Annals of Gastroenterology (2026) **39,** 1-13

A decade after the Hellenic consensus conference on *Helicobacter pylori* infection: what has changed since, and why an update is due

Christos Zavos

Bioclinic Hospital of Thessaloniki, Thessaloniki, Greece

Abstract

The Hellenic consensus on *Helicobacter pylori* (*H. pylori*) infection was published in the *Annals of Gastroenterology* in 2020, after the experts had met in Athens in June 2017 with the help of the Hellenic Society of Gastroenterology, the voting on 2 statements being completed in 2018. The authors had stated that the guidelines would require periodic revision as new data appeared. A substantial body of evidence and guidance has accumulated since. The Maastricht VI/Florence consensus, the World Gastroenterology Organisation global guideline, the American College of Gastroenterology guideline, the Real-world Gastritis Initiative, the third update on the management of epithelial precancerous conditions of the stomach, the Taipei Global Consensus II, and the working group report of the International Agency for Research on Cancer have been published, together with the first regional consensus for the Middle East, new national documents from several European countries, and updated pediatric guidance. Over the same period, 2 large randomized trials and an updated meta-analysis supported *H. pylori* eradication to prevent gastric cancer, molecular and stool-based susceptibility testing became clinically feasible, potassium-competitive acid blockers entered the international algorithms, and Greek surveillance data documented high primary and secondary antimicrobial resistance. This narrative review summarizes the developments since then, as regards the indications, screening, diagnosis, treatment, surveillance and pediatric care, compares them with the corresponding Hellenic statements, and considers the practical constraints of drug availability and laboratory capacity in Greece. These developments justify the need to hold a second Hellenic consensus meeting and update the statements in the modern era.

Keywords *Helicobacter pylori*, consensus, guidelines, gastric cancer prevention, antimicrobial resistance, Greece

Ann Gastroenterol 2026; 39 (X): 1-13

Introduction

Helicobacter pylori (*H. pylori*) infection affects nearly half of the world's population, and, although its prevalence is falling in high-income settings, it remains a significant burden in southern Europe [1,2]. *H. pylori* is responsible for almost all non-cardia gastric adenocarcinomas and for most peptic ulcers, and its eradication attenuates both risks [2].

In January 2020 the Hellenic Society of Gastroenterology published the first Hellenic consensus on *H. pylori* infection, comprising 39 statements produced by 41 delegates from all Greek regions and covering indications and diagnosis, extragastric associations, treatment and gastric malignancy [3]. The supporting literature was closed in June 2017, when the committee convened in Athens, Greece, with the Maastricht V/Florence report and the 2017 American College of Gastroenterology (ACG) guideline being the reference texts. Online voting on the 2 statements for which changes had been requested was concluded in 2018, and the full set was finalized. The panel wrote that, as new data became available from well-designed clinical trials, the statements would be revised regularly [3]. Correspondence published shortly afterwards in the same journal, *Annals of Gastroenterology*, and the authors' reply both anticipated that revision would come quickly, particularly for treatment, in a

Department of Gastroenterology, Bioclinic Hospital of Thessaloniki, Thessaloniki, Greece

Conflict of Interest: None

Correspondence to: Christos Zavos, MD, PhD, FEBGH, Astypalaias 2B, 54248, Thessaloniki, Greece,
e-mail: czavos@ymail.com, website: https://peptiko.gr

Received 1 August 2026; accepted 7 September 2026;
published online 6 November 2026

DOI: https://doi.org/10.20524/aog.2026.1128

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms

© 2026 Hellenic Society of Gastroenterology

country where bismuth-based regimens were not an option at the time [4,5].

Almost a decade has passed, and the interval has been extremely productive. Three international consensus documents [6-8], 2 European guideline updates [9,10], a World Health Organization agency report [11], an updated pediatric guideline [12], a series of European national documents [13-18] and the first regional consensus for a high-prevalence non-European region [19] have been published since. Randomized and long-term cohort evidence on population-level prevention has matured, molecular diagnostics have moved into routine practice, and a new class of acid suppressant has been incorporated in the international algorithms.

The aim of this review is: (a) to summarize what has been published since the Hellenic consensus was written; (b) to align these developments with the corresponding Greek statements; (c) to position them against the contemporary Greek resistance surveillance and drug availability; and (d) to raise the questions that a second national consensus would need to address.

Materials and methods

PubMed was searched for consensus reports, guidelines and position statements on *H. pylori* published between 2020, when the Hellenic consensus appeared, and August 2026, using combinations of the terms "*Helicobacter pylori*", "consensus", "guideline", "recommendations" and "statement" in the Title field. The timeframe started with the publication of the Hellenic consensus in 2020, since the aim of the present review was to compare the contemporary international recommendations with Greek practice from that point to the present, and to guide and urge for a second Hellenic consensus [3]. Documents were retained if: (a) they were international in scope; (b) they were European and represented the most recent position of a national society; or (c) if they addressed gastric cancer prevention and gastritis staging in a way that has a direct impact on *H. pylori* management. Regional documents from outside Europe were retained where the setting combined high prevalence, high antimicrobial resistance and constrained drug availability, since those problems resemble those in Greece. Where a Society had issued more than 1 document, only the most recent version was considered. The documents are compared in Table 1. A statement-level alignment between the Hellenic consensus and current guidance is presented in Table 2. Greek antimicrobial resistance data reported by the Laboratory of Medical Microbiology of the Hellenic Pasteur Institute, Athens, Greece, at a recent Panhellenic Congress of *Helicobacter pylori* and Human Microbiota are summarized in the section on antimicrobial resistance below.

From a treatment to a communicable disease and prevention paradigm

The most important development since the Hellenic consensus was published concerns the rationale for treatment. The Kyoto consensus had already defined *H. pylori* gastritis as an infectious disease [20], and the entity subsequently entered the 11th revision of the International Classification of Diseases. Maastricht VI/Florence argued that *H. pylori* infection always causes gastritis, irrespective of symptoms or complications, and the indication for treatment is no longer restricted to patients with clinical symptoms [6]. Reinforcing this notion, the Taipei Global Consensus II, updating the first Taipei consensus [21], concluded that *H. pylori* eradication is an effective prevention strategy that should be offered to all infected adults [7].

The Hellenic consensus is organized around disease-specific indications: peptic ulcer, gastric mucosa-associated lymphoid tissue lymphoma, users of non-steroidal anti-inflammatory drugs and aspirin, patients starting long-term proton pump inhibitor (PPI) therapy, unexplained iron deficiency anemia, immune thrombocytopenic purpura and vitamin B12 deficiency, together with screen-and-treat in high-risk communities and high-risk individuals [3]. Although not much has changed with respect to these indications, what has been added internationally is the principle that a confirmed *H. pylori* infection is itself an indication for treatment. The latter has practical consequences for how: (a) an incidentally positive test in an asymptomatic adult is handled in primary care; (b) household members of an index case are approached; and (c) *H. pylori* eradication is presented to patients.

Screening

The Hellenic consensus set the test-and-treat threshold at 45 years, and referred older patients or those with alarm features for gastroscopy, adding that the strategy should be re-evaluated if *H. pylori* prevalence in the population below 45 years fell below 20%, implying that Greek *H. pylori* prevalence would require continuous monitoring [3]. Maastricht VI/Florence used a threshold of 50 years, with a range of 45-55 depending on local gastric cancer risk [6]. The difference is small, and both positions remain reasonable; the monitoring the Hellenic panel called for has not yet been organized nationally as of 2026 [22,23].

Population-level prevention is where the literature has advanced the most. A pragmatic randomized trial in 152,503 individuals in Taiwan combined *H. pylori* stool antigen testing with fecal immunochemical testing and showed a reduction in gastric cancer incidence after adjustment for adherence [24]. A cluster-randomized trial in more than 180,000 participants in China showed reduced incidence, particularly in those successfully treated [25]. An updated meta-analysis found a lower incidence of gastric cancer after *H. pylori* eradication in healthy infected individuals (risk ratio [RR] 0.64, 95% confidence interval [CI] 0.48-0.84) and in patients undergoing endoscopic mucosal resection of gastric neoplasia (RR 0.52, 95%CI 0.38-0.71); gastric cancer mortality was lower in the first group only (RR 0.78, 95%CI 0.62-0.98), with no effect on all-cause mortality [26]. Two decades of follow up on the Matsu Islands documented parallel falls in prevalence, atrophy and cancer incidence [27].

