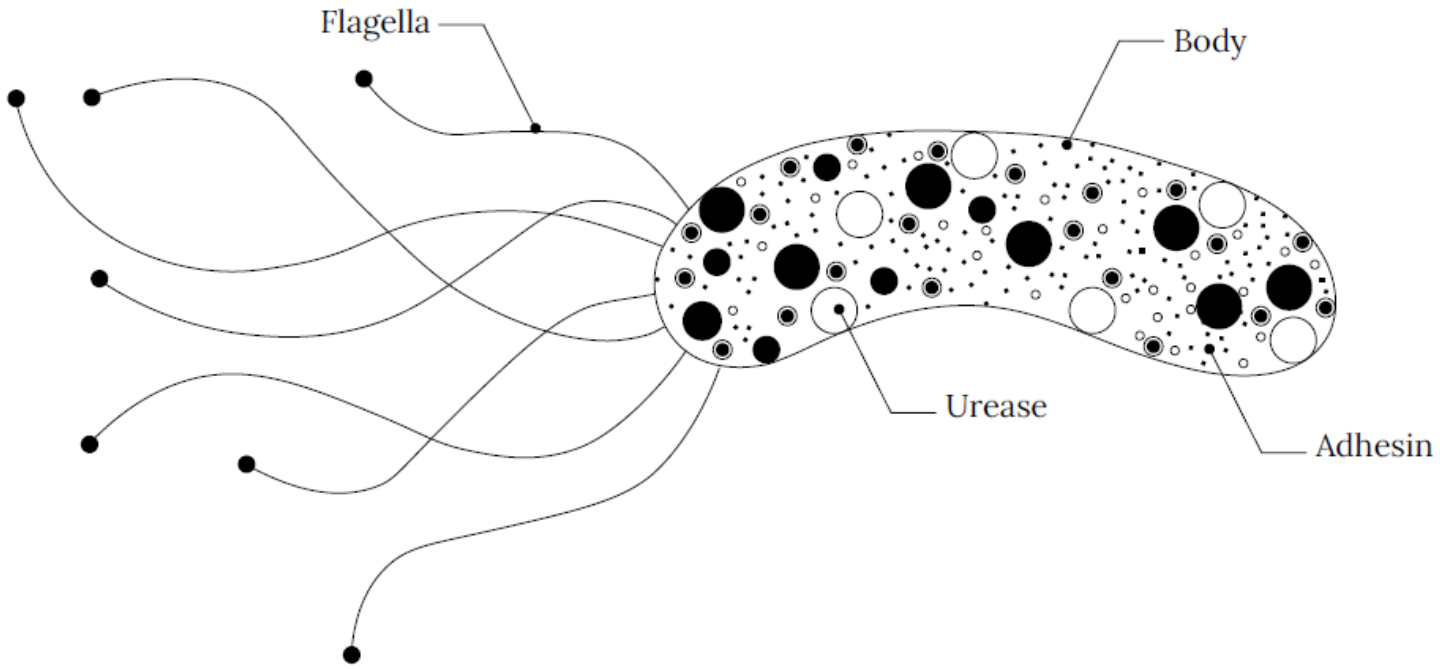


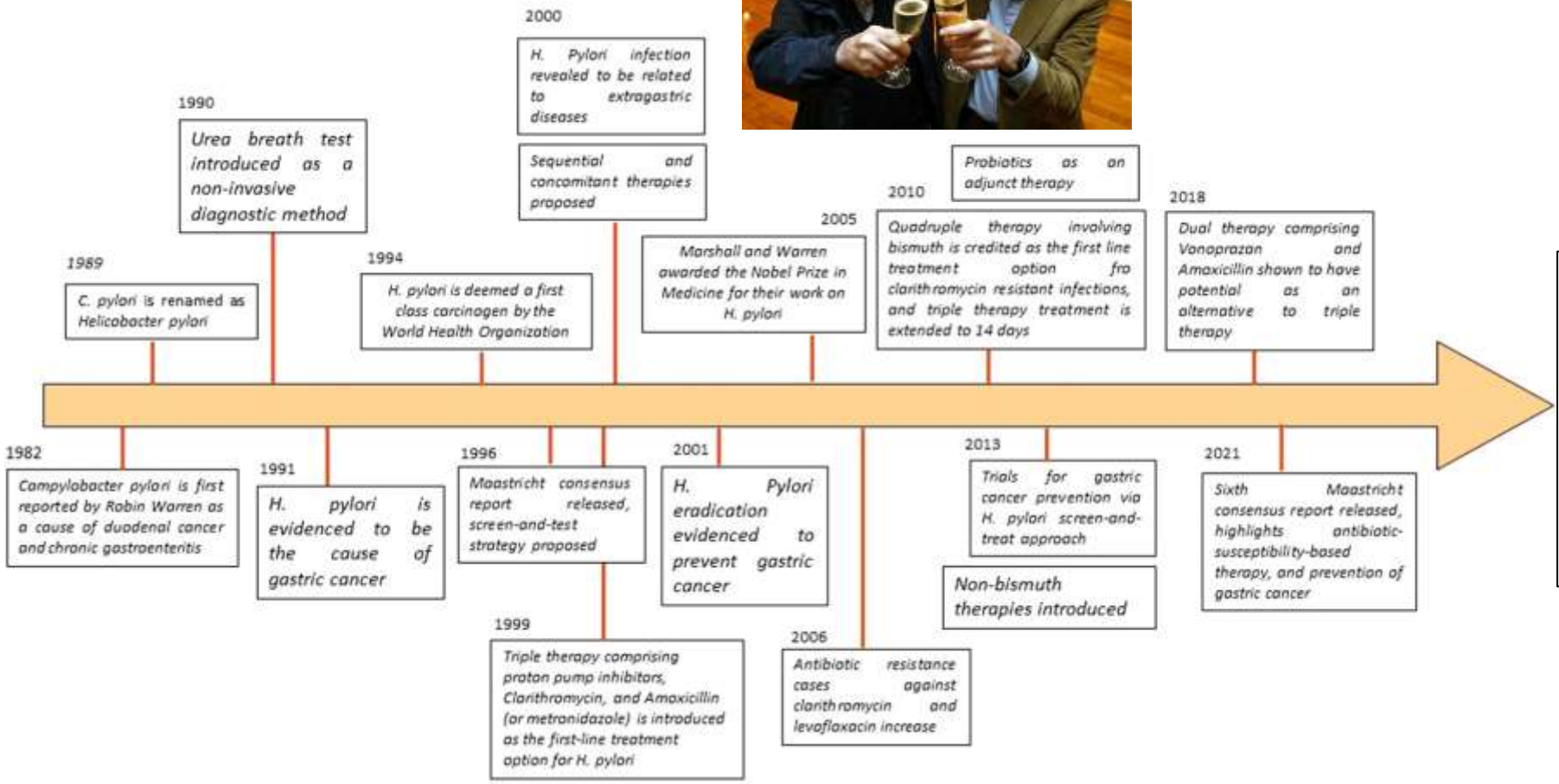
2024 ACG Clinical Guideline: Treatment of *Helicobacter pylori* Infection

