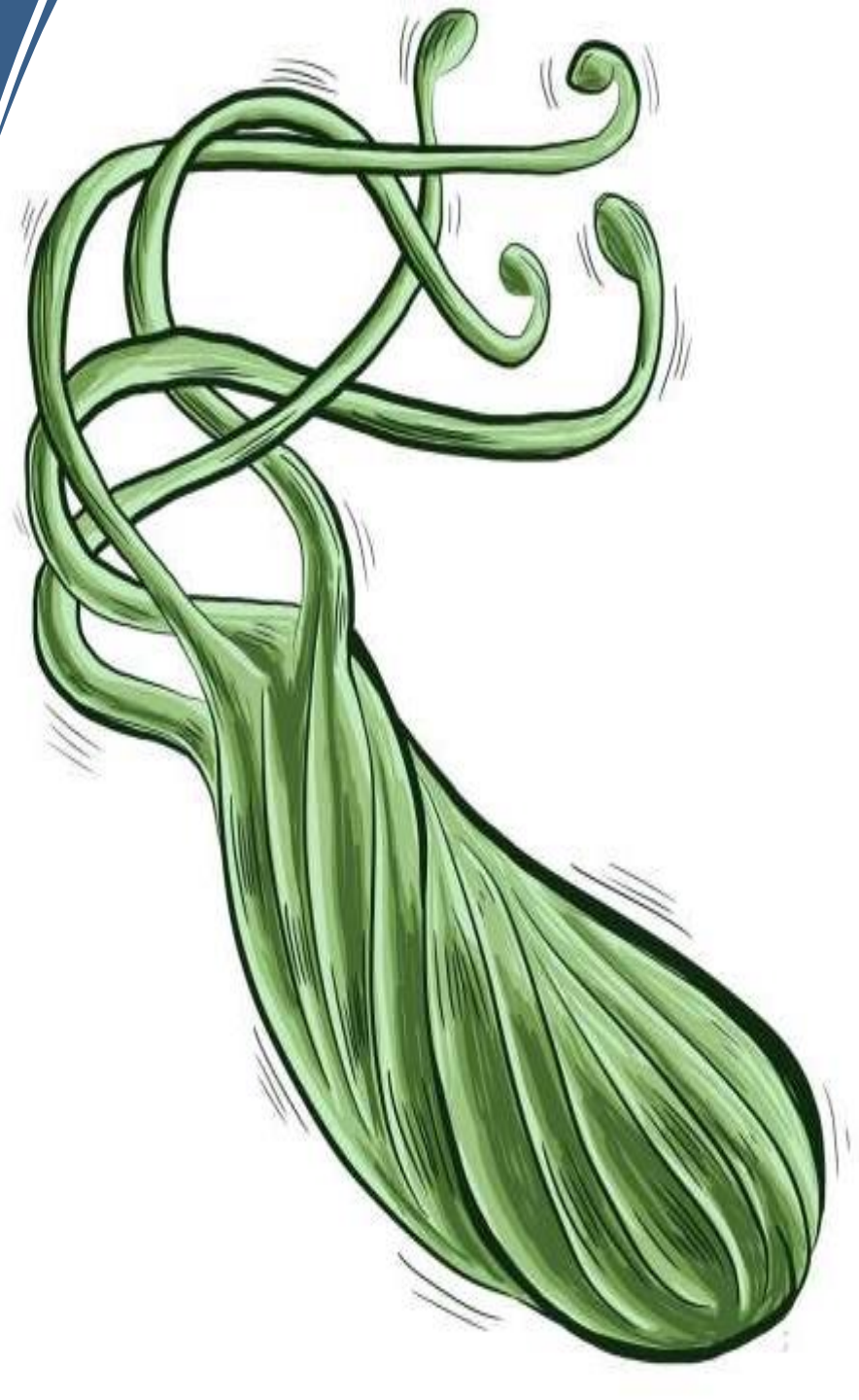
MANAGEMENT OF HELICOBACTER PYLORI INFECTION

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October 17, 2024–Tehran-Iran





Co-Winners of Nobel Prize in 2005

for their discovery of HP



Barry Marshall & Robin Warren

Helicobacter pylori Discovery

- **In 1983**, two Australian researchers **discovered** the bacterium Helicobacter pylori and explained its role in gastritis and peptic ulcer disease.
- They were awarded the **Nobel Prize in Physiology or Medicine** in **2005**.

Introduction

Helicobacter pylori is a **Gram-negative, spiral-shaped bacterium**

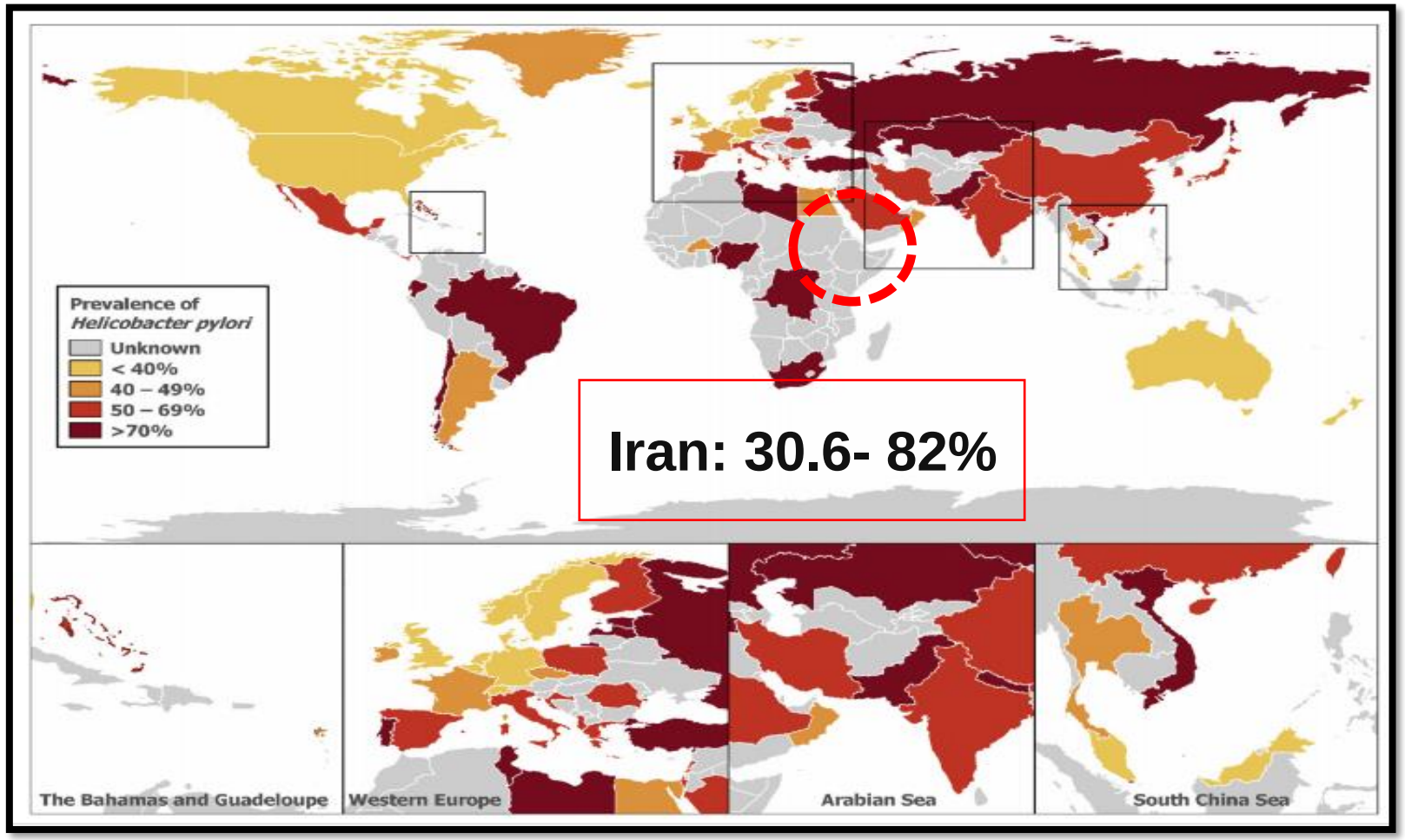
One of the **most common chronic bacterial infections of humans worldwide**

A leading cause of **infection-associated cancer globally**

WHO International Agency for Research on Cancer as a **group I (definite) carcinogen** because of its causal association with gastric cancer.

Hooi JKY, et al. Global prevalence of Helicobacter pylori infection: Systematic review and meta-analysis. Gastroenterology 2017;153(2):420–9.
de Martel C, Georges D, Bray F, et al. Global burden of cancer attributable to infections in 2018: A worldwide incidence analysis. Lancet Glob Health 2020;8(2):e180–90.c





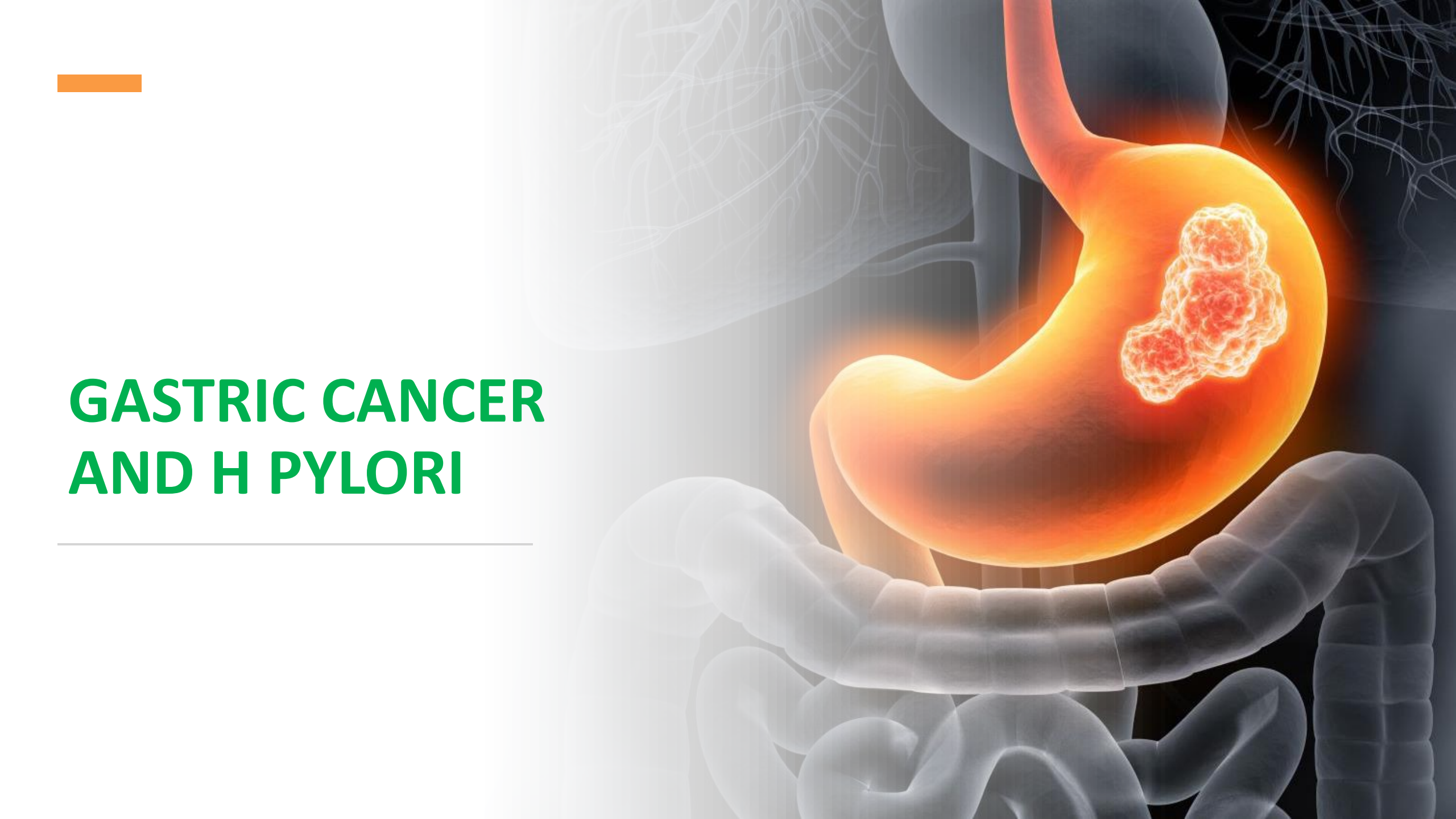
The crude global prevalence of H pylori: **43.1%**