Table 1 Guidelines on *Helicobacter pylori* infection considered in this review (mentioned in a chronological order starting from the most recent)

Guidelines (year) [ref.]	Society	Scope	Main focus	Methodology
MAPS III (2025) [10]	ESGE, EHMSG, ESP	European	Precancerous conditions and early gastric neoplasia	GRADE
Taipei Global Consensus II (2025) [7]	Asian Pacific Alliance on Helicobacter and Microbiota and partner societies	Global	Screening and eradication for gastric cancer prevention	28 statements; GRADE; Delphi; 80% agreement threshold
Middle East regional consensus (2025) [19]	Expert panel from 6 Middle Eastern countries with an international expert	Regional (Middle East)	Diagnosis, treatment, prevention and gut microbiota in a high-resistance region	Statements adopted from Maastricht VI; 2 Delphi rounds; GRADE; 80% agreement threshold
Korean guidelines, 2025 revised edition (2025) [46]	Korean College of Helicobacter and Upper Gastrointestinal Research	National (Korea)	Diagnosis and treatment; tailored and empirical strategies; P-CABs	9 key questions; systematic review and meta-analysis; modified Delphi with 64 experts
IARC working group report (2025) [11]	International Agency for Research on Cancer	Global	Implementation of population-based screen-and-treat programs	Working group consensus
RE.GA.IN. (2024) [9]	International gastritis initiative	International	Diagnosis, classification and staging of gastritis	Consensus statements
ACG guideline (2024) [33]	American College of Gastroenterology	North America	Treatment	GRADE for 11 questions; 6 expert key concepts
DGVS S2k update (2024) [17]	German Society of Gastroenterology, Digestive and Metabolic Diseases	National (Germany)	*H. pylori* and gastroduodenal ulcer disease	S2k consensus
Second Irish consensus (2024) [18]	Irish *H. pylori* Working Group	National (Ireland)	Diagnosis and treatment in adults	GRADE; Delphi
ESPGHAN/NASPGHAN update (2024) [12]	European and North American pediatric societies	International, pediatric	Children and adolescents	GRADE; evidence-to-decision framework
Belgian consensus (2023) [15]	Belgian expert panel	National (Belgium)	Diagnosis and management in adults and children	GRADE
WGO global guideline (2023) [8]	World Gastroenterology Organisation	Global, resource-tiered	Diagnosis and treatment across resource settings	Cascade approach
Polish recommendations (2023) [16]	Polish Society of Gastroenterology	National (Poland)	Diagnosis and treatment	Expert working group
Maastricht VI/ Florence (2022) [6]	European Helicobacter and Microbiota Study Group	International	Indications, diagnosis, treatment, prevention, gut microbiota	5 working groups; GRADE; Delphi; 80% agreement threshold
SIGE/SIED guidelines (2022) [13]	Italian Society of Gastroenterology; Italian Society of Digestive Endoscopy	National (Italy)	Diagnosis and treatment	Evidence-based recommendations
V Spanish Consensus (2022) [14]	Spanish gastroenterology and primary care societies	National (Spain)	Treatment	GRADE; Delphi
Hellenic consensus (2020) [3]	Hellenic Society of Gastroenterology	National (Greece)	Indications, diagnosis, extragastric associations, treatment, gastric malignancy	39 statements; Oxford levels of evidence; 70% agreement threshold

ACG, American College of Gastroenterology; DGVS, German Society of Gastroenterology, Digestive and Metabolic Diseases; EHMSG, European Helicobacter and Microbiota Study Group; ESGE, European Society of Gastrointestinal Endoscopy; ESP, European Society of Pathology; ESPGHAN, European Society for Paediatric Gastroenterology, Hepatology and Nutrition; GRADE, Grading of Recommendations Assessment, Development and Evaluation; H. pylori, Helicobacter pylori; IARC, International Agency for Research on Cancer; MAPS, management of epithelial precancerous conditions and lesions in the stomach; NASPGHAN, North American Society for Pediatric Gastroenterology, Hepatology and Nutrition; RE.GA.IN., Real-world Gastritis Initiative; SIED, Italian Society of Digestive Endoscopy; SIGE, Italian Society of Gastroenterology; WGO, World Gastroenterology Organisation

Table 2 Hellenic consensus statements and corresponding developments since its publication

Domain	Hellenic consensus 2020 [3]	Current international guidance [6,7,10,33]	What has changed since its publication	Implications for Greece/ suggested issues for the next Hellenic consensus
Conceptual framework	Disease-based indications for eradication	*H. pylori* gastritis is an infectious disease; eradication offered to all infected adults	Entry into ICD-11 and adoption of the infectious disease framing	State the *H. pylori* infection framing, and establish the indications for its eradication
Test-and-treat threshold	Below 45 years for uninvestigated dyspepsia	Below 50 years (range 45-55) adjusted to local gastric cancer risk	Threshold refined; national prevalence monitoring still required	Define the Greek age threshold on current national prevalence data
Population screening	Screen-and-treat for high-risk communities and individuals	Program framework covering target population, age of initiation, test selection, integration with existing screening, quality assurance and cost-effectiveness	Two large randomized trials, an updated meta-analysis and IARC implementation guidance [11,24-26]	Decide whether Greece adopts organized screening, with a cost-effectiveness analysis on Greek incidence and cost data
Opportunistic screening	Not addressed	Screening for gastric cancer and staging of precancerous conditions at every diagnostic gastroscopy	New recommendation in MAPS III [10]	Available now without a screening program; define the biopsy protocol at diagnostic gastroscopy
Immigrants from high-incidence countries	Not addressed	Screening recommended	New statement in Maastricht VI/ Florence and Taipei Global Consensus II	Add a statement on immigrants from high-incidence countries
Family-based case-finding	Not addressed	Family-based screening and eradication may reduce transmission and reinfection	Large family-based epidemiological data [30]	Add targeted screening of first-degree relatives of patients with gastric cancer
Preferred non-invasive test	^{13}C-urea breath test; stool antigen test not preferred in adults	^{13}C-urea breath test and validated monoclonal stool antigen test both appropriate, including for population screening	Reappraisal of monoclonal stool antigen testing for large-scale use	Reconsider the standing of the monoclonal stool antigen test, above all if screening is contemplated
Urea breath test protocol	Test meal not specified	Citric acid an essential component of the protocol	Specified in Maastricht VI	Specify citric acid in the national protocol
Serology	Positive IgG indicates past, not necessarily current, infection; local cutoffs required	Locally validated serology acceptable for screening in low-prevalence settings, with confirmatory non-serological testing before treatment	Two-stage screening pathway defined	Name the assays that have been locally validated
Susceptibility testing before first-line therapy	Not recommended; reserved as a rescue option	Reasonable to perform routinely for stewardship; clarithromycin susceptibility testing before any clarithromycin-containing regimen	Directional change in international guidance	Decide the Greek position, taking account of laboratory capacity and reimbursement
Molecular and stool-based resistance testing	Promising; clinical and economic data awaited	Real-time polymerase chain reaction, whole-genome and next-generation sequencing endorsed; biopsies from the rapid urease test reusable	Next-generation stool sequencing validated against biopsy [34]	Map laboratory capacity and reimbursement before recommending routine use
Gastric functional serology	Not addressed	Pepsinogens I and II and gastrin-17 recommended for non-invasive assessment of atrophy	Incorporated into Maastricht VI/ Florence and MAPS III	Settle availability and reimbursement of pepsinogen and gastrin-17 testing

(*Contd...*)

Table 2 (*Continued*)

