***Helicobacter pylori* Testing**

Policy Number: AHS – G2044 – *Helicobacter pylori* Testing	Effective Date: 11/01/2026

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I. Policy Description

Helicobacter pylori (*H. pylori*) is a spiral-shaped, gram-negative bacteria that thrives while living in acidic environments, growing in close association with the stomach lining. H. *pylori* infection causes chronic inflammation (infection) in the stomach and is associated with conditions such as peptic ulcer disease, chronic gastritis, gastric adenocarcinoma, and gastric mucosa associated lymphoid tissue (MALT) lymphoma.[1]

II. Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request.

1) For individuals who are 18 years of age and older, urea breath testing **or** stool antigen testing to diagnose an *H. pylori* infection **MEETS COVERAGE CRITERIA** in **any** of the following situations:
   a) For individuals with dyspepsia (see Note 1).
   b) For individuals with active peptic ulcer disease (PUD).
   c) For individuals with past PUD and who have had recurrent symptoms.
   d) For individuals with low-grade gastric mucosa-associated lymphoid tissue (MALT) lymphoma.
   e) For individuals with a history of resection of early gastric cancer (EGC).
   f) For individuals with gastric intestinal metaplasia (GIM).
   g) For individuals initiating chronic treatment with or who have been on a long-term aspirin or non-steroidal anti-inflammatory drug (NSAID) treatment.
   h) For individuals with unexplained iron deficiency anemia.
   i) For individuals with idiopathic thrombocytopenic purpura (ITP).
   j) For individuals with a family history of gastric cancer.
   k) For individuals who are first-generation immigrants from a high prevalence area.

2) For individuals who are 18 years of age and older and who are undergoing endoscopic examination or who have alarm symptoms (see Note 2), a biopsy-based endoscopic histology test and **either** a rapid urease test **or** a culture with susceptibility testing to diagnose an *H. pylori* infection **MEETS COVERAGE CRITERIA**.

3) For individuals who are less than 18 years of age, urea breath testing **or** stool antigen testing to diagnose an *H. pylori* infection **MEETS COVERAGE CRITERIA** in **any** of the following situations:
   a) For individuals who have gastric or duodenal ulcers or erosions.
   b) For individuals who have a family history of gastric cancer.

4) For individuals who are less than 18 years of age and who have refractory iron deficiency anemia, a biopsy-based endoscopic histology test and **either** a rapid urease test **or** a culture with susceptibility testing to diagnose an *H. pylori* infection **MEETS COVERAGE CRITERIA.**

5) For all individuals who have tested positive for *H. pylori*, urea breath testing **or** stool antigen testing to measure the success of eradication of *H. pylori* infection, with testing performed at least four weeks post-treatment, **MEETS COVERAGE CRITERIA**.

6) For individuals with a refractory *H. pylori* infection, susceptibility testing (culture or nucleic acid based) **MEETS COVERAGE CRITERIA.**

7) Urea breath testing **or** stool antigen testing to diagnose an *H. pylori* infection **DOES NOT MEET COVERAGE CRITERIA** for **any** of the following situations:
   a) For asymptomatic individuals of all ages.
   b) For individuals 18 years and older with typical symptoms of gastroesophageal reflux disease (i.e., heartburn, regurgitation) who do not have a history of peptic ulcer disease (PUD).

8) For individuals of all ages, serologic testing for *H. pylori* infection **DOES NOT MEET COVERAGE CRITERIA**.

9) For individuals less than 18 years of age, a biopsy-based endoscopic histology test and a rapid urease test **or** a culture with susceptibility testing to diagnose an *H. pylori* infection **DOES NOT MEET COVERAGE CRITERIA** in **any** of the following situations:
   a) For children with functional abdominal pain.
   b) As part of an initial investigation in children with iron deficiency anemia.
   c) When investigating causes of short stature.

10) For individuals with recent use of antibiotics, proton pump inhibitors (PPIs), or bismuth, the urea breath test, stool antigen, **or** biopsy-based testing to diagnose an *H. pylori* infection **DOES NOT MEET COVERAGE CRITERIA**.

11) To diagnose an H. pylori infection, concurrent testing with **any** combination of the urea breath test, stool antigen testing, **and/or** biopsy-based testing **DOES NOT MEET COVERAGE CRITERIA**.

12) For all other situations not described above, nucleic acid testing for *H. pylori* **DOES NOT MEET COVERAGE CRITERIA**.

NOTES:

Note 1: "Dyspepsia refers to bothersome upper abdominal symptoms that are often meal related. The predominant symptoms are fullness (or bloating) after meals, early satiety (inability to finish a normal-sized meal because of postprandial discomfort), or epigastric pain (or burning) that may or may not be related to meals. If dyspepsia is chronic, epigastric pain is a less common feature than postprandial fullness or satiety. Pain is not required to make a diagnosis of dyspepsia."[2]

Note 2: Alarm features of dyspepsia: vomiting, gastrointestinal bleeding, unexplained iron deficiency, or weight loss.[3]

III. Table of Terminology

Term	Definition
ACG	American College of Gastroenterology
AGA	American Gastroenterological Association
ASH	American Society of Hematology
BQT	Bismuth Quadruple Therapy
CAG	Canadian Association of Gastroenterology
CLIA '88	Clinical Laboratory Improvement Amendments of 1988
CMS	Centers for Medicare and Medicaid
CYP2C19	Cytochrome P450 Family 2 Subfamily C Member 19
EAGEN	European Association for Gastroenterology, Endoscopy and Nutrition
EGC	Early gastric cancer
EIA	Enzyme immunoassay
ELISA	Enzyme-linked immunosorbent assay
ESNM	European Society of Neurogastroenterology and Motility
ESPGHAN	European Society for Pediatric Gastroenterology Hepatology and Nutrition
FDA	Food and Drug Administration
FIA	Fluorescence immunoassay
GERD	Gastroesophageal reflux disease
GIM	Gastric intestinal metaplasia
gyrA	Deoxyribonucleic acid gyrase subunit A
HpSA-LFIA	*Helicobacter pylori* stool antigen lateral flow immunochromatography assay
H. pylori	*Helicobacter pylori*
HP	*Helicobacter pylori*
ID	Iron deficiency
IDA	Iron deficiency anemia
IgG	Immunoglobulin G
ITP	Immune thrombocytopenic purpura
LDTs	Laboratory-developed tests
MALT	Mucosa associated lymphoid tissue
NAFLD	Non-alcoholic fatty liver disease
NASPGHAN	North American Society for Pediatric Gastroenterology, Hepatology and Nutrition

NGS	Next-generation sequencing
NICE	National Institute for Health and Care Excellence
NSAID	Non-steroidal anti-inflammatory drug
OR	Odds ratio
PCAB	Potassium-competitive acid blockers
PCR	Polymerase chain reaction
Pg	Pepsinogen
PLA	Proprietary laboratory analyses
PPI	Proton pump inhibitor
PUD	Peptic ulcer disease
qPCR	Quantitative polymerase chain reaction
RNA	Ribonucleic acid
rRNA	Ribosomal ribonucleic acid
RUT	Rapid urease test
SA	Stool antigen
SAT	Stool antigen test
UBT	Urea breath test
USS	Updated Sydney system

IV. Scientific Background

Infection with *H. pylori* is common, with conservative estimates at 50% of the world's population affected. Prevalence in the United States is significant, estimated to be 30 – 40% in the general population.[4] *H. pylori* is associated with many conditions, such as peptic ulcer disease, chronic gastritis, and gastric mucosa associated lymphoid tissue (MALT) lymphoma. Other conditions such as dyspepsia have been attributed to *H. pylori* as well.[1] Common symptoms of these conditions include gastritis, dyspepsia, heartburn, and stomach pain.[2,5]

