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Mistakes in the diagnosis and treatment of *Helicobacter pylori* infection in daily clinical practice

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Abstract

Background: An adequate diagnostic and therapeutic approach to *Helicobacter pylori* (*H. pylori*) infection is the cornerstone to avoid overdiagnosis, overuse of health resources, and increase in antibiotic resistances. The aim of the study was to evaluate the most common errors in clinical practice and the associated risk factors.

Materials and Methods: This is a retrospective observational study including patients with *H. pylori* infection and no previous treatment belonging to two defined areas of the National Health System in Spain; some of them were enrolled in the European Registry on *H. pylori* management (Hp-EuReg). Patients were attended by gastroenterologists between 2010 and 2019. According to current guidelines, we evaluated indications for *H. pylori* investigation, appropriateness of diagnostic test used in dyspeptic patients and discontinuation of surveillance after treatment.

Results: A total of 1730 patients were included, receiving 2260 eradication regimens. *H. pylori* infection was investigated in 1.7% cases in absence of a formal indication. Oral endoscopy was incorrectly used in 56% of patients with dyspepsia under 55 years without alarm signs, and urea breath test (UBT) was incorrectly used in 22.4% of patients with dyspepsia ≥55 years or red flags. Levofloxacin containing regimens were used as first-line therapy in 7.5% of non-allergic to penicillin patients. After first-line failure, clarithromycin was repeated in 2.6% of the patients who received second-line therapy. Confirmatory test of *H. pylori* status was absent in 2.5% cases. Men, patients under 55 years, and patients diagnosed by UBT had a higher risk of not undergoing a confirmatory test.

Conclusions: Investigation of *H. pylori* infection by gastroenterologists is rare in absence of a formal indication; however, endoscopy is commonly used for dyspeptic patients <55 years without red flags and non-invasive tests are still used for dyspeptic patients ≥55 years or presenting alarm signs. Men, patients under 55 years, and patients diagnosed by UBT have an increased risk of being lost to follow-up after eradication treatment.

KEYWORDS
diagnosis, *Helicobacter pylori*, loss to follow-up, mistakes, treatment

Inés Ariño-Pérez and Samuel J. Martínez-Domínguez: Equal contribution.

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1 | INTRODUCTION

Helicobacter pylori (*H. pylori*) is a spiral, microaerophilic and gram-negative bacillus that chronically infects gastric mucosa in approximately 50% of the world population, becoming the most frequent infection worldwide. Its ability to hydrolyze urea into ammonium increasing the pH and its morphology allow *H. pylori* to survive in a hostile environment.[1–3]

The infection is associated with benign pathology such as gastric or duodenal ulcer and chronic gastritis. However, *H. pylori* infection is also the most common infectious cause of cancer, with an age-adjusted incidence rate of 8.7 cases per 100,000 person-years. Gastric adenocarcinoma is the most frequent tumor associated with *H. pylori*, followed by mucosa-associated lymphoid tissue (MALT) lymphoma. Nonetheless, *H. pylori* screening is not recommended in the general population of low-risk areas like Spain.[4–6]

Consequently, national and international scientific societies have established indications to investigate the infection in order to avoid overdiagnosis, unnecessary costs, and avoidable treatments. The "Test and treat" strategy has demonstrated to be an effective strategy for dyspeptic patients under 55 years without alarm signs, avoiding upper endoscopy as first step. However, upper GI endoscopy should be considered as the first test in dyspeptic patients over the age of 55 years, since several studies found that the risk of gastric cancer increases significantly above that age.[7–9]

The prevalence of antibiotic resistance in *H. pylori* infection has steadily increased over the last four decades.[10] In fact, numerous efforts are being made to investigate this topic, such as detecting mutations that cause resistance and reducing the dependence on methods like culture.[11,12] Resistances to clarithromycin, metronidazole, and levofloxacin are the most clinically relevant, whereas amoxicillin, bismuth, or tetracycline resistances have less impact. Indeed, clarithromycin should not be repeated in subsequent lines after first-line failure, due to an effectiveness rate of 46% in that context.[13]