Domain	Hellenic consensus 2020 [3]	Current international guidance [6,7,10,33]	What has changed since its publication	Implications for Greece/ suggested issues for the next Hellenic consensus
Autoimmune gastritis	Not addressed	Defined diagnostic pathway using gastrin, pepsinogen ratio and autoantibodies	Formalized in Maastricht VI/ Florence and RE.GA. IN. [9,39]	Add a diagnostic pathway for autoimmune gastritis
Gastritis staging	OLGA/OLGIM endorsed; surveillance for stages III-IV	Histological staging mandatory; endoscopic grading and Kimura–Takemoto classification incorporated	RE.GA.IN. and MAPS III [9,10]	Align staging and endoscopic quality standards with RE.GA.IN. and MAPS III
First-line therapy	Concomitant non-bismuth quadruple therapy for at least 10 days; hybrid 14 days as alternative	Bismuth quadruple therapy for 14 days preferred; concomitant therapy for 14 days where bismuth is unavailable; rifabutin triple and P-CAB–amoxicillin dual therapy as additional first-line options	Bismuth now marketed in Greece; combination product anticipated	Decide whether Greek first-line treatment moves to bismuth quadruple therapy
Bismuth quadruple dosing	Not applicable; bismuth unavailable when Hellenic consensus was published	Optimized regimen defined as standard-dose PPI b.i.d., bismuth 300 mg q.i.d., tetracycline 500 mg q.i.d. and metronidazole 1500-2000 mg daily; doxycycline not an acceptable substitute	Dosing definition introduced [33,52]	State the dose in full and rule out substitution of doxycycline, since tetracycline is unavailable as a separate product
Concomitant versus bismuth quadruple therapy	Concomitant therapy preferred, bismuth being unavailable	Comparable eradication with concomitant and bismuth quadruple therapy in randomized trials (intention-to-treat 86% vs. 88%; RD − 0.01, 95%CI − 0.04 to 0.03; $P = 0.63$); concomitant therapy discouraged on stewardship grounds	Updated meta-analysis of randomized trials [53]	Both regimens remain defensible; choose on stewardship grounds and on local effectiveness
Treatment duration	At least 10 days for concomitant therapy	14 days unless a shorter schedule is proven effective locally	Duration recommendation strengthened	Recommend 14 days unless Greek data support a shorter schedule
Potassium-competitive acid blockers	Mentioned narratively; approved in Japan at the time	Central to first- and second-line algorithms	New class in international algorithms; not marketed in Greece	Not marketed in Greece; define the evidence and the position of the Society should authorization and reimbursement follow
Choice of proton pump inhibitor	High-dose second-generation PPI	Esomeprazole or rabeprazole preferred where CYP2C19 rapid or ultrarapid metabolism is known or likely; otherwise an increased dose	Pharmacogenomic data linking CYP2C19 phenotype to eradication failure [33,58]	Name esomeprazole or rabeprazole, a change that needs no new drug approval
Penicillin allergy	Empirical clarithromycin plus fluoroquinolone regimen	Bismuth quadruple therapy first-line; P-CAB-based regimens without amoxicillin as alternative; formal allergy testing encouraged	Bismuth availability now permits alignment	Align with bismuth quadruple therapy now that bismuth is marketed
Second-line therapy	Levofloxacin triple therapy for at least 10 days	Clarithromycin and levofloxacin not reused; empirical levofloxacin-based rescue regimens only where levofloxacin resistance is below 10%	Secondary levofloxacin resistance in Greece 10-19% in 2019-2022	Empirical levofloxacin rescue is hard to defend at Greek secondary resistance levels
Rifabutin	Third line or later	First-line option in the ACG guideline; rescue option elsewhere	Expanded evidence base	Consider earlier placement, subject to availability

(*Contd...*)

Table 2 (*Continued*)

Domain	Hellenic consensus 2020 [3]	Current international guidance [6,7,10,33]	What has changed since its publication	Implications for Greece/ suggested issues for the next Hellenic consensus
High-dose dual therapy	Option worth considering after multiple failures	Rescue option	Systematic evaluation [59]	Define its place in the Greek treatment sequence
Confirmation of eradication	^{13}C-urea breath test at least 2 weeks after PPI and 4 weeks after antibiotics	Confirmatory testing 4-6 weeks after completion of therapy	Interval harmonized internationally	Harmonize the interval at 4-6 weeks after completion of therapy
Local audit of eradication success	Not addressed	Universal test of cure; empirical regimen reconsidered where local eradication falls below about 85%	Confirmation reframed as a quality measure [8,33]	Set a national effectiveness threshold below which an empirical regimen is abandoned
Post-eradication surveillance	Surveillance for OLGA/ OLGIM III-IV	Every 2-3 years for advanced atrophy or extensive intestinal metaplasia; additional triggers include open-type atrophy and abnormal pepsinogen profile	Intervals and risk markers defined in MAPS III and Taipei Global Consensus II	Adopt defined intervals for advanced atrophy and intestinal metaplasia
Antimicrobial stewardship	National registries recommended	Stewardship framework structuring the treatment recommendations	Explicit framework introduced [35]	Make stewardship an explicit chapter, supported by a functioning national registry
Probiotics as an adjunct	Not addressed	Meta-analyses and European registry data show higher eradication and fewer adverse events with probiotic co-prescription	Evidence base updated since the ACG guideline [64-69]	Decide whether to recommend probiotics, naming the preparation and the regimen
Resource-adapted guidance	Not addressed	Cascade pathways graded by available resources; regional adaptation of Maastricht VI/ Florence where drug availability is constrained	WGO global guideline [8] and Middle East regional consensus [19]	A workable model for matching statements to Greek drug and laboratory availability
Gut microbiota and resistome	Alteration acknowledged; clinical significance unclear	Disruption transient with recovery within 6-12 months; population-level ecological effects flagged for research	Randomized long-term data [60]	Reassure on transience, and continue to argue stewardship on resistance grounds
Genetic risk stratification	Not addressed	Conditional recommendation in individuals with a family history of gastric cancer	New statement in Taipei Global Consensus II	Premature for a national statement; keep under review
Children and adolescents	Not addressed	Updated international pediatric guideline	ESPGHAN/ NASPGHAN update 2024 [12]	Add a pediatric section aligned with ESPGHAN/ NASPGHAN

ACG, American College of Gastroenterology; CI, confidence interval; ESPGHAN, European Society for Paediatric Gastroenterology, Hepatology and Nutrition; H. pylori, Helicobacter pylori; IARC, International Agency for Research on Cancer; ICD-11, International Classification of Diseases 11th revision; IgG, immunoglobulin G; MAPS, management of epithelial precancerous conditions and lesions in the stomach; NASPGHAN, North American Society for Pediatric Gastroenterology, Hepatology and Nutrition; OLGA, operative link on gastritis assessment; OLGIM, operative link on gastric intestinal metaplasia assessment; P-CAB, potassium-competitive acid blocker; PPI, proton pump inhibitor; RE.GA.IN., Real-world Gastritis Initiative

Following these data, the Taipei Global Consensus II devoted 11 statements to screening, covering prioritization of high-incidence regions and high-risk groups, screening of adult residents of and immigrants from high-incidence countries, integration into existing preventive health programs, an optimal starting age that remains uncertain but is practically reasonable between 35 and 45 years, and the opportunity to pair *H. pylori* testing with colorectal cancer screening [7]. Maastricht VI/Florence recommends that population-based programs be adapted to regional requirements and integrated into healthcare priorities [6]. The International Agency for Research on Cancer working group report published in 2025 provides implementation guidance on readiness assessment, test selection, responsible antibiotic use and cost containment [11]. MAPS III adds a complementary approach: every diagnostic gastroscopy should include screening for gastric cancer and the diagnosis and staging of precancerous conditions, irrespective of country of origin, so that individual

risk is stratified opportunistically in patients who are older or otherwise at higher risk [10].

A modeling study in 185 countries projected 15.6 million gastric cancers among people born between 2008 and 2017, of which 76% are attributable to *H. pylori* and therefore potentially preventable [28]. European activity has also become concrete, with the GISTAR trial in Latvia, the EUROHELICAN study of screen-and-treat in young adults, and the TOGAS pilots examining feasibility, stakeholder views and cost-effectiveness across several member states [29]. Disappointingly, Greece has taken part in none of them.

As regards intrafamilial transmission, this is now regarded as the dominant route of acquisition. A national family-based survey of more than 10,000 Chinese households quantified household risk [30], and both Maastricht VI/Florence and the Taipei Global Consensus II endorse family-based screening and eradication to reduce transmission and reinfection [6,7]. The Hellenic consensus, written before these data, addressed neither family-based approaches nor the growing Greek population of immigrants from high-incidence countries.

Diagnosis

Several Hellenic diagnostic positions remain concordant with current guidance, including the preference for the ^{13}C-urea breath test as the noninvasive method of choice, the use of 2 biopsies for the rapid urease test, and histochemistry as the reference method for *H. pylori* detection [3,6,31].