The global prevalence of H pylori infection has **declined by 15.9%** during the last 3 decades in adults, but not in children and adolescents.

- *Hooi et al., Gastroenterology, 2017*
- *Eshraghian, Ahad. WJG 20.46 (2014): 17618.*
- *Yi-Chu Chen et al., Gastroenterology, 2024*

Prevalence of *H. pylori* Infection

GASTRIC CANCER AND H PYLORI



H pylori and gastric cancer

H. pylori infection is the **primary etiological factor for gastric adenocarcinoma**, including proximal gastric cancer (PGC) [A1 100.00%]

H. pylori eradication offers the chance for gastric cancer prevention at any age in adulthood. The magnitude of the benefit **decreases with age**. [A1 100.00%]



Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.

H pylori and gastric cancer

Severe atrophy (OLGA3/4) in the context of H. pylori gastritis carries a much **higher risk for gastric cancer** development as compared with atrophy in the context of autoimmune gastritis. [A1 100.00%]

H. pylori eradication eliminates **a)** the active inflammatory response in chronic active non-atrophic gastritis and **b)** prevents progression to atrophy and intestinal metaplasia in chronic non-atrophic gastritis. [A1 100.00%]

H. pylori eradication may **reverse gastric atrophy and to some extent intestinal metaplasia** and may halt the progression from chronic atrophic gastritis to neoplastic lesions in a subset of patients. [A1 97.00%]



Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.

H pylori and gastric cancer

Diagnostic tests used to screen H**. pylori infection for the purpose of gastric cancer prevention** should preferably be **non-invasive**.[C2 89.00%]

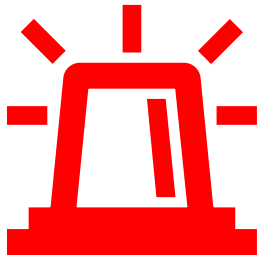
Endoscopy with biopsies is recommended in **asymptomatic individuals with a family history of gastric cancer** (does not refer to hereditary gastric cancer) **at age 45 and above**. [C2 89.00%]

Screening modalities for gastric cancer prevention (noninvasive or endoscopic) **combined with colorectal cancer screening** is an opportunity [C2 81.00%]



Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.

Indications/associations



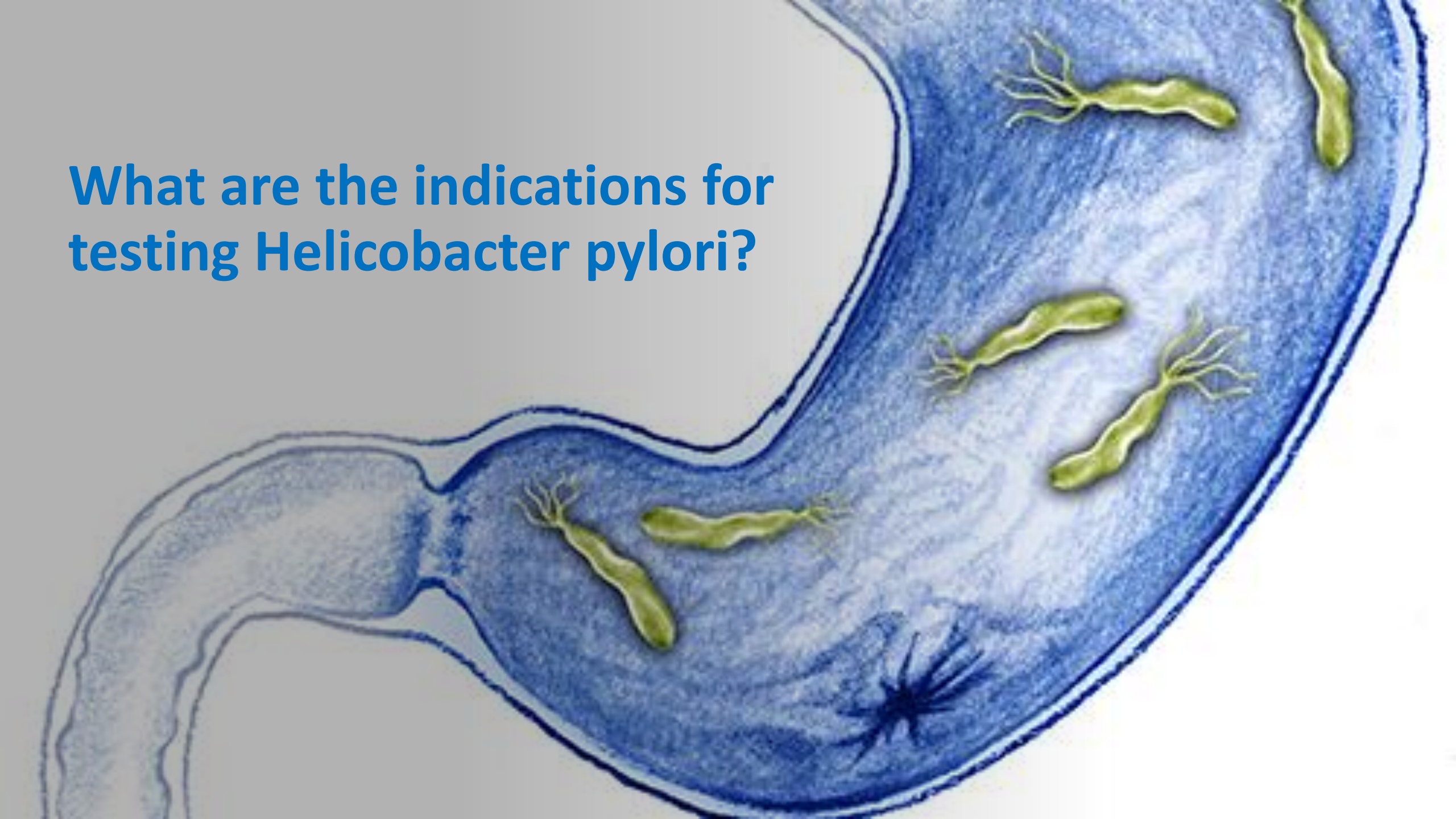
H. pylori infects more than half of the world’s population

Always chronic gastritis that may progress to severe complications such as **peptic ulcer disease, gastric adenocarcinoma, and gastric MALT lymphoma**.



Sugano K, et al. Kyoto global consensus report on Helicobacter pylori gastritis. Gut 2015;64:1353–67
Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.

What are the indications for testing Helicobacter pylori?



Indications for Helicobacter pylori testing

- Gastric marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)
- Active peptic ulcer disease
- History of peptic ulcer if cure of *H. pylori* has not been documented
- Early gastric cancer
- Prior to long-term treatment with NSAIDs and/or low-dose aspirin
- Unexplained iron deficiency anemia
- Adults with immune thrombocytopenia
- Unexplained vitamin B12 deficiency



Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.
Chey, William D., et al. "ACG Clinical Guideline: Treatment of Helicobacter pylori Infection 2024

Indications for Helicobacter pylori testing

- Uninvestigated dyspepsia in patients <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



Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.
Chey, William D., et al. "ACG Clinical Guideline: Treatment of Helicobacter pylori Infection 2024

Indications for Helicobacter pylori testing

- **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



Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.
Chey, William D., et al. "ACG Clinical Guideline: Treatment of Helicobacter pylori Infection 2024

Q: What is your preferred test specifically for active peptic ulcer bleeding?

Patients undergoing upper endoscopy

*No active peptic ulcer bleeding?

- No recent PPI/bismuth/antibiotic use and no indication for gastric biopsy→ RUT
- Recent PPI/bismuth/antibiotic use or indication for gastric biopsy→ Histology
- Prior antibiotic treatment failures → Culture and antibiotic sensitivity

Active peptic ulcer bleeding? Gastric mucosal biopsy, or **RUT after some weeks

Patients not undergoing upper endoscopy

Test for active infection (stool antigen assay or urea breath test).



Medications that should be discontinued prior to testing

PPI use within 1-2 weeks and **bismuth/antibiotic use within 4 weeks** of testing can decrease the sensitivity of all endoscopy-based tests and noninvasive tests of active H. pylori infection (stool antigen and urea breath test).

In the short-term post-eradication (4–6 weeks) follow-up, no antibiotics or bismuth should be used to permit optimum testing for H. pylori. PPIs should be stopped 14 days before testing

Agreement 96% Grade A1



Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.

Q: Which statement regarding RUT is true?

-Acute upper gastrointestinal bleeding can lead to false-negative results in the RUT

- The use of PPIs, antibiotics, or bismuth-containing compounds can cause false-negative results in RUT.

-Taking samples from both the gastric antrum and the fundus increases the sensitivity of the RUT.

- Obtaining a final result after 24 hours increases the sensitivity of the RUT.

- All of the above factors can impact the accuracy of the RUT.



Q: Which statement regarding histology is false?

Biopsy for histology should be taken from both the antrum and body.

The accuracy of diagnosing H. pylori histology can be improved by special stains such as Giemsa or specific immune stains.

The sensitivity of histology may be increased in patients with acute peptic ulcer bleeding.

