Diagnosis and Treatment Patterns Among Patients with *Helicobacter pylori* Infection in the United States: A Linked EMR-Claims Database Analysis

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BACKGROUND

- *Helicobacter pylori* infects approximately 36% of the United States (US) population, although there is variation by birth cohort, race, ethnicity, and immigration status, among other factors.[1]
- *H. pylori* eradication reduces the risk of peptic ulcer disease complications and gastric cancer compared to no eradication.[2,3,4]
- To prevent complications associated with persistent *H. pylori* infection, current US guidelines recommend eradication therapy for all people diagnosed with active *H. pylori* infection and eradication confirmation testing ≥4 weeks post-treatment.[5]
- Declining rates of successful eradication using current first-line regimens in the US undermine the potential benefits of *H. pylori* eradication.

OBJECTIVES

To characterize current *H. pylori* testing and treatment patterns among insured individuals using a real-world data set.

RESULTS

Table 2. Patient Characteristics During the 12-month Baseline Period

Characteristic	(n = 60,593)
Age, mean (SD)	54.2 (14.5)
Female, n (%)	39,699 (65.5%)
Clinical Conditions, n (%)	
Cardiovascular disease	37,814 (62.4%)
Hypertension (primary)	33,159 (54.7%)
Diabetes	19,578 (32.3%)
Anxiety	14,869 (24.5%)
Osteoarthritis	14,368 (23.7%)
Depression	12,289 (20.3%)
Upper GI Conditions, n (%)	
GERD	29,803 (49.2%)
Gastritis	23,885 (39.4%)
Atrophic gastritis	1,903 (3.1%)
Dyspepsia	18,497 (30.5%)
Esophagitis	9,326 (15.4%)
Functional dyspepsia	5,818 (9.6%)
Gastric/duodenal ulcer	4,132 (6.8%)
Gastric polyp	1,518 (2.5%)
Medications, n (%)	
Any antibiotic	33,398 (55.1%)
Penicillins	16,409 (27.1%)
Macrolides	13,251 (21.9%)
Fluoroquinolones	10,565 (17.4%)
Cephalosporins	8,044 (13.3%)
Nitroimidazoles (metronidazole, tinidazole)	4,959 (8.2%)
Tetracyclines	4,622 (7.6%)
Other	3,157 (5.2%)
NSAIDs/COX-2 inhibitors	24,590 (40.6%)
Proton pump inhibitors	28,516 (47.1%)
H2-receptor antagonists	10,579 (17.5%)

COX-2, cyclooxygenase-2; GERD, gastroesophageal reflux disease; H2, histamine type-2; NSAID, non-steroidal anti-inflammatory drug; SD, standard deviation.

H. pylori Eradication Regimens (HPER)

- Only 68.2% (n = 41,340) of patients included in the study had ≥1 guideline recommended HPER (**Table 3**).
  - Among the 31.8% of people with *H. pylori* who did not receive a guideline recommended HPER, 57.0% received an antibiotic and 52.5% received a proton pump inhibitor (PPI) during the first 12 months of follow-up.
- Most patients (80.2%) with ≥1 HPER received PPI, amoxicillin, clarithromycin (PAC) as first-line treatment; 6.6% received bismuth quadruple (BQUAD) and 5.1% received levofloxacin triple (LTRIP).

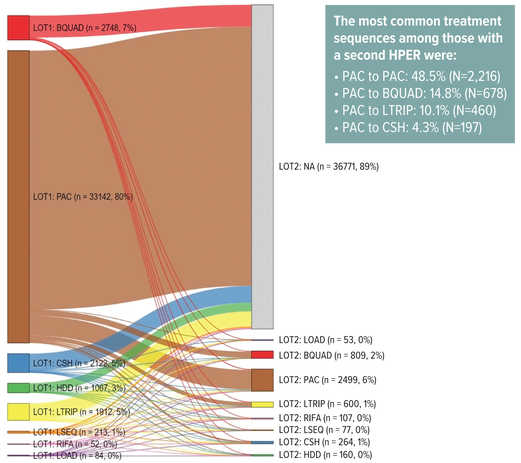
Table 3. *H. pylori* Eradication Regimens During the Follow-up Period

	1st HPER (n = 41,340)	2nd HPER (n = 4,569)	3rd HPER (n = 972)
Eradication Therapy, n (%)			
Clarithromycin Triple	33,142 (80.2%)	2,499 (54.7%)	439 (45.2%)
Clarithromycin triple fixed-dose combination	4,628 (14.0%)	243 (9.7%)	36 (8.2%)
Bismuth Quadruple	2,748 (6.6%)	809 (17.7%)	164 (16.9%)
Bismuth quadruple fixed-dose combination	2,233 (81.3%)	541 (66.9%)	113 (68.9%)
Concomitant/Sequential/Hybrid	2,122 (5.1%)	264 (5.8%)	75 (7.7%)
Levofloxacin Triple	1,912 (4.6%)	600 (13.1%)	153 (15.7%)
High-dose Dual	1,067 (2.6%)	160 (3.5%)	49 (5.0%)
Levofloxacin Sequential	213 (0.5%)	77 (1.7%)	18 (1.9%)
LOAD	84 (0.2%)	53 (1.2%)	16 (1.6%)
Rifabutin Triple	52 (0.1%)	107 (2.3%)	58 (6.0%)

HPER: *H. pylori* eradication regimen; LOAD: levofloxacin, omeprazole, nitazoxanide, and doxycycline.