However, there have been 3 significant changes since the Hellenic consensus was published: (1) the relative standing of the monoclonal stool antigen test has risen. The Hellenic consensus judged it not to be the preferred method in Greek adults, partly because of the reluctance of patients to collect stool samples [3]. Contemporary guidance treats a properly validated monoclonal stool antigen test as an appropriate test before and after treatment, and the Taipei Global Consensus II names it, alongside the ^{13}C-urea breath test, as one of the 2 preferred options for population-based screening, largely on grounds of cost and scalability [6,7,32]. Should a Greek screening initiative be considered, the position on stool antigen testing would need revisiting; (2) Maastricht VI/Florence specifies citric acid as an essential component of the urea breath test protocol, since it delays gastric emptying and improves sensitivity, particularly in atrophic stomachs [6]—a point the Hellenic text does not cover; and (3) the position of susceptibility testing has changed considerably. The Hellenic consensus stated that culture and antimicrobial susceptibility testing are not recommended before first-line therapy, and should be reserved as a rescue option, particularly after a second-line treatment has failed, noting that culture was then performed in very few Greek centers [3]. Maastricht VI/Florence now considers it reasonable to perform susceptibility testing routinely, even before first-line treatment, in the interest of antibiotic stewardship, and recommends clarithromycin susceptibility testing before prescribing any clarithromycin-containing regimen [6]. The ACG guideline advises testing whenever the choice of therapy is not otherwise clear [33], and the Taipei Global Consensus II organizes its treatment section around the mindful use of antibiotics [7]. The technical basis has also shifted: gastric biopsies recovered from the rapid urease test can be reused for polymerase chain reaction [6]; next-generation sequencing of stool has been shown to give results comparable to gastric biopsy [34]; and a framework for constructing therapy guidelines around stewardship has been published [35].

As regards the expected gain, in a meta-analysis, susceptibility-guided first-line treatment was modestly better than empirical treatment (RR 1.15, 95%CI 1.11-1.20), but the advantage was no longer apparent where the empirical comparator was a quadruple regimen, and none was demonstrated for second-line or third-line therapy [33,36]. The ACG therefore ties the indication to local performance: testing adds little where empirical bismuth quadruple therapy achieves eradication above 85% locally, and is advised before any clarithromycin- or levofloxacin-containing regimen [33]. The World Gastroenterology Organisation (WGO) adds that culture has a limited role after failures, since secondary clarithromycin resistance is common enough that confirming it changes nothing, and that a failed regimen should not be repeated [8].

Recent advances on the assessment of the gastric mucosa are remarkable. The Hellenic consensus endorsed the operative link on gastritis assessment (OLGA) and the operative link on gastric intestinal metaplasia assessment (OLGIM) staging systems, and recommended surveillance for stages III and IV [3]. Since then: (a) RE.GA.IN. has clarified the endoscopic and histological diagnosis of gastritis and formalized the place of autoimmune gastritis [9]; (b) MAPS III has set the current European standard for the management of precancerous conditions and early neoplasia, superseding MAPS II [10,37]; and (c) gastric functional serology with pepsinogens I and II and gastrin-17, the Kimura–Takemoto endoscopic classification and endoscopic grading of gastric intestinal metaplasia have all been incorporated into international recommendations [6,7,10,38,39]. Autoimmune gastritis in particular currently has a defined diagnostic pathway based on gastrin, the pepsinogen ratio, and antibodies to intrinsic factor and parietal cells [6,39,40], a topic the 2020 Hellenic consensus document did not cover.

Antimicrobial resistance in Greece

The Hellenic consensus classified Greece as a high-resistance area, citing rates of 32-37% for metronidazole, 24-27% for clarithromycin and 7-8% for levofloxacin in adults, with limited data on secondary resistance [3]. Surveillance data that included the COVID-19 period from the Hellenic Pasteur Institute extended that picture. Primary clarithromycin resistance rose from 2.3% in 1998 to 28% in 2018, primary metronidazole resistance has fluctuated between 25% and 43% without a downward trend, and primary levofloxacin resistance has remained between 7.7% and 9.5% since 2008.

Secondary resistance measured between 2019 and 2022 was considerably higher: clarithromycin 67-78%, metronidazole 38-51% and levofloxacin 10-19%, with the levofloxacin figure approximately doubling over those 4 years.

These figures are consistent with the European survey conducted in 2018—in which primary clarithromycin resistance in Greece was among the higher national estimates, and fluoroquinolone resistance tracked community antibiotic consumption [41]—and with a prospective molecular study in Thrace that found clarithromycin resistance of 23.2% in treatment-naïve patients [42]. Greece has contributed to the European Registry on *H. pylori* Management since its inception, and Greek first-line prescribing and effectiveness have been analyzed within it [43,44].

In the systematic review used by the WGO guideline, pooled primary resistance in the European region was 18% (95%CI 16-20) for clarithromycin, 32% (95%CI 27-36) for metronidazole and 11% (95%CI 9-13) for levofloxacin, with secondary resistance of 48% (95%CI 38-57), 48% (95%CI 38-58) and 19% (95%CI 14-24), respectively [8,45]. Greek primary clarithromycin and metronidazole resistance exceed these estimates, and Greek secondary clarithromycin resistance of 67-78% is well above them.

The secondary levofloxacin data have direct bearing on one Hellenic statement. The consensus recommends a levofloxacin triple regimen for at least 10 days as the preferred second-line treatment, explicitly on the basis that levofloxacin resistance in Greece was then below the critical limit of 10%, while noting an increasing trend that jeopardized its use [3]. In the population in which second-line therapy is actually given, resistance now exceeds that limit. Maastricht VI/Florence and the Taipei Global Consensus II both advise that clarithromycin and levofloxacin should not be reused in rescue therapy**,** and Maastricht VI/Florence recommends empirical levofloxacin-based triple or quadruple rescue regimens in areas where levofloxacin resistance is below 10% [6,7].

Adapting international guidance to local resources

The WGO global guideline is built on a cascade structure, in which pathways are graded by the resources actually available rather than against a single standard of care [8]. Its principles are that recommendations derived in one region may not be transferrable to another, that local resistance data and local audit of eradication outcomes are priorities, and that previous personal exposure to a macrolide or a quinolone should be taken as evidence of resistance [8]. Where bismuth or tetracycline are not registered nationally, generic products can often be used with the permission of the relevant authorities, which aligns with the current Greek position on tetracycline [8].

The first regional consensus for the Middle East, published in 2025, applied such reasoning in a setting that resembles the Greek one: high prevalence, clarithromycin resistance above 15% or unmeasured, no national surveillance, and uneven access to bismuth [19]. The panel adopted the Maastricht VI/Florence statements, re-evaluated each against regional conditions using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach and 2 Delphi rounds, recommended single-capsule bismuth quadruple therapy for 10 days where clarithromycin resistance is high or unknown, and graded several treatment statements as low-quality evidence where regional data were absent [19].

A second example is the Korean guidelines, revised in 2025. Faced with a rise in clarithromycin resistance from 17.8% to 33.3%, the panel restricted empirical clarithromycin triple *H. pylori* eradication therapy to defined conditions, removed sequential therapy, adopted a dual strategy of susceptibility-guided and empirical quadruple treatment, accepted potassium-competitive acid blockers (P-CABs) in place of PPIs, and extended the indications for eradication to gastric cancer prevention [46]. Greece faces a comparable set of constraints, and the transferable element is the method rather than the content.

Treatment

First-line therapy

The Hellenic consensus recommended non-bismuth quadruple concomitant therapy for at least 10 days as the preferred first-line option in Greece, with a 14-day hybrid regimen as an alternative, and advised against standard triple therapy of 7-10 days and against fluoroquinolone-containing first-line regimens [3]. These recommendations were based on Greek randomized and prospective data [47-49], and on the absence of bismuth-based options.

International guidance has since agreed on the use of bismuth quadruple therapy for 14 days as the preferred empirical first-line regimen, on the grounds that its efficacy is not affected by clarithromycin or levofloxacin resistance, and that metronidazole resistance is largely overcome by dose and duration [6,7,33]. Where a non-bismuth quadruple regimen is used, Maastricht VI/Florence specifies 14 days unless a 10-day schedule has been shown to be effective locally [6]. The ACG guideline has additionally introduced 2 first-line options that were not available for consideration when the Hellenic consensus was drafted: rifabutin triple therapy and dual therapy with a P-CAB and amoxicillin [33]. Real-world European registry data support cure rates above 90% with single-capsule bismuth quadruple therapy in first-line use [50], and network meta-analyses have compared the available first-line regimens directly [51].