The sensitivity of histology may be reduced in patients on PPI therapy, due to the proximal migration of H. pylori from the antrum to the corpus.



PPI and topography of H.pylori gastritis.

Long-term treatment with PPIs alters the topography of H.pylori gastritis.

Agreement 94% Grade A1

Long-term PPI treatment is associated with the spread of gastritis **from the antrum to the corpus**, and **increased body atrophic gastritis**

Lundell L, Vieth M, Gibson F, et al. Aliment Pharmacol Ther 2015;42:649–63.
Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.



Q: What challenges are associated with bacterial culture and sensitivity testing?

Before the forceps are contaminated with formalin, biopsies for culture should be obtained.

The **tissue should be placed into a container with a few drops of saline**.

Despite its high specificity, it has **low sensitivity because H. pylori is difficult to culture.**



Q: Which non-invasive test for H. pylori do you prefer?

A. UBT

B. stool antigen assay

C. H. pylori serology

D. A and B

H. pylori serology can be **positive in active or prior infection patients**.

UBT and stool antigen assay are tests of **active Infection**

False-negative results of UBT and stool antigen assay in patients who are taking PPIs, bismuth, or antibiotics and in the setting of active peptic ulcer bleeding

Other infrequently used tests: 13C-urea assay, PCR



Molecular methods and susceptibility testing

Molecular methods (real-time-PCR, whole-genome sequencing, and digital PCR) allow detection of H. pylori mutations associated with resistance to clarithromycin, levofloxacin, tetracycline, and rifampicin.

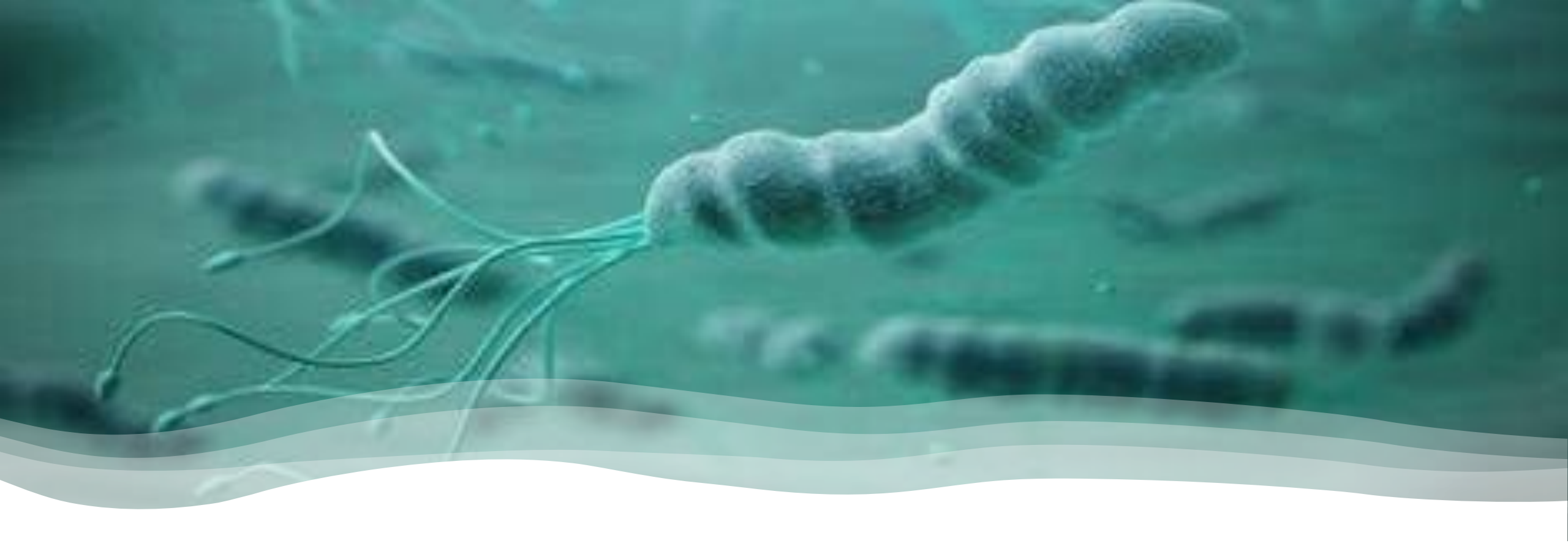
Agreement 100% Grade A1

Clarithromycin susceptibility testing, if available, is recommended before prescribing any clarithromycin-containing therapy.

Agreement 91% Grade A1



Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.



Who should be treated?

Q:Does everyone who is infected need H. pylori eradication?

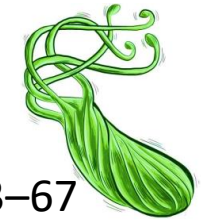


Dyspepsia

H. pylori-induced gastritis

Q: Is H. pylori-induced gastritis always symptomatic? Yes◯ No◯

Kyoto H. pylori consensus in 2015→H. pylori-induced gastritis is an infectious disease regardless of clinical symptoms and complications



Sugano K, Tack J, Kuipers EJ, et al. Kyoto global consensus report on Helicobacter pylori gastritis. Gut 2015;64:1353–67

Uninvestigated dyspepsia

What is the best management strategy in uninvestigated dyspepsia?

- **Test-and-treat approach**
- **Acid suppression**
- **Prompt endoscopy for all or only H. pylori-positive patients**
- **non-invasive testing for H. pylori infection in age< 50 without alarm symptoms**



Endoscopy in dyspepsia

Q: Is upper GI endoscopy necessary for the initial investigation of dyspepsia? **Yes◯ No◯**

Endoscopy is **not necessary** in the initial investigation of dyspepsia in **low H. pylori prevalence areas**.

Agreement 92% Grade A1

The prevalence of serious upper GI lesions in dyspepsia in the age groups below 50 (45–55), depending on geographical area, is very low. the prevalence of gastric cancer was only 0.4% and was even lower in those aged below 45



Ford AC, et al. Clin Gastroenterol Hepatol 2010;8:830–7. 7 e1-2.
Sung JJ, et al. I. Gastrointest Endosc 2001;54:454–8.
Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.

Uninvestigated dyspepsia.

Q: Is "test-and-treat" an appropriate strategy for uninvestigated dyspepsia?

Test-and-treat is an appropriate strategy for uninvestigated dyspepsia.

Agreement 94% Grade A1

Test-and-treat approach ranked first over acid suppression or prompt endoscopy for all or only H. pylori-positive patients

Beresniak A, Helicobacter pylori "Test-and-Treat" strategy with urea breath test . Helicobacter 2020;25:e12693
Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.
Eusebi LH, et al. systematic review and network meta-analysis. BMJ 2019;51:l6483



Q: Is H. pylori eradication superior to placebo or acid suppressive therapy for long-term relief of dyspepsia?



H. pylori eradication or acid suppressive therapy

Overall, H. pylori eradication is superior to placebo or acid suppressive therapy for **long-term relief of dyspepsia**, but the magnitude of the benefit is small.

Agreement 100% Grade A1

Ford AC, et al.. Gut 2022. doi:10.1136/gutjnl-2021-326583. [Epub ahead of print: 12 Jan 2022].
Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.



Gastritis in long- term PPI

H. pylori eradication improves gastritis in long- term PPI users.

Agreement 97% Grade A1

Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.

Q: When should upper gastrointestinal (GI) endoscopy be considered for patients with dyspepsia: under 50 or over 50?

In **young dyspeptic < 50** with no alarm symptoms, **non-invasive testing for H. pylori infection** is recommended.

Agreement 97% Grade A1

In dyspeptic patients >50 years, upper GI endoscopy is required.

Agreement 94% Grade B1



Alarm features in dyspepsia

Unintentional weight loss
Dysphagia
Odynophagia
Unexplained iron deficiency anemia
Persistent vomiting
Palpable mass or lymphadenopathy
Family history of upper gastrointestinal cancer



Functional dyspepsia

H. pylori gastritis has to be excluded before a reliable diagnosis of functional dyspepsia (FD) can be made.

Agreement 100% Grade B1

Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.
Hansen JM, et al. Effect of a community screening for Helicobacter pylori: a 5-Yr follow-up study. Am J Gastroenterol 2008;103:1106–13.
Madisch A, et al. The diagnosis and treatment of functional dyspepsia. Dtsch Arztebl Int 2018;115:222–32.
Moayyedi P,, et al. Acg and CAG clinical guideline: management of dyspepsia. Am J Gastroenterol 2017;112:988–1013.



Aspirin and NSAIDs

Aspirin and NSAIDs –HPE?

Q: Which statement is true?

H. pylori testing and treatment for high-risk patients who are already on long-term aspirin.

H. pylori testing and treatment for naïve patients starting long-term NSAID therapy.

Continue additional PPI therapy after HPE

All of the above



Bleeding rate of H pylori infected population

Aspirin or NSAIDs increase the risk of peptic ulcer disease and its complications in H. pylori-infected subjects.

Agreement 100% Grade A1

H. pylori testing and treatment are advisable for high-risk patients who are already on **long-term aspirin**.

H. pylori testing and treatment are advisable for **naïve patients starting long-term NSAID therapy**. Those at high risk may need additional PPI therapy.

Agreement 100% Grade A1



Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.

ANTICOAGULANTS

Bleeding rate of H pylori infected population

Bleeding rate of H pylori infected population

There is no evidence to suggest that anticoagulants (coumarins, direct oral, and vitamin K antagonists) increase the risk of bleeding in patients with H. pylori infection.

Agreement 94% Grade A1



Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.

Treatment



Important question before treatment

Q: Which question do you ask before treatment?

Is the patient treatment-naïve or have they been exposed to treatment?

Is antibiotic susceptibility known?

Does the patient have a penicillin allergy?



Chey WD, et al. ACG Clinical Guideline. 2024 Sep 1;119(9):1730-53.