Doris H. Toro, MD AGAF, FACG, FACP

Disclosures:

- This presentation is based on published ACG Clinical Guideline: Treatment of *Helicobacter pylori* Infection at The American Journal of Gastroenterology 119(9):p 1730-1753, September 2024 and additional review of the relevant literature.
- The contents of this presentation do not represent the views of the Veterans Affairs Caribbean Healthcare System, the U.S. Department of Veterans Affairs, or the United States Government.
- I have no financial conflicts to disclose.

H. pylori Timeline



2024 ACG Clinical Guideline: Treatment of *Helicobacter pylori* Infection

doi: 10.20944/preprints202312.1242.v1

Updated 2024 Treatment Guidelines

Updates 2017 guidelines and includes 6 key concepts and 12 recommendations.

6 Key Concepts

- Decreasing prevalence of infection through time and changing epidemiology.
- Updated testing indications
- All patients with confirmed infection should be offered treatment and testing to confirm cure.
- Rising rates of resistance to key antibiotics in both treatment naïve and experienced patients.
- Incorporate novel treatment regimens and role of next-generation gastric acid-suppressing agents (i.e., potassium-competitive acid blockers; PCABs) in treatment-naive individuals.

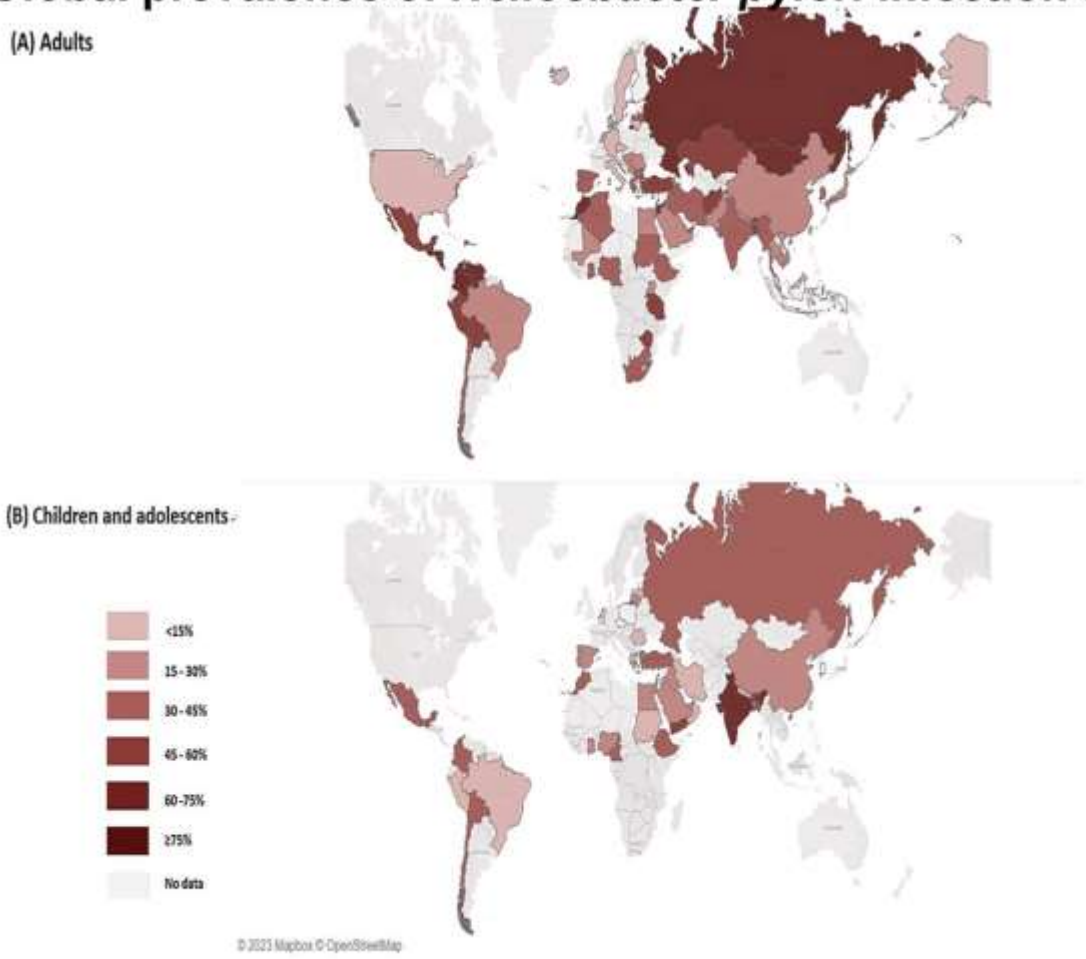
12 Recommendations

- For treatment Naïve patients.
  - Provides different alternatives as first line treatment
  - Advocates against use of clarithromycin and levofloxacin treatment in the absence of susceptibility tests and concomitant treatment using (PPI, clarithromycin, amoxicillin, and metronidazole)
- For patients with persistent infection.
  - Provides possible regimes, including empiric and susceptibility based.