Appropriate prescription of antibiotics to treat *H. pylori* infection in those patients who have an approved indication is a common responsibility of all physicians who must prescribe empirical or culture-guided regimens according to national or international guidelines in order to achieve the maximal benefit minimizing potential adverse effects. In fact, the Food and Drugs Administration (FDA) and the European Medicines Agency (EMA) recently published alerts about severe adverse effects linked to quinolone use, and they should be used as rescue therapy for mild or moderate infections like *H. pylori* infection.[13–15]

Although gastroenterologists can decide the indication, the diagnostic method, and the antibiotic regimen prescribed, collaboration of patients during the diagnostic and therapeutic process is essential. Confirmation of *H. pylori* eradication must be carried out in all cases, as it is the only way to ensure cure of the infection and, in addition, it allows monitoring effectiveness in real clinical practice. The absence of confirmatory test is not rare and can be ignored by both physicians and patients, so identifying susceptible populations will allow us to develop specific measures for them.[7]

Therefore, the aim of the study was to evaluate the most common errors in daily clinical practice of gastroenterologists regarding indications for *H. pylori* investigation, appropriateness of diagnostic test used in dyspeptic patients, appropriateness of prescribed eradication regimens and loss to follow-up after treatment.

2 | MATERIALS AND METHODS

2.1 | Study design

This is a retrospective observational study that evaluates mistakes in the diagnosis and treatment of *H. pylori* infection in daily clinical practice of gastroenterologists. This study was performed between January 2010 and December 2019 in the outpatient unit of two defined areas of the Regional Health System in Aragón ("Lozano Blesa" University Hospital of Zaragoza and "Obispo Polanco" Hospital of Teruel, Spain). In both hospitals, specialized care is provided by gastroenterologists, being reference centers for approximately 350,000 people belonging to 38 primary care centers.

This is a parallel extension of the sub-analysis from our cases included in the European Registry on *Helicobacter pylori* management (Hp-EuReg), an international, multicenter, non-interventional registry promoted by the European Helicobacter and Microbiota Study Group (EHMSG). Records reflect the real clinical practice at the discretion of the gastroenterologist; no special protocol was followed for belonging to the study.

Patients aged 18+ years or older diagnosed of current *H. pylori* infection without previous eradication treatment (naive) were included. Exclusion criteria were as follows: eradication treatment prior to 2010 (not naïve) and absence of baseline, diagnosis or treatment data.

For initial diagnosis of the infection histology in gastric samples, urea breath test with[13] CO ≥ 2.5 ‰ (UBTest®, Otsuka Pharmaceutical), serology or stool antigen test was used. For eradication confirmation, histology in gastric samples and urea breath test with[13] CO ≥2.5 ‰ were used. No cultures or antibiotic sensitivity tests were performed. Our national health system provided free access to UBT and endoscopy for both gastroenterologists and general practitioners. All visits and complementary examinations were fully financed, so the choice of diagnostic tests was not based on economic issues. Finally, gastroenterologists did not have any reminder system about diagnostic or therapeutic strategy.

2.2 | Definition of agreement with guidelines

Indications for investigation of *H. pylori infection* were considered appropriate if they were included in III Spanish Consensus Conference of 2013.[7] That conference reported similar recommendations than

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Maastricht IV consensus developed in 2012.[16] From the beginning of the study, the different consensus documents recommended a "Test and treat" strategy for diagnosis of patients <55 years of age with dyspepsia in absence of red flags. Performance of upper GI endoscopy as first step in dyspeptic patients <55 years without alarm signs was considered inappropriate. In addition, diagnosis of *H. pylori* using non-invasive tests in dyspeptic patients ≥55 years of age or with red flags was also considered erroneous.[9]

2.3 | Variables

The following variables were reviewed from medical records and collected in an electronic database: age, gender, penicillin allergy, center, diagnostic test (for initial diagnosis and for confirmation of eradication), diagnosis date, indication, prescription date, prescribed antibiotic regimen and duration, proton pump inhibitor (PPI) treatment and agreement with current clinical practice guidelines.

2.4 | Statistical analysis and Ethics statement

Qualitative variables were presented as frequencies and percentages (%). Quantitative variables were presented as mean and standard deviation (SD), and normality was assessed using Kolmogorov–Smirnov test.

The relationship between qualitative variables was assessed using chi-square test or Fisher's test. In addition, a logistic regression multivariate analysis was performed, presented as adjusted odds ratio (OR) and a 95% confidence interval (95% CI). A *p*-value <.05 was considered statistically significant.