ACG Clinical Practice Guideline

Treatment of *H. pylori* Infection in North America				
	Treatment Naïve	***Treatment-Experienced (Salvage)***		***Penicillin Allergy***
Regimen		Empiric	Proven antibiotic sensitivity	
Optimized Bismuth Quadruple	☑☑☑	☑☑	☑☑	☑☑☑ *
Rifabutin Triple	☑☑	☑☑	☑☑	
Vonoprazan Dual	☑☑	?	?	
Vonoprazan Triple			☑☑	
Levofloxacin Triple			☑☑	

☑☑☑ Recommended ☑☑ Suggested ? May be considered when other treatments are not options

* When Bismuth Quadruple Therapy not an option, consider referral for formal penicillin allergy testing and/or desensitization

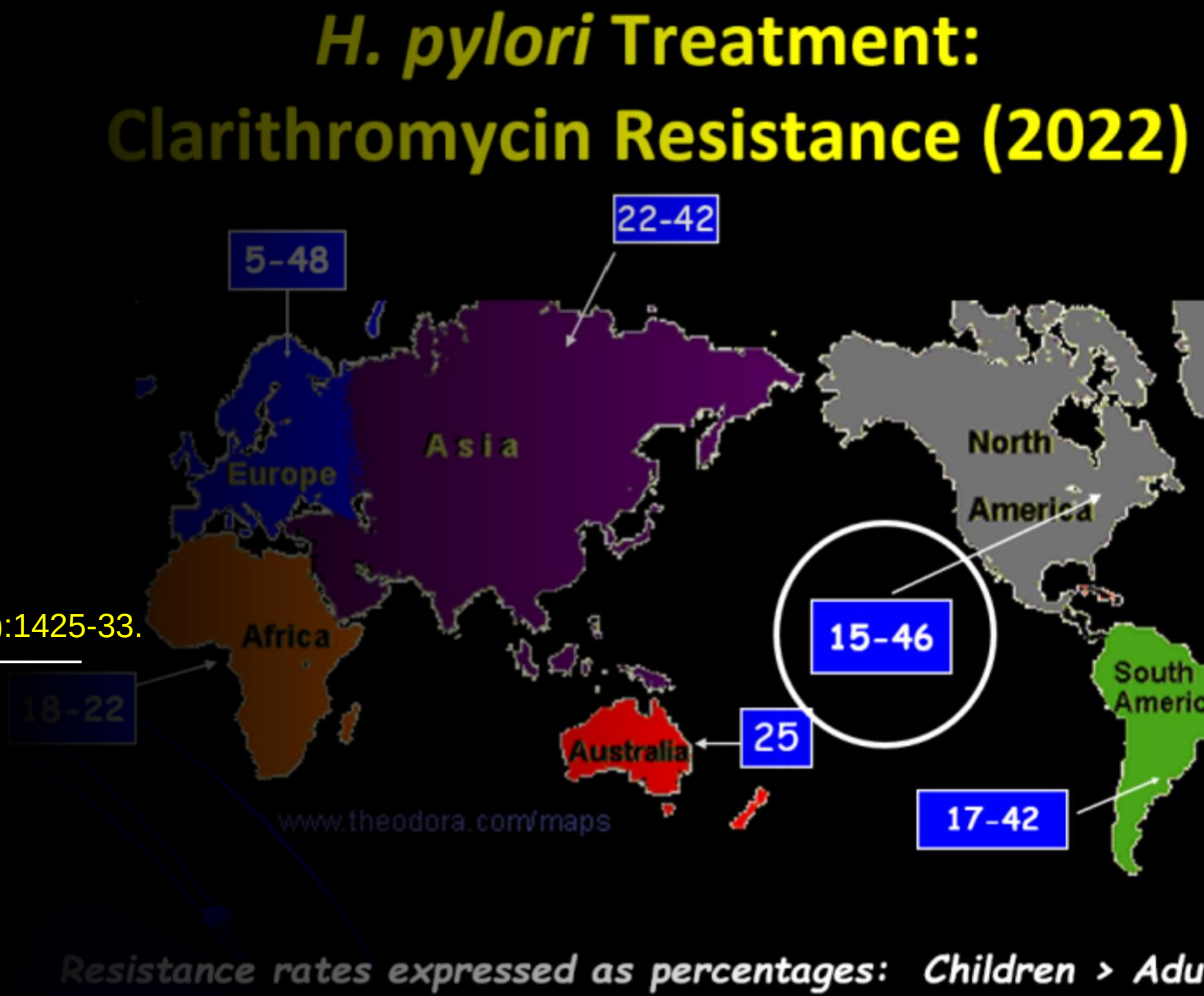


Am J Gastroenterol 2024;119:1730–1753.

Overall CLA resistance rate was 27.53%, worldwide

Clinical Laboratory. 2023 Jul 1;69(7):1425-33.

Clarithromycin resistance in Helicobacter pylori has reached concerning levels globally



H. pylori Antibiotic Resistance Rates in the US

a

Antibiotic(s)	% Resistant (N=2669 strains)
Clarithromycin	31.5
Levofloxacin	37.6
Metronidazole	42.1
Tetracycline	0.9
Amoxicillin	2.6
Rifabutin	0.2
Dual Metronidazole /Clarithromycin	11.7

Antibiotic susceptibility testing performed on 2669 strains from the US between 2011-2021

Ho J et al, Am J Gastroenterol 2022;117:1221

b

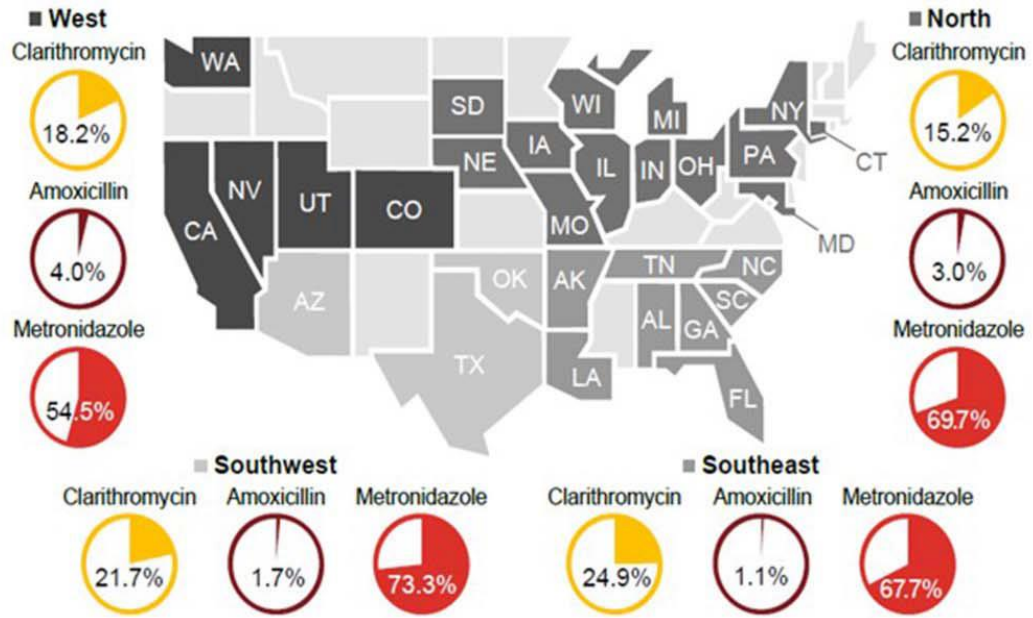
Overall resistance rates:

Clarithromycin **22.2%**

Amoxicillin **1.2%**

Metronidazole **69.2%**

US resistance rates by subregion:



381 patients with *H. pylori* from the US underwent antibiotic sensitivity testing between 12/2019-1/2021

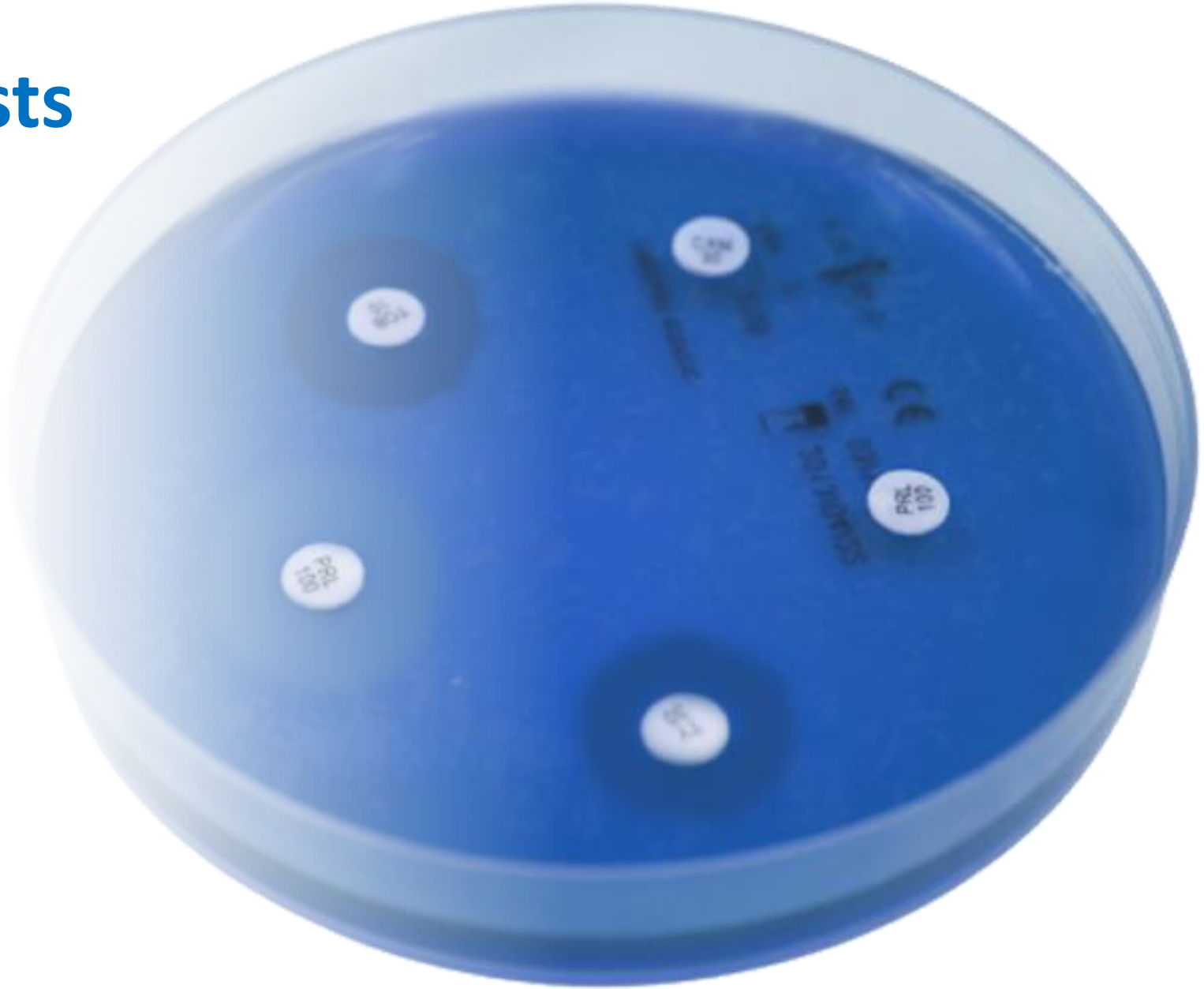
Megraud et al. Am J Gastroenterol 2023;118:269–275

Megraud F, Graham DY, Howden CW, et al. Rates of antimicrobial resistance in Helicobacter pylori isolates from clinical trial patients across the US and Europe. Am J Gastroenterol 2023;118(2):269–75.

Chey WD, et al. ACG Clinical Guideline. 2024 Sep 1;119(9):1730-53.

