Clinical Practice Guidelines on the Management of Gastric Cancer and *Helicobacter pylori* in the Philippines

Quick Reference Guide

March 2024

Executive Summary

This clinical practice guideline for the Management of Gastric Cancer and *Helicobacter pylori* infection in the Philippines is a collaborative effort between the Department of Health, the National Institutes of Health - Institute of Clinical Epidemiology, Bicol Medical Center, and the Philippine Society of Digestive Endoscopy.

The CPG systematically synthesizes evidence to standardize practices in certain priority topics regarding the screening, diagnosis, management, and surveillance of gastric cancer and *Helicobacter pylori* infection in the country. Equal emphasis is placed on addressing *H. pylori* infection, given its significant role as a major risk factor for the development of gastric cancer.

The guideline development process adhered to the widely accepted Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach, including GRADE Adolopment—a systematic process adapting evidence summaries—and the GRADE Evidence to Decision (EtD2) framework. This involved:

1. Identifying critical questions and outcomes
2. Retrieving current evidence
3. Assessing and synthesizing the evidence base
4. Formulating draft recommendations
5. Convening a multi-sectoral stakeholder panel to discuss values, preferences, and assess recommendation strength
6. Planning for dissemination, implementation, impact evaluation, and updates.

The CPG offers eighteen (18) recommendations and five (5) good practice statements derived from assessing the best available evidence on ten (10) prioritized clinical questions related to screening, diagnosis, management, and surveillance of gastric cancer and *H.pylori* infection. The recommendations in this CPG will remain valid and will be updated every three years or when new evidence emerges.

Target Population

This CPG is designed for individuals diagnosed with gastric cancer and for both children and adults infected with *H. pylori* bacteria. Some guideline questions target populations suspected to have gastric cancer, high-risk individuals, as well as the asymptomatic general population.

Intended Users

These recommendations are designed for use by healthcare practitioners of all levels of care. They can also be used by policymakers and allied health professionals who treat patients with gastric cancer and *H. pylori*.

Guideline Questions

#	Topic	Guideline Question	Type
1	Gastric cancer screening using alarm signs in patients with dyspepsia	GQ: Should we use alarm signs and symptoms for the early diagnosis of gastric cancer among patients with dyspepsia? RQ: Among patients with dyspepsia, how accurate are alarm signs and symptoms for the early diagnosis of gastric cancer?	Diagnosis
2	Non-invasive tests for diagnosing gastric cancer	GQ: Should we do non-invasive tests to diagnose gastric cancer? RQ: Among patients with alarm signs and symptoms, how accurate are non-invasive tests (imaging and biochemical tests) compared to biopsy/histopathology in diagnosing gastric cancer?	Diagnosis
3	Conventional CT vs. CT + EUS/PET for pre-operative staging of gastric cancer	GQ: Should we use FDG-PET CT or endoscopic ultrasound (EUS) on top of contrast CT to guide pre-operative staging in patients with gastric cancer? RQ: Among patients diagnosed with gastric cancer, how safe, accurate, and effective is contrast CT alone compared to contrast CT with adjunctive diagnostic modalities (EUS, FDG-PET-CT) in pre-operative staging?	Diagnosis
4	Multidisciplinary team approach for managing patients with gastric cancer	GQ: Should we use a multidisciplinary team approach for patients with gastric cancer? RQ: Among patients with gastric cancer, how effective is a multidisciplinary team approach in improving gastric-cancer related outcomes?	Treatment
5	Non-surgical hemostatic interventions for bleeding	GQ: Should we use non-surgical hemostatic interventions in patients with unresectable gastric cancer with tumoral bleeding? RQ: Among patients with unresectable gastric cancer presenting with tumoral bleeding, how effective are non-surgical hemostatic interventions in improving survival and bleeding control?	Treatment
6	Mass screening for H pylori in asymptomatic general population	GQ: Should we do mass or targeted screening for *H. pylori* infection in asymptomatic individuals? RQ: Among asymptomatic individuals, how safe, accurate, and effective is mass screening compared to targeted screening for detecting *H. pylori* infection and decreasing *H. pylori*-related morbidity and gastric cancer incidence?	Diagnosis
7	Non-invasive tests for H pylori diagnosis	GQ: Should we use non-invasive tests to diagnose active *H. pylori* infection in patients with dyspepsia? RQ: Among patients with dyspepsia, how accurate, safe, and effective are non-invasive tests in diagnosing active H pylori infection?	Diagnosis
8	Standard antibiotic therapy vs. other antibiotic therapy	GQ: Should we use the 14-day triple therapy in patients with *H. pylori* infection? RQ: Among patients with H pylori infection, how effective and safe is 14-day triple therapy compared to novel drug combinations in patients with *H. pylori* infection?	Treatment
9	Post-treatment surveillance for H pylori	GQ: Should we use confirmatory tests to decrease incidence of gastric cancer in patients who completed eradication treatment? RQ: Among patients who completed eradication treatment for *H. pylori*, how effective is confirmatory testing compared to no testing in decreasing incidence of gastric cancer, *H. pylori* related morbidity, and drug resistance rates?	Diagnosis, Prognosis
10	Routine surveillance EGD for gastric cancer prevention	GQ: Should we do monitoring and surveillance of precancerous lesions? RQ: Among patients diagnosed with premalignant gastric lesions, how effective is periodic monitoring using EGD in decreasing gastric cancer-related mortality and morbidity?	Diagnosis, Prognosis