Identification of *H. pylori* infection is accomplished with one or more of the several tests available. The choice of test is guided by the reason for the test, cost and availability of the test, the patient's age and clinical presentation, prevalence in a population, and the patient's use of certain medications. Testing for *H. pylori* infection is done for two main reasons; to detect an active infection that will be treated and to confirm eradication of the infection post-treatment. Invasive and non-invasive approaches have been used. Endoscopy and collection of biopsy specimens for evaluation of *H. pylori* infection and early gastric cancer detection typically is done in older individuals and those with "alarm" symptoms, including bleeding, unexplained anemia, unexplained weight loss, progressing dysphagia, recurrent vomiting, a family history of gastrointestinal cancer, or a personal history of esophagogastric malignancy. Tissue samples can be tested for *H. pylori* via methods such as a rapid urease test, culture, or staining. Molecular methods include PCR and next-generation sequencing, and serological methods include ELISA, immunoassays, and dried blood spots. Other non-invasive methods include urea breath test and stool antigen test. Testing for eradication of infection may be performed with the same tests used for diagnosis.[1]

Analytical Validity

Non-invasive options for detection of active *H. pylori* infection include urea breath tests and stool antigen testing. The stool antigen test is an immunoassay that detects the presence of *H. pylori* in a stool sample. The test is reported to have greater than 90% sensitivity and specificity for detection of active *H. pylori* infection, and its use has been FDA cleared for all ages. This test may be used for initial diagnostic purposes and for post-treatment testing. Urea breath tests, which take advantage of the bacteria's urease activity, may also be used to detect active *H. pylori* infection. The patient ingests a solution containing either ^{13}C or ^{14}C labeled urea, after a set amount of time, the patient's breath is collected and analyzed for the presence of ^{13}C or ^{14}C labeled CO_2. If *H. pylori* is present, it will have metabolized the labeled urea and labeled CO_2 will be detected, thus indicating infection with *H. pylori*. This test takes approximately 15-20 minutes.[1]

ELISA-based serological tests are also available for detection of *H. pylori*. However, serological tests often need validation at the local level, which may not be practical in routine practice. Furthermore, serological tests do not distinguish between past and present infections. Serological tests also have a very low positive predictive value in populations with low or average prevalence, as the antibodies will be detected even after an infection has been treated or naturally resolved. In these low-prevalence areas, a positive serological test is more likely to be a false positive.[1]

Other tests such as PCR-based tests are infrequently used. The PCR test, despite its high accuracy, is often too expensive for routine use. In fact, nested PCR tests have approached 100% sensitivity and 100% specificity for detection of *H. pylori*, but the test may not be widely available and may be of limited use due to high cost.[1,6,7] PCR tests have been used for diagnostic purposes as well as identifying genetic variants of the bacteria and pathogenic genes present in a patient. A variety of body fluids, such as stool and saliva, have been used in PCR tests for this bacterial species.[7]

Some medications are known to inhibit the growth or urease activity of *H. pylori* and can cause a false negative *H. pylori* test result. Proton pump inhibitors, antibiotics, and bismuth-containing medications may decrease sensitivity of tests, thereby increasing rates of a false negative. Eradication testing is often done weeks after treatment is completed.[1]

Dechant, et al. (2020) evaluated the accuracy of various rapid urease tests (RUTs) and compared it with histopathology results. No differences were detected in the sensitivity or specificity of the various RUTs and RUTs had comparable results to histology; however, in patients treated with proton pump inhibitors and antibiotics. RUTs seemed to be more sensitive compared to histology. Pohl, et al. (2019) discuss the drawbacks of RUTs, including false negative test results if the bacterial load is less than 10^4 in the gastric biopsy and false positive test results with some urease positive bacteria, affecting the sensitivity and specificity of RUTs. Commercially available RUTs, such as HpFast, CLOTest, and HpOne, have reported specificities ranging from 95% to 100%, but their sensitivity is moderate (85% to 95%).[9]

Hussein, et al. (2021) compared the sensitivity, specificity, positive, and negative predictive values of invasive tests (RUT and gastric tissue culture) and noninvasive tests (^{14}C-Urea breath test (^{14}C-UBT), stool antigen test, and CagA-IgG serology) to the gold standard quantitative PCR (qPCR) tests for *H. pylori* in Iraq. One hundred and fifteen participants strongly suspected of *H. pylori* infection were tested. Overall, the prevalence rates ranged from 47.8% to 70.4% depending on the test method. "The ^{14}C-UBT showed the highest overall performance with 97.5% sensitivity, 97% specificity, and total accuracy of 97.3% followed by SAT, RUT, Cag-IgG, and culture method." SAT had a sensitivity of 95.0% and a specificity of 91.2%. RUT had a sensitivity of 93.8% and a specificity of 94.1%. CagA-IgG had a sensitivity of 75.3% and a specificity of 85.3%. Gastric tissue culture had a sensitivity of 67.9% and a specificity of 79.4%. The authors conclude that ^{14}C-UBT "may be recommended as first choice due to its higher performance

compared to other methods."[10] Hassan, et al. (2021) compared the accuracy, specificity, and sensitivity of the stool antigen test and the urea breath test in 45 children who underwent esophagogastroduodenoscopy between 2013 and 2019 in Sulaymaniyah City, Iraq. Histopathological findings from biopsies were used as a confirmatory diagnosis tool. The authors found that "UBT has a statistical significant correlation with result of biopsy, also it is more accurate and more sensitive than SAT, but they share same positive predictive value and same specificity." The authors conclude that UBT is preferred over SAT in children above six years.[11]

Abdelmalek, et al. (2022) evaluated the accuracy and utility assurance of *H. pylori* stool antigen lateral flow immunochromatography assay (HpSA-LFIA) in Egypt. The study used stool samples from 200 gastric patients and compared HpSA-LFIA results to the monoclonal antibody-based ELISA kit. The authors report that HpSA-LFIA achieved sensitivity of 93.75%, specificity of 59.76%, a negative predictive value of 98.00%, positive predictive value of 31.25%, and accuracy of 65.31%. The authors conclude that "HpSA-LFIA was not accurate enough to be the sole test for diagnosis and needs other confirmatory tests in case of positive conditions."[12]

Clinical Utility and Validity

The stool antigen test has been shown to have strong accuracy. A meta-analysis by Gisbert, et al. (2006) focusing on 2499 patients of 22 studies found the diagnostic test to have a sensitivity of 0.94 and a specificity of 0.97. The monoclonal version of the test was shown to be more sensitive than the polyclonal one (0.95 vs 0.83). The authors also evaluated the diagnostic test after eradication of the bacteria in 957 patients of 12 studies. The authors evaluated the antigen test at 0.93 sensitivity and 0.96 specificity post-eradication.[13]

A new automated LIAISON® Meridian H. pylori SA assay, a chemiluminescent immunoassay that uses novel monoclonal antibodies for capture and detection of the H. pylori stool antigen, was evaluated for its clinical performance. Opekun, et al. (2020) studied the utility of this assay on 277 patients who tested positive for *H. pylori* infection from an endoscopy. Comparing histology, culture, and rapid urease test results, the assay delivered a sensitivity of 95.5% and specificity of 97.6%. The authors conclude that LIAISON® "brings reliable noninvasive testing for H. pylori to the laboratory that is in very good agreement with the current, more invasive biopsy-based methods such as histology, culture, or rapid urease test."[14]

The rapid in-office, monoclonal test is widely used and provides significant benefit in terms of availability and speed. However, a study using the test as a reference to compare against a new test found the in-office test to only have a 0.50 sensitivity and 0.96 specificity out of 162 patients.[15]

The UBT has also been well-validated. A meta-analysis by Ferwana, et al. (2015) including 3999 patients of 23 studies found the diagnostic test to have a pooled sensitivity of 0.96 and a pooled specificity of 0.93. The authors noted that their populations had significant heterogeneity but concluded that the UBT had high diagnostic accuracy for detecting an *H. pylori* infection.[16] This test is often considered the gold standard for diagnosing an *H. pylori* infection.[7]

Serological tests to assess infection have also been used. A meta-analysis by Loy, et al. (1996) focused on commercial serological kits assessing *H. pylori*. Loy, et al. (1996) found these kits to have a pooled sensitivity of 0.85 and specificity of 0.79. The authors concluded that there was no major difference in accuracy between any of the kits tested.[17]