Ho JJ, et al . Helicobacter pylori antibiotic resistance in the United States between 2011 and 2021: a systematic review and meta-analysis ACG. 2022 Aug 1;117(8):1221-30.

Susceptibility tests



Susceptibility tests

It is reasonable to recommend that susceptibility tests (molecular or after culture) are **routinely performed**, **even before prescribing first-line treatment**, regarding antibiotic stewardship.

However, the **generalized use** of such a susceptibility-guided strategy in routine clinical practice remains to be established.

Agreement 91% Grade D2



Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.



Antibiotic stewardship

First-line treatment of HPE?

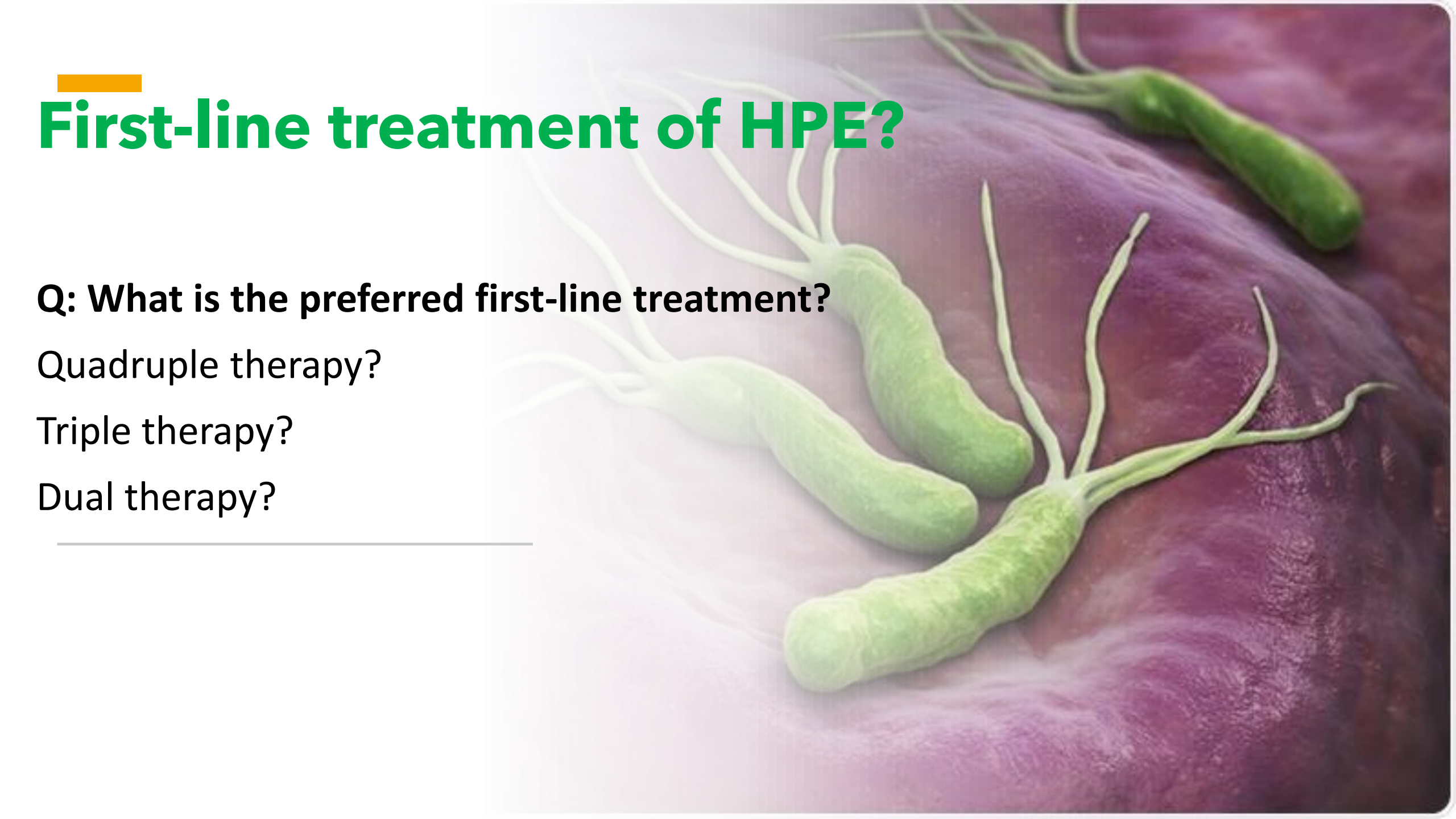
First-line treatment of HPE?

Q: What is the preferred first-line treatment?

Quadruple therapy?

Triple therapy?

Dual therapy?

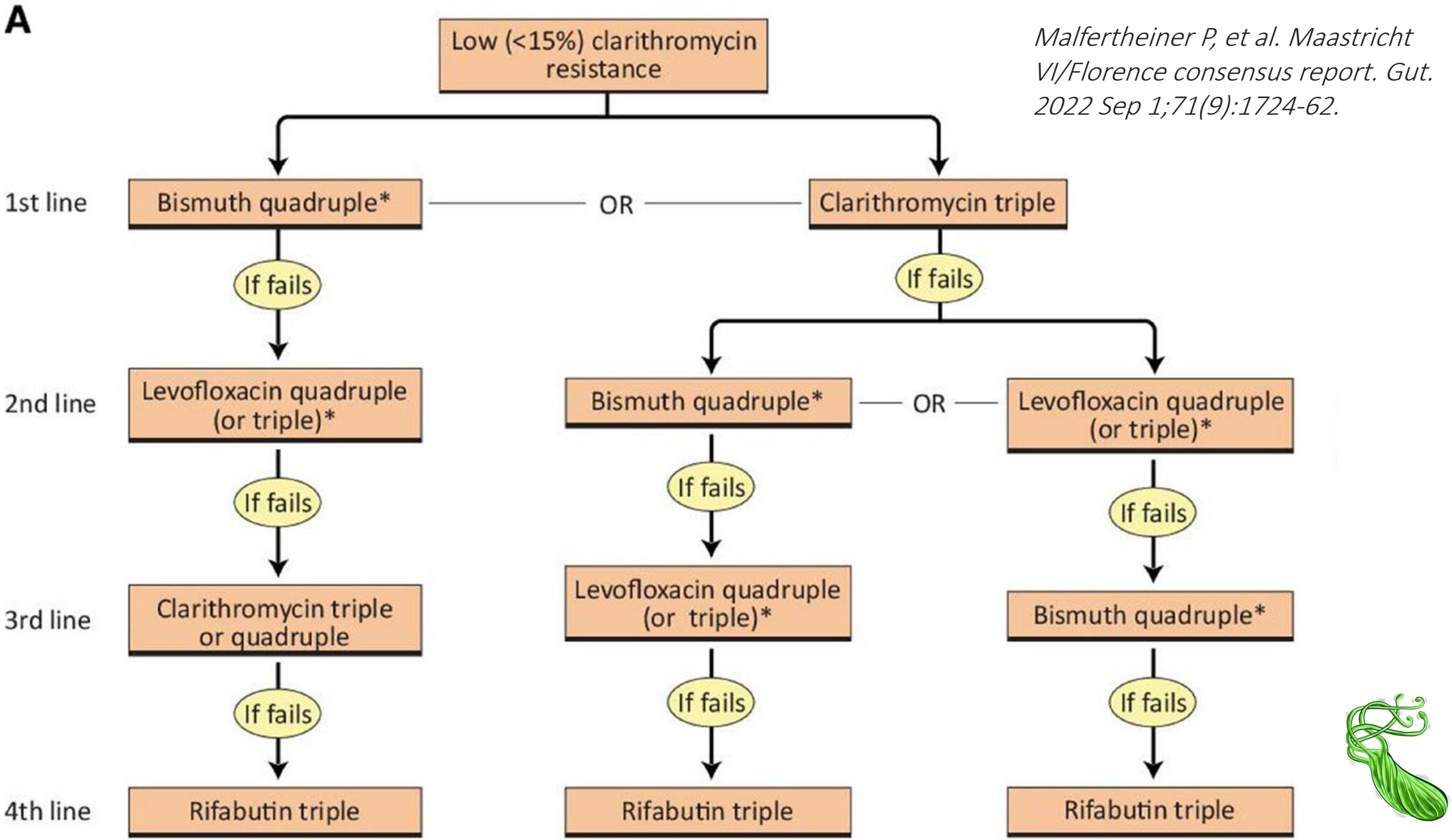


Which of the following option(s) do you prefer as your first choice? Why?

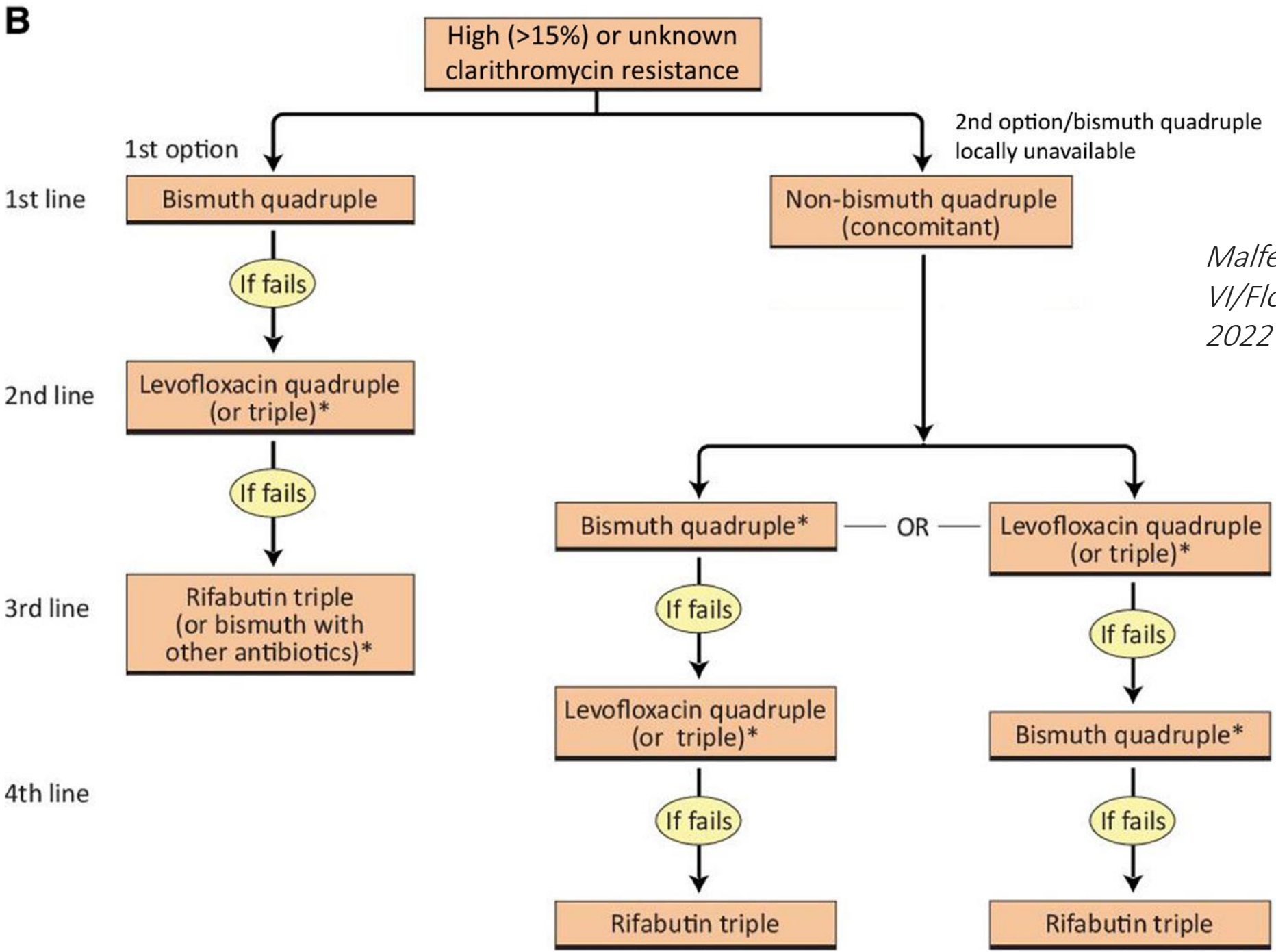
PPI+ Amoxicillin + Bismuth subcitrate+ Clarithromycin
PPI+ Amoxicillin+ Bismuth subcitrate+ Metronidazole
PPI+ Amoxicillin+ Bismuth subcitrate+ Furazolidone/Metronidazole
PPI+ Bismuth subcitrate+ Amoxicillin+ Levofloxacin
PPI+ Bismuth subcitrate+ Tetracycline+ Metronidazole.
PPI+ Amoxicillin +Metronidazole + Clarithromycin
PPI+ Amoxicillin+ Levofloxacin