Certainty of Evidence

Each recommendation was formulated with an accompanying certainty of evidence rating. The certainty of evidence reflects the assessment of the CPG developers regarding the level of confidence in the stated effects of the intervention/diagnostic test. An initial high rating was assigned to randomized controlled trials (RCTs), while observational studies were rated low. This initial rating for RCTs has been subject to downgrade based on factors such as risk of bias, inconsistency, indirectness, imprecision, and publication bias. Observational studies, on the other hand, have received upgraded certainty of evidence when a large effect, dose-response relationship, and/or a significant effect despite confounding effects were observed.

Certainty	Definition and Implications	Randomized Controlled Trials	Observational Studies
HIGH ⊕⊕⊕⊕	The group is very confident that the true effect lies close to that of the estimate of the effect (Further research is very unlikely to change confidence in the effect estimate)	No serious flaws in study quality	Extremely strong association and no major threats to validity
MODERATE ⊕⊕⊕◯	The group is moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that is substantially different. (Further research is likely to have an important impact)	Serious flaws in design or execution; quasi-experimental design	Strong consistent association and no plausible confounders
LOW ⊕⊕◯◯	Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of effect. (Further research is very likely to have an important impact)	Very serious flaws in design or execution	No serious flaws in study quality
VERY LOW ⊕◯◯◯	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect. (The estimate of the effect is very uncertain)	Very serious flaws and at least one other serious threat to validity	Serious flaws in design and execution

Summary of Recommendations

No.	Recommendations	Strength of Recommendation	Certainty of Evidence	Considerations
Gastric cancer screening using alarm signs in patients with dyspepsia				
1	Among adults with dyspepsia, we suggest using alarm signs and symptoms* to identify those who may need an upper gastrointestinal endoscopy. **Includes any of the following: unintended weight loss (at least 5% of usual body weight in the preceding 6-12 months), dysphagia or odynophagia, bleeding, anemia, vomiting, abdominal mass, age ≥ 50 years old*	**Weak**	**Very Low** ⊕◯◯◯	Using alarm signs and symptoms for gastric cancer screening may be justified, as the benefits may outweigh the risks of false positive cases. Based on local data showing higher gastric cancer incidence, a cut-off age of ≥50 is suggested for screening, as screening may not be cost-effective for children and adolescents due to the low prevalence. However, there may be a potential for higher false positives in this age group, leading to a weak recommendation for those with ≥3 alarm signs. This recommendation may result in high direct medical costs associated with further testing, and its implementation would be affected by endoscopy availability and patient preference.
Non-invasive tests for diagnosing gastric cancer				
2.1	The gold standard for diagnosing gastric cancer is through biopsy, histopathology obtained through esophagogastroduodenoscopy (EGD) and/or surgery.	**Good practice statement**		Non-invasive tests are integral components of the diagnostic process for cancer, often used early on or as additional tools for diagnosis. However, it is essential to recognize that more invasive procedures, such as biopsy through surgery or endoscopy, remain the gold standard for confirmation of diagnosis due to their reliability.
2.2	Among patients with alarm signs and symptoms, we recommend against the use of non-invasive tests in place of biopsy for diagnosing gastric cancer.	**Strong**	**Very Low** ⊕◯◯◯	