As costs of sequencing decreases, use of Next Generation Sequencing (NGS) to detect *H. pylori* infection and its antibiotic resistance has increased. In a study by Nezami, et al. (2019), 133 *H. pylori* positive specimens from histological evaluation were analyzed by NGS to detect mutations in gyrA, 23S rRNA, and 16s rRNA genes. NGS detected *H. pylori* in 126/133 cases (95% sensitivity). NGS also detected multiple mutations associated with resistance in 92 cases (73%), one mutation in 63 cases (50%), and mutations in several genes in 29 cases (23%). In the 58 cases where treatment history was available, therapy failure was observed in cases where the number of mutated genes was high. Therapy failed in 11/16 cases with multiple gene mutations and 5/27 cases with one gene mutation.[18]

Yang, et al. (2019) performed a meta-analysis investigating the association between *H. pylori* and colorectal cancer. Twenty-seven studies encompassing 14357 cases were included. The authors found an increased rate of colorectal cancer with *H. pylori* infection (odds ratio [OR] = 1.27). The authors also identified odds ratios for certain subgroups, such as Western countries (OR = 1.34), serological testing (OR = 1.20), multiple methods of testing (OR = 2.63), and cross-sectional studies (OR = 1.92).[19]

Wang, et al. (2019) performed a meta-analysis assessing the association between *H. pylori* and osteoporosis. Twenty-one studies totaling 9655 patients were analyzed. The authors found that *H. pylori* infection was associated with an increased risk of osteoporosis with an odds ratio of 1.39. However, the decrease of bone mineral density in *H. pylori* positive patients was not found to be significant compared to *H. pylori* negative patients.[20]

Zhou, et al. (2019) investigated the association between *H. pylori* infection and non-alcoholic fatty liver disease (NAFLD). Fifteen studies including 97228 patients were evaluated. The authors identified an increased risk of NAFLD in *H. pylori* positive patients compared to *H. pylori* negative patients by an odds ratio of 1.19. Similar results were found despite differing subgroups, such as geographical locations. Testing method did not significantly change the results, and there was no significant difference when using multiple detection methods.[21]

Halland, et al. (2021) assessed two novel enzyme assays (EIA), H. PYLORI QUIK CHEK™ and H. PYLORI CHEK™, for the detection of *H. pylori* antigen in stool from 271 patients in America, Germany, and Bangladesh. The EIA results were compared to clinical diagnosis, which included histological analysis and rapid urease test. H. PYLORI QUIK CHEK™ had a sensitivity of 92% and a specificity of 91%. H. PYLORI CHEK™ had a sensitivity of 91% and a specificity of 100%. The authors concluded that "the H. PYLORI QUIK CHEK™ and H. PYLORI CHEK™ assays demonstrate excellent clinical performance compared the composite reference method."[22] Marrero Rolon, et al. (2022) have developed and tested a real-time PCR assay to simultaneously detect *H. pylori* infection and genotypic markers of clarithromycin resistance. *H. pylori* infection can be treated with clarithromycin-based therapy; The American College of Gastroenterology (ACG) recommends clarithromycin-based triple therapy as first-line treatment in regions where clarithromycin resistance is known to be below 15% in patients with no history of macrolide exposure. "Clarithromycin resistance is most commonly caused by point mutations in the 23S rRNA (rRNA) gene, including A2143G, A2142G, and A2142C, which result in decreased macrolide binding to the 23S rRNA ribosomal subunit; clarithromycin resistance is considered the main cause of clarithromycin therapy failure." The authors tested 524 stool samples. *H. pylori* stool antigen tests were used as a control test for *H. pylori* detection. Sanger sequencing was used as control tests for genetic susceptibility. PCR results were positive for 98% of positive antigen stool tests. "The clarithromycin-based triple therapy success was lower when resistance was predicted by PCR (41%) than when no resistance was predicted (70%; P = 0.03)." The authors conclude that the PCR assay can diagnose *H.*

pylori infection and provide genetic susceptibility information. The authors suggest the need for susceptibility-guided therapy when clarithromycin-based therapy is considered.[23]

Nguyen Wenker, et al. (2023) studied the predictive performance of current guidelines about *H. pylori* testing in the United States. The authors investigated the association between *H. pylori* presence and *H. pylori* risk factors. *H. pylori* presence was determined based on histopathology, stool antigen, urea breath test, immunoglobulin G serology, or prior treatment. The risk factors were selected based on the Houston Consensus Conference and American College of Gastroenterology guidelines. The study included 942 patients undergoing upper endoscopy with gastric biopsies for any indication from one hospital in Houston, Texas. Overall, the risk factors with the highest predictive performance were "first-generation immigrant" and "Hispanic or black race/ethnicity." The other seven risk factors included had low predictive values. The authors concluded that "the performance of individual risk factors identified by the Houston Consensus Conference and ACG was generally low for predicting H pylori infection except for black or Hispanic race/ethnicity and first-generation immigrant status."[24]

V. Guidelines and Recommendations

American Gastroenterological Association (AGA)

The AGA recommends that "patients 55 years or younger without alarm features should receive *H. pylori* test and treat followed by acid suppression if symptoms remain" and note that "*H. pylori* testing is optimally performed by a 13C-urea breath test or stool antigen test." Alarm features include symptoms such as recurrent vomiting and weight loss. Additionally, the AGA indicates that "although the yield of endoscopy is low, it is recommended for patients older than 55 years of age and for younger patients…presenting with new-onset dyspepsia." They reason that endoscopy with biopsy is the preferred test for this age group because upper gastrointestinal malignancy becomes more common after age 55 years.[25]

In 2015 the AGA published a technical review on Upper Gastrointestinal biopsy to evaluate dyspepsia in the absence of visible mucosal lesions and found that:

- In the defined population, biopsy of normal-appearing gastric mucosa can detect HP [*H. pylori*] infection that would be missed on the exam without biopsies. The quality of evidence is very low, and there are noninvasive methods to detect HP infection.
- "Detection of HP infection with tissue biopsy and its eradication in patients with dyspepsia is associated with symptom improvement and reduction of risk for HP-related comorbidities, including gastric cancer compared with no biopsy (or no eradication). The quality of evidence is moderate. The effect on symptom resolution is not universal, and it does not appear to improve well-being. Quality of evidence for this statement is low."[26]

The AGA also released guidelines focusing on gastric intestinal metaplasia. In it, they recommend testing for *H. pylori* (followed by eradication) over no testing and eradication.[27]

The AGA released guidelines on gastrointestinal evaluation of iron deficiency anemia. AGA recommends that patients with iron deficiency anemia, without other identifiable etiology after bidirectional endoscopy, should undergo noninvasive testing for H. *pylori* over no testing at all to reduce the incidence of gastric cancer.[28]

In 2021, the AGA released a clinical practice update on the management of refractory *H. pylori* infection. The AGA recommends that "after two failed therapies with confirmed patient adherence, *H. pylori* susceptibility testing should be considered to guide the selection of subsequent regimens." They further note that "as an alternative, molecular resistance testing (using a variety of platforms) is simpler, more likely to yield results, and can also be performed on archival specimens including the formalin-fixed paraffin-embedded gastric biopsy tissue remaining after routine diagnostic histopathological testing. This obviates the need for specialized tissue handling by the endoscopist."[29]

The AGA highlights that treatment adherence is critical and recommends that providers "explain the rationale for therapy, dosing instructions, expected adverse events, and the importance of completing the full therapeutic course." They emphasize that inadequate acid suppression is a key contributor to treatment failure, stating that "the use of high-dose and more potent PPIs, PPIs not metabolized by *CYP2C19*, or potassium-competitive acid blockers if available, should be considered in cases of refractory *H. pylori* infection."[29]

To improve treatment outcomes, the AGA recommends that providers "explain the rationale for therapy, dosing instructions, expected adverse events, and the importance of completing the full therapeutic course." They advise that inadequate acid suppression contributes to treatment failure and recommend "the use of high-dose and more potent PPIs, PPIs not metabolized by *CYP2C19*, or potassium-competitive acid blockers if available." Additionally, the AGA recommends longer treatment durations for improved eradication success, including that "a 14-day therapeutic duration should be used for refractory *H. pylori* infection."[29]