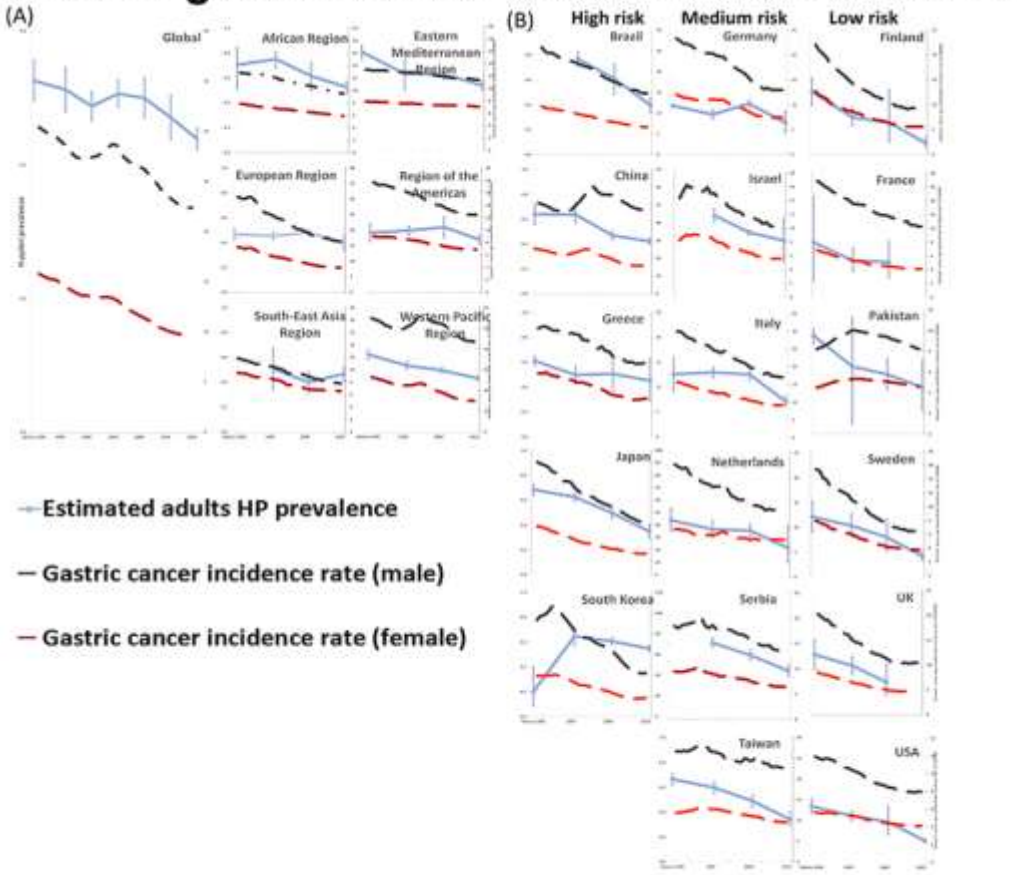
Key Concept 1:

The prevalence of *H. pylori* infection in North America is decreasing over time but remains substantial at **30%–40%.** The infection is typically acquired in childhood and is more prevalent among non-White races and ethnicities, those living in crowded or poor sanitary conditions, and early generation immigrants from countries where *H. pylori* is endemic.

Global prevalence of *Helicobacter pylori* infection and incidence of gastric cancer between 1980 and 2022



The latest (2010~2022) *H pylori* prevalence



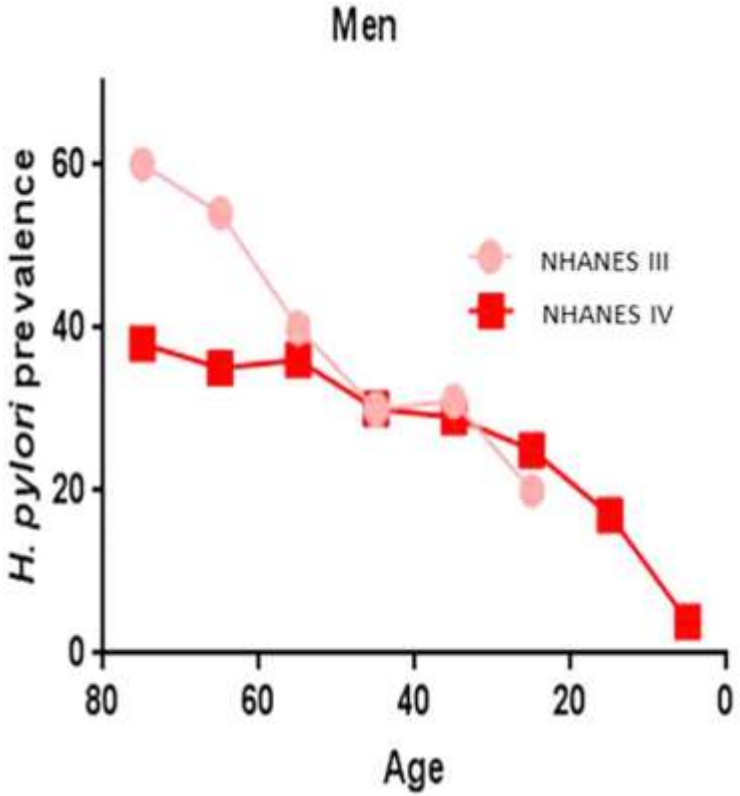
Secular trends of gastric cancer incidence and *H pylori* prevalence