The ACG defines what it means by an optimized bismuth quadruple regimen, and the definition matters for a country introducing one: a standard-dose PPI b.i.d., bismuth 300 mg q.i.d., tetracycline 500 mg q.i.d., and metronidazole 1500-2000 mg daily in divided doses [33]. Substituting doxycycline for tetracycline and underdosing metronidazole both reduce effectiveness: in a single-center series eradication fell from 87% with 14 days of the optimized regimen to 70% when doxycycline replaced tetracycline [33,52]. Since tetracycline is

not available in Greece as a separate product, while doxycycline is, this is the substitution most likely to be made and the one a national statement should preempt.

The comparison that matters most for the current Hellenic recommendation is between concomitant therapy (PPI, amoxicillin, clarithromycin and metronidazole given concurrently) and bismuth quadruple therapy (PPI, bismuth, tetracycline and metronidazole). In a more recent meta-analysis restricted to randomized trials (11 trials, 3448 patients), concomitant therapy was comparable to bismuth quadruple therapy with tetracycline and nitroimidazole: intention-to-treat 86% versus 88% (risk difference [RD] −0.01, 95%CI −0.04 to 0.03; P=0.63) and per-protocol 90% versus 92% (RD −0.02, 95%CI −0.04 to 0.01; P=0.17), with moderate heterogeneity between groups (I^2=45% and I^2=37%, respectively). A sensitivity analysis against single-capsule bismuth quadruple therapy (2 studies, 473 patients) gave an intention-to-treat efficacy of 92% with both regimens (RD 0.03, 95%CI −0.10 to 0.15; P=0.66; I^2=79%) and per-protocol 93% versus 94% (RD −0.01, 95%CI −0.06 to 0.04; P=0.70; I^2=17%) [53]. The ACG advises against concomitant therapy, mainly on the grounds of mindful use of antibiotics, since it exposes every patient to clarithromycin and metronidazole while resistance to both is rising [33], an argument that carries particular weight in Greece and must be set against the Greek trial data supporting the 2020 recommendation [47-49].

The Greek position on bismuth then reflected availability. Instead, in 2026, bismuth as a single agent is marketed in Greece, and a fixed combination of bismuth, metronidazole and tetracycline is expected but has not yet been released; tetracycline as a separate product remains unavailable, though it can be obtained via a galenic pharmacy store. A revised consensus would therefore be written at a point when a genuine choice between bismuth-based and bismuth-free first-line algorithms becomes possible for the first time since 2010, and this alone is a substantive reason to reopen the treatment chapter.

Acid suppression and P-CABs

The Hellenic consensus referred to vonoprazan in narrative form only, noting that it had at that time been approved for clinical use in Japan alone, and recommended instead that acid suppression be optimized with a high-dose, second-generation PPI [3]. Since then, Maastricht VI/Florence has concluded that P-CAB-based combinations are superior or not inferior to conventional PPI-based triple therapies in first- and second-line treatment, and superior in patients with antimicrobial-resistant infection [6]. The ACG guideline suggests P-CAB–amoxicillin dual therapy as a first-line option and prefers P-CAB–clarithromycin triple therapy over the PPI equivalent when clarithromycin susceptibility is unknown [33]. The Taipei Global Consensus II positions P-CAB-based regimens as alternatives to bismuth quadruple therapy [7]. A randomized trial conducted in the United States and Europe defined both the potential and the limitations of these regimens in Western populations [54], and a network meta-analysis has compared P-CAB-based dual, triple and quadruple schedules [55]. A 2026 meta-analysis of 11 randomized trials in 2877 patients found that vonoprazan–amoxicillin dual therapy improved eradication only when given for 14 days (RR 1.08, 95%CI 1.01-1.15; P<0.001), with no advantage at 7 days (RR 0.97, 95%CI 0.91-1.04; P=0.30), and with fewer adverse events (RR 0.66, 95%CI 0.52-0.84; P<0.001) [56].

As P-CABs are not marketed in Greece, a national document cannot recommend them for current use, but it can define the evidence, the situations in which they would be preferred, and the position of the Society should authorization and reimbursement follow [57].

That absence also makes the choice among PPIs more consequential. Omeprazole, lansoprazole and pantoprazole are extensively metabolized by CYP2C19, and rapid and ultrarapid metabolizers, who carry an increased-function allele present in about 20% of European populations, have a 2.5- to 4.4-fold higher likelihood of eradication failure with these agents, an association not seen with esomeprazole or rabeprazole [33,58]. The ACG therefore suggests esomeprazole or rabeprazole, or an increased dose of another PPI [33]. Naming the preferred agent and dose, rather than referring generically to a high-dose second-generation PPI, is a change that requires no new drug approvals.

Second-line and rescue therapies

Beyond the levofloxacin issue outlined above, 2 further treatment options have gained ground. Rifabutin, confined in the Hellenic consensus to third-line or subsequent attempts [3], is now listed among first-line options in the ACG guideline [33]. High-dose dual therapy with amoxicillin and potent acid suppression, described in the Hellenic text as an option worth considering when multidrug-resistant infection is suspected after multiple failures [3], has since been examined more systematically and features in international rescue algorithms [6,59].

The ACG is more reserved, finding the North American evidence insufficient to recommend either for or against high-dose dual therapy in treatment-experienced patients and confining it to situations in which optimized bismuth quadruple or rifabutin triple therapy cannot be used [33].

Penicillin allergy

For patients with documented penicillin allergy the Hellenic consensus proposed an empirical clarithromycin- and fluoroquinolone-containing regimen, with bismuth quadruple therapy prescribed after failure and procured through the national pharmaceutical agency where necessary [3]. Maastricht VI/Florence and the Taipei Global Consensus II now recommend bismuth quadruple therapy as the first-line regimen in penicillin allergy, with P-CAB-based regimens excluding amoxicillin as the alternative [6,7]. Both

documents also emphasize formal allergy testing, since true immunoglobulin E-mediated allergy is present in a small minority of those who report it. With bismuth now available in Greece, this is one of the statements most readily brought into line with international practice.

Both the ACG and the WGO quantify that point: the true prevalence is below 1%, and formal assessment with specific antibodies, skin testing and, if negative, a supervised oral challenge shows that up to 80% of lower-risk patients are not allergic and can receive amoxicillin-containing therapy [8,33]. The ACG advises referral for assessment, and consideration of desensitization, when optimized bismuth quadruple therapy is unsuitable [33].

Confirmation of *H. pylori* eradication

The Hellenic consensus specified the ^{13}C-urea breath test performed at least 2 weeks after PPI discontinuation and 4 weeks after antibiotics and bismuth [3], while current guidance frames the interval as 4-6 weeks after completion of therapy [6,7]. The Hellenic panel also recommended national registries to monitor treatment efficacy and safety in clinical practice; Greek participation in the European Registry has continued [43,44], while a national resistance surveillance network with periodic public reporting has yet to be established. Antimicrobial stewardship, which now structures the treatment sections of both Maastricht VI/Florence and the Taipei Global Consensus II [6,7,35], was not an explicit topic discussed in the Greek consensus conference.

The ACG frames confirmation as universal rather than selective, at least 4 weeks after the end of treatment, with PPIs withheld for 2 weeks and serology excluded; the effect of P-CABs on these tests has not been adequately studied [33]. It also treats testing as a quality measure, since it lets a service detect first-line eradication below about 85% and change its empirical regimen; post-treatment testing in the United States rose from under 25% in 2005 to 60-80% by 2019 [33]. No comparable Greek figure has been published.

Post-eradication surveillance and the gastric cancer agenda

The gastric malignancy chapter of the Hellenic consensus anticipated much of what followed: *H. pylori* eradication is most effective before severe atrophy develops, screen-and-treat prevents gastric cancer in high-risk communities, image-enhanced endoscopy improves detection of preneoplastic lesions, and OLGA/OLGIM stages III and IV warrant surveillance endoscopy [3].