American College of Gastroenterology/Canadian Association of Gastroenterology

The ACG and CAG have released guidelines on testing for *H. pylori*:

- All patients with active peptic ulcer disease (PUD), a past history of PUD (unless previous cure of *H. pylori* infection has been documented), low-grade gastric mucosa-associated lymphoid tissue (MALT) lymphoma, or a history of endoscopic resection of early gastric cancer (EGC) should be tested for *H. pylori* infection. Those who test positive should be offered treatment for the infection.
- In patients with uninvestigated dyspepsia who are under the age of 60 years and without alarm features, non-endoscopic testing for *H. pylori* infection is a consideration. Those who test positive should be offered eradication therapy.
- When upper endoscopy is undertaken in patients with dyspepsia, gastric biopsies should be taken to evaluate for *H. pylori* infection. Infected patients should be offered eradication therapy.
- Patients with typical symptoms of gastroesophageal reflux disease (GERD) without history of PUD need not be tested for *H. pylori* infection. For those who are found to be infected, treatment should be offered, acknowledging that effects on GERD symptoms are unpredictable.
- In patients taking long-term low-dose aspirin, testing for *H. pylori* infection could be considered.
- Patients initiating chronic treatment with a non-steroidal anti-inflammatory drug (NSAID) should be tested for *H. pylori* infection. Those who test positive should be offered eradication therapy.
- Patients with unexplained iron deficiency (ID) anemia despite an appropriate evaluation or idiopathic thrombocytopenic purpura should be tested for *H. pylori* infection.
- There is insufficient evidence to support routine testing and treating of *H. pylori* in asymptomatic individuals with a family history of "gastric cancer or patients with lymphocytic gastritis, hyperplastic gastric polyps and hyperemesis gravidarum."

- The ACG recommends the breath test and fecal stool antigen test as eradication tests, supported by moderate evidence.[30]

Another set of joint guidelines from the ACG and Canadian Association of Gastroenterology (CAG) noted that dyspepsia patients under 60 should be tested for *H. pylori.*

In 2024, the ACG released independent guidelines outlining recommendations for *H. pylori* treatment. "The populations of interest included both treatment-naive and treatment-experienced adult (≥18 years) patients with active *H. pylori* infection. Interventions considered were proton pump inhibitor (PPI)-clarithromycin triple therapy, bismuth quadruple therapy (BQT), concomitant therapy, rifabutin triple therapy, PCAB dual therapy, PCAB triple therapy, quinolone-based therapy, high-dose PPI dual therapy, susceptibility-guided therapy, and probiotics."[3]

"Recommendations for treatment-naive patients with *Helicobacter pylori* infection

- In treatment-naive patients with *H. pylori* infection, optimized BQT is recommended as a first-line treatment option (strong recommendation; moderate quality evidence)
- In treatment-naive patients with *H. pylori* infection, rifabutin triple therapy is suggested as a first-line treatment option (conditional recommendation; low quality evidence)
- In treatment-naive patients with *H. pylori* infection, dual therapy with a PCAB and amoxicillin is suggested as a first-line treatment option (conditional recommendation; moderate quality evidence)
- In treatment-naive patients with *H. pylori* infection and unknown clarithromycin susceptibility, PCAB-clarithromycin triple therapy is suggested over PPI-clarithromycin triple therapy (conditional recommendation; moderate quality evidence)
- In treatment-naive patients with *H. pylori* infection, concomitant therapy is not suggested over bismuth quadruple therapy (conditional recommendation; low quality evidence)

Recommendations for treatment-experienced patients with persistent H. pylori infection

- In treatment-experienced patients with persistent *H. pylori* infection who have not previously received bismuth quadruple therapy, optimized bismuth quadruple therapy is suggested (conditional recommendation; very low quality of evidence)
- In treatment-experienced patients with persistent *H. pylori* infection who have previously received PPI-clarithromycin triple therapy, optimized bismuth quadruple therapy is suggested (conditional recommendation; low quality of evidence)
- In treatment-experienced patients with persistent *H. pylori* infection who have received bismuth quadruple therapy, rifabutin triple therapy is suggested (conditional recommendation; low quality of evidence)
- In treatment-experienced patients with persistent *H. pylori* infection who have not previously received optimized bismuth quadruple therapy, optimized bismuth quadruple therapy is suggested over quinolone-based therapy (conditional recommendation; low quality of evidence)
- In treatment-experienced patients with persistent *H. pylori* infection, levofloxacin triple therapy is suggested in patients with known levofloxacin-sensitive *H. pylori* strains and when optimized bismuth quadruple or rifabutin triple therapies have previously been used or are unavailable (conditional recommendation, low quality of evidence)

- In treatment-experienced patients with persistent *H. pylori* infection, there is insufficient evidence from North America to recommend high-dose PPI or PCAB dual therapy (no recommendation; evidence gap)
- There is insufficient evidence to suggest that the use of probiotic therapy improves the efficacy or tolerability of *H. pylori* eradication therapy (conditional recommendation; low quality of evidence)."[3]

"*H. pylori* infection is an infectious disease with the potential for serious clinical consequences, including gastric cancer. Therefore, all patients with an indication for testing should be offered effective treatment if confirmed to have active infection—and should subsequently undergo a test-of-cure after treatment."[3]

The indications to test for and treat *H. pylori* infection are summarized below:

"Groups to test and treat for *H. pylori* infection:
- Peptic ulcer disease: prior history or active disease
- Marginal zone B-cell lymphoma, MALT type
- Uninvestigated dyspepsia in patients who are under the age of 60 years
  - In high-risk populations for gastric cancer, test and treat at age 45-50 years
  - Functional dyspepsia
- Adult household members of individuals who have a positive non-serological test for *H. pylori*
- Patients taking long-term NSAIDs or starting long-term treatment with low-dose aspirin
- Patients with unexplained iron deficiency anemia
- Patients with idiopathic (autoimmune) thrombocytopenic purpura
- Primary and secondary prevention of gastric adenocarcinoma
  - Current or history of gastric premalignant conditions (GPMC)
  - Current or history of early gastric cancer resection
  - Current or prior history of gastric adenocarcinoma
  - Patients with gastric adenomas or hyperplastic polyps
  - Persons with a first degree relative with gastric cancer
  - Individuals at increased risk for gastric cancer including certain non-White racial/ethnic groups, immigrants from high gastric cancer incidence regions/countries, hereditary cancer syndromes associated with an increased risk for gastric cancer
  - Patients with autoimmune gastritis."[3]

The ACG recommends that patients under 60 years of age presenting with dyspepsia and without alarm features should undergo non-invasive testing for H. pylori infection, followed by appropriate eradication therapy if positive. Preferred diagnostic methods include the urea breath test or stool antigen test. Alarm features necessitating prompt endoscopic evaluation include vomiting, GI bleeding, unexplained iron deficiency, or weight loss. The ACG emphasizes that patients aged 60 and older, or those exhibiting any alarm features, should undergo upper endoscopy to exclude malignancy or other serious gastrointestinal conditions.[3,30]

National Institute for Health and Care Excellence (NICE)

The NICE recommends testing for *H. pylori* with a carbon-13 urea breath test or a stool antigen test. A re-test should be with a breath test. Office-based serological tests are not recommended. NICE recommends a "2-week washout period after proton pump inhibitor (PPI) use before testing for *Helicobacter pylori.*" NICE recommends that individuals with positive *H. pylori* tests be offered therapy to eradicate the

bacteria; however, they note that re-testing to confirm eradication should not be routinely offered. NICE limits the recommendation for post-treatment testing to **"**people with peptic ulcer (gastric or duodenal)…6 to 8 weeks after beginning treatment, depending on the size of the lesion."[31]

Further guidelines were released in 2015 reaffirming the carbon-13 urea breath test and the stool antigen test to test for *H. pylori*. A locally validated lab-based serology test may also be used to assess *H. pylori*. NICE reaffirms the two week washout period before testing for *H. pylori* if the patient is on PPIs as well as the four week washout period if the patient is on antibiotics.[32]