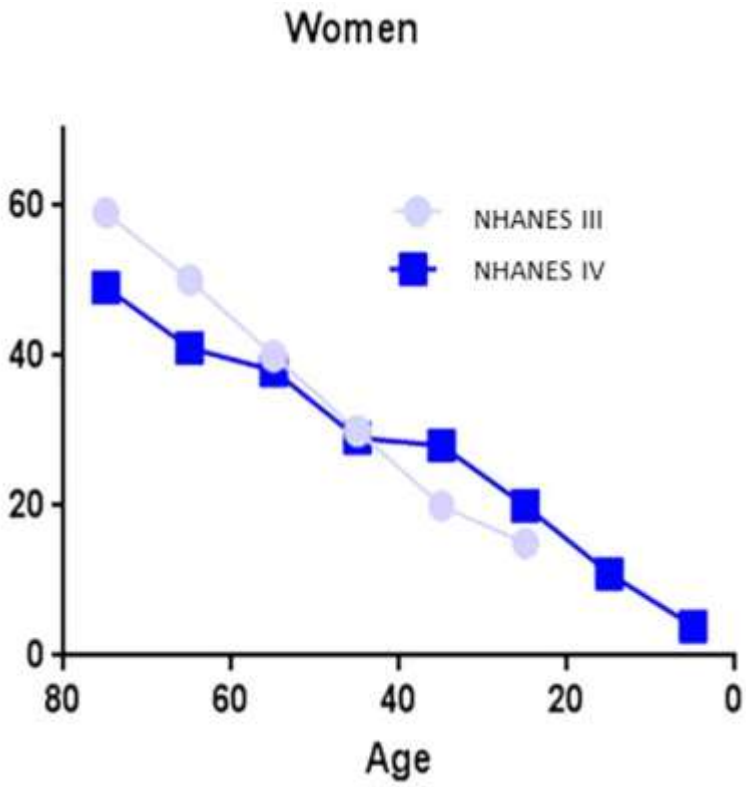
Gastroenterology

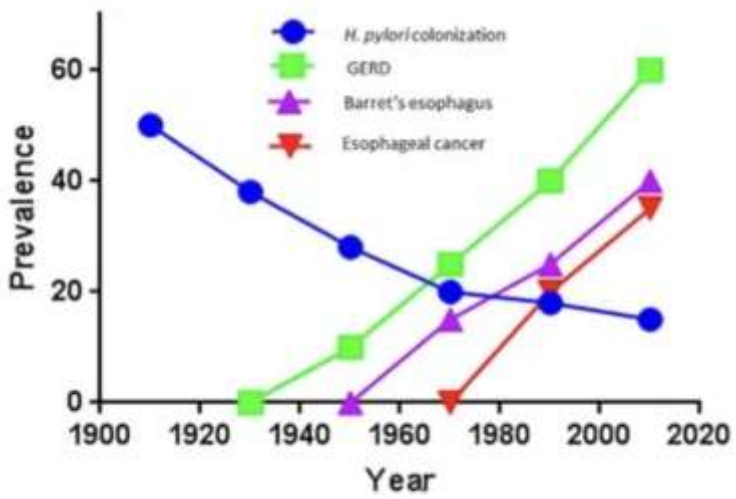
Global prevalence has declined from 58.2 % (1980-1990) to 43.1% (2011-2020)

Gastroenterology 2024 April;166(4):605-619

Evolving *H. pylori* Epidemiology in USA

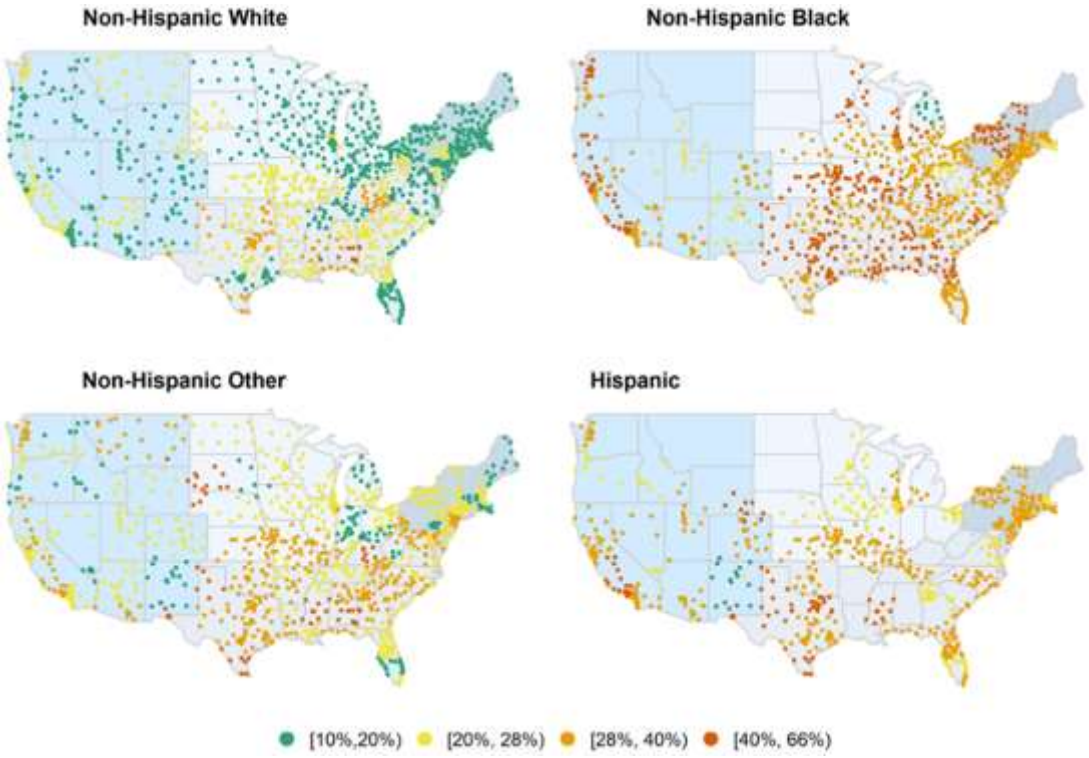






Decline in *H. pylori* prevalence observed in two population studies NHANES (National Health and Nutrition Examination Survey) III Phase I (1988–1991) and NHANES IV 1999–2000. https://doi.org/10.3389/fmicb.2018.00609

H. pylori Positivity According to Race and Ethnicity



- Nationwide retrospective VHA study.
- The primary outcome was H pylori positivity overall, as well as according to zip code-level geography, race, ethnicity, age, sex, and time period.
- Data included 913,328 individuals who had H pylori testing between 1999 and 2018.
- Overall prevalence was 25.8%, highest in blacks (40.2%) and Hispanics (36.7%)
- Positivity declined through time in all race and ethnicity groups.

Clin Gastroenterol Hepatol 2024 Jan;22(1):42-50.e26.
doi: 10.1016/j.cgh.2023.05.016.Epub 2023 May 26.

Key Concepts 2 and 4

The determination of when to test for—and treat—*H. pylori* should be viewed as a single, rather than 2 separate and distinct, decisions.

All patients who are 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.

