Recommendations for gastric cancer prevention and control in the Americas

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Historically, gastric (stomach) cancer (GC) in the Americas has received little attention from policymakers, research funding agencies, and health providers despite the significant health burden in several populations. Most patients with GC are diagnosed at late stages, and ~97,000 individuals die from this cancer each year in the region (Globocan 2020). The disease burden is greatest in low- and middle-income countries,[1] and specific marginalized groups in high-income countries.[2] Due to aging and growing of high-risk populations, the absolute burden of GC is estimated to rise in the Americas. In addition, this cancer is increasing in young individuals in several low and high-incidence countries, including the United States (US).[3] This unfavorable trend might be associated with a potential increase in autoimmune gastritis. The regional health systems are not prepared to properly manage this growing burden of a too often fatal disease.

Gastric carcinogenesis is a multifactorial, slowly progressive process with well-defined preneoplastic stages. GC is curable if diagnosed at early stages. Unfortunately, there is no routine screening for GC in the Americas. Most individuals do not receive adequate care because of ineffective and fragmented health systems, inadequate services, disparities in access to esophagogastroduodenoscopy (EGD), lack of knowledge, and high financial costs. There is also low public awareness of risk factors and warning symptoms, and self-medication increases delays in GC diagnosis and management. Population-based screening using EGD has substantially reduced GC mortality in high-risk East Asian countries.[4] However, this secondary prevention strategy is not yet practical in the Americas, mainly due to its high cost and lack of trained professionals. The cornerstone of primary prevention of GC is eradication of *Helicobacter pylori* infection, the main known cause. Randomized clinical trials suggest that anti-*H. pylori* treatment reduces both incidence and mortality from GC by ~40%.[5] The effectiveness of available treatment regimens varies and has progressively decreased due to increasing antimicrobial resistance. Organized *H. pylori* eradication programs are not actually taking place anywhere, but accumulating data suggest they might be cost-effective in high-risk populations.[6] Further data on the benefits or adverse effects of *H. pylori* eradication should come from ongoing clinical trials in China (MITS), South Korea (HELPER), the United Kingdom (HPSS), and Latvia (GISTAR).

A significant proportion of GC cases and deaths can be avoided if preventive interventions are taken. Accordingly, we propose a strategic framework to achieve effective prevention and control of GC across the Americas. This information can be used as a resource for public policy decisions and development of funding priorities. Our recommendations are based on the best available evidence and expert opinion. Adoption of most of these recommendations may be easier to achieve if they begin as small-scale demonstrative research projects in each country. Table 1 summarizes the recommendations, rationale, and potential specific actions to be implemented by key national stakeholders.

The burden of *H. pylori* in the Americas varies across areas, with lower (<25%) seroprevalence in North America and higher (~70%) in Central America, and across demographic groups within countries. The prevalence trend continues to decline with better sanitation, food preservation, and use of antibiotics. We anticipate improvements in diagnostics capacity for *H. pylori* infection through development of unexpensive, quick, and easy to use tests. Research is needed to identify more cost-effective approaches (e.g., *H. pylori* vaccines) and address new etiological challenges (e.g., increasing burden of autoimmune gastritis-driven GC).

We hope this commentary brings attention to the lack of public health actions on GC. We believe that even the smallest change would start the path forward to control this major, but preventable cause of mortality.

