Chapter 3.2.

Gastric cancer prevention in Latin America and the Caribbean

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Summary

- Gastric cancer is a leading cause of cancer-related death in the Latin America and the Caribbean region, which contributes about 8% of the new cases globally. The burden of gastric cancer is greatest in the mountainous areas of the Pacific littoral.
- The most common anatomical subsite of gastric cancer in populations in Latin America and the Caribbean is *H. pylori*-driven non-cardia gastric cancer, and its late diagnosis is associated with poor outcomes.
- The burden of *H. pylori* infection in populations is high (> 60% in adults) and is relatively homogeneous across the region. Two multicentre studies in countries in Latin America and the Caribbean address *H. pylori* diagnosis and treatment schemes (Hp-LATAM-Reg) and *H. pylori* antibiotic resistance (Hp-RESLA).
- There are limited strategies for gastric cancer prevention and control embedded in public health policies in the region.
- Chile has taken a leading role in implementing demonstrative studies of prevention that could inform national and regional regulations to reduce gastric cancer mortality.

3.2.1 Introduction

Latin America and the Caribbean (LAC) is a region with a low to moderate risk of gastric cancer. LAC accounts for about 8% of new cases of gastric cancer globally [1]. The greatest burden of gastric cancer in LAC is concentrated in the mountainous areas of the Pacific littoral [2]. Based on the limited incidence data that are available, the risk of gastric cancer has been decreasing for several decades in both men and women in

LAC (Fig. 3.2.1) [3]. Gastric cancer is a leading cause of cancer-related deaths in LAC; it is responsible for about 58 000 deaths per year in the region [1].



Age-Standardized Rate (World) per 100 000, Incidence, Females Stomach Argentina* - Chile* - Colombia* - Costa Rica - Ecuador* - Puerto Rico





Fig. 3.2.1. Country-specific trends of gastric cancer incidence in (top) men and (bottom) women in Latin America and the Caribbean. * Subnational data. Source: Ervik et al. (2024) [3].

According to GLOBOCAN 2022, the countries in LAC with the highest overall gastric cancer incidence and mortality rates are Chile, Colombia, Costa Rica, Ecuador, Guatemala, and Peru (Fig. 3.2.2) [1]. The countries with the lowest gastric cancer incidence and mortality rates are Barbados, Belize, Guyana, Suriname, and Trinidad and Tobago. The Central America Four region (El Salvador, Guatemala, Honduras, and Nicaragua) is the largest low- and middle-income region in the Western Hemisphere, with a population of about 41 million; in addition, about 6 million people who now live in the USA have emigrated from the Central America Four region. Accurate mortality data are lacking for the Central America Four region, and underreporting hinders national and regional cancer control programmes [4]. The gastric cancer burden in the Central America Four region is projected to increase by 73% by 2030, primarily because of population growth and ageing, unless prevention strategies are implemented [4]. In contrast, the Caribbean has a heterogeneous incidence of gastric cancer, with an intermediate estimated incidence in Haiti (10 cases per 100 000 person-years) and a relatively low estimated incidence in the Dominican Republic (6 cases per 100 000 person-years) (Fig. 3.2.2) [1].



Age-Standardized Rate ((World) per	r 100 000. Incidence	Both sexes.	in 2022
Age-Standardized Nate	(world) per	100 000, melacifice	, Dotti Seves,	111 2022

Population	ASR (W)
Suriname	4.6
Guyana	4.5
Trinidad and Tobago	4.0
Puerto Rico	2.8

Age-Standardized Rate (World) per 100 000, Mortality, Both sexes, in 2022 Stomach



ASR

3.5

3.1

3.0

2.4

Fig. 3.2.2. Gastric cancer (A) incidence and (B) mortality in both sexes, age-standardized rates (ASRs) (world) per 100 000 person-years in Latin America and the Caribbean. Source: Ferlay et al. (2024) [1].





Fig. 3.2.3. Median 5-year observed survival of patients with gastric cancer in Latin America and the Caribbean, in both sexes combined. Source: Soerjomataram et al. (2023) [6].

The most common anatomical subsite of gastric cancer in populations in LAC is *H. pylori*-driven non-cardia gastric cancer [5]. In LAC, patients with gastric cancer are often diagnosed at an advanced stage of the disease, and the overall median 5-year survival rate is < 35% (Fig. 3.2.3) [6]. People in rural Central America have an even worse prognosis after a gastric cancer diagnosis, with a 5-year survival rate of < 10% [7].