Updated Indications for H. Pylori Testing and Treatment

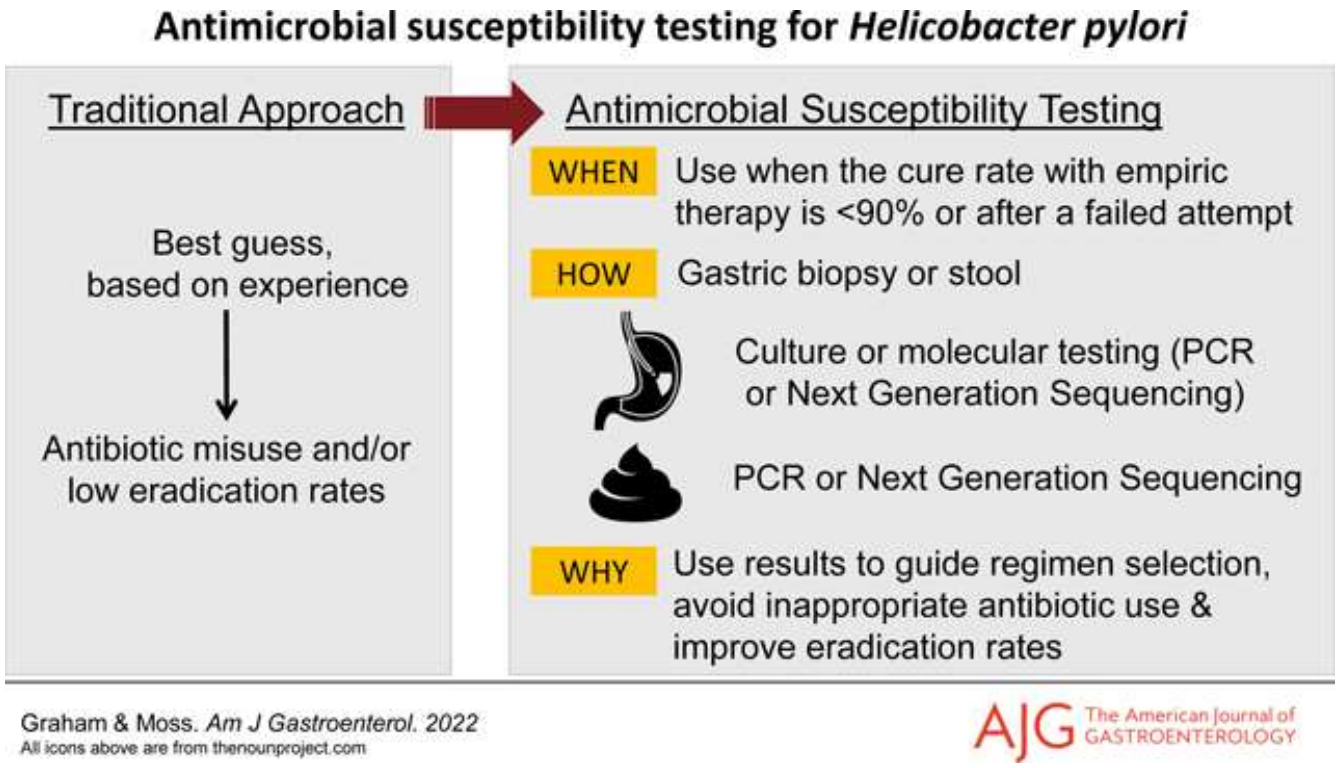
- Patients with peptic ulcer disease
- Marginal zone Lymphoma, MSLT type
- Uninvestigated dyspepsia in patients < 60 years old
  - In patients at high risk of gastric cancer, test and treat at age 45-50
- Functional dyspepsia
- **Adult household members of individuals who have a positive non-serological test for H. pylori**
- **Patients on long term NSAIDS or low dose aspirin**
- **Patients with unexplained iron deficiency anemia**
- **Patients with autoimmune thrombocytopenic purpura (ITP)**

- **Primary or secondary prevention of gastric adenocarcinoma:**
  - Patients with premalignant lesions such as atrophic gastritis, intestinal metaplasia and dysplasia
  - Current or history of early gastric cancer resection or gastric adenocarcinoma
  - Patients with **gastric adenomas or hyperplastic polyps**
  - Persons with a **first degree relative with gastric cancer**
  - Immigrants from high cancer incidence regions
  - Hereditary cancer syndromes with higher risk for gastric cancer
  - Patients with **autoimmune gastritis**

H. pylori Testing

- If you test you should treat and confirm eradication
- Standard testing modalities remain the same:
  - Fecal antigen test
  - Breath tests
  - Serology
- Some advances in antibiotic sensitivity testing
  - Molecular testing to identify gene mutations associated to antibiotic resistance

Tests to Assess Antibiotic Resistance: Key Concept



- *H. pylori* antibiotic susceptibility tests are becoming increasingly available in the United States.
- The benefit of selecting an eradication regimen "tailored" to the antibiotic susceptibility profile remains to be adequately studied—for both treatment-naive and treatment-experienced patients.
- 2024 guideline recommends **using antibiotic susceptibility testing whenever the choice of therapy remains unclear after taking into consideration any previous treatments for *H. pylori* infection, past antibiotic exposure, and whether there is a history of penicillin allergy.**

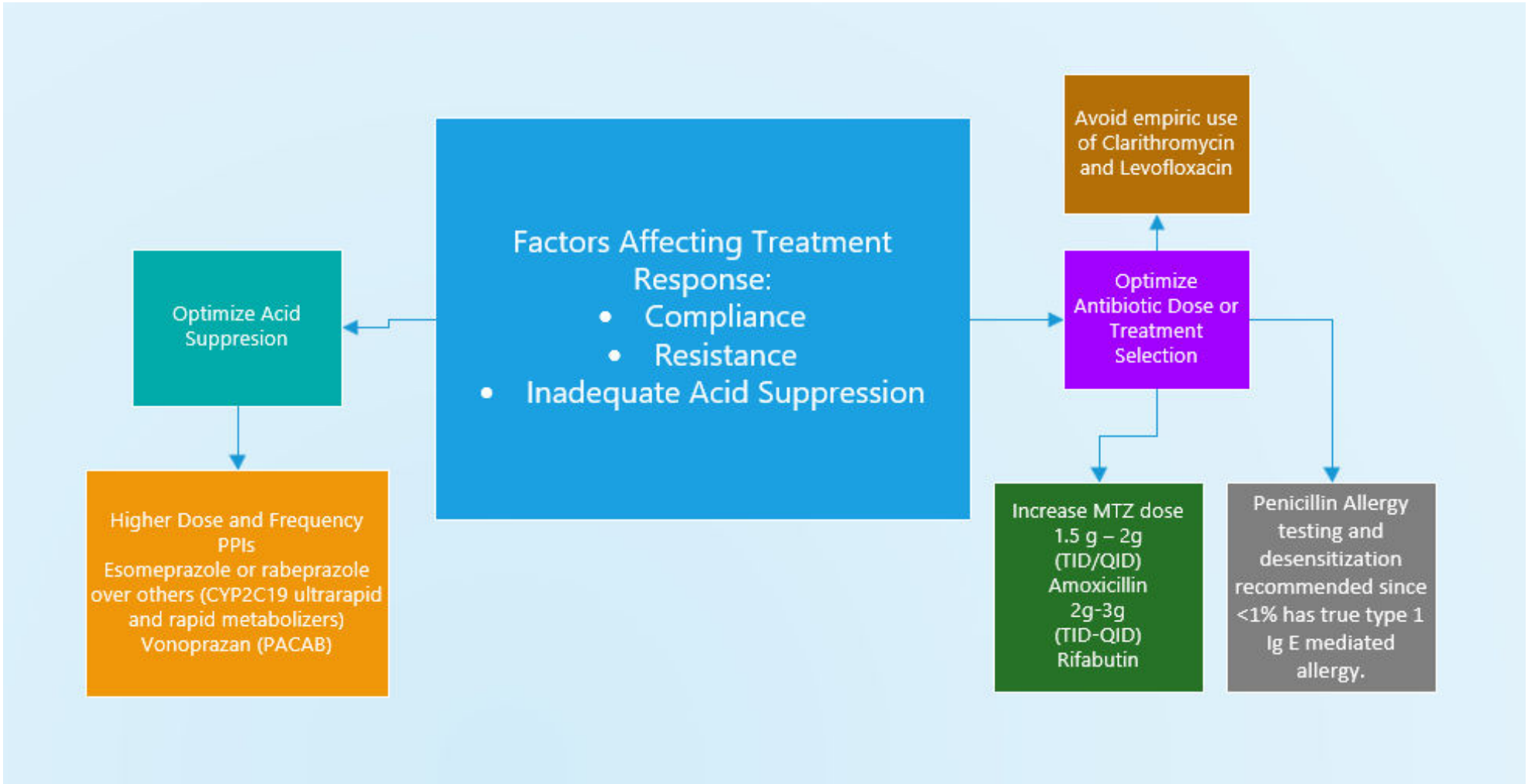
Antimicrobial Susceptibility Testing for Helicobacter pylori is Now Widely available: The Who's, When's, and How's