American College of Cardiology

The American College of Cardiology recommends testing for and eradicating *H. pylori* in patients with a history of ulcer disease before starting chronic antiplatelet therapy.[33]

World Gastroenterology Organization

The World Gastroenterology Organization Global Guidelines on *Helicobacter pylori* recommends testing for *H. pylori* based on evidence-based indications, noting that these indications may differ in different regions of the world based on prevalence, resources, competing needs, and individual patient factors. The guidelines state that "peptic ulcer disease is the prime indication in most of the world." The guidelines list other indications for the treatment of *H. pylori* as: past or present duodenal and/or gastric ulcer (with or without complications), gastric MALT lymphoma, gastric mucosal atrophy and/or intestinal metaplasia, resection of gastric cancer, first-degree relatives with gastric cancer, functional dyspepsia, NSAID use, before long-term aspirin therapy in patients at high risk of ulcers and ulcer-related complications, during long-term low-dose aspirin therapy in patients with a history of upper gastrointestinal bleeding and perforation, patients with gastroesophageal reflux disease who require long-term proton-pump inhibitors, as a strategy for gastric cancer prevention in communities with a high incidence, and unexplained iron-deficiency anemia or idiopathic thrombocytopenic purpura.[34]

European Association for Gastroenterology, Endoscopy and Nutrition (EAGEN), European Society of Neurogastroenterology and Motility (ESNM), and European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN)

The pan-European guideline recommends the use of ^{13}C -urea breath tests as a noninvasive alternative for testing for "all indications of *Helicobacter pylori* testing if endoscopy is not required or if biopsies are contraindicated" and as "a preferred option for conformation of *Helicobacter pylori* eradication in adults and children." Alternatively, when there is indication for endoscopy and no contraindication for biopsy, the guidelines recommend RUT as the first-line diagnostic tests.[35]

ESPGHAN and The North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN)

The ESPGHAN and NASPGHAN have issued updated guidelines for management of *H. pylori* in children and adolescents. They have proposed recommendations for diagnosis and management of *H. pylori* infection in pediatric patients. They have defined pediatric patients as children and adolescents below 18 years of age. The following recommendations were stated:

- "We recommend that the primary goal of clinical investigation of gastrointestinal symptoms should be to determine the underlying cause of the symptoms and not solely the diagnosis of *H. pylori.*

- We recommend that testing for *H. pylori* be performed in children with gastric or duodenal ulcers and/or erosions. If *H. pylori* infection is identified, then treatment should be administered, and eradication confirmed.
- We recommend that diagnostic testing (invasive or noninvasive) for *H. pylori* infection in children with functional abdominal pain, a disorder of gut–brain interaction (DGBI), is not indicated.
- We suggest that when investigating other diseases such as IBD, celiac disease, or EoE, specific diagnostic biopsies for *H. pylori* infection are not indicated. We suggest that if *H. pylori* is an incidental finding during endoscopy performed for other GI diseases (IBD, celiac disease, EoE), treatment may be considered after discussion of the risks and benefits of treatment with the patient/family.
- We recommend against noninvasive testing for *H. pylori* in the initial investigation or management of IDA. We suggest that if endoscopy is indicated after failure of therapy for IDA, testing for *H. pylori* may be considered and treated if found. We suggest treating H. pylori infection identified during upper endoscopy in children with IDA after failed iron supplementation in which other causes of IDA have been ruled out.
- We recommend against testing for *H. pylori* infection when investigating causes of short stature.
- We suggest against testing (invasive or noninvasive) for *H. pylori* infection when investigating causes of cITP in children.
- We suggest that children with history of GC in a first-degree relative have a noninvasive test for H. pylori.
- We recommend against screening for *H. pylori* in children belonging to racial/ethnic groups at increased risk for GC that are living in North America/Europe.
- We recommend that the diagnosis of *H. pylori* infection should be gastric biopsy-based using the following tests: (a) culture or molecular tests and (b) histopathology according to Sydney system.
- We recommend that at least six gastric biopsies (three from corpus and three from antrum) should be obtained for the diagnosis of *H. pylori* infection during upper endoscopy.
- We recommend that before invasive testing for diagnosis and noninvasive testing confirmation of *H. pylori* eradication, to wait at least 2 weeks after stopping PPIs and 4 weeks after stopping antibiotics and bismuth salts.
- We suggest against the use of stool for molecular tests or culture for H. pylori infection detection or for susceptibility testing."[36]

Japanese Society for Pediatric Gastroenterology, Hepatology and Nutrition (JSPGHAN)

The JSPGHAN have updated their guidelines for *H. pylori* testing in pediatrics, including recommendations for diagnostic methods in children.

For diagnosis using endoscopic biopsy specimens, the guidelines recommend considering the performance and accuracy of the rapid urease test, recommending an additional urea breath test or stool antigen test when there is inconsistency between histopathology and the rapid urease test. The guidelines further recommend histological examination of gastric biopsies, and culture diagnostic tests to diagnose active *H. pylori* infection.[37]

For diagnosis without endoscopic biopsy specimens, the guidelines recommend ^{13}C-urea breath test and stool antigen tests. To increase the diagnosis accuracy, the guidelines recommend more than two tests (two noninvasive tests or a biopsy-based and a noninvasive test) be completed. The guidelines recommend urea breath test or stool antigen test four or more weeks after treatment to confirm eradication of *H. pylori* and recommend against using endoscopic biopsy methods and single serological

tests to confirm eradication. The guidelines also recommend against anti-*H. pylori* antibody tests as a single test to diagnose *H. pylori* in a clinical setting.[37]

Maastricht V/Florence Consensus Report

The Maastricht V/Florence Consensus report was published in 2017 on behalf of the European Helicobacter and Microbiota Study Group and Consensus panel. The panel reports that UBT is "the most investigated and best recommended non-invasive test in the context of a 'test-and-treat strategy". The panel also notes that monoclonal tests can be used and that serological tests can be used only after validation. However, rapid "office" serology tests are not recommended and "should be avoided". The guidelines recommend the rapid urease test (RUT) as a first line diagnostic test if there is an indication for endoscopy and no contraindication for biopsy. The guideline state that *H. pylori* is linked to "unexplained iron deficiency anaemia (IDA), idiopathic thrombocytopenic purpura, and vitamin B12 deficiency", and in these disorders, an *H. pylori* infection should be "sought and eradicated." The guidelines state that PPIs should be stopped two weeks and antibiotics, and other bismuth compounds should be stopped four weeks before testing for *H. pylori*. In cases of chronic (active) gastritis in which *H. pylori* is not detected by histochemistry, immunohistochemical testing of *H. pylori* can be used as an ancillary test. If histology is normal, no immunohistochemical staining should be performed. It is recommended to perform clarithromycin susceptibility testing when a standard clarithromycin-based treatment is considered as the first-line therapy, except in populations or regions with well documented low clarithromycin resistance (<15%). Pepsinogen (Pg) serology is considered the most useful non-invasive test to explore gastric mucosa status (non-atrophic vs atrophic). The PgI/PgII ratio can never be assumed as a biomarker of gastric neoplasia. UBT is the best option for confirmation of *H. pylori* eradication and monoclonal SAT is an alternative. It should be performed at least four weeks after completion of therapy.[38]

The Maastricht IV from 2012 also addressed testing for the cagA and vacA variants, stating that no specific genetic or virulence markers can be recommended at this time.[39]

American Society of Hematology (ASH)

American Society of Hematology (ASH) published an update to the immune thrombocytopenic purpura guidelines in 2019. In it, they "suggest" that "Screening for *H pylori* be considered for patients with ITP in whom eradication therapy would be used if testing is positive." However, ASH still recommends against "routine testing for *H pylori* in children with chronic ITP."[40]

Houston Consensus Conference

This conference included 11 experts on "management of adult and pediatric patients with *H. pylori*, from different geographic regions of the United States" and was convened to "discuss key factors in diagnosis of *H. pylori* infection, including identification of appropriate patients for testing, effects of antibiotic susceptibility on testing and treatment, appropriate methods for confirmation of infection and eradication, and relevant health system considerations." Two cohorts of approval were present: one of the 11 experts, and another consisting of a selected group of United States-based gastroenterologists. These recommendations were intended to provide practical advice for US practitioners, and guidelines to be adopted by US health care systems.

