 (2013): 564–572.

22. M. Leja, J. Y. Park, R. Murillo, et al., "Multicentric Randomised Study of *Helicobacter pylori* Eradication and Pepsinogen Testing for Prevention of Gastric Cancer Mortality: The GISTAR Study," *BMJ Open* 7, no. 8 (2017): e016999.

23. J. Y. Park, ed., *Population-Based Helicobacter Pylori Screen-And-Treat Strategies for Gastric Cancer Prevention: Guidance on Implementation (IARC Working Group Reports No. 12)* (International Agency for Research on Cancer, 2025), https://publications.iarc.who.int/648.