David Y Graham , Steven F Moss

Test	Laboratory	Web address	Catalog #
Culture	AURP Laboratories	https://ltd.aruplab.com/Tests/Pub/2006686	2006686
Culture	Mayo Clinical Laboratories	https://www.mayocliniclabs.com/test-catalog/Overview/62769	HELIS
Culture	QUEST	https://testdirectory.questdiagnostics.com/test/test-detail/8395/helicobacter-pylori-culture?cc=MASTER	369949
Culture	LabCorp	https://www.labcorp.com/tests/180885/i-helicobacter-pylori-i-culture	18085
Culture	Microbiology Specialists Inc.	https://microbiologyspecialists.com/helicobacter-pylori-testing/	058, 238
Reflex Stool by polymerase chain reaction	Mayo Clinical Laboratories	https://www.mayocliniclabs.com/test-catalog/Overview/607594	HPFRP
Next Generation Sequencing	American Molecular Laboratories	http://amlaboratories.com/testing-services/helicobacter-pylori-detection-antibiotic-resistant-analysis/	PyloriAR™/AmHPR®
Reflex Stool by Next Generation sequencing	American Molecular Laboratories	http://amlaboratories.com/testing-services/helicobacter-pylori-detection-antibiotic-resistant-analysis/	PyloriAR™/AmHPR®

Am J Gastroenterol. 2022 Apr 1;117(4):524–528.
doi: 10.14309/ajg.0000000000001659

Guidelines Focuses on Optimizing Current Treatments



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

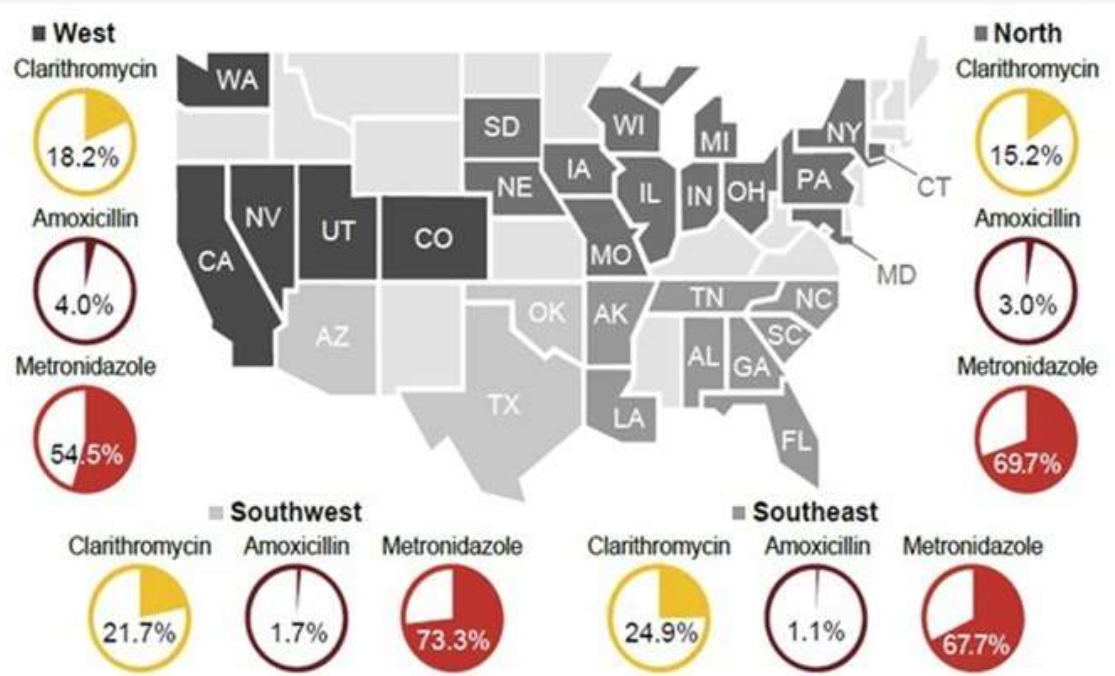
Overall resistance rates:

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

OFFICIAL JOURNAL OF THE AMERICAN COLLEGE OF GASTROENTEROLOGY | ACG

Key Concept: Clarithromycin and Levofloxacin containing regimens SHOULD BE AVOIDED in the absence of demonstrated macrolide and quinolone susceptibility, respectively.

Key Concept:

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

	Levofloxacin-based treatment	Clarithromycin-based treatment
14-day regimen	80.9%	66.3%
10-day regimen	62.7%	41.2%

Table 1: Comparison of *H. pylori* eradication rates

NOT FOR EMPIRIC TREATMENT

PPI vs PCAB

Table 1. Potassium-Competitive Acid Blocker and Proton Pump Inhibitor Class Comparison

Variable	P-CAB	PPI
Effect of gastric acid	Acid-stable	Acid-labile (note enteric coating)
Prodrug	No	Yes (converted to sulfonamide compounds in acidic environment)
Binding to proton pump	Ionic (reversible) binding (blocks access of K^+ to potassium-binding site of pump)	Binds covalently (irreversible) to cysteines on active pumps (blocks exchange of H^+ and K^+)
Half-life estimates, *h*[5–7]	6–9	1–2
Timing of administration	Independent of mealtimes (not restricted, given longer half-life)	30–60 min before meals (so presence in secretory canaliculus coincides with postprandial peak in active pumps)
Dosing range, *d*, for maximal acid suppression[5,7,8]	1	3–5
Examples	Revaprazan, vonoprazan, tegoprazan, fexuprazan, linaprazan, zastaprazan, and keverprazan	Dexlansoprazole, esomeprazole, lansoprazole, omeprazole, pantoprazole, and rabeprazole