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Recommendation	Rationale	Potential implementation actions
Strengthen population-based cancer registries	- High-quality and comprehensive cancer registries ensure that policymakers have accurate and timely data on incidence, treatment, and survivorship to make decision on cancer control. - The epidemiology of GC is changing in the Americas. Thus, periodical, and detailed registry-based analyses should be performed. - Most North American populations have a satisfactory level of coverage by population-based cancer incidence registration, while only ~20% of the Latin American populations are covered.	- Maintain adequate funding for existing registries. - Establish new population-based registries in high-risk areas with no coverage.
Support development and dissemination of standards for quality care aimed at GC prevention	- High quality care must be a tenet for all health care providers in the cancer continuum.	- In collaboration with clinical and academic organizations: * Improve the suboptimal quality of EGD, considering the structure (i.e., facilities and equipment), procedure, outcome, and adverse events. * Procure better quality endoscopy equipment with high magnification and narrow-band imaging. * Increase the number of highly trained specialist endoscopists and surgeons. * Establish clear guidelines for standardized biopsy collection protocols (e.g., Sydney or adequate representation of both antral and oxyntic mucosa). * Establish protocols for optimal quality histotechnology and for better and consistent reporting of histopathologic findings. The use of Operative link for Gastritis (OLGA) and/or Gastric Intestinal Metaplasia (OLGIM) Assessments should be implemented. * Promote multidisciplinary (i.e., endoscopic, surgical, oncologic, and palliative) care in control and prevention strategies of GC, and establish combined guidelines.
Enable training of health care workforce specialized in GC	- Health care providers with specialized training can effectively limit morbidity and mortality associated with GC. - Training in patient-centered medicine can increase the ability of health care providers to individualize care according to patients' risk factors and provide more effective care by considering patients' values, preferences, and circumstances.	- In collaboration with clinical and academic organizations, establish high quality training in GC prevention for health providers at every level. Specific topic training may include: * All providers: the value of patient-centered care in achieving more effective health outcomes, particularly in historically underserved groups. * Primary care physicians: indications for *H. pylori* eradication, and risk factors for GC. * Gastroenterologists/endoscopists: endoscopic diagnosis of atrophy, indications for biopsy and biopsy collection protocols. * Histotechnologists: histological preparations of optimal quality. * Pathologists: atrophy classifications. * Oncologists: risk assessment for relatives of patients with GC. * Endoscopist gastroenterologists and surgeons: endoscopic mucosal resection and endoscopic submucosal dissection and gastrectomy.
Conduct research and advocacy aimed at getting GC prevention strategies adopted and paid for by health systems	- The US Preventive Services Task Force (USPSTF) makes evidence-based recommendations about preventive services such as screenings, behavioral counseling, and preventive medications. The USPSTF posted a draft research plan on screening for *H. pylori* infection in November 2022, but in August 2023 announced that it will not move into the final research plan stage and evidence review at this time. - Other countries in the Americas may have similar panels of experts in disease prevention and evidence-based medicine. - Stakeholder-engaged research approaches such as community-driven research and patient-oriented research engage stakeholders to keep research centered on their goals, priorities, values, and circumstances, thereby generating knowledge of direct relevance to stakeholders. - By generating evidence aligned with local circumstances and motivations, community-driven research facilitates the movement of knowledge to action.	- In collaboration with clinical and academic organizations, as well as patient advocacy groups and high-risk communities, conduct studies that generate information to fill knowledge gaps encountered by decision makers. - Facilitate community-driven research conducted by partnerships between academic researchers and high-risk communities aimed at developing and evaluating community-based prevention strategies. - Facilitate patient-oriented research aimed at developing and evaluating clinic-based prevention strategies.
Establish *H. pylori* treatment registries	- There is a high burden of *H. pylori* infection in several populations in the Americas. - An optimal anti-*H. pylori* regimen is defined as one that consistently cures ≥90% of treated individuals.[6] - Clarithromycin-based standard triple therapy is still the most used first-line regimen in many countries in the Americas despite their failure in ≥20% of patients. - Information on actual clinical practice is essential for continuous assessment of the coherence of clinical guidelines with temporal trends in management options and outcomes.	- In collaboration with clinical and academic organizations, establish a large-scale long-term prospective registry of *H. pylori*-positive patients receiving eradication therapy. * Registry activities could be modelled after the European Registry on *H. pylori* Management, *Hp*-EuReg.