Others?





Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.



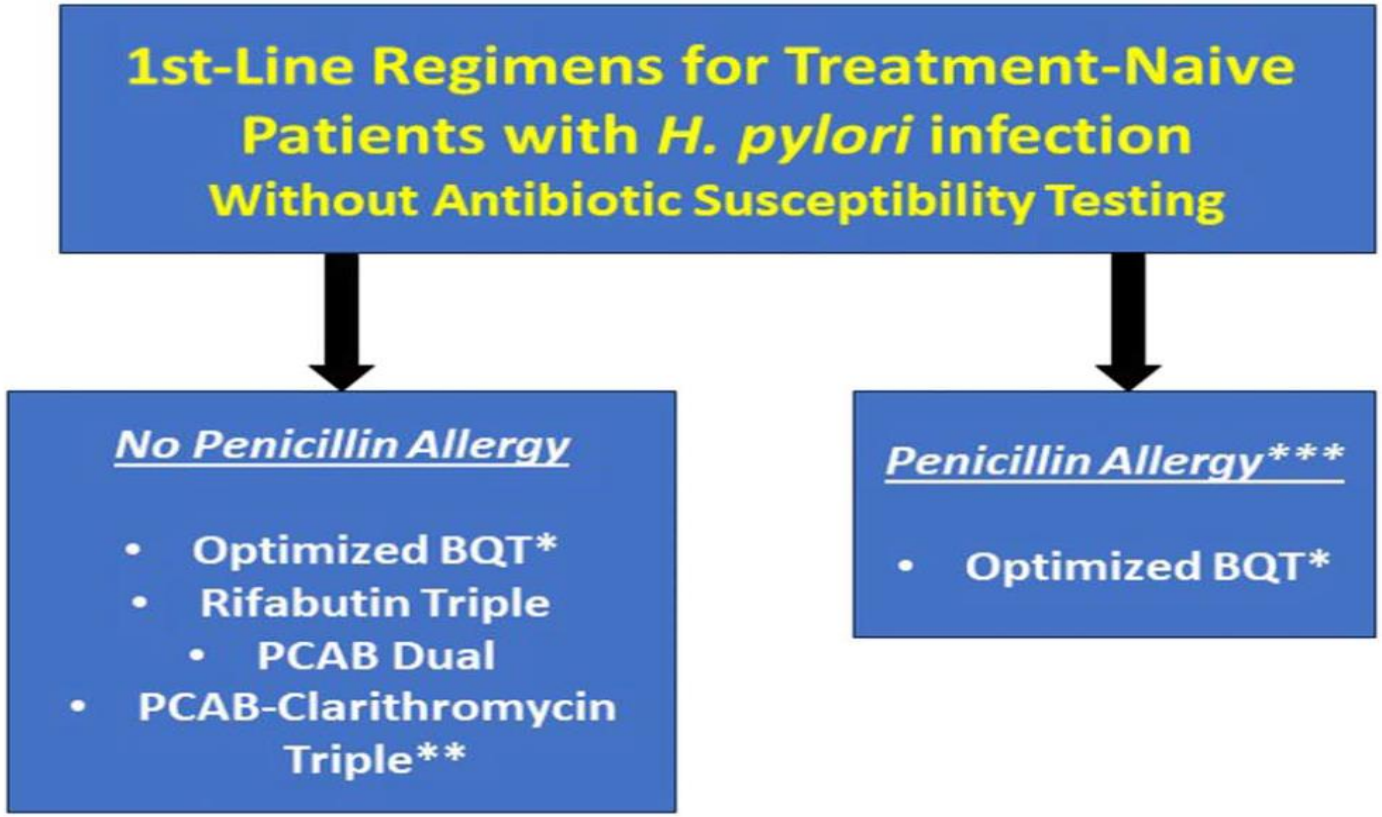
Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.

Table 5. Recommended regimens for treatment-naive patients with *H. pylori* infection

Regimen	Drugs (doses)	Dosing frequency	FDA approval	Recommendation
Optimized bismuth quadruple[a]	PPI (standard dose)[b] Bismuth subcitrate (120–300 mg) or subsalicylate (300 mg)[d] Tetracycline (500 mg)[e] Metronidazole (500 mg)	b.i.d. q.i.d. q.i.d. t.i.d. or q.i.d.	No[c]	Strong (moderate quality of evidence)
Rifabutin triple (Talicia)[f]	Omeprazole (10 mg)[b] Amoxicillin (250 mg) Rifabutin (12.5 mg)	4 capsules t.i.d.	Yes	Conditional (low quality of evidence)
PCAB dual (Voquezna DualPak)[g]	Vonoprazan (20 mg) Amoxicillin (1,000 mg)	b.i.d. t.i.d.	Yes	Conditional (moderate quality of evidence)
PCAB triple (Voquezna TriplePak)[h]	Vonoprazan (20 mg) Clarithromycin (500 mg) Amoxicillin (1,000 mg)	b.i.d.	Yes	Conditional (moderate quality of evidence)

Chey WD, et al. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. Official journal of the American College of Gastroenterology| ACG. 2024 Sep 1;119(9):1730-53.





BQT, bismuth quadruple therapy, PCAB, potassium-competitive acid blocker
*Includes appropriately dosed PPI, bismuth, nitroimidazole, and tetracycline (not doxycycline)
** Avoid in those with previous macrolide exposure
*** May require formal allergy testing

Chey WD, et al. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. Official journal of the American College of Gastroenterology| ACG. 2024 Sep 1;119(9):1730-53.

Susceptibility testing is not available

If individual susceptibility testing is not available, in areas of high (>15%) or unknown clarithromycin resistance is bismuth quadruple therapy.

Bismuth quadruple: PPI, bismuth, tetracycline, and metronidazole.

If this is not available, non-bismuth concomitant quadruple therapy may be considered.

PPI, amoxicillin, clarithromycin, and a nitroimidazole administered concurrently

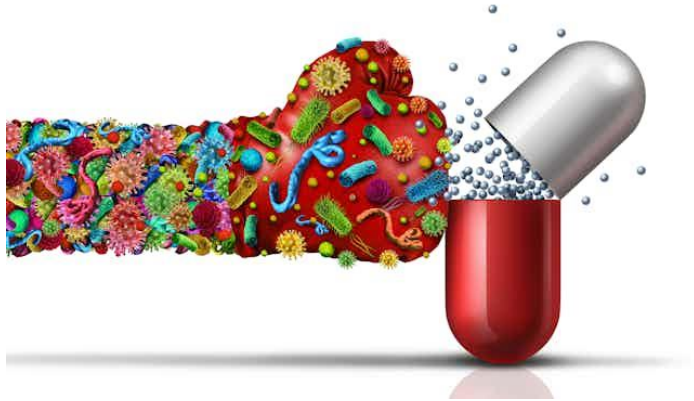


Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.

Low clarithromycin resistance

In areas of low clarithromycin resistance, bismuth quadruple therapy or clarithromycin-containing triple therapy may be recommended as first-line empirical treatment, if proven effective locally.

Clarithromycin triple: PPI, clarithromycin and amoxicillin



Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.

AST- Rates of resistance

Clarithromycin- and levofloxacin-containing treatment regimens **should be avoided** in the absence of demonstrated **macrolide and quinolone susceptibility**, respectively.

Rates of resistance to clarithromycin and levofloxacin have been significantly increasing among H. pylori strains in many regions of the world and are associated with high rates of treatment failure

Chey WD, et al. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. Official journal of the American College of Gastroenterology| ACG. 2024 Sep 1;119(9):1730-53.

Savoldi A, et al. Prevalence of antibiotic resistance in Helicobacter pylori: A systematic review and meta-analysis in World Health Organization regions. Gastroenterology 2018;155(5): 1372–82.e17.

Low clarithromycin resistance

In areas of **low clarithromycin resistance**, BQT or clarithromycin-containing triple therapy may be recommended as first-line empirical treatment, if proven effective locally.

Agreement 94% Grade B1



Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.

Empiric second-line

Rescue therapies

Experienced patient

Which option(s) do you prefer as your second choice? Why?

PPI+ Amoxicillin + Bismuth subcitrate+ Clarithromycin
PPI+ Amoxicillin+ Bismuth subcitrate+ Metronidazole
PPI+ Amoxicillin+ Bismuth subcitrate+ Furazolidone/Metronidazole
PPI+ Bismuth subcitrate+ Amoxicillin+ Levofloxacin
PPI+ Bismuth subcitrate+ Tetracycline+ Metronidazole.
PPI+ Amoxicillin +Metronidazole + Clarithromycin
PPI+ Amoxicillin+ Levofloxacin

Others?