No.	Recommendations	Strength of Recommendation	Certainty of Evidence	Considerations
Conventional CT (computed tomographic) vs. CT + endoscopic ultrasonography/positron emission tomography (EUS/PET) for pre-operative staging of gastric cancer				
3.1	Among patients with gastric cancer, we recommend the use of MDCT for staging gastric cancer prior to surgery.	**Strong**	**Low** ⊕⊕◯◯	MDCT, the standard diagnostic exam for staging gastric cancer, may not be widely available across the country, and there is a shortage of trained specialists to interpret the results. While MDCT scans are crucial for determining metastatic makeup, endoscopic ultrasound may offer the most benefit for early-stage gastric cancer. FDG-PET scans, although available, are not ideal due to false positives and cost considerations. Moreover, standard CT scans are generally deemed sufficient for detecting metastatic diseases. However, in cases like node-positive and intraperitoneal metastatic gastric cancer, CT scans may sometimes miss lesions. FDG-PET scans are not consistently more accurate in these instances based on the reviewed studies.
3.2	Among patients with early gastric cancer, we suggest the use of EUS as an adjunct to multidetector computed tomography (MDCT) in areas where it is available and technical expertise is present.	**Weak**	**Very Low** ⊕◯◯◯	
3.3	Among patients with gastric cancer, we do not recommend the routine use of FDG-PET/CT as an adjunct to MDCT for staging.	**Strong**	**Low** ⊕⊕◯◯	
Multidisciplinary team approach for managing patients with gastric cancer				
4	Among patients with gastric cancer, we recommend the use of a multidisciplinary team approach.	**Strong**	**Very Low** ⊕◯◯◯	Despite the very low certainty of evidence regarding its benefits, multidisciplinary team (MDT) discussions have the potential to enhance clinical decision-making, particularly for cases of advanced gastric cancer. Patients perceive this approach as advantageous for their welfare and well-being, although it may come with increased costs. Integrating MDT discussions into standardization and policy-making processes was suggested as a strategy to mitigate these costs. However, potential harms, such as overstaging, and concerns about feasibility and availability in low-resource areas must be carefully considered.