MAPS III and the Taipei Global Consensus II recommend surveillance every 2-3 years for advanced atrophic gastritis or extensive intestinal metaplasia, with a longer interval for intermediate stages, and identify open-type atrophy on the Kimura–Takemoto classification and an abnormal pepsinogen profile as additional triggers for surveillance [7,10]. Follow up after endoscopic resection of early gastric cancer is similarly codified [10]. Two further topics have emerged: genetic risk stratification in individuals with a family history of gastric cancer, addressed as a conditional recommendation in the Taipei Global Consensus II [7], and the longer-term consequences of eradication for the gut microbiota and resistome, where randomized data now indicate recovery within 6-12 months at the individual level while population-level effects remain to be defined [7,60].

Whether *H. pylori* eradication still helps once intestinal metaplasia or dysplasia is present has also been addressed by a meta-analysis of 16 randomized trials in 15,027 such patients, and found a lower gastric cancer risk after eradication (RR 0.55, 95%CI 0.46-0.67; P<0.001), with reductions in both dysplasia (RR 0.51, 95%CI 0.32-0.82; P=0.005) and intestinal metaplasia (RR 0.61, 95%CI 0.40-0.93; P=0.022) [61]. The point of no return is therefore relative rather than absolute.

Evidence has also accumulated on the prevention of ulcer complications in older patients on aspirin, where a large primary-care randomized trial showed a reduction in ulcer bleeding during the first 2.5 years after eradication that was not maintained over longer follow up [62]. This refines rather than contradicts the Hellenic statements on nonsteroidal anti-inflammatory drug and aspirin users.

Pediatric practice

The Hellenic consensus provided recommendations for adult patients. Instead, the European and North American pediatric societies updated their joint guidance in 2024, revising the recommended antimicrobial regimens, reaffirming that diagnostic testing is not indicated in children with functional abdominal pain, and prioritizing susceptibility-guided therapy [12]. Greece has no national pediatric position, and a revised adult consensus could usefully signpost the international pediatric document and define the interface between adult and pediatric services, particularly in the context of family-based case-finding.

Current Greek practice

A national survey of 180 members of the Hellenic Society of Gastroenterology, published in 2024 with a response rate of 31.4%, found that more than 90% of respondents test for *H. pylori* in patients with active peptic ulcer disease, gastric lymphoma, a family history of gastric cancer, or an endoscopic appearance suggestive of gastritis, and that the majority conform to international guidance, with the exception of testing in gastroesophageal reflux disease; adjunctive probiotic use was common [63]. The survey indicates a receptive audience for national guidance and provides a baseline against which the effect of an updated consensus could later be measured.

Adjunctive probiotics were commonly prescribed, whereas the ACG concluded that the evidence is insufficient to show that probiotics improve the efficacy or tolerability of eradication

therapy [33]. Evidence published since that guideline supports their use as adjuncts: meta-analyses of randomized trials report higher eradication rates and fewer adverse events when probiotics are added to bismuth quadruple therapy or to non-bismuth quadruple concomitant therapy [64-67], and real-world data from the European Registry point in the same direction, with better effectiveness and fewer adverse events among treatments co-prescribed with probiotics, and a specific gain for *Saccharomyces boulardii* added to concomitant therapy [68-70]. Strain, dose and duration still differ between trials, so a national statement would need to name the preparation and the regimen with which it is to be given.

Implications for a future Hellenic consensus: evidence gaps and priorities

The evidence analyzed above can be summarized in 6 priority areas that a second Hellenic consensus would need to address:

1. Contemporary national resistance data are the foundation. The Pasteur Institute series provides a primary and secondary resistance picture up to 2018 and 2022, respectively; extending it prospectively, with regional representation and periodic publication, would allow empirical algorithms to be defended on Greek evidence.
2. The position on susceptibility-guided therapy is the area in which international guidance has moved furthest since the Hellenic consensus was published, and a national statement would need to define which centers can offer culture or molecular testing, when testing should be requested, and how results feed into the treatment algorithm.
3. With bismuth marketed, and a bismuth, metronidazole and tetracycline combination anticipated, the Society will have to decide whether Greek first-line therapy converges with the international bismuth quadruple standard, and to specify the fallback while the combination product remains unavailable, including whether tetracycline should be imported as a generic or galenic product, rather than replaced by doxycycline [8,33].
4. A prevention chapter with operational content: eligibility and age of initiation, choice of test at population scale, the option of pairing *H. pylori* testing with colorectal cancer screening, opportunistic screening with risk stratification of precancerous conditions at every diagnostic gastroscopy [10], targeted screening of first-degree relatives of patients with gastric cancer and of immigrants from high-incidence countries, and a cost-effectiveness analysis based on Greek incidence and cost data [6,7,11].
5. Alignment of the diagnostic and surveillance chapters with RE.GA.IN. and MAPS III, including surveillance intervals, gastric functional serology, endoscopic grading of atrophy and intestinal metaplasia, and the diagnostic pathway for autoimmune gastritis [9,10].
6. Universal confirmation of eradication, a stated local threshold of effectiveness below which an empirical regimen is abandoned, continued audit of first-line outcomes through the European Registry, and an explicit position on adjunctive probiotics would give a revised consensus something against which its implementation could later be assessed [8,33,43].

Methodological questions also arise. The Hellenic consensus used the Oxford levels of evidence and a 70% acceptance threshold [3], whereas contemporary international panels apply GRADE with an 80% threshold and a formal Delphi process [6,7,33]. Adopting these would improve comparability with the documents against which the Greek statements will inevitably be read.

Concluding remarks

The 2020 Hellenic consensus was a carefully constructed document that took proper account of Greek epidemiology, Greek trial data and the medicines actually available in Greece, and much of it remains serviceable. Its authors explicitly foresaw the need for periodic revision. The case for acting on that provision is now strong. The conceptual framework has shifted from disease-based treatment towards a communicable disease and cancer prevention model; randomized evidence for population-level prevention has matured; susceptibility-guided therapy has moved from a rescue option to an expectation of mindful use of antibiotics with a workable technical basis; bismuth quadruple therapy of 14 days has become the international reference first-line regimen, and bismuth has returned to the Greek market; a new class of acid suppressant occupies a central place in every major algorithm; surveillance of precancerous gastric conditions has acquired defined intervals and additional risk markers; and national surveillance shows secondary resistance to clarithromycin approaching 80%, and to levofloxacin rising above the threshold on which the current second-line recommendation was based. The experience of other high-resistance regions working under constrained drug supply suggests a workable method: adopt the international statements, then state explicitly which of them—Greek resistance data, Greek trial data or Greek drug availability—need to be modified [8,19]. Convening a second Hellenic consensus, supported by prospective national resistance surveillance and a Greek cost-effectiveness analysis, would be a timely response.

References

1. Li Y, Choi H, Leung K, Jiang F, Graham DY, Leung WK. Global prevalence of *Helicobacter pylori* infection between 1980 and 2022: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol* 2023;**8**:553-564.
2. Malfertheiner P, Camargo MC, El-Omar E, et al. *Helicobacter pylori* infection. *Nat Rev Dis Primers* 2023;**9**:19.
3. Georgopoulos SD, Michopoulos S, Rokkas T, et al. Hellenic consensus on *Helicobacter pylori* infection. *Ann Gastroenterol* 2020;**33**:105-124.
4. Papaefthymiou A, Doulberis M, Polyzos SA, Kountouras J.