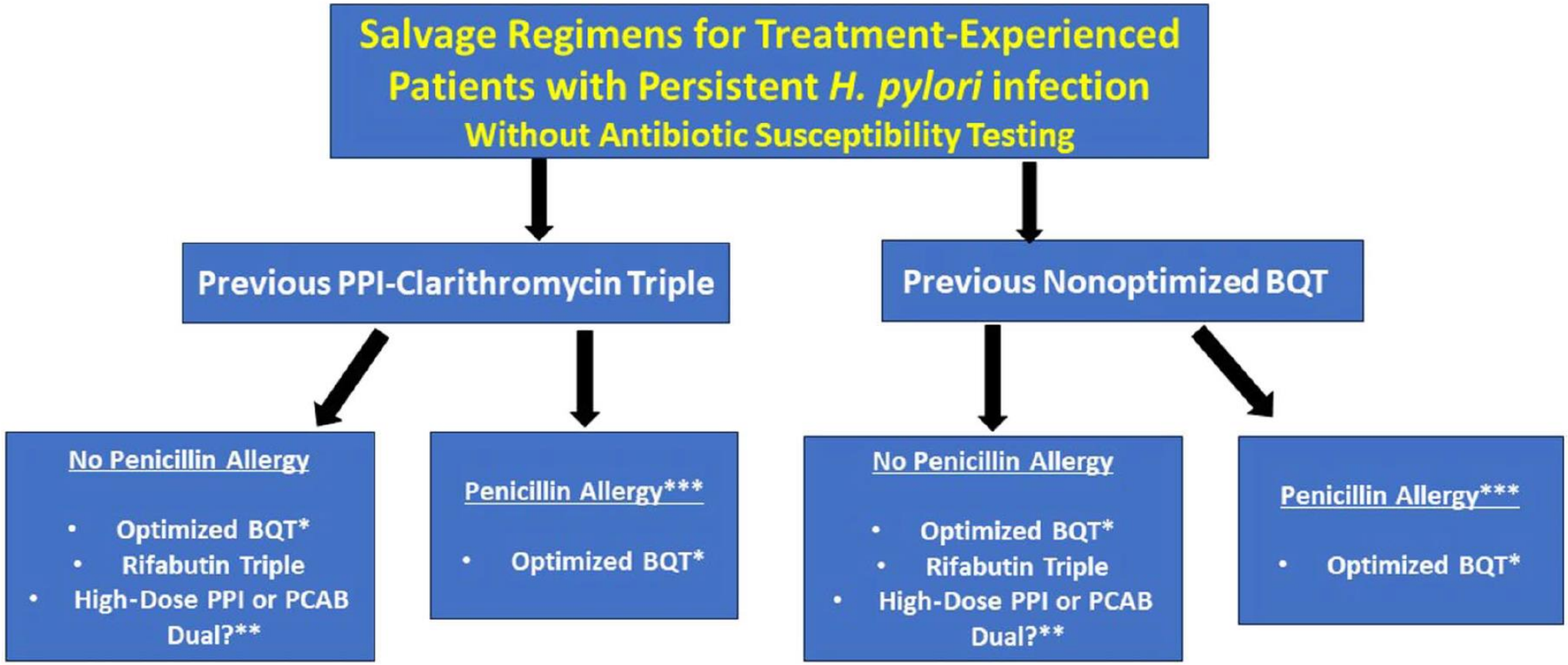
Table 6. Recommended salvage regimens for treatment-experienced patients with persistent *H. pylori* infection

Regimen	Drugs (doses)	Dosing frequency	AST required?	Recommendation
Optimized bismuth quadruple[a]	PPI (standard dose)[b] Bismuth subcitrate (120–300 mg) or subsalicylate (300 mg) Tetracycline (500 mg) Metronidazole (500 mg)	b.i.d. q.i.d. q.i.d. t.i.d. or q.i.d.	No	Conditional (very low quality of evidence)
Rifabutin triple	PPI (standard to double dose)[b] Amoxicillin (1,000 mg) Rifabutin (50–300 mg)[c]	b.i.d. b.i.d. or t.i.d. q.d., b.i.d., or (Talicia which contains 50 mg t.i.d.)[c]	No	Conditional (low quality of evidence)
Levofloxacin triple[d]	PPI (standard dose)[b] Levofloxacin (500 mg)[d] Amoxicillin (1,000 mg) or metronidazole[e] (500 mg)	b.i.d. q.d. b.i.d.	Yes	Conditional (low quality of evidence)
P-CAB triple (Voquezna TriplePak)[f]	Vonoprazan (20 mg) Clarithromycin (500 mg) Amoxicillin (1,000 mg)	b.i.d	Yes	No recommendation (evidence gap)
High-dose dual therapy[g]	Vonoprazan (20 mg)[h] or PPI (double dose) Amoxicillin (1,000 mg)	b.i.d. or t.i.d. t.i.d	No	No recommendation (evidence gap)

*Optimized bismuth quadruple therapy includes appropriately dosed PPI, bismuth, nitroimidazole (1,500–2,000 mg in divided doses), and tetracycline



Chey WD, et al. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. Official journal of the American College of Gastroenterology| ACG. 2024 Sep 1;119(9):1730-53..



Lists of treatments are meant to present appropriate options but are *not* meant to present a treatment hierarchy

BQT, bismuth quadruple therapy
***Includes appropriately dosed PPI, bismuth, nitroimidazole, and tetracycline (not doxycycline)**
****Consider only when optimized BQT or rifabutin triple therapy is not an option and antibiotic susceptibility testing is unavailable**
***** May require formal allergy testing**

Chey WD, et al. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. Official journal of the American College of Gastroenterology| ACG. 2024 Sep 1;119(9):1730-53.

Salvage Regimens for Treatment-Experienced Patients with Persistent *H. pylori* infection

Antibiotic Susceptibility Testing

Clarithromycin- and levofloxacin-sensitive

- Clarithromycin Triple*
- Optimized BQT**
- Rifabutin Triple
- Levofloxacin Triple

Clarithromycin-resistant, levofloxacin-sensitive

- Optimized BQT**
- Rifabutin Triple
- Levofloxacin Triple

Clarithromycin-sensitive, levofloxacin-resistant

- Clarithromycin Triple*
- Optimized BQT**
- Rifabutin Triple

Clarithromycin- and levofloxacin-resistant

- Optimized BQT**
- Rifabutin Triple
- High-Dose PPI or PCAB Dual?***

PCAB, potassium-competitive acid blocker, BQT, bismuth quadruple therapy

Lists of treatments are meant to present appropriate options but are *not* meant to present a treatment hierarchy except that levofloxacin should only be used when other options are inappropriate. The choice of salvage therapy should also be guided by previous treatments received for *H. pylori*.

* Can be prescribed with a PPI or PCAB, **Includes appropriately dosed PPI, bismuth, nitroimidazole, and tetracycline (not doxycycline), ***Consider only when optimized BQT or rifabutin triple therapy is not an option

Chey WD, et al. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. Official journal of the American College of Gastroenterology| ACG. 2024 Sep 1;119(9):1730-53.

Empiric second-line

Empiric second-line and rescue therapies should be guided by **local resistance patterns** assessed by **susceptibility testing** and eradication rates in order to optimize treatment success.

Agreement 94% Grade D2



Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.

Fluoroquinolone-containing therapy

After the **failure of bismuth-containing quadruple therapy**, a **fluoroquinolone-containing quadruple (or triple) therapy or the high-dose PPI-amoxicillin dual therapy** may be recommended.

In cases of high fluoroquinolone resistance, combining bismuth with other antibiotics or rifabutin may be an option.

Agreement 83% Grade C2



Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.

Failure of PPI-clarithromycin-amoxicillin

After failure of PPI-clarithromycin-amoxicillin triple therapy, a bismuth-containing quadruple therapy, a fluoroquinolone-containing quadruple (or triple) therapy or a PPI-amoxicillin high-dose dual therapy are recommended as a second-line treatment.

Agreement 84% Grade C2



Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.

Failure of a non-BQT

After failure of a non-BQT, either a **BQT or a fluoroquinolone-containing quadruple (or triple) therapy** is recommended. PPI-amoxicillin high-dose dual therapy might also be considered.

Agreement 87% Grade C2



Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.

Bismuth-based quadruple therapy.

After failure of the first-line treatment with **clarithromycin-containing triple or non-BQTs**, and second-line treatment with **fluoroquinolone-containing therapy,** it is recommended to use the bismuth-based quadruple therapy.

If bismuth is not available, high-dose PPI-amoxicillin dual or a rifabutin-containing regimen could be considered.

Agreement 84% Grade B2



Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.

Failure to first and second-line treatment

After failure of first-line treatment with bismuth quadruple and second-line treatment with fluoroquinolone-containing therapy, it is recommended to use a **clarithromycin-based triple or quadruple therapy only if from an area of low (<15%) clarithromycin resistance**.

Otherwise, a high-dose PPI-amoxicillin dual therapy, a rifabutin-containing regimen or a combination of bismuth with different antibiotics should be used.

Agreement 90% Grade C2



Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.

First-line treatment in “Proven penicillin allergy”

In patients with proven penicillin allergy, for a first-line treatment, BQT **(PPI-bismuth- tetracycline-metronidazole)** should be recommended.

As second-line therapy, BQT (if not previously prescribed) and fluoroquinolone-containing regimen may represent empirical second-line rescue options.

Agreement 85% Grade C2



Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.

Role of P-CAB

Potassium-competitive acid blockers (P-CAB)—antimicrobial combination treatments:

- ✓ Superior, or not inferior, to conventional PPI-based triple therapies for first-line and second-line treatment
- ✓ Superior in patients with evidence of antimicrobial-resistant infections.

Agreement 100% Grade B2



Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.



Duration of treatment

Duration of treatment

The treatment duration of BQT should be **14 days**, unless 10-days equally effective therapies are available.

Agreement 85% Grade D2

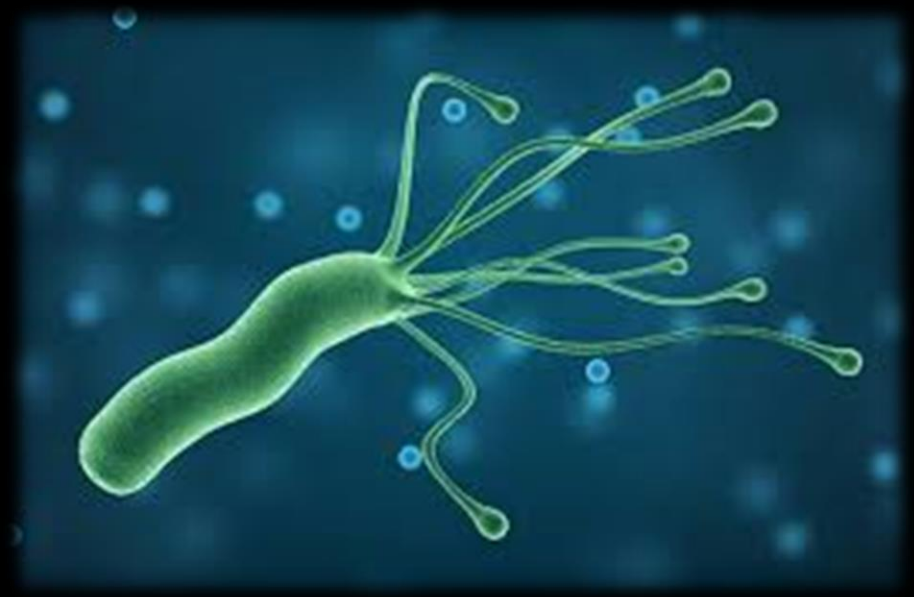
The recommended treatment duration of non-BQT (concomitant) is 14 days.