Patel A. et al. Gastroenterology 2024;167:1228-1238

Recommended Regimens for Treatment-Naive Patients with *H. pylori* Infection

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

Regimen	Drugs (doses)	Dosing frequency	FDA approval	Recommendation
Optimized bismuth quadruple[a] Relative contraindication in women of childbearing potential and those with photosensitivity	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] Myelotoxicity has not been reported with total daily dose of 150 mg	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] Avoid if previous macrolide exposure	Vonoprazan (20 mg) Clarithromycin (500 mg) Amoxicillin (1,000 mg)	b.i.d.	Yes	Conditional (moderate quality of evidence)

ACG Clinical Guideline: Treatment of Helicobacter pylori Infection

Always provide 14 days of treatment

Eradication of *H. Pylori* in Treatment Naïve Patients (Empiric)

1st-Line Regimens for Treatment-Naive Patients with *H. pylori* infection Without Antibiotic Susceptibility Testing

No Penicillin Allergy

- Optimized BQT*
- Rifabutin Triple
- PCAB Dual
- PCAB-Clarithromycin Triple**

Penicillin Allergy*

- Optimized BQT*

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

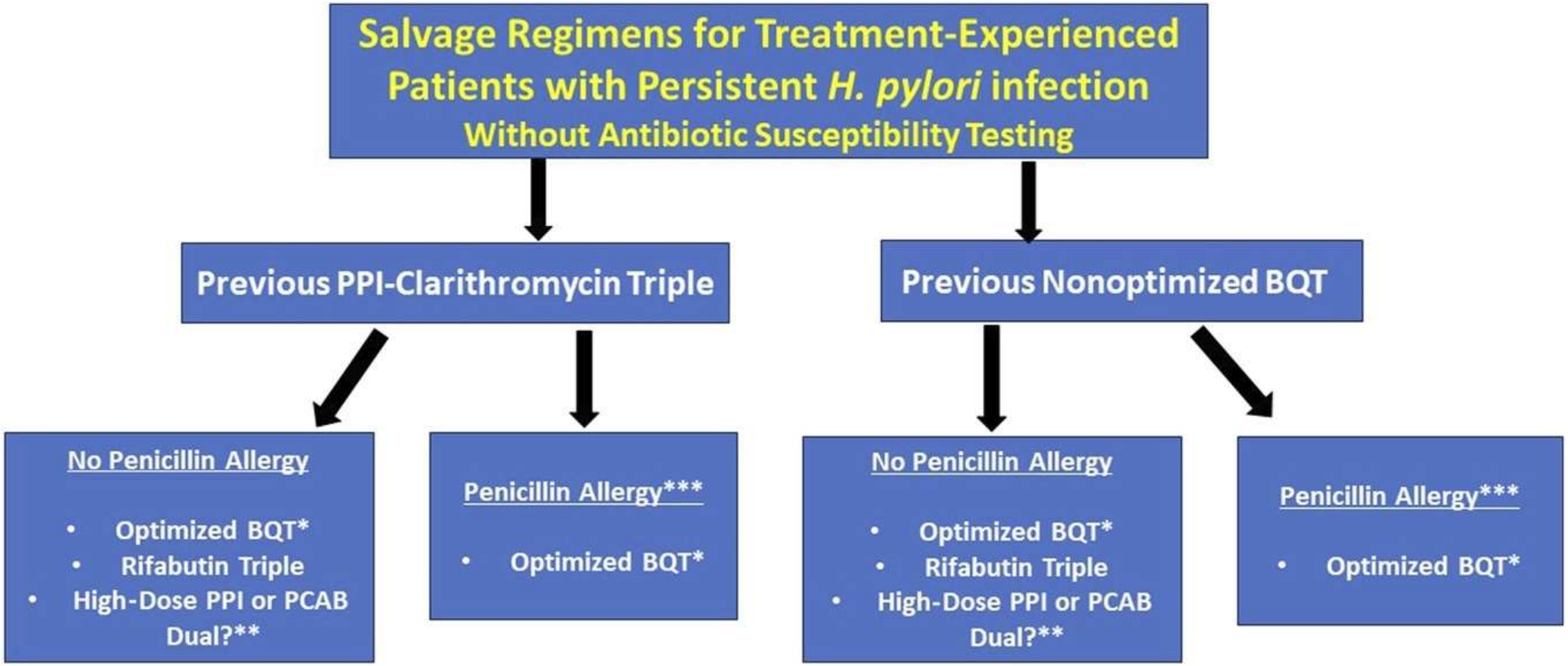
Vonoprazan: FDA approved in 2022

- 30 tablets is around $800.
- Dual pack: $920
- Triple pack: $999

Talicia cost: $800-900

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)



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

BQT, bismuth quadruple therapy

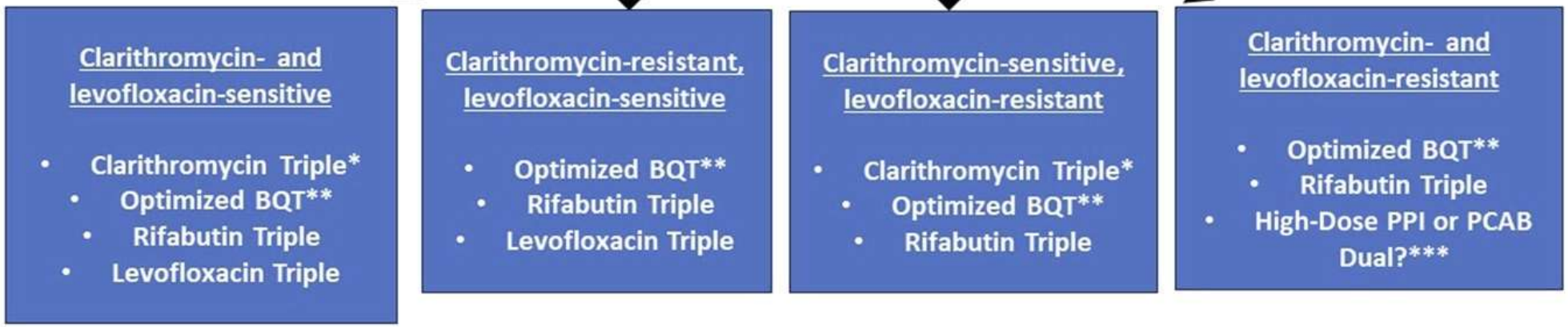
*Includes appropriately dosed PPI, bismuth, nitroimidazole, and tetracycline (not doxycycline)