- 21.0% of patients with PAC as first-line had at ≥1 prescription for a macrolide antibiotic during the 12-month baseline period (note: the time period prior to 12 months was not captured).
- Most (88.9%) patients did not receive a second HPER.
- Of the people treated with a recommended first-line HPER, 11.1% received salvage therapy; PAC remained the most common second treatment (54.7%), followed by BQUAD (17.7%) and LTRIP (13.1%) therapies.
- Among patients with a second HPER, 53.4% received the same regimen as the first HPER (**Figure 2**).
- The mean time between first and second HPERs was 314.4 days (median = 153 days).

Figure 2. First and Second *H. pylori* Eradication Regimens



The most common treatment sequences among those with a second HPER were:

- PAC to PAC: 48.5% (N=2,216)
- PAC to BQUAD: 14.8% (N=678)
- PAC to LTRIP: 10.1% (N=460)
- PAC to CSH: 4.3% (N=197)

BQUAD: bismuth quadruple; CSH: concomitant, sequential, or hybrid; HDD: high-dose dual (amoxicillin, PPI); LOAD: levofloxacin/nitazoxanide/doxycycline/PPI; LOT: line of therapy; LSEQ: levofloxacin sequential; LTRIP: levofloxacin triple; PAC: PPI, amoxicillin, clarithromycin; PPI: proton pump inhibitor; RIFA: rifabutin triple.

- As a separate analysis, the overall rate of treatment with US guideline recommended HPERs in the claims database (with no link to the EMR) in calendar year 2019 was computed.

Patients with US Guideline Recommended HPERs in 2019

Individuals continuously enrolled in claims data in 2019
n = 33,281,517

→ Age 18–64 on Jan. 1, 2019
n = 22,224,940 (66.8%)

→ Had a US guideline recommended *H. pylori* treatment in 2019 (and an *H. pylori* diagnostic test within 60 days prior)
N = 44,257 (0.20%)

H. pylori Testing Patterns

- In the month prior to the index date, only 27.7% of patients received an *H. pylori* lab test, and 1.4% were given an antibiotic resistance test (**Table 4**).

Table 4. *H. pylori* Testing During the Baseline Period

	1 Month Before Index Date (n = 60,593)	3 Months Before Index Date (n = 60,593)
Diagnostic Test[a], n (%)		
EGD	16,935 (27.9%)	21,125 (34.9%)
H. pylori lab test	16,794 (27.7%)	18,985 (31.3%)
Urea breath test	11,205 (18.5%)	12,372 (20.4%)
Fecal antigen test	4,580 (7.6%)	5,295 (8.7%)
Serum antibody test	1,497 (2.5%)	2,063 (3.4%)
Rapid urease test	15 (<0.1%%)	18 (<0.1%)
Antibiotic resistance testing	823 (1.4%)	1,894 (3.1%)

[a]Tests reported in this table were measured from procedure codes in the EMR and claims data, and do not have associated test results.
EGD, esophagogastroduodenoscopy.

- Among patients with at least one HPER, 32.6% did not have follow-up *H. pylori* testing identified; among those with repeat testing, the mean [SD] time to testing after the end of the first HPER was 227.9 [326.6] days (standard deviation = 326.6 days; median = 75 days) (**Table 5**).

Table 5. First *H. pylori* Test After First-Line Eradication Therapy

	All Treated Patients (n = 41,340)		
Diagnostic Test[a]	Patients, n (%)	Days to Test, mean	Days to Test, median
No lab tests	13,462 (32.6%)		
First lab test	27,878 (67.4%)	228	75
Urea breath test	12,885 (46.2%)	148	56
EGD	7,882 (28.3%)	400	235
Fecal antigen	6,424 (23.0%)	161	64
Serum antibody	630 (2.3%)	354	225.5
Rapid urease test	21 (0.1%)	206	34
Unknown test type	36 (0.1%)	306	120

[a]Tests reported in this table were measured from procedure codes in the EMR and claims data, and do not have associated test results.
EGD, esophagogastroduodenoscopy; SD, standard deviation.