The recommended treatment duration of PPI-clarithromycin-Based triple therapy is 14 days.

Agreement 100% Grade B1



Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.



High dose PPI

High-dose PPI twice daily

The use of **high-dose PPI twice daily** increases the efficacy of **triple therapy.**

It remains unclear whether high-dose PPI twice daily can improve the efficacy of quadruple therapies.

Agreement 97% Grade C2



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Post-treatment



Which patients treated for H. pylori infection should undergo a test to confirm eradication?

HPE confirmation

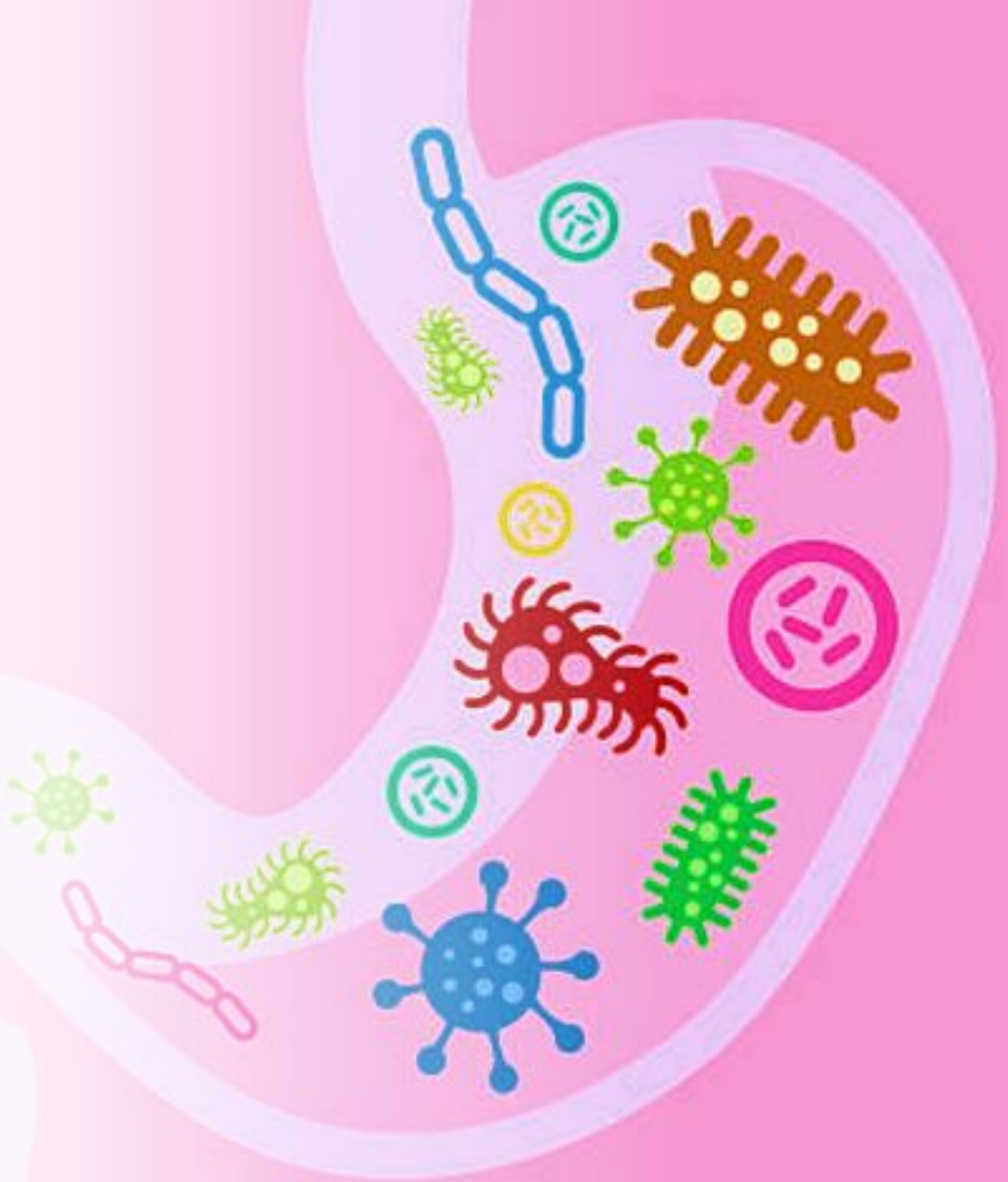
All patients treated for H. pylori infection should have their eradication confirmed.

All patients treated for H. pylori infection should undergo a test of cure with an appropriately conducted urea breath test, fecal antigen test, or biopsy-based test at least 4 weeks after completion of therapy.



Chey WD, et al. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. Official journal of the American College of Gastroenterology| ACG. 2024 Sep 1;119(9):1730-53.

Role of probiotics in H. pylori eradication



Role of probiotics in H. pylori eradication

Certain probiotics have been shown to be effective in **reducing GI side effects caused by H. pylori eradication therapies**.

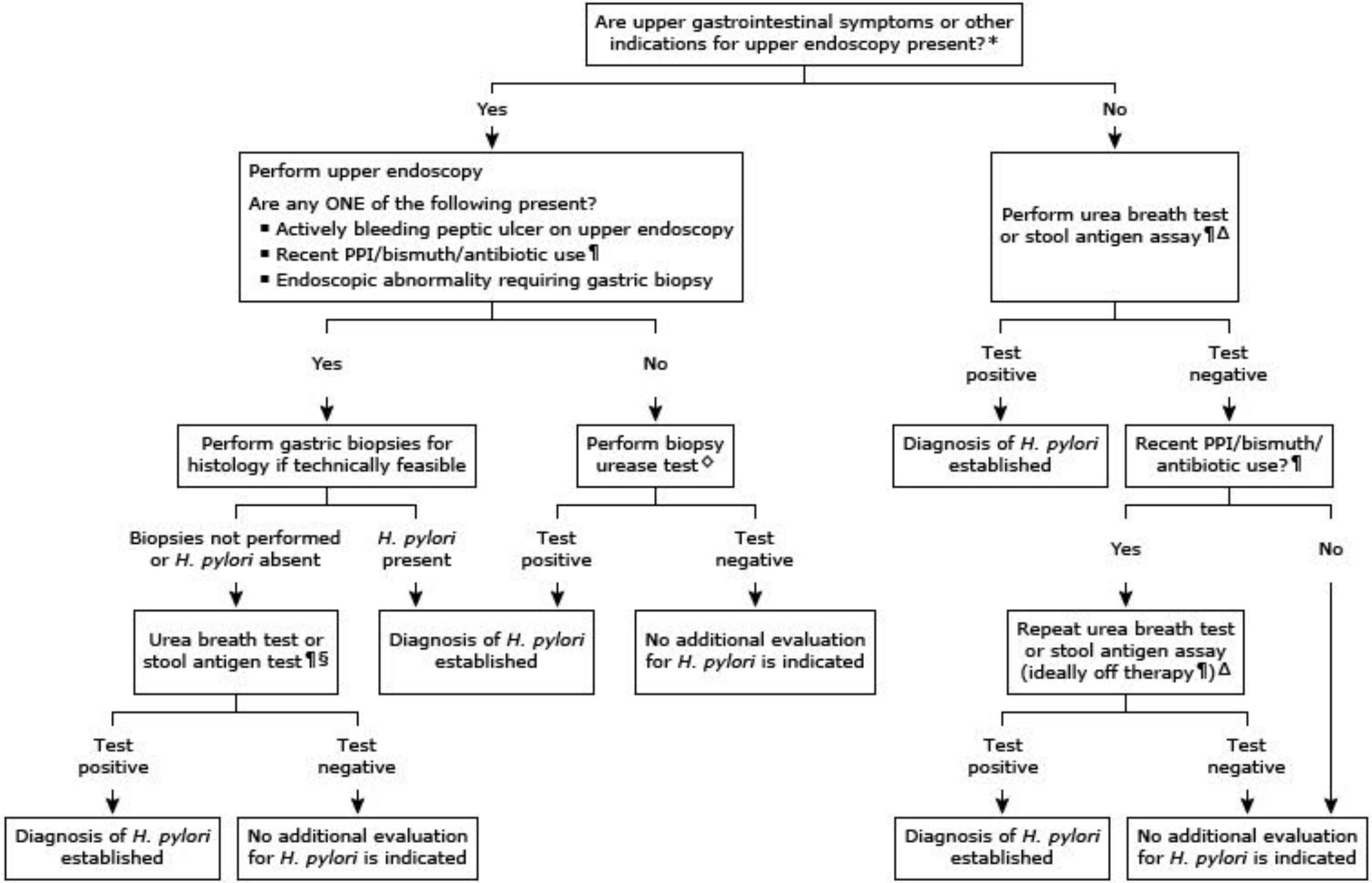
There is **insufficient evidence to suggest** that the use of probiotic therapy improves the efficacy or tolerability of H. pylori eradication therapy (conditional recommendation; low quality of evidence).

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Malfertheiner P, et al. Maastricht VI/Florence consensus report. Gut. 2022 Sep 1;71(9):1724-62.



Take home




Are upper gastrointestinal symptoms or other indications for upper endoscopy present?*
Yes
No
Perform upper endoscopy
Are any ONE of the following present?
Actively bleeding peptic ulcer on upper endoscopy
Recent PPI/bismuth/antibiotic use¶
Endoscopic abnormality requiring gastric biopsy
Perform urea breath test or stool antigen assay¶Δ
Yes
No
Test positive
Test negative
Perform gastric biopsies for histology if technically feasible
Perform biopsy urease test◇
Diagnosis of H. pylori established
Recent PPI/bismuth/ antibiotic use?¶
Biopsies not performed or H. pylori absent
H. pylori present
Test positive
Test negative
Yes
No
Urea breath test or stool antigen test¶§
Diagnosis of H. pylori established
No additional evaluation for H. pylori is indicated
Repeat urea breath test or stool antigen assay (ideally off therapy¶)Δ
Test positive
Test negative
Test positive
Test negative
Diagnosis of H. pylori established
No additional evaluation for H. pylori is indicated
Diagnosis of H. pylori established
No additional evaluation for H. pylori is indicated

Thank you for your attention

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