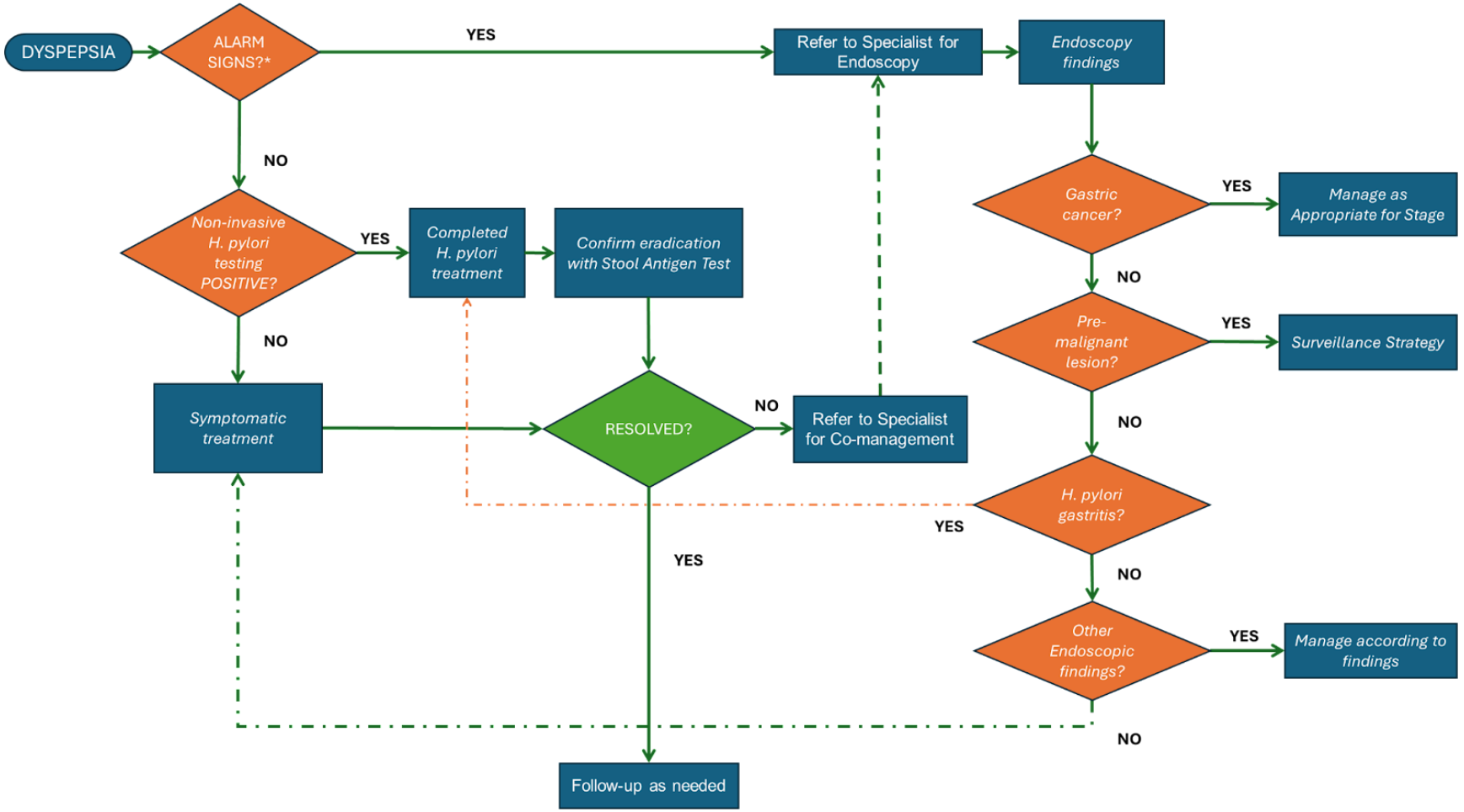
No.	Recommendations	Strength of Recommendation	Certainty of Evidence	Considerations
Non-surgical hemostatic interventions for bleeding				
5.1	Shared decision making for the palliative control of tumor bleeding by endoscopic techniques and/or radiotherapy should be discussed to the patient as deemed necessary.	**Good practice statement**		Non-surgical hemostatic interventions may have limited efficacy in patients with lower functional status (ECOG 3+). Endoscopic treatments, including clips, are considered appropriate for cases of unresectable bleeding. Concerns about potential harms from transarterial embolization (TAE), such as spleen infarction and pyloric stenosis, were highlighted. While TAE was favored by the panel, its use was subject to the condition of a low risk of bleeding impacting other organs. Hemospray was viewed as a more acceptable option for patients, while radiotherapy posed challenges due to limited accessibility outside Metro Manila and additional costs associated with transportation and logistics. A good practice statement emphasized the importance of shared decision-making between patients and healthcare providers, considering factors like cost-effectiveness, physician expertise, logistical support, and practical feasibility, rather than endorsing a specific procedure outright.
5.2	Among patients with unresectable gastric cancer with tumor bleeding, we suggest the use of hemostatic spray powder application or transarterial embolization as bridging therapy for more definitive treatment for tumor bleeding where accessible.	**Weak**	**Very Low** ⊕◯◯◯	
Screening for *H. pylori* in asymptomatic general population				
6.1	Among asymptomatic individuals, we suggest against mass screening for *H. pylori.*	**Weak**	**Very Low** ⊕◯◯◯	Mass screening for gastric cancer in the Philippines is not recommended due to a lack of local evidence regarding disease burden and risk distribution. The prevalent strains of Helicobacter pylori in the country are not proven to be carcinogenic. Implementing mass screening was considered less feasible and cost-effective without substantial incidence data to support it. Instead, individualized screening may be conducted under specific conditions, which would be more realistic and sustainable in the long term.

No.	Recommendations	Strength of Recommendation	Certainty of Evidence	Considerations
Non-invasive tests for *H. pylori* diagnosis				
7.1	Among adults with dyspepsia without alarm signs and symptoms, we recommend the test-and-treat strategy in the non-invasive testing of *H pylori* infection.	**Strong**	**Low** ⊕⊕◯◯	The stool antigen test (SAT) is strongly recommended for diagnosing H. pylori infection in adults due to its accuracy, cost-effectiveness, and ease of implementation. SAT is more readily available than urea breath tests (UBT) and exhibits sensitivity comparable to other diagnostic methods. In cases where patients present with alarm signs and symptoms, conducting endoscopy and testing for H. pylori using the rapid urease test (RUT) is suggested by the consensus panel. However, patient reluctance to handle stool samples may affect the test's acceptability in routine medical practice. Although serology is the most widely available and cost-effective option, it cannot distinguish between past and current infections. Qualitative tests may remain positive for up to 3 years post-treatment, and quantitative levels may persist for 6 to 12 months after treatment. UBT may face availability challenges in hospitals, limiting its applicability to the general population. However, UBT could be beneficial for patients on anticoagulants, with low platelet counts, or at high risk of cardiac complications. It is not recommended for children due to low specificity and sensitivity, as well as challenges in compliance. Patient acceptability tends to favor UBT, with high satisfaction rates compared to endoscopy. Factors influencing UBT accuracy include the presence of *Helicobacter heilmannii,* certain infections causing false positives, and recent antibiotic or bismuth compound use leading to potential false negatives.
7.2	Among adults with dyspepsia without alarm signs and symptoms, we recommend the use of stool antigen tests to diagnose *H. pylori* infection.	**Strong**	**Low** ⊕⊕◯◯	
7.3	Among adults with dyspepsia without alarm signs and symptoms, we suggest the use of 13C or 14C Urea Breath test (UBT) to diagnose *H. pylori* infection.	**Weak**	**Low** ⊕⊕◯◯	
7.4	Among adults with dyspepsia without alarm signs and symptoms, we suggest against the use of serology to diagnose *H. pylori* infection.	**Weak**	**Low** ⊕⊕◯◯	
7.5	Among children with dyspepsia without alarm signs and symptoms, we recommend against non-invasive testing (13C/14C UBT, serology, stool antigen tests) for *H. pylori* infection.	**Strong**	**Low** ⊕⊕◯◯	