National consensus on *Helicobacter pylori* infection: the next-day challenge. *Ann Gastroenterol* 2020;**33**:324-325.
5. Georgopoulos SD, Apostolopoulos P, Michopoulos S, Rokkas T. Authors' reply. *Ann Gastroenterol* 2020;**33**:325.
6. Malfertheiner P, Megraud F, Rokkas T, et al; European Helicobacter and Microbiota Study group. Management of *Helicobacter pylori* infection: the Maastricht VI/Florence consensus report. *Gut* 2022;**71**:1724-1762.
7. Liou JM, Malfertheiner P, Hong TC, et al; Asian Pacific Alliance on Helicobacter and Microbiota (APAHAM). Screening and eradication of *Helicobacter pylori* for gastric cancer prevention: Taipei Global Consensus II. *Gut* 2025;**74**:1767-1791.
8. Katelaris P, Hunt R, Bazzoli F, et al. *Helicobacter pylori* World Gastroenterology Organization global guideline. *J Clin Gastroenterol* 2023;**57**:111-126.
9. Rugge M, Genta RM, Malfertheiner P, et al; RE GA IN. RE.GA. IN.: the Real-world Gastritis Initiative-updating the updates. *Gut* 2024;**73**:407-441.
10. Dinis-Ribeiro M, Libânio D, Uchima H, et al. Management of epithelial precancerous conditions and early neoplasia of the stomach (MAPS III): European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter and Microbiota Study Group (EHMSG) and European Society of Pathology (ESP) guideline update 2025. *Endoscopy* 2025;**57**:504-554.
11. Park JY, editor. Population-based *Helicobacter pylori* screen-and-treat strategies for gastric cancer prevention: guidance on implementation (IARC Working Group Reports No. 12). Lyon: International Agency for Research on Cancer; 2025.
12. Homan M, Jones NL, Bontems P, et al; on behalf of ESPGHAN/NASPGHAN. Updated joint ESPGHAN/NASPGHAN guidelines for management of *Helicobacter pylori* infection in children and adolescents (2023). *J Pediatr Gastroenterol Nutr* 2024;**79**:758-785.
13. Romano M, Gravina AG, Eusebi LH, et al; Members of SIED National Council. Management of *Helicobacter pylori* infection: guidelines of the Italian Society of Gastroenterology (SIGE) and the Italian Society of Digestive Endoscopy (SIED). *Dig Liver Dis* 2022;**54**:1153-1161.
14. Gisbert JP, Alcedo J, Amador J, et al. V Spanish Consensus Conference on *Helicobacter pylori* infection treatment. *Gastroenterol Hepatol* 2022;**45**:392-417.
15. Garcés-Duran R, Kindt S, Kotilea K, et al. Belgian consensus for *Helicobacter pylori* management 2023. *Acta Gastroenterol Belg* 2023;**86**:74-91.
16. Jaroń K, Pietrzak A, Daniluk J, et al. Diagnostic and therapeutic recommendations on *Helicobacter pylori* infection. Recommendations of the Working Group of the Polish Society of Gastroenterology. *Prz Gastroenterol* 2023;**18**:225-248.
17. Fischbach W, Bornschein J, Hoffmann JC, et al. Update S2k-guideline *Helicobacter pylori* and gastroduodenal ulcer disease of the German Society of Gastroenterology, Digestive and Metabolic Diseases (DGVS). *Z Gastroenterol* 2024;**62**:261-321.
18. Smith SM, Boyle B, Buckley M, et al. The second Irish Helicobacter pylori Working Group consensus for the diagnosis and treatment of *Helicobacter pylori* infection in adult patients in Ireland. *Eur J Gastroenterol Hepatol* 2024;**36**:1000-1009.
19. Sharara AI, Alsohaibani FI, Alsaegh A, et al. First regional consensus on the management of *Helicobacter pylori* infection in the Middle East. *World J Gastroenterol* 2025;**31**:107138.
20. Sugano K, Tack J, Kuipers EJ, et al; faculty members of Kyoto Global Consensus Conference. Kyoto global consensus report on *Helicobacter pylori* gastritis. *Gut* 2015;**64**:1353-1367.
21. Liou JM, Malfertheiner P, Lee YC, et al; Asian Pacific Alliance on Helicobacter and Microbiota (APAHAM). Screening and eradication of *Helicobacter pylori* for gastric cancer prevention: the Taipei global consensus. *Gut* 2020;**69**:2093-2112.
22. Kouvaras SN, Koumarianos IG, Ekmektzoglou K, et al. Prevalence of *Helicobacter pylori* infection and gastric intestinal metaplasia in Greek patients. *Ann Gastroenterol* 2025;**38**:604-609.
23. Kountouras J, Polyzos SA, Papanikolaou IS, Doulberis M, Liatsos C, Vardaka E. Impact of *Helicobacter pylori* eradication on the progression of Correa's cascade. *Ann Gastroenterol* 2026;**39**:278-279.
24. Lee YC, Chiang TH, Chiu HM, et al; Collaborators of Taiwan Community-based Integrated Screening Group. Screening for *Helicobacter pylori* to prevent gastric cancer: a pragmatic randomized clinical trial. *JAMA* 2024;**332**:1642-1651.
25. Pan KF, Li WQ, Zhang L, et al. Gastric cancer prevention by community eradication of *Helicobacter pylori*: a cluster-randomized controlled trial. *Nat Med* 2024;**30**:3250-3260.
26. Ford AC, Yuan Y, Park JY, Forman D, Moayyedi P. Eradication therapy to prevent gastric cancer in *Helicobacter pylori*-positive individuals: systematic review and meta-analysis of randomized controlled trials and observational studies. *Gastroenterology* 2025;**169**:261-276.
27. Chiang TH, Chang WJ, Chen SL, et al. Mass eradication of *Helicobacter pylori* to reduce gastric cancer incidence and mortality: a long-term cohort study on Matsu Islands. *Gut* 2021;**70**:243-250.
28. Park JY, Georges D, Alberts CJ, Bray F, Clifford G, Baussano I. Global lifetime estimates of expected and preventable gastric cancers across 185 countries. *Nat Med* 2025;**31**:3020-3027.
29. Leja M, Ražuka-Ebela D, Tepes B, et al; TOGAS Study Group. Overview of gastric cancer prevention initiatives in Europe. *Helicobacter* 2026;**31**:e70126.
30. Zhou XZ, Lyu NH, Zhu HY, et al; National Clinical Research Center for Digestive Diseases (Shanghai), Gastrointestinal Early Cancer Prevention & Treatment Alliance of China (GECA), Helicobacter pylori Study Group of Chinese Society of Gastroenterology and Chinese Alliance for Helicobacter pylori Study. Large-scale, national, family-based epidemiological study on *Helicobacter pylori* infection in China: the time to change practice for related disease prevention. *Gut* 2023;**72**:855-869.
31. Best LM, Takwoingi Y, Siddique S, et al. Non-invasive diagnostic tests for *Helicobacter pylori* infection. *Cochrane Database Syst Rev* 2018;**3**:CD012080.
32. Zavos C. Letter to the editor regarding "Discordance between stool antigen and urea breath testing for *Helicobacter pylori* after Roux-en-Y gastric bypass". *J Gastrointest Surg* 2026;**30**:102564.
33. Chey WD, Howden CW, Moss SF, et al. ACG clinical guideline: treatment of *Helicobacter pylori* infection. *Am J Gastroenterol* 2024;**119**:1730-1753.
34. Moss SF, Dang LP, Chua D, Sobrado J, Zhou Y, Graham DY. Comparable results of *Helicobacter pylori* antibiotic resistance testing of stools vs gastric biopsies using next-generation sequencing. *Gastroenterology* 2022;**162**:2095-2097.
35. Graham DY, Liou JM. Primer for development of guidelines for *Helicobacter pylori* therapy using antimicrobial stewardship. *Clin Gastroenterol Hepatol* 2022;**20**:973-983.
36. Nyssen OP, Espada M, Gisbert JP. Empirical vs. susceptibility-guided treatment of *Helicobacter pylori* infection: a systematic review and meta-analysis. *Front Microbiol* 2022;**13**:913436.
37. Pimentel-Nunes P, Libânio D, Marcos-Pinto R, et al. Management of epithelial precancerous conditions and lesions in the stomach (MAPS II): European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter and Microbiota Study Group (EHMSG), European Society of Pathology (ESP), and Sociedade Portuguesa de Endoscopia Digestiva (SPED) guideline update 2019. *Endoscopy* 2019;**51**:365-388.
38. Rugge M, Genta RM, Fassan M, et al. OLGA gastritis staging for the prediction of gastric cancer risk: a long-term follow-up study of 7436 patients. *Am J Gastroenterol* 2018;**113**:1621-1628.
39. Lenti MV, Rugge M, Lahner E, et al. Autoimmune gastritis. *Nat Rev*