The study was carried out according to Declaration of Helsinki and was authorized by both hospitals. The Hp-EuReg protocol was approved by the Ethics Committee of "La Princesa" University Hospital (Madrid, Spain) and was registered at ClinicalTrials.gov (code NCT02328131). Informed consent was not obtained from participants because this was an observational retrospective study of real clinical practice with anonymized data.

3 | RESULTS

3.1 | Baseline characteristics

A total of 1730 patients were included, receiving 2260 eradication regimens: 1730 in first line, 428 in second line, 88 in third line, 12 in fourth line, and 2 in fifth line. The mean age at diagnosis of *H. pylori* infection was 50.5 ± 15.8 years, and 1035 (59.8%) were women. Penicillin allergy was previously diagnosed in 86 (5%) patients (by either confirmatory tests or information provided by the patient).

Dyspepsia followed by gastric or duodenal ulcer were the most frequent indications for *H. pylori* treatment (Table 1). Significant differences were observed for the indication according to gender and age. Peptic ulcer disease was frequent indication among men ($p < .001$) and patients ≥55 years ($p < .001$) while dyspepsia and suspected celiac disease (Marsh 1 in duodenal biopsies) were frequent indications among women ($p < .001$ and $p = .033$, respectively) and patients under 55 years ($p = .002$ and $p < .001$, respectively).

Histology (70.1%) and UBT (28.8%) were the most common diagnostic test used, far followed by serology (0.6%), rapid urease test (0.4%), and stool antigen test (0.1%). Significant differences were observed for the diagnostic test used according to the age. Histology was frequently used in patients ≥55 years of age ($p < .001$) whereas UBT was frequently used in patients under 55 years ($p < .001$). No differences were observed based on gender.

Triple therapies were the most prescribed between 2010 and 2015. From 2015, quadruple therapies were more used. The duration of eradication treatment in patient non-allergic to penicillin ranged from 7 to 14 days (6.6% 7 days, 60.5% 10 days, and 32.9% 14 days).

TABLE 1 Distribution of indications for *Helicobacter pylori* treatment in 1730 patients.

	Total (*N* = 1730)	Male (*N* = 695)	Female (*N* = 1035)	*p*-Value	<55 years (*N* = 1003)	≥55 years (*N* = 727)	*p*-Value
Indication				**<.001**			**<.001**
Dyspepsia	1003 (58)	346 (49.8)	657 (63.5)	**<.001**	614 (61.2)	389 (53.5)	**.002**
Peptic ulcer	278 (16.1)	171 (24.6)	107 (10.3)	**<.001**	134 (13.4)	144 (19.8)	**<.001**
Suspected celiac disease[a]	130 (7.5)	41 (5.9)	89 (8.6)	**.033**	107 (10.7)	23 (3.2)	**<.001**
Anemia	100 (5.9)	36 (5.2)	66 (6.4)	.349	44 (4.4)	58 (8.0)	**.002**
FH gastric cancer	78 (4.5)	37 (5.3)	41 (4.0)	.194	45 (4.5)	33 (4.5)	1.000
Rosacea	19 (1.1)	7 (1.0)	12 (1.2)	.819	8 (0.8)	11 (1.5)	.114
Chorioretinopathy	11 (0.6)	6 (0.9)	5 (0.5)	.560	6 (0.6)	5 (0.7)	1.000
Other	109 (6.3)	51 (7.3)	58 (5.6)	.158	45 (4.5)	64 (8.8)	**<.001**

Note: Data are presented as *n* (%). Chi-square test or Fisher's test was used as appropriate. *p*-Values in bold format indicate statistical significance (*p*-value <.05).

Abbreviation: FH, Family History.

[a]Finding of Marsh 1 in duodenal biopsies of infected patients with suspected celiac disease.

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3.2 | Mistakes in diagnostic and therapeutic management of *H. pylori* infection

Diagnosis of *H. pylori* infection was performed in 30 (1.7%) cases despite the absence of formal indication, according to current guidelines. Inappropriate indications were 19 (1.1%) patients with rosacea and 11 (0.6%) patients with chorioretinopathy. Serology was not used to confirm eradication in any case.