The epidemiological pattern of gastric cancer is evolving. A trend analysis in Hispanic populations in Puerto Rico and 16 countries in LAC showed that gastric cancer mortality had increased slightly or was stable in people younger than 50 years [8]. This is consistent with an increasing incidence of non-cardia gastric cancer in young non-Hispanic White people and in Hispanic people in the USA, particularly in women [9]. Additional surveillance is needed in populations in LAC.

3.2.2 Risk factors for gastric cancer in populations in LAC

Improvements in hygiene and sanitation have contributed to the global decrease in the prevalence of *H. pylori* infection, and these factors still contribute to the varying prevalence of *H. pylori* infection across regions. The prevalence of *H. pylori* infection is about 50% in the population worldwide and is > 60% in most countries in LAC. Fig. 3.2.4 shows the prevalence of *H. pylori* infection and the age-standardized rates (world) of gastric cancer per 100 000 population in 2020 attributable to *H. pylori* infection in selected countries [10]. In a meta-analysis that included 22 studies in Latin America (in 14 countries) in 1987–2012, the prevalence of *H. pylori* infection was 69.3% in adults and 48.4% in children and adolescents [11]. In Chile, the historical seroprevalence of *H. pylori* infection [12], but a recent study suggested that there has been a drastic decrease, with an observed prevalence of 29% in adults in urban areas, mainly related to water sanitization [13, 14]. In participants in the Hispanic Community Health Study/Study of Latinos, the overall weighted *H. pylori* seroprevalence was 57%, with a seropositivity of 38% in people born in the USA and a seropositivity of 62% in people born outside the USA [15].



Fig. 3.2.4. Prevalence of *H. pylori* infection (in red) and age-standardized rates (world) of gastric cancer per 100 000 population (in blue) in 2020 attributable to *H. pylori* infection in selected countries. Compiled from Ferlay et al. (2024) [1]. Panel illustrated by Valentina Riquelme.

In Latin America, the associations of risk factors for gastric cancer are based on case–control comparisons. The specific factors that have been identified and their magnitudes of association are largely similar to those identified in other populations [5]. An association between altitude and gastric cancer incidence and mortality has been observed in the countries of western Latin America, located along the Pacific rim; this is known as the Andes enigma [2]. South American countries that are located along the Atlantic coast also have some populations at high risk of gastric cancer. For example, people in north-eastern Brazil have the highest rates of gastric cancer in the country [16]. These observed variations in risk may be attributed to differences in ancestry, salt intake, environmental factors, the prevalence of *H. pylori* CagA-positive strains, and the presence of other gastrointestinal coinfections [17].

3.2.3 Gastric cancer prevention in LAC

In most countries in LAC, health sectors have inadequate financial protection against health-care costs, and service delivery is fragmented [18]. Few health efforts in the region are focused on preventive medicine. Prevention strategies for gastric cancer are urgently needed in LAC to reduce the high social and economic costs of this disease.

An evidence-based strategic framework to achieve effective prevention and control of gastric cancer in the Americas was recently proposed, and this framework could guide immediate action [19]. In addition, under the umbrella of the World Code Against Cancer Framework, the 2023 Latin America and the Caribbean Code Against Cancer recommends screening and treatment for *H. pylori* infection in the context of specific public health programmes [20].

Gastric cancer prevention activities before 2013

The 2014 IARC Working Group Report on H. pylori eradication as a strategy for preventing gastric cancer [21] summarized the strategies used against gastric cancer in countries in LAC. At that time, only Chile, Costa Rica, Ecuador, the Bolivarian Republic of Venezuela, and Peru had explicit initiatives related to gastric cancer prevention. In Chile, the Ministry of Health initiated an opportunistic nationwide gastric cancer detection programme in 2006 that focused on symptomatic individuals. Also, H. pylori eradication (standard triple therapy) was recommended for any patient who had undergone oesophago-gastro-duodenoscopy (OGD) with a diagnosis of H. pylori infection and duodenal or stomach ulcer, atrophic gastritis, lymphoma, adenoma, gastric cancer, and/or a family history of gastric cancer [22]. In Ecuador, the Sociedad de Lucha Contra el Cáncer, a national non-profit organization, provides education about gastric cancer and specific recommendations for its treatment [23]. In Peru, the National Plan to Strengthen Cancer Prevention and Control in Peru, published in 2006, recommended (i) promoting research studies on methods for early detection of gastric cancer, including endoscopy; (ii) promoting the incorporation of early detection methods for gastric cancer and other cancers among health-care providers and the general public; and (iii) supporting actions to control *H. pylori* infection and to improve eating habits [24].