Lab-Confirmed *H. pylori* Eradication Rates

- 8.4% of treated patients (n = 3,479) had *H. pylori* lab results after first-line eradication therapy.
- Guideline recommended first-line therapy failed to eradicate *H. pylori* in 21.7% of patients with available lab results.

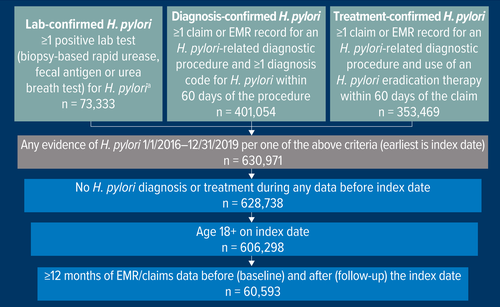
CONCLUSIONS

- In a population of patients with *H. pylori* infection, only 68.2% received an HPER that aligned with current US guidelines.
- Clarithromycin triple therapy is still the most common first-line regimen while bismuth-based quadruple therapy is used infrequently.
  - Among those with clarithromycin triple therapy as first-line and with a second line of treatment, almost half received a second course of clarithromycin triple therapy, which is contrary to current guideline recommendations.
- Our findings suggest a suboptimal eradication rate; 21.7% of patients failed to eradicate *H. pylori* following guideline-recommended first-line treatment and of these, only 11% received subsequent *H. pylori* treatment.
- We also found poor *H. pylori* re-testing rates; only 67.4% of patients received a diagnostic *H. pylori* lab test after first-line therapy to confirm eradication.
- Focused efforts are warranted to improve *H. pylori* testing and treatment practices.

METHODS

- **Data Source:** The Veradigm Health Insights Ambulatory electronic medical record (EMR) Database linked to Komodo medical and pharmacy claims.
- **Cohort Selection:** See **Figure 1**.

Figure 1. Cohort Selection Criteria



[a]Serology tests were not included as they are not used to confirm active *H. pylori* infection.
EMR: electronic medical record

Identifying Guideline-recommended Treatment Regimens

- Patients receiving *H. pylori* eradication regimens (HPERs) recommended by current US evidence-based guidelines were identified via pharmacy claims per **Table 1**.[5]

H. pylori Lab Test Results and Estimation of *H. pylori* Eradication Rate

- A subset of patients with completed rapid urease, fecal antigen, or urea breath test results following the first HPER was identified.
- Test results between the end of the first HPER and the earlier of the start of the second HPER or the end of follow-up were used to estimate *H. pylori* eradication rate following first-line treatment
  - Eradication success rate was calculated as the total number with negative *H. pylori* test results divided by the total number with any available *H. pylori* test results.

Table 1. US Guideline-recommended *H. pylori* Eradication Regimens[5]

Eradication Regimen[a,b]	Drug 1[c]	Drug 2	Drug 3	Drug 4
PAC	PPI	clarithromycin	amoxicillin	n/a
		clarithromycin	metronidazole	n/a
BQUAD	PPI	bismuth	tetracycline	metronidazole
CSH	PPI	clarithromycin	amoxicillin	metronidazole
		clarithromycin	amoxicillin	tinidazole
LTRIP	PPI	levofloxacin	amoxicillin	n/a
LSEQ	PPI	levofloxacin	amoxicillin	metronidazole
		levofloxacin	amoxicillin	tinidazole
LOAD	PPI	levofloxacin	nitazoxanide	doxycycline
RIFA	PPI	amoxicillin	rifabutin	n/a
HDD	PPI	amoxicillin (>3000 mg/day)	n/a	n/a

[a]HPERs were flagged when prescription fills for all medications in the regimen were observed in a 14-day period.
[b]We required a non-serologic *H. pylori* test (EGD, urea breath test, fecal antigen test, or rapid urease test) in the 60 days prior to each regimen.
[c]PPIs are often purchased over-the-counter and may not be captured in claims or EMR data; only the non-PPI medications in the regimens were required for a regimen to be identified. If a PPI was observed in the data, its presence and identity was recorded.
BQUAD: bismuth quadruple; CSH: concomitant, sequential, or hybrid; EGD: esophagogastroduodenoscopy; EMR, electronic medical record; HDD: high-dose dual; HPER: *H. pylori* eradication rate; LOAD: levofloxacin, omeprazole, nitazoxanide, and doxycycline; LSEQ: levofloxacin sequential; LTRIP: levofloxacin triple; PAC: PPI, amoxicillin, clarithromycin; PPI: proton pump inhibitor; RIFA: rifabutin triple.

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Disclosures/Conflicts of Interest
SS and **RY** are consultants for Phathom Pharmaceuticals. **KC**, **RS**, and **MB** are employees of Veradigm. **CP** and **RJ** are employees of Phathom Pharmaceuticals.

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