**Consider only when optimized BQT or rifabutin triple therapy is not an option and antibiotic susceptibility testing is unavailable

***May require formal allergy testing

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

Antibiotic Susceptibility Testing



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

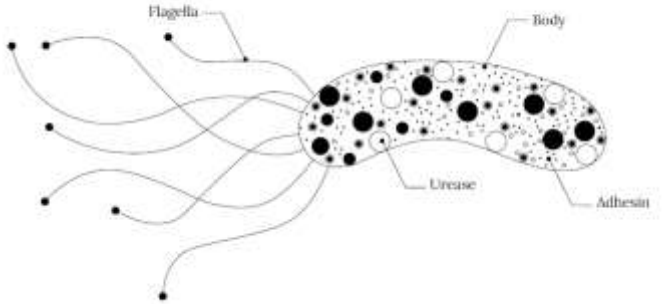
Lists of treatments are meant to present appropriate options but are *not* meant to present a treatment hierarchy except that levofloxacin should only be used when other options are inappropriate. The choice of salvage therapy should also be guided by previous treatments received for *H. pylori*.

* 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

Probiotics and *H pylori* Treatment

- 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).
- Single metanalysis of 40 studies and 8,924 patients using probiotics showed a modest eradication benefit and lower side effects when used with BQT .
- Lactobacillus and multi-strain probiotics were associated with the highest eradication rates.
- Additional studies are needed to define the the most appropriate probiotic strains, dosages, durations, and combinations with antibiotics that might benefit *H. pylori* treatment efficacy and/or tolerability.

Key Points:



- Although H. pylori prevalence has decreased, it remains an important global pathogen and leading cause of cancer death.
- There are expanded testing indications, including households of infected patients.
- If you test for H. pylori, treat and confirm eradication with urea breath test or stool antigen. Schedule test 4 weeks after completing antibiotics/bismuth and stop PPIs/PCABs 2 weeks before the test.
- Eradication rates are suboptimal due to increasing antibiotic resistance for which treatment selection is very important.
  - Avoid levofloxacin and clarithromycin-based therapy in the absence of susceptibility testing.
  - BQT remains as the first line option
  - Refer to Allergist those patients with a history of penicillin allergy and BQT is not an option.
- Antibiotic susceptibility testing is now an option that can help us guide treatment.

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			☑☑	

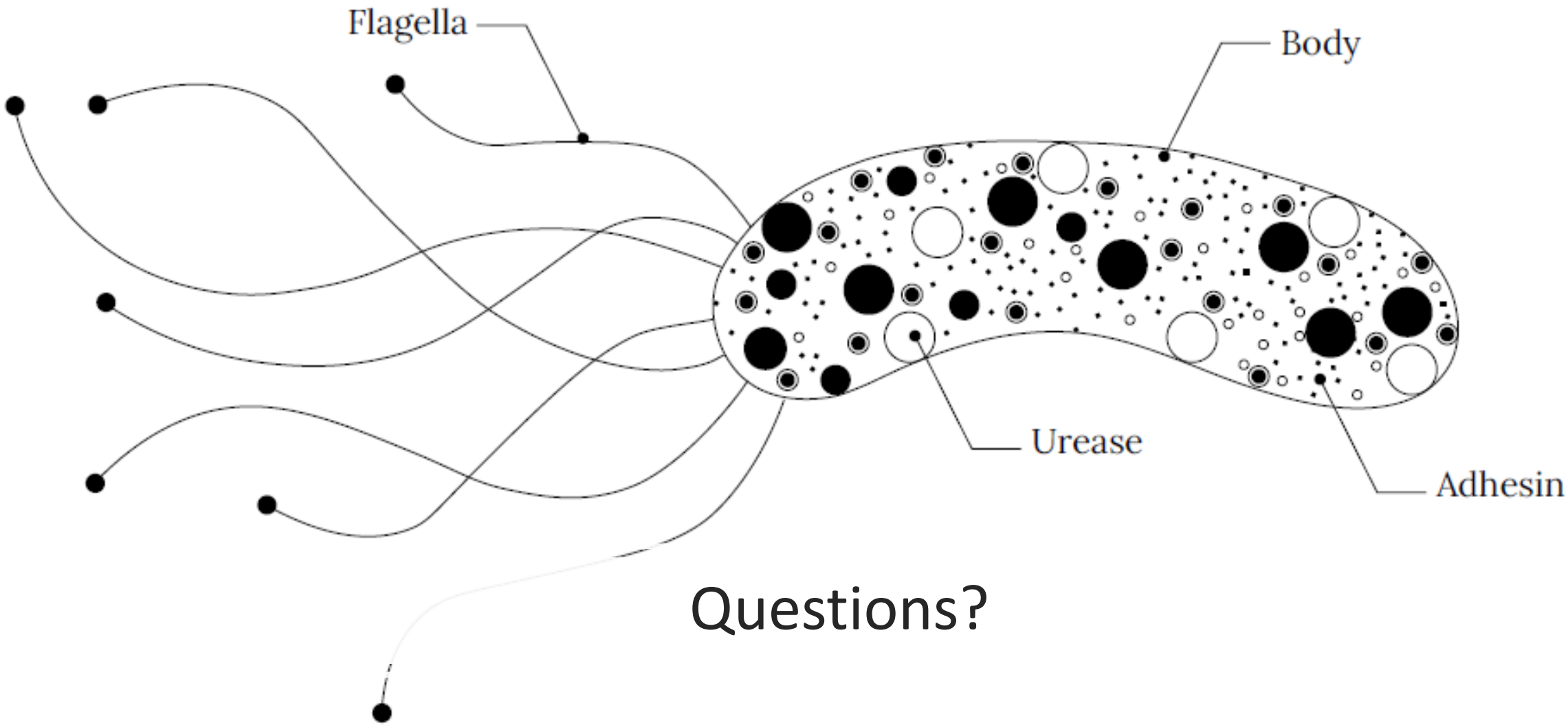
☑☑☑ Recommended ☑☑ Suggested ? May be considered when other treatments are not options

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

Chey et al. *Am J Gastroenterol.* 2024. doi:10.14309/ajg.0000000000002968

All icons above are from Microsoft Powerpoint.

AJG The American Journal of GASTROENTEROLOGY
OFFICIAL JOURNAL OF THE AMERICAN COLLEGE OF GASTROENTEROLOGY | ACG



Questions?