Appropriateness of diagnostic tests for dyspepsia was analyzed based on patient's age, according to the cutoff referred by national guidelines described in Methods. Oral endoscopy was performed in 344 (56%) patients with dyspepsia under 55 years of age. In addition, UBT was used in 87 (22.4%) of patients with dyspepsia and 55 years or older.

Levofloxacin containing regimens were used as first-line therapy in 123 (7.5%) non-allergic to penicillin patients, with a decreasing prescription trend between 2010 and 2014 and was rarely prescribed between 2014 and 2019. Patients with penicillin allergy were prescribed PCL (PPI, clarithromycin and levofloxacin) in 14 (16.3%) of cases and PML (PPI, metronidazole and levofloxacin) in 11 (12.8%) cases.

Among the 24 non-allergic to penicillin patients receiving a second-line regimen based on clarithromycin, 9 (37.5%) had already received clarithromycin as first-line therapy.

Clarithromycin-based therapies failed in 421 (29.6%) of the first-line eradications of patients non-allergic to penicillin. After first-line failure, clarithromycin was repeated in nine (2.6%) of the 352 patients who received second-line therapy.

3.3 | Risk factors for discontinuing clinical surveillance of *H. pylori* infection after eradication treatment

Of 1730 patients with a total of 2260 prescribed regimens, 57 (2.5%) patients were considered lost to follow-up due to lack of confirmation test. The percentage of patients lost to follow-up increased with the subsequent line, reaching 5.7% in the third-line (Table 2). Patients who stopped clinical surveillance had a mean age of 42.5 ± 13.9 years.

Gender, age at diagnosis of *H. pylori* infection, and type of diagnostic test used were associated with loss to follow-up in univariate analysis. Multivariate analysis, adjusted by age, sex, and diagnostic test (Figure 1), confirmed an increased risk for discontinuing clinical surveillance in men (OR 1.79 95% CI: 1.05–3.07), patients under 55 years (OR 2.07 95% CI: 1.09–3.91), and patients diagnosed using UBT as the first initial *H. pylori* test (OR 3.41 95% CI: 1.96–5.91).

4 | DISCUSSION

Helicobacter pylori infection is highly prevalent, consuming a large amount of human and economic resources. Some errors are frequently repeated in real clinical practice, so improving them can significantly optimize infection management.

The first step is to test for *H. pylori* infection only when it is indicated because this strategy avoids treatments on conditions with no or little clinical relevance. Although we detected 1.7% of non-indicated diagnoses, this finding is actually low and less frequent than that reported for gastroenterologists in a study previously published by our group (7.2%).[17] In addition, inappropriate indications for *H. pylori* diagnosis are still higher at primary care level (up to 35.9%).[17]

The use of non-invasive and cost-effective diagnostic tests is essential for both patient safety and sustainability of healthcare systems. This strategy is supported by European and American scientific societies[18,19]; however, we found an overuse of endoscopy in 56% of cases in this study. None of the study investigators had a financial incentive to perform endoscopies. Similarly, a study conducted in Canada reported that 65% of gastroscopies performed in patients with dyspepsia were based on the presence of alarm signs;[20] however, other study carried out in United Kingdom found that only 14.8% of gastroscopies in dyspeptic patients associated red flags.[21]

Alarm features have limited value to distinguish organic and functional dyspepsia and endoscopy should be offered to patients to rule out malignancies in patients over 55 years of age, according to current national guidelines.[22,23] Nevertheless, we found that 22.4% of the patients with alarm signs underwent a non-invasive test, with the subsequent risk of underdiagnosing malignancy. It should be noted that it is unknown if these patients had a previous upper endoscopy without macroscopic abnormalities, so this finding should be interpreted with caution.