During the mid-1980s and the 1990s, as an international cooperation between the governments of Japan and of several LAC countries, gastric cancer screening programmes based on photofluorography were established in high-risk areas. In Peru, OGD examinations were conducted in > 30 000 symptomatic patients in 1985–2002. In the Bolivarian Republic of Venezuela, a screening programme conducted > 100 000 examinations in 1980–1989 in the high-risk region of Tachira [25]. Both of these programmes have been discontinued. In Costa Rica, the Cancer Early Detection Center in Cartago was opened in 1995, and 10 064 individuals were screened in 1996–1999 [26]. The impact evaluation of this intervention concluded that although X-ray mass

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screening seems to be able to reduce mortality from gastric cancer, the high cost of the procedure may prevent this intervention from being scaled up to cover the entire country [27]. The Cancer Early Detection Center still operates as a patient care centre, as part of the Caja Costarricense de Seguro Social (CCSS). Residents in the target areas are invited for a gastrointestinal series, and individuals with an altered series and those referred (from within or outside the CCSS) for previous suspicious endoscopy findings have diagnostic OGDs. At the Cancer Early Detection Center, most cases of gastric cancer are diagnosed at an early stage of the disease, and they are treated by an expert multidisciplinary team.

Gastric cancer prevention activities after 2013

In recent years, the Pan American Gastroenterology Organization (Organización Panamericana de Gastroenterología; OPGE), in collaboration with organizations in Europe and North America, including the European Registry on *H. pylori* Management (Hp-EuReg), the Spanish Gastroenterology Association, and the United States National Cancer Institute, has led key regional initiatives related to the primary prevention of gastric cancer.

Local guidelines

In 2014, under the sponsorship of the Chilean Society of Gastroenterology, a consensus report on the management of *H. pylori* infection in Latin America was published by a multidisciplinary group of adult and paediatric gastroenterologists, epidemiologists, and scientists with expertise in *H. pylori* infection and associated diseases and evidence-based medicine [28]. In a parallel effort, the Chilean Association of Digestive Endoscopy (ACHED) published a consensus report on endoscopic diagnosis and follow-up of gastric premalignant lesions. The ACHED group recommended that (i) endoscopists should perform systematic biopsies and specific examinations to detect early lesions, (ii) pathologists should adopt the updated Sydney protocol and include the Operative Link on Gastritis Assessment (OLGA) or Operative Link on Gastric Intestinal Metaplasia Assessment (OLGIM) staging in the histopathological report, and (iii) endoscopy services and pathological anatomy services should implement administrative processes to ensure that patients receive notifications and appointments for endoscopies if needed [29]. These two consensus reports helped to launch several initiatives (described below) for the prevention and control of gastric cancer in LAC. The ACHED group is working on

an updated version of the guidelines on gastric premalignant conditions, to be published in 2025, which will incorporate new data.

The Latin American Registry on the Management of H. pylori Infection

In 2019, the Latin American Registry on the Management of H. pylori Infection (Hp-LATAMReg) was created, with the support of the Hp-EuReg and the Spanish Gastroenterology Association, to describe and evaluate the main H. pylori eradication therapies and their eradication rates, adherence, and side-effects in countries in LAC. Eight countries (Argentina, Chile, Colombia, Costa Rica, Ecuador, Guatemala, Mexico, and Peru) have joined the Hp-LATAMReg and have provided retrospective and prospective (2015–2023) information to the Hp-LATAMReg. In 2024, a preliminary analysis reported that 1378 individuals have been registered, including 1218 (88%) treatment-naive patients. Preliminary results showed that (i) most of the treatment regimens used were 14 days long (n = 1051; 96%) and administered high-dose proton pump inhibitors; (ii) dual therapy and bismuth-containing quadruple therapies were significantly more effective than standard triple therapy; (iii) the most frequently used diagnostic test was histology (66%), and the most frequently used tests to confirm eradication were the stool antigen test (39%) and the ¹³C-urea breath test (29%) [30, 31]; and (iv) the eradication rates for several schemes were strongly associated with rates of *H. pylori* antibiotic resistance. Findings from the Hp-LATAMReg are already providing relevant information to enable updates of the national and regional guidelines for *H. pylori* treatment. For example, quadruple and dual therapies should be considered as the first-line treatment for *H. pylori* eradication in LAC.