Recommendations approved by both groups are listed below:

- "Statement 1: We recommend that all patients with active *H pylori* infection be treated (100% agree/strongly agree, Grade 1A).
- Statement 2: All patients with current or past gastric or duodenal ulcers should be tested for *H pylori* infection (100% agree/strongly agree; Grade 1A).
- Statement 3: We recommend that all patients with uninvestigated dyspepsia be tested for *H pylori* infection (100% agree/strongly agree, Grade 1A).
- Statement 4: We recommend routine testing for *H pylori* infection in patients with reflux symptoms only if they are at high risk for *H pylori*-related disease (91% agree/strongly agree, Grade 1C).
- Statement 5: We recommend that patients with gastric mucosa-associated lymphoid tissue (MALT) lymphoma be tested for *H pylori* infection (100% agree/strongly agree, Grade 1B).
- Statement 6: We recommend that individuals with family history of gastric cancer be tested for *H pylori* infection (100% agree/strongly agree, Grade 1B).
- Statement 7: We recommend that patients who are first-generation immigrants from high prevalence areas be tested for *H pylori* infection (82% agree/strongly agree, Grade 1B).
- Statement 8: We suggest that patients of Latino and African American racial or ethnic groups may be considered for *H pylori* testing due to their high risk of infection (91% agree/strongly agree, Grade 2C)."
- Statement 17: We recommend that validated diagnostic testing of stool or gastric mucosal biopsy by culture and susceptibility, or molecular analysis be universally available (100% agree/strongly agree, Grade 1)
- Statement 18: We suggest that antibiotics that may be routinely evaluated for susceptibility include amoxicillin, clarithromycin, levofloxacin, metronidazole, and tetracycline (100% agree/strongly agree, Grade 2C).
- Statement 20: We recommend the use of tests for active *H pylori* infection (ie, UBT, HpSAg testing) for the initial diagnosis (100% agree/strongly agree, Grade 1A).
- Statement 22: We recommend that serology not be utilized for detection of active *H pylori* infection (100% agree/strongly agree, Grade 1A).
- Statement 23: We recommend that bismuth and antibiotics be stopped at least 4 weeks before *H pylori* testing with tests for active infection (ie, UBT, and HpSAg testing and histology; 100% agree/strongly agree, Grade 1C).
- Statement 27: We recommend that all patients receiving treatment for *H pylori* receive posttreatment confirmation of eradication. We recommend that only tests that evaluate for active infection, such as UBT, HpSAg test, or histology (if endoscopy is required for other reasons), are utilized for this purpose (100% agree/strongly agree, Grade 1A).
- Statement 28: Once appropriate testing has confirmed eradication, we recommend against further *H pylori* testing, (100% agree/strongly agree, Grade 1C)"

The following recommendations reached a consensus by the expert panel, but not the external group:

- "Statement 9: We recommend that patients with idiopathic thrombocytopenia be tested for *H pylori* infection (experts vs survey: 100% vs 68% agree/strongly agree, Expert Grade 1B)
- Statement 10: We suggest that patients receiving long-term PPIs (>1 month) be tested for *H pylori* infection (experts vs survey: 82% vs 68% agree/strongly agree, Expert Grade 2C)
- Statement 11: We recommend that family members residing in the same household of patients with proven active *H pylori* infections undergo *H pylori* testing (experts vs survey: 91% vs 78% agree/strongly agree, Expert Grade 1B)

- Statement 12: We recommend that individuals with a family history of peptic ulcer disease be tested for *H pylori* infection (experts vs survey: 91% vs (73% agree/strongly agree, Expert Grade 1B)."[41]

VI. Applicable State and Federal Regulations

Food and Drug Administration (FDA)

Many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). LDTs are not approved or cleared by the U. S. Food and Drug Administration; however, FDA clearance or approval is not currently required for clinical use.

On Feb 22, 2012, the FDA approved the BreathTek UBT for *H. pylori* Kit created by Otsuka America Pharmaceutical, Inc. TheBreathTek UBT for *H. pylori* Kit (BreathTek UBT Kit) is intended for use in the qualitative detection of urease associated with *H. pylori* in the human stomach and is indicated as an aid in the initial diagnosis and post-treatment monitoring of *H. pylori* infection in adults, and pediatric patients three to 17 years old. The test may be used for monitoring treatment if used at four weeks following completion of therapy. The FDA notes its sensitivity and specificity to be 0.958 and 0.992 respectively.[42]

On Jan 17, 2002, the FDA approved the BreathTek UBiT for *H. pylori* created by Meretek Diagnostics Inc. The scientific basis underlying the BreathTek UBT and the BreathTek UBiT UBT kit is identical. The urea breath test is FDA cleared for use in individuals 18 years of age and older.[43]

The BreathTek product line was bought by Meridian Biosciences and as of July 1, 2024 the entire BreathTek line, including BreathTek UBT and the BreathTek UBiT have been discontinued.[44]

On February 18, 2020, the FDA approved the PyloPlus UBT System created by ARJ Medical Inc. PyloPlus detects urease associated with *H. pylori* in the stomach and is indicated as an aid in the initial diagnosis of *H. pylori* infection in adults 18 years and older.[45]

VII. Applicable CPT/HCPCS Procedure Codes

Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all inclusive and is subject to updates. In addition, codes listed are not a guarantee of payment.

CPT	Code Description
83009	Helicobacter pylori, blood test analysis for urease activity, non-radioactive isotope (eg, C-13)
83013	Helicobacter pylori; breath test analysis for urease activity, non-radioactive isotope (eg, C-13)
83014	Helicobacter pylori; drug administration
86318	Immunoassay for infectious agent antibody(ies), qualitative or semiquantitative, single step-method (eg, reagent strip);
86677	Antibody; Helicobacter pylori
87070	Culture, bacterial; any other source except urine, blood or stool, aerobic, with isolation and presumptive identification of isolates
87077	Culture, bacterial; aerobic isolate, additional methods required for definitive identification, each isolate

CPT	Code Description
87081	Culture, presumptive, pathogenic organisms, screening only;
87149	Culture, typing; identification by nucleic acid (DNA or RNA) probe, direct probe technique, per culture or isolate, each organism probed
87150	Culture, typing; identification by nucleic acid (DNA or RNA) probe, amplified probe technique, per culture or isolate, each organism probed
87153	Culture, typing; identification by nucleic acid sequencing method, each isolate (eg, sequencing of the 16S rRNA gene)
87181	Susceptibility studies, antimicrobial agent; agar dilution method, per agent (eg, antibiotic gradient strip)
87186	Susceptibility studies, antimicrobial agent; microdilution or agar dilution (minimum inhibitory concentration [MIC] or breakpoint), each multi-antimicrobial, per plate
87205	Smear, primary source with interpretation; Gram or Giemsa stain for bacteria, fungi, or cell types
87338	Infectious agent antigen detection by immunoassay technique, (eg, enzyme immunoassay [EIA], enzyme-linked immunosorbent assay [ELISA], fluorescence immunoassay [FIA], immunochemiluminometric assay [IMCA]) qualitative or semiquantitative; Helicobacter pylori, stool
87339	Infectious agent antigen detection by immunoassay technique, (eg, enzyme immunoassay [EIA], enzyme-linked immunosorbent assay [ELISA], fluorescence immunoassay [FIA], immunochemiluminometric assay [IMCA]) qualitative or semiquantitative; Helicobacter pylori
87513	Infectious agent detection by nucleic acid (DNA or RNA); Helicobacter pylori (H. pylori), clarithromycin resistance, amplified probe technique
88305	Level IV - Surgical pathology, gross and microscopic examination - Stomach biopsy
0008U	Helicobacter pylori detection and antibiotic resistance, DNA, 16S and 23S rRNA, gyrA, pbp1, rdxA and rpoB, next generation sequencing, formalin-fixed paraffin-embedded or fresh tissue or fecal sample, predictive, reported as positive or negative for resistance to clarithromycin, fluoroquinolones, metronidazole, amoxicillin, tetracycline, and rifabutin Proprietary test: AmHPR H. Antibiotic Resistance Panel Lab/Manufacturer: American Molecular Laboratories, Inc