Dis Primers 2020;**6**:56.
40. Rokkas T, Rugge M. Atrophic gastritis of distinct etiologies: malignant potential in *Helicobacter pylori*-associated and autoimmune forms. *Ann Gastroenterol* 2026;**39**:283-293.
41. Megraud F, Bruyndonckx R, Coenen S, et al; European Helicobacter pylori Antimicrobial Susceptibility Testing Working Group. Resistance to antibiotics in Europe in 2018 and its relationship to antibiotic consumption in the community. *Gut* 2021;**70**:1815-1822.
42. Karvelas A, Martinez-Gonzalez B, Papadopoulos VP, Panopoulou M, Sgouras D, Mimidis K. Real-time PCR detection of *Helicobacter pylori* clarithromycin resistance in Thrace, Greece. *Hippokratia* 2021;**25**:51-55.
43. Rokkas T, Georgopoulos S, Michopoulos S, et al; Hp-EuReg Investigators. Assessment of first-line eradication treatment in Greece: data from the European Registry on *Helicobacter pylori* management (Hp-EuReg). *Ann Gastroenterol* 2022;**35**:42-47.
44. Nyssen OP, Bordin D, Tepes B, et al; Hp-EuReg Investigators. European Registry on *Helicobacter pylori* management (Hp-EuReg): patterns and trends in first-line empirical eradication prescription and outcomes of 5 years and 21 533 patients. *Gut* 2021;**70**:40-54.
45. Savoldi A, Carrara E, Graham DY, Conti M, Tacconelli E. Prevalence of antibiotic resistance in *Helicobacter pylori*: a systematic review and meta-analysis in World Health Organization regions. *Gastroenterology* 2018;**155**:1372-1382.
46. Bang CS, Kang SJ, Lim H, et al; Korean College of Helicobacter and Upper Gastrointestinal Research. Evidence-based guidelines for the diagnosis and treatment of *Helicobacter pylori* infection in Korea: 2025 revised edition. *Helicobacter* 2026;**31**:e70149.
47. Georgopoulos SD, Xirouchakis E, Martinez-Gonzales B, et al. Randomized clinical trial comparing ten day concomitant and sequential therapies for *Helicobacter pylori* eradication in a high clarithromycin resistance area. *Eur J Intern Med* 2016;**32**:84-90.
48. Georgopoulos SD, Papastergiou V, Martinez-Gonzalez B, et al. Hybrid therapy as first-line regimen for *Helicobacter pylori* eradication in a high clarithromycin resistance area: a prospective open-label trial. *Ann Gastroenterol* 2018;**31**:205-210.
49. Apostolopoulos P, Ekmektzoglou K, Georgopoulos S, et al. 10-day versus 14-day quadruple concomitant nonbismuth therapy for the treatment of *Helicobacter pylori* infection: results from a randomized prospective study in a high clarithromycin resistance country. *J Clin Gastroenterol* 2020;**54**:522-527.
50. Nyssen OP, Perez-Aisa A, Castro-Fernandez M, et al; Hp-EuReg investigators. European Registry on *Helicobacter pylori* management: single-capsule bismuth quadruple therapy is effective in real-world clinical practice. *United European Gastroenterol J* 2021;**9**:38-46.
51. Rokkas T, Gisbert JP, Malfertheiner P, et al. Comparative effectiveness of multiple different first-line treatment regimens for *Helicobacter pylori* infection: a network meta-analysis. *Gastroenterology* 2021;**161**:495-507.
52. Alsamman MA, Vecchio EC, Shawwa K, Acosta-Gonzales G, Resnick MB, Moss SF. Retrospective analysis confirms tetracycline quadruple as best *Helicobacter pylori* regimen in the USA. *Dig Dis Sci* 2019;**64**:2893-2898.
53. Parra P, Nyssen OP, Gisbert JP. Non-bismuth quadruple concomitant treatment for *Helicobacter pylori* eradication: a systematic review and meta-analysis. *Helicobacter* 2026;**31**:e70099.
54. Chey WD, Mégraud F, Laine L, López LJ, Hunt BJ, Howden CW. Vonoprazan triple and dual therapy for *Helicobacter pylori* infection in the United States and Europe: randomized clinical trial. *Gastroenterology* 2022;**163**:608-619.
55. Rokkas T, Ekmektzoglou K, Niv Y, Graham DY. Comparative efficacy and safety of potassium-competitive acid blocker-based dual, triple, and quadruple regimens for first-line *Helicobacter pylori* infection treatment: a systematic review and network meta-analysis. *Am J Gastroenterol* 2025;**120**:787-798.
56. Bharia U, Goel A, Raja F, et al. Vonoprazan-amoxicillin dual therapy improves 14-day eradication and reduces adverse events in patients with *Helicobacter pylori* infection: an updated landmark systematic review and meta-analysis of 11 randomized trials with subgroup analysis. *Ann Gastroenterol* 2026;**39**:294-302.
57. Zavos C. Local price and clarithromycin resistance shape the cost of vonoprazan triple therapy for *Helicobacter pylori* eradication. *Helicobacter* 2026;**31**:e70160.
58. Shah SC, Tepler A, Chung CP, et al. Host genetic determinants associated with *Helicobacter pylori* eradication treatment failure: a systematic review and meta-analysis. *Gastroenterology* 2021;**161**:1443-1459.
59. Shah SC, Iyer PG, Moss SF. AGA clinical practice update on the management of refractory *Helicobacter pylori* infection: expert review. *Gastroenterology* 2021;**160**:1831-1841.
60. Liou JM, Chen CC, Chang CM, et al; Taiwan Gastrointestinal Disease and Helicobacter Consortium. Long-term changes of gut microbiota, antibiotic resistance, and metabolic parameters after *Helicobacter pylori* eradication: a multicentre, open-label, randomised trial. *Lancet Infect Dis* 2019;**19**:1109-1120.
61. Fu Q, Yu H, Liu M, et al. Effect of *Helicobacter pylori* eradication on gastric cancer risk in patients with intestinal metaplasia or dysplasia: a meta-analysis of randomized controlled trials. *Front Microbiol* 2025;**16**:1530549.
62. Hawkey C, Avery A, Coupland CAC, et al; HEAT Trialists. *Helicobacter pylori* eradication for primary prevention of peptic ulcer bleeding in older patients prescribed aspirin in primary care (HEAT): a randomised, double-blind, placebo-controlled trial. *Lancet* 2022;**400**:1597-1606.
63. Protopapas AA, Papagiouvanni I, Protopapas AN, Goulis I. *Helicobacter pylori* infection diagnosis and management: current practices of Greek gastroenterologists. *Ann Gastroenterol* 2024;**37**:15-21.
64. Zhou S, Yu Y, Tian J, Wang X, Zeng M, Song H. Efficacy and safety of probiotics combined with bismuth-containing quadruple therapy for *Helicobacter pylori* eradication: a systematic review and meta-analysis. *Front Microbiol* 2025;**16**:1704508.
65. Liu YH, Zhang J, Li DH, et al. The impact of probiotics on *Helicobacter pylori* eradication with bismuth quadruple therapy: a systematic review and meta-analysis. *Int J Antimicrob Agents* 2025;**66**:107600.
66. Ma F, Huang H, Tian K, Wang W. Efficacy and safety of *Saccharomyces boulardii* with standard quadruple therapy for eradication of *Helicobacter pylori* in adults: meta-analysis. *J Coll Physicians Surg Pak* 2025;**35**:1440-1446.
67. Li M, Wang X, Dong X, Teng G, Dai Y, Wang W. *Lactobacillus reuteri* compared with placebo as an adjuvant in *Helicobacter pylori* eradication therapy: a meta-analysis of randomized controlled trials. *Ther Adv Gastroenterol* 2024;**17:** 17562848241258021.
68. Casas Deza D, Alcedo J, Lafuente M, et al; Hp-EuReg investigators. Probiotics prescribed with *Helicobacter pylori* eradication therapy in Europe: usage pattern, effectiveness, and safety. results from the European Registry on *Helicobacter pylori* management (Hp-EuReg). *Am J Gastroenterol* 2025;**120**:2644-2659.
69. Nyssen OP, Jonaitis L, Pérez-Aísa Á, et al; Hp-EuReg investigators. Real-world effectiveness and safety of *Saccharomyces boulardii* CNCM I-745 as adjunct therapy for *Helicobacter pylori* eradication: data from the European Registry on *H. pylori* management (Hp-EuReg). *Helicobacter* 2026;**31**:e70119.
70. Zavos C. *Saccharomyces boulardii* as an adjunct to *Helicobacter pylori* eradication therapy: the role of clarithromycin resistance and product definition. *J Dig Dis* 2026 (in press) doi: 10.1111/1751-2980.70076