H. pylori-antibiotics RESistance in Latin America (Hp-RESLA)

A systematic review and meta-analysis of studies in Latin America published up to October 2013 reported that the overall prevalence of *H. pylori* primary antimicrobial resistance among adults was 12% for clarithromycin, 53% for metronidazole, 4% for amoxicillin, 6% for tetracycline, 3% for furazolidone, 15% for fluoroquinolones, and 8% for dual clarithromycin and metronidazole resistance [32]. The prevalence of resistance varied substantially by country but not by year of sample collection. In 2019, a meta-analysis of studies on clarithromycin resistance in adults in Santiago, Chile, showed a higher prevalence of clarithromycin resistance (26%) and a suboptimal *H. pylori* eradication rate (63%) [33]. Another study in Santiago showed that levofloxacin

resistance was higher in women than in men (39% vs 13%; P < 0.001) [34]. Additional studies should be conducted to further explore potentially differential effects by sex. Accordingly, since 2019, the OPGE has supported Hp-RESLA, a multicentre study on molecular *H. pylori* antibiotic resistance in LAC, which aims to create a regional laboratory network for polymerase chain reaction (PCR), using gastric biopsies that were originally collected for rapid urease tests, and next-generation sequencing, using formalin-fixed, paraffin-embedded blocks.

GC-GAP index

The Gastric Cancer Global Action Preparedness (GC-GAP) study, led by the OPGE, aims to develop a preparedness index using published public policies against gastric cancer. Three rounds of Delphi panels were held, with the participation of 45 international experts. These experts represented all continents and included representatives from all the gastroenterology societies in the Americas (OPGE members), representing 98% of the population of the continent. The objectives of the three rounds were to define the domains, to define the indicators, and to adjust and agree on the final preparedness index. The index is made up of public policy domains and their respective indicators to classify countries according to their level of preparedness in each domain: low, intermediate, or high. Consensus (i.e. > 80% agreement) was reached on nine domains of public policies in favour of gastric cancer awareness, screening for risk factors and early-stage disease, availability of gastric cancer treatment, increasing the availability of drinking-water, and policies against H. pylori infection, obesity, tobacco use, and alcohol consumption. The use of a preparedness index will enable a standardized evaluation of public policies against gastric cancer in the Americas, including countries in LAC, based on global standards [35].

National activities in Chile

During the past decade, Chile has developed several initiatives and laws related to cancer prevention that may have a positive impact on gastric cancer. The 2015 Choose a Healthy Lifestyle programme promotes healthy eating, physical activity, outdoor lifestyles, and family life [36]. The 2016 Law of Food Labelling aims to reduce purchases of foods with sodium, sugars, saturated fats, or calories above the recommended limits ("high-in" foods) [37]. The 2022 Cancer Law aims for the integrated management of

patients with cancer [38]. In 2023, the Center for Cancer Prevention and Control was established to generate evidence that could guide public policies on cancer prevention and control [39].

As part of efforts for gastric cancer prevention, universal health coverage for gastric cancer and *H. pylori* infection includes access to therapy for all health-care systems and types of insurance [40]. The 2006 public health policy of offering OGD screening to symptomatic individuals aged \geq 40 years has led to long waiting lists in several areas of Chile. To determine the best strategy to reduce these waiting lists, the Ministry of Health is conducting a pilot study using non-invasive biomarkers for risk stratification of gastric premalignant conditions and gastric cancer. The preliminary (unpublished) results of this study, using data on pepsinogen I/II ratios, immunoglobulin G (IgG), *H. pylori* serology, serum gastrin-17 levels, age, sex, and first-degree relatives with gastric cancer, showed an area under the receiver operating characteristic curve of 0.74, with a negative predictive value of 88% in the Maule region of Chile and of 90% in Santiago. This will enable the Ministry of Health to prioritize access to OGD in the next stage of the project. However, these findings are not sufficient to avoid OGD screening for patients on the waiting list, and they cannot be extrapolated to asymptomatic individuals in population-based studies.



Fig. 3.2.5. Strategies for the non-invasive detection of *H. pylori* in an asymptomatic population aged 35–44 years. IgG, immunoglobulin G; UHC, universal health coverage. Reproduced from Corsi Sotelo et al. (2024) [41]. Copyright Elsevier 2024.