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VIII. Evidence-based Scientific References

1. Lamont JT. Indications and diagnostic tests for Helicobacter pylori infection. July 13, 2023. https://www.uptodate.com/contents/indications-and-diagnostic-tests-for-helicobacter-pylori-infection
2. Longstreth G, Lacy, Brian. Approach to the adult with dyspepsia. Updated January 16, 2025. https://www.uptodate.com/contents/approach-to-the-adult-with-dyspepsia
3. Chey WD, Howden CW, Moss SF, et al. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. *Official journal of the American College of Gastroenterology | ACG*. 2024;119(9):1730-1753. doi:10.14309/ajg.0000000000002968
4. Siao D, Somsouk M. Helicobacter pylori: evidence-based review with a focus on immigrant populations. *Journal of general internal medicine*. Mar 2014;29(3):520-8. doi:10.1007/s11606-013-2630-y

5. Jensen P, Feldman, Mark. Acute and chronic gastritis due to Helicobacter pylori. Updated September 5, 2023. https://www.uptodate.com/contents/acute-and-chronic-gastritis-due-to-helicobacter-pylori
6. Singh V, Mishra S, Rao GR, et al. Evaluation of nested PCR in detection of Helicobacter pylori targeting a highly conserved gene: HSP60. *Helicobacter*. Feb 2008;13(1):30-4. doi:10.1111/j.1523-5378.2008.00573.x
7. Patel SK, Pratap CB, Jain AK, Gulati AK, Nath G. Diagnosis of Helicobacter pylori: what should be the gold standard? *World journal of gastroenterology*. Sep 28 2014;20(36):12847-59. doi:10.3748/wjg.v20.i36.12847
8. Dechant FX, Dechant R, Kandulski A, et al. Accuracy of Different Rapid Urease Tests in Comparison with Histopathology in Patients with Endoscopic Signs of Gastritis. *Digestion*. 2020;101(2):184-190. doi:10.1159/000497810
9. Pohl D, Keller PM, Bordier V, Wagner K. Review of current diagnostic methods and advances in Helicobacter pylori diagnostics in the era of next generation sequencing. *World journal of gastroenterology*. Aug 28 2019;25(32):4629-4660. doi:10.3748/wjg.v25.i32.4629
10. Hussein RA, Al-Ouqaili MTS, Majeed YH. Detection of Helicobacter Pylori infection by invasive and non-invasive techniques in patients with gastrointestinal diseases from Iraq: A validation study. *PLoS One*. 2021;16(8):e0256393. doi:10.1371/journal.pone.0256393
11. Hassan AM, Faraj HHA, Mohammad HF. Comparison between stool antigen test and urea breath test for diagnosing of Helicobacter pylori infection among Children in Sulaymaniyah City. *Mustansiriya Medical Journal*. 2021;20(1):6.
12. Abdelmalek S, Hamed W, Nagy N, Shokry K, Abdelrahman H. Evaluation of the Diagnostic Values and Utility of Helicobacter Pylori Stool Antigen Lateral Immunochromatography Assay. 2022;
13. Gisbert JP, de la Morena F, Abraira V. Accuracy of monoclonal stool antigen test for the diagnosis of H. pylori infection: a systematic review and meta-analysis. *The American journal of gastroenterology*. Aug 2006;101(8):1921-30. doi:10.1111/j.1572-0241.2006.00668.x
14. Opekun AR, Zierold C, Rode A, et al. Clinical Performance of the Automated LIAISON® Meridian H. pylori SA Stool Antigen Test. *Biomed Res Int*. 2020;2020:7189519. doi:10.1155/2020/7189519
15. Korkmaz H, Findik D, Ugurluoglu C, Terzi Y. Reliability of stool antigen tests: investigation of the diagnostic value of a new immunochromatographic Helicobacter pylori approach in dyspeptic patients. *Asian Pacific journal of cancer prevention : APJCP*. 2015;16(2):657-60.
16. Ferwana M, Abdulmajeed I, Alhajiahmed A, et al. Accuracy of urea breath test in Helicobacter pylori infection: meta-analysis. *World journal of gastroenterology*. Jan 28 2015;21(4):1305-14. doi:10.3748/wjg.v21.i4.1305
17. Loy CT, Irwig LM, Katelaris PH, Talley NJ. Do commercial serological kits for Helicobacter pylori infection differ in accuracy? A meta-analysis. *The American journal of gastroenterology*. Jun 1996;91(6):1138-44.
18. Nezami BG, Jani M, Alouani D, Rhoads DD, Sadri N. Helicobacter pylori Mutations Detected by Next-Generation Sequencing in Formalin-Fixed, Paraffin-Embedded Gastric Biopsy Specimens Are Associated with Treatment Failure. *J Clin Microbiol*. Jul 2019;57(7)doi:10.1128/jcm.01834-18
19. Yang F, Xu YL, Zhu RF. Helicobacter pylori infection and the risk of colorectal carcinoma: a systematic review and meta-analysis. *Minerva medica*. Oct 2019;110(5):464-470. doi:10.23736/s0026-4806.19.05942-1
20. Wang T, Li X, Zhang Q, et al. Relationship between Helicobacter pylori infection and osteoporosis: a systematic review and meta-analysis. *BMJ open*. Jun 27 2019;9(6):e027356. doi:10.1136/bmjopen-2018-027356

21. Zhou BG, Yang HJ, Xu W, Wang K, Guo P, Ai YW. Association between Helicobacter pylori infection and nonalcoholic fatty liver disease: A systematic review and meta-analysis of observational studies. *Helicobacter*. Jun 2019;24(3):e12576. doi:10.1111/hel.12576
22. Halland M, Haque R, Langhorst J, Boone JH, Petri WA. Clinical performance of the H. PYLORI QUIK CHEK™ and H. PYLORI CHEK™ assays, novel stool antigen tests for diagnosis of Helicobacter pylori. *Eur J Clin Microbiol Infect Dis*. May 2021;40(5):1023-1028. doi:10.1007/s10096-020-04137-7
23. Marrero Rolon R, Cunningham SA, Mandrekar JN, Polo ET, Patel R. Clinical Evaluation of a Real-Time PCR Assay for Simultaneous Detection of Helicobacter pylori and Genotypic Markers of Clarithromycin Resistance Directly from Stool. *J Clin Microbiol*. Apr 20 2022;59(5)doi:10.1128/jcm.03040-20
24. Nguyen Wenker T, Peng FB, Emelogu I, et al. The Predictive Performance of Contemporary Guideline Recommendations for Helicobacter pylori Testing in a United States Population. *Clin Gastroenterol Hepatol*. Jul 2023;21(7):1771-1780. doi:10.1016/j.cgh.2022.10.009
25. Talley NJ. American Gastroenterological Association medical position statement: evaluation of dyspepsia. *Gastroenterology*. Nov 2005;129(5):1753-5. doi:10.1053/j.gastro.2005.09.019
26. Allen JI, Katzka D, Robert M, Leontiadis GI. American Gastroenterological Association Institute Technical Review on the Role of Upper Gastrointestinal Biopsy to Evaluate Dyspepsia in the Adult Patient in the Absence of Visible Mucosal Lesions. *Gastroenterology*. Oct 2015;149(4):1088-118. doi:10.1053/j.gastro.2015.07.040
27. Gupta S, Li D, El Serag HB, et al. AGA Clinical Practice Guidelines on Management of Gastric Intestinal Metaplasia. *Gastroenterology*. 2020;158(3):693-702. doi:10.1053/j.gastro.2019.12.003
28. Ko CW, Siddique SM, Patel A, et al. AGA Clinical Practice Guidelines on the Gastrointestinal Evaluation of Iron Deficiency Anemia. *Gastroenterology*. 2020;159(3):1085-1094. doi:10.1053/j.gastro.2020.06.046
29. Shah SC, Iyer PG, Moss SF. AGA Clinical Practice Update on the Management of Refractory Helicobacter pylori Infection: Expert Review. *Gastroenterology*. Apr 2021;160(5):1831-1841. doi:10.1053/j.gastro.2020.11.059
30. Chey WD, Leontiadis GI, Howden CW, Moss SF. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. *The American journal of gastroenterology*. Feb 2017;112(2):212-239. doi:10.1038/ajg.2016.563
31. NICE. Gastro-oesophageal reflux disease and dyspepsia in adults: investigation and management. Dyspepsia and Gastro-Oesophageal Reflux Disease: Investigation and Management of Dyspepsia, Symptoms Suggestive of Gastro-Oesophageal Reflux Disease, or Both https://www.nice.org.uk/guidance/cg184
32. NICE. Dyspepsia and gastro-oesophageal reflux disease in adults. https://www.nice.org.uk/guidance/qs96/resources/dyspepsia-and-gastrooesophageal-reflux-disease-in-adults-investigation-and-management-2098972399813
33. Bhatt DL, Scheiman J, Abraham NS, et al. ACCF/ACG/AHA 2008 expert consensus document on reducing the gastrointestinal risks of antiplatelet therapy and NSAID use: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents. *Circulation*. Oct 28 2008;118(18):1894-909. doi:10.1161/circulationaha.108.191087
34. Katelaris P, Hunt R, Bazzoli F, et al. Helicobacter pylori World Gastroenterology Organization Global Guideline. *J Clin Gastroenterol*. Feb 1 2023;57(2):111-126. doi:10.1097/mcg.0000000000001719
35. Keller J, Hammer HF, Afolabi PR, et al. European guideline on indications, performance and clinical impact of 13C-breath tests in adult and pediatric patients: An EAGEN, ESNM, and ESPGHAN consensus, supported by EPC. *UEG Journal*. 2021;doi:10.1002/ueg2.12099