No.	Recommendations	Strength of Recommendation	Certainty of Evidence	Considerations
Standard triple antibiotic therapy for *H. pylori*				
8.1	Among adults and children with *H. pylori* infection, we suggest using the 14-day concomitant triple therapy containing clarithromycin.	**Weak**	**Very Low** ⊕◯◯◯	The 14-day triple therapy is suggested for both adults and children, in accordance with common practice. However, the panel opted to lower the strength of this recommendation due to concerns regarding the rising clarithromycin resistance observed in the country. Local data regarding the extent of this increase was unavailable, and routine testing for resistance was not commonly conducted locally, leading to an information gap. Alternative regimens may be considered for retreatment, albeit they are costlier compared to the 14-day triple therapy. While deliberating the inclusion of probiotics in recommendations for children, a decision was deferred due to insufficient clinical data supporting their use.
8.2	Among adults with *H. pylori* infection, we suggest using alternative regimens*. **14D clarithromycin-based sequential, 14D levofloxacin-based sequential, 10-14D bismuth-containing quadruple, 7D vonoprazan-containing triple therapy*	**Weak**	**Very Low** ⊕◯◯◯	
8.3	Among children with *H. pylori* infection, we suggest using alternative regimens*. **14D sequential, bismuth-based quadruple therapy*	**Weak**	**Very Low** ⊕◯◯◯	
Post-treatment surveillance of *H. pylori*				
9.1	In adults and children who completed eradication treatment for *H. pylori* infection, clinicians should consider doing tests of cure using urea breath test or stool antigen test to confirm eradication of *H. pylori*.	**Good practice statement**		A good practice statement was formulated in recognition of the potential benefits of post-treatment surveillance, notwithstanding the absence of direct evidence. The recommendation discourages re-testing for individuals with negative results but advocates for re-testing for those who initially test positive and undergo antibiotic treatment. Subsequent retesting is deemed
9.2	Biopsy-based testing for cure may be considered only if there are other indications for a repeat EGD.	**Good practice statement**		

No.	Recommendations	Strength of Recommendation	Certainty of Evidence	Considerations
9.3	Tests of cure should be done at least 4 weeks after the completion of antibiotic therapy and after proton pump inhibitor (PPI) therapy has been withheld for 1-2 weeks.	**Good practice statement**		unnecessary once a negative outcome is achieved, unless symptoms reappear. Anticipated challenges pertaining to logistics, particularly concerning costs and test availability, are expected, particularly in provincial areas. The decision to consolidate pediatric and adult statements was justified by the non-practice of test-and-treat in pediatrics due to the non-standardized urea breath test (UBT) and the absence of routine stool antigen tests in the Philippines. However, the necessity for local studies and eradication therapy was underscored.
Surveillance for precancerous lesions				
10	Among patients with gastric premalignant conditions, we suggest periodic surveillance using upper gastrointestinal endoscopy. ● **Atrophic gastritis:** within 3 years ● **Gastrointestinal metaplasia:** within 3 years ○ **Dysplasia:** endoscopic resection, if available, or annual surveillance	**Weak**	**Low** ⊕⊕◯◯	Endoscopic surveillance every 3 years is recommended considering the relatively low incidence rate of gastric cancer in the Philippines. The consensus panel underscored the importance of enhancing not only equipment but also the quality of training for individuals performing endoscopy to ensure the highest standard of surveillance. Given the rapid development of gastric cancer compared to certain other cancers, regular surveillance was emphasized for its potential to mitigate false positives in diagnosis, alleviate the risks and anxieties associated with additional tests such as biopsy, and ultimately influence the overall costs of prevention and diagnosis.

Algorithm for Recommendations 1, 7, 9, and 10



Quick Reference Figure 1. Algorithm summarizing Recommendations 1, 7, 9 and 10