The Chilean consensus report for gastric cancer prevention [41], published in 2024, recommended a screen-and-treat strategy for *H. pylori* infection using non-invasive tests (primary prevention) for individuals aged 35–44 years (Fig. 3.2.5) and a combined strategy (IgG, *H. pylori* serology, and OGD) for individuals aged \geq 45 years (primary and secondary prevention) (Fig. 3.2.6). This recommendation is aligned with the Maastricht VI/Florence Consensus report [42] and could be applicable in other high-risk countries in LAC.





Fig. 3.2.6. Primary and secondary strategies for gastric cancer prevention in an asymptomatic population aged \geq 45 years. IgG, immunoglobulin G; OGD, oesophago-gastro-duodenoscopy; OLGA, Operative Link on Gastritis Assessment; UHC, universal health coverage. Reproduced from Corsi Sotelo et al. (2024) [41]. Copyright Elsevier 2024.

ECHOS retrospective study

In the Endoscopic Cohort and Histological OLGA Staging (ECHOS) study, a retrospective cohort was assembled of 685 individuals who underwent > 2 OGDs with biopsies > 6 months apart in 2015–2021 and who had atrophic gastritis staged by OLGA and OLGIM [43]. In this study, OLGA and OLGIM stages III–IV were independently associated with a higher risk of progression to high-grade dysplasia and gastric cancer. A microsimulation model based on the ECHOS study and other data sets showed that surveillance of incidentally detected intestinal metaplasia every 5 years is associated with reduced gastric cancer incidence and mortality and is cost-effective from a health-care sector perspective [44]. These combined results support the role of endoscopic surveillance in patients in Latin America with advanced OLGA and OLGIM stages.

HOPE-Hp-GC study

In 2023, the Center for Cancer Prevention and Control launched the Hospital and Outpatient Prevention Program to Eradicate H. pylori and Gastric Cancer (HOPE-Hp-GC) study in Molina, a high-risk area in the Maule region of Chile. This study is based on the Chilean consensus report for gastric cancer prevention [41], and other centres in Chile and other countries in LAC will join this study in the near future. In the first level of the study, individuals aged < 40 years are screened for *H. pylori* infection using the urea breath test and are offered *H. pylori* eradication treatment using dual therapy or quadruple concomitant therapy for mass eradication. Currently, 3000 of the 50 000 inhabitants of Molina have been tested, and by the second year of the project, H. pylori positivity had decreased from 49% to 34%. In contrast, individuals aged 40-75 years are screened using *H. pylori* pepsinogen serology, considering individual baseline comorbidities to assess the level of gastric cancer risk, i.e. low risk or intermediate to high risk, followed by H. pylori treatment if the individual tests positive for H. pylori infection at the second level. Finally, individuals with intermediate to high risk of gastric cancer undergo OGD using the Sydney protocol, followed by an OLGA assessment, which is conducted after H. pylori treatment or directly if the individual tested negative for H. pylori infection. Individuals with intermediate to high risk of gastric cancer are followed up every 4 years for OLGA stages 0-1 with persistent H. pylori infection and for OLGA stage II regardless of H. pylori status, and every 2 years for OLGA stages III-IV. Surveillance was not recommended for OLGA stages 0-I with no H. pylori infection; this

is in accordance with the updated ACHED protocol. In the preliminary results of OGDs performed in Molina, 12% were at OLGA stages III–IV. As part of this study, a new endoscopy unit was established at Molina Hospital, and this helped to reduce the waiting list for OGDs by 63%. In 2025, patients at OLGA stages III–IV will be offered follow-up endoscopy alongside the other study activities.

Recent and ongoing national activities in other countries in LAC

In the Bolivarian Republic of Venezuela, the Society Against Cancer (Sociedad Anticancerosa) launched a screening programme for premalignant lesions in firstdegree relatives of patients with gastric cancer at Caracas Hospital in 2023. If this initiative is successful, it will be expanded to other areas of the country [45].

In Ecuador, the National Strategy for Comprehensive Cancer Care (2017–2023) recommended that screening for gastric cancer in the population aged > 50 years should be conducted using a combination of serology tests to determine *H. pylori* infection status and pepsinogen levels combined with OGD to detect gastric cancer. The intervals at which endoscopic studies should be done should be determined by the ABCD method [46].

3.2.4 Conclusions and future directions

In summary, gastric cancer prevention is an important public health programme in LAC. Continued and targeted prevention efforts are needed to reduce the morbidity and mortality burden of gastric cancer. Several new research initiatives are under way in key countries in LAC, but there are limited strategies for gastric cancer prevention and control embedded in laws and public health policies. Ongoing research work should inform future efforts and guide changes in regional and local clinical guidelines.

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