36. Homan M, Jones NL, Bontems P, et al. Updated joint ESPGHAN/NASPGHAN guidelines for management of Helicobacter pylori infection in children and adolescents (2023). *J Pediatr Gastroenterol Nutr*. Sep 2024;79(3):758-785. doi:10.1002/jpn3.12314
37. Kato S, Shimizu T, Toyoda S, et al. The updated JSPGHAN guidelines for the management of Helicobacter pylori infection in childhood. *Pediatr Int*. Dec 2020;62(12):1315-1331. doi:10.1111/ped.14388
38. Malfertheiner P, Megraud F, Morain CA, et al. Management of Helicobacter pylori infection—the Maastricht V/Florence Consensus Report. *Gut*. 2017;66(1):6. doi:10.1136/gutjnl-2016-312288
39. Malfertheiner P, Megraud F, Morain CA, et al. Management of Helicobacter pylori infection—the Maastricht IV/ Florence Consensus Report. *Gut*. 2012;61(5):646. doi:10.1136/gutjnl-2012-302084
40. Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood Advances*. 2020;3(23):3829-3866. doi:10.1182/bloodadvances.2019000966
41. El-Serag HB, Kao JY, Kanwal F, et al. Houston Consensus Conference on Testing for Helicobacter pylori Infection in the United States. *Clinical Gastroenterology and Hepatology*. 2018/07/01 2018;16(7):992-1002.e6.
42. FDA. Summary of Safety and Effectiveness. https://www.accessdata.fda.gov/cdrh_docs/pdf10/P100025B.pdf
43. FDA. 510k summary. https://www.accessdata.fda.gov/cdrh_docs/pdf/K014225.pdf
44. Biosciences M. BreathTek® UBT for H. pylori. Updated July 1, 2024. https://www.meridianbioscience.com/diagnostics/disease-areas/gastrointestinal/h-pylori/breathtek-ubt-for-h-pylori
45. FDA. PyloPlus UBT System - P170022/S003. Updated January 11, 2024. https://www.fda.gov/medical-devices/recently-approved-devices/pyloplus-ubt-system-p170022s003

IX. Revision History

Revision Date	Summary of Changes
01/01/2022	Initial Effective Date
07/19/2022	Updated background, guidelines and recommendations, and evidence-based scientific references. Literature review did not necessitate modification to coverage criteria. Addition of “or” to several coverage criteria for clarity. Revised code disclaimer statement
06/28/2023	Updated background, guidelines and recommendations, and evidence-based scientific references. Literature review did not necessitate modification to coverage criteria. Policy edited for clarity and consistency. Committee approved: 06/28/2023
05/14/2024	Reviewed and Updated: Updated the background, guidelines and recommendations, and evidence-based scientific references. Literature review did not necessitate any modifications to coverage criteria. Committee approved: 05/14/2024
05/21/2025	Reviewed and Updated: Updated background, guidelines, and evidence-based scientific references. Literature review necessitated the following changes in coverage criteria: Clarity edits made to CC1, CC2, CC3, and CC4.

	CC1.a., changed “dyspeptic” to “dyspepsia (see Note 1)”. CC1.c., replaced “without H. pylori history” with “and who have had recurrent symptoms.” CC1.e., removed “endoscopic” Removed former CC1.g. due to repetition with CC1.a. Former CC1.h., now CC1.g., added “or who have been on a” and “aspirin”, now reads: “g) For individuals initiating chronic treatment with or who have been on a long-term aspirin or non-steroidal anti-inflammatory drug (NSAID) treatment.” Former CC1.j., change “chronic immune” to “idiopathic” and removed “and suspected H. pylori infection” Removed former CC2 (follow up testing now found in new CC5) Former CC4, now CC3, removed chronic ITP, follow up (now in CC5), added ulcers/erosions and family history. Now reads: 3) For individuals who are less than 18 years of age, urea breath testing or stool antigen testing to diagnose an H. pylori infection MEETS COVERAGE CRITERIA in any of the following situations: a) For individuals who have gastric or duodenal ulcers or erosions. b) For individuals who have a family history of gastric cancer.” Former CC5, now CC4, removed gastric ulcers (noninvasive testing now allowed in CC3), reworded criteria since it now only pertains to those with refractory IDA. Now reads: “4) For individuals who are less than 18 years of age and who have refractory iron deficiency anemia, a biopsy-based endoscopic histology test and either a rapid urease test or a culture with susceptibility testing to diagnose an H. pylori infection MEETS COVERAGE CRITERIA.” New CC5and CC6: “5) For all individuals who have tested positive for H. pylori, urea breath testing or stool antigen testing to measure the success of eradication of H. pylori infection, with testing performed at least four weeks post-treatment, MEETS COVERAGE CRITERIA. 6) For individuals with a refractory H. pylori infection, susceptibility testing (culture or nucleic acid based) MEETS COVERAGE CRITERIA.” Former CC6.b., now CC7.b., added “(i.e., heartburn, regurgitation)” Allowance of nucleic acid based susceptibility testing in CC6 results in changes to CC12, addition of “for all other situations not described above”. Now reads: “12) For all other situations not described above, nucleic acid testing for H. pylori DOES NOT MEET COVERAGE CRITERIA.” New Note 1 and Note 2: “Note 1: “Dyspepsia refers to bothersome upper abdominal symptoms that are often meal related. The predominant symptoms are fullness (or bloating) after meals, early satiety (inability to finish a normal-sized meal because of postprandial discomfort), or epigastric pain (or burning) that may or may not be related to meals. If dyspepsia is chronic, epigastric pain is a less common feature than postprandial fullness or satiety. Pain is not required to make a diagnosis of dyspepsia.” Note 2: Alarm features of dyspepsia: vomiting, gastrointestinal bleeding, unexplained iron deficiency, or weight loss.” Added CPT code 87513 Committee approved: 05/21/2025
06/17/2026	CAB Review Q2 2026: Reviewed and Updated: Updated the background, guidelines and recommendations, and evidence-based scientific references. Literature review did not necessitate any modifications to coverage criteria.

	Committee Approved: 06/17/2026