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Recommendation	Rationale	Potential implementation actions
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	- Registry data on *H. pylori* clinical management would help to determine the most effective treatment strategies, regionally and locally, thereby improving the alignment of routine clinical practice with the best standards of care.	
Establish a surveillance system of *H. pylori* antibiotic resistance	- The World Health Organization (WHO) has identified *H. pylori* as a global priority pathogen due to growing global resistance to antimicrobial medicines. - The selection of regimens to be used in each population must be based on studies of antibiotic resistance in the same population.[6] - Resistance to clarithromycin is one of the major factors affecting *H. pylori* eradication success, and the rate of resistance to this antibiotic is steadily increasing in many geographical areas.[6] - Resistance of *H. pylori* strains to common antibiotics is increasing in frequency in the Americas.[7,8] - Genomic testing provides comparable results to phenotypic antimicrobial susceptibility methods and facilitates surveillance because it is more feasible and affordable.	- Strengthen antimicrobial regulations. - Raise awareness of the misuse of antibiotics in various sectors, including the potential deleterious effects on gastric and gut microbiome. - Build high-quality antimicrobial resistance laboratory networks to provide accurate and timely services. - In collaboration with clinical organizations, establish large-scale and periodical (i.e., every 5–10 years) surveys of *H. pylori* resistance to commonly used antibiotics based on genomic testing of gastric biopsies.
Assure optimal *H. pylori* testing and treatment protocols	- Accumulating evidence from randomized clinical trials and observational studies indicates that treatment to eliminate *H. pylori* infection reduces the risk of GC in high-risk populations.[5] - Repeat *H. pylori* testing after treatment is essential to confirm eradication.[6] - There is a significant reduction in metachronous GC after *H. pylori* eradication therapy in patients with previously resected early-stage GC.[9]	- Build high-quality laboratory networks for *H. pylori* testing to provide accurate, timely and affordable services. - In collaboration with clinical organizations, patient advocacy groups and high-risk communities conduct patient-oriented research to: * Develop effective age-specific messaging for patients at increased risk of GC regarding pros and cons of treatment to eliminate *H. pylori* infection. * Develop effective strategies to improve treatment adherence and increase the frequency of post-treatment testing. - Consider family-based therapy in *H. pylori*-positive individuals with indication for treatment. - Adopt the recommendation of *H. pylori* eradication in patients with previously resected early GC.
Ensure endoscopic surveillance of patients with high-risk gastric intestinal metaplasia (IM)	- There is an excellent interobserver agreement in the diagnosis of IM. - Globally, IM is present in up to 25% of individuals with dyspeptic symptoms. - Individuals with IM have a higher risk of developing GC than those without this histological lesion. The risk of GC is higher in individuals with IM that simultaneously involves the antrum and the body of the stomach,[6] and in those with incomplete-type IM. - According to international clinical guidelines, individuals with high-risk OLGIM stages III and IV should be followed-up endoscopically every two-three years.[6] - Accumulating evidence suggest that EGD combined with colonoscopy for positive fecal immunochemical test may represent an efficient strategy for GC screening.	- Adopt the use of the new ICD-10-CM codes (K31A0-29) for IM. - Identify and stratify patients with IM: * In a retrospective fashion, patients diagnosed with IM could be identified based on medical records. Individuals with a diagnosis at least three years in the past could be recalled for an updated risk assessment using a validated protocol for EGD with biopsies. * In a prospective fashion, all patients diagnosed with IM could be risk stratified using the OLGIM system. * Individuals with high-risk IM (OLGIM stages III and IV) should be followed according to international guidelines. Follow-up in individuals with OLGIM II should be considered based on other risk factors. - Opportunistic EGD during colonoscopy should be considered in high-risk individuals.
Establish key interventions directed to GC families	- Relatives of patients with GC have a higher risk of developing GC than individuals without a family history of GC. - Familial clustering of GC may reflect shared genetic or environmental factors (including *H. pylori* infection), or both. - Young patients with GC may harbor mutations related to hereditary GC syndromes, mainly in cases of diffuse-type.	- Clinical care teams of GC patients could discuss with them the possibility of inviting their relatives for risk assessment. - Adult (>20 years) relatives of GC could undergo *H. pylori* testing and get treated if they test positive. - Relatives aged 45–65 years could be offered EGD with biopsies for risk stratification (based on OLGA and/or OLGIM staging). Individuals with high-risk stages (III and IV) should be followed according to international guidelines. Follow-up in individuals with OLGIM II should be considered based on other risk factors. - Molecular investigations should be provided to early-onset GC cases, and if high risk genetic variants are found, their relatives should also be offered diagnostic evaluation.
Conduct endoscopic campaigns in high-risk populations with limited access to health care (e.g., rural residents), focusing on individuals with major risk factors	- Mobile screening services have served to expand access to cancer screening in diverse contexts. - In the US, several ethnic groups have increased GC incidence and mortality compared to non-Hispanic White individuals.[2] - In Latin America and the Caribbean, individuals with lower socioeconomic status have increased GC incidence and mortality.[1] - Across the Americas, Indigenous peoples have increased GC incidence and mortality.[1,2]	- In collaboration with clinical and academic organizations, perform endoscopic campaigns focused on high-risk individuals (i.e., adults aged ≥50 years, male sex, smokers, family history of GC) and ideally symptomatic. Treatments and referrals should be guaranteed through the available health system. - A model of a successful endoscopic campaign in Chile has been described by Gonzalez et al.[10]

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Strengthen smoking regulations	- Smoking increases the risk of GC. - Smoking increases the likelihood of *H. pylori* treatment failure.	- Maintain adequate funding for existing prevention strategies. - Reinforce smoking-cessation services in primary-care settings. - Establish standard recommendations of smoking cessation in patients receiving *H. pylori* treatment.
Strengthen strategies to reduce salt (sodium) intake	- High salt intake increases the risk of GC. - Salt may synergize the pathogenic effects of chronic *H. pylori* infection.	- Adopt WHO recommendations for salt intake reduction. - Reinforce salt reduction interventions in primary-care settings.
Establish community education programs	- Health literacy empowers individuals to take an active role in their healthcare.	- Adopt general recommendations against cancer based on healthy lifestyles, such as the *Latin America and the Caribbean Code Against Cancer.* - In collaboration with clinical organizations and patient advocacy groups, generate educational materials on GC risk factors.

Table 1: **Recommendations, rationale, and potential specific actions for gastric cancer prevention and control in the Americas.**

Contributors

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Data sharing statement

There are no data to be shared.

Declaration of interests

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