Once the patient is diagnosed, it is crucial to choose the most adequate eradication therapy. In our area, a resistance rate to clarithromycin of 17%–18% has been reported.[13] Therefore, quadruple therapies are currently recommended to achieve the 90% effectiveness threshold for any eradication regimen to be considered adequate. However, lower effectiveness rates have been reported in many studies assessing daily clinical practice. Low adherence to recommendations of scientific societies may explain, at least partially, this finding.[24] In fact, we observed an overuse of levofloxacin as first-line therapy (7.5%) and clarithromycin as second-line after first-line failure (2.6%), despite recommendations against these practices by official guidelines.[13] Previous studies reported great variability in the repetition of clarithromycin in second-line after first-line failure depending on the country (from 6% in Slovenia and 8% in Spain to 61% in Russia).[25–27]

Performance of a confirmatory test after *H. pylori* treatment is important since it confirms effectiveness both at the individual level and for epidemiological purposes. Possible reasons why 2.5% of patients did not undergo a confirmatory test could be clinical improvement after treatment, development of side effects during treatment or interruption of the treatment. Hp-EuReg, a source of many publications, found that 6% of cases did not check eradication success;

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TABLE 2 Loss to follow-up in 2260 eradication regimens, detailed by line of treatment.

	Total (*N* = 2260)	First-line (*N* = 1730)	Second-line (*N* = 428)	Third-line (*N* = 88)	*p*-Value
Loss to follow-up	57 (2.5)	34 (2)	18 (4.2)	5 (5.7)	
Gender					
Female	27 (2.6)	16 (1.5)	8 (2.9)	3 (5.4)	.055
Male	30 (4.3)	18 (2.6)	10 (6.4)	2 (6.1)	
Age (years)					
Range	19–69	24–69	19–69	39–67	**.003**
Mean ± SD	42.5 ± 13.9	43.1 ± 13.6	40 ± 15.2	48 ± 11.9	
≥55 years	13 (1.8)	9 (1.2)	3 (1.7)	1 (2.4)	
<55 years	44 (4.4)	25 (2.5)	15 (5.9)	4 (8.5)	
Indication					
Ulcer	9 (3.2)	8 (2.9)	1 (1.8)	0 (0)	.432
Dyspepsia	36 (3.6)	18 (1.8)	14 (5.2)	4 (7.7)	
Anemia	0 (0)	0 (0)	0 (0)	0 (0)	
FH gastric cancer	3 (3.8)	2 (2.6)	0 (0)	1 (11.1)	
Rosacea	0 (0)	0 (0)	0 (0)	0 (0)	
Other	4 (3.7)	2 (1.8)	2 (10.5)	0 (0)	
Chorioretinopathy	1 (9.1)	1 (9.1)	0 (0)	0 (0)	
Suspected celiac disease[a]	4 (3.1)	3 (2.3)	1 (4.2)	0 (0)	
Diagnostic test					
Histology	23 (1.9)	10 (0.8)	9 (3.1)	4 (6.8)	**<.001**
UBT	33 (6.6)	23 (4.6)	9 (6.6)	1 (3.4)	

Note: Data are presented as *n* (%). *p*-values in bold format indicate statistical significance (*p*-value < .05).

Abbreviations: FH, Family History; SD, Standard Deviation; UBT, Urea Breath Test.

[a]Finding of Marsh 1 in duodenal biopsies of infected patients with suspected celiac disease.

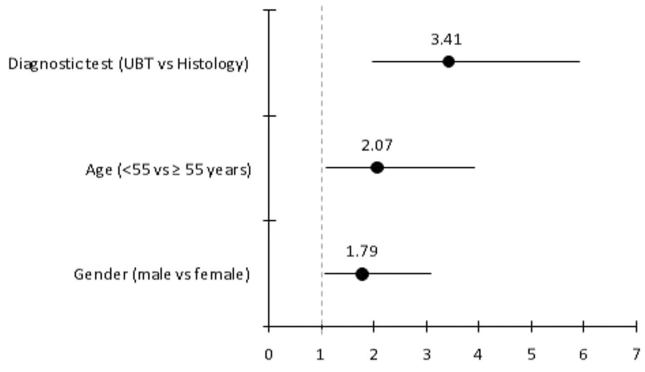

FIGURE 1 Multivariate analysis of risk factors associated with loss to follow-up after *Helicobacter pylori* treatment. UBT, Urea Breath Test. Results are expressed as odds ratio (OR) and confidence interval. Adjusted by age, sex and diagnostic test.

however, we found higher follow-up rates.[25] Other study performed in United States including 27,185 patients reported that only 23.9% of patients were retested after treatment.[28] One hypothesis about the increase in follow-up losses with subsequent lines is that it could be related to poor patient cooperation.

In addition, the absence of a confirmatory test was more frequent in men and patients ≥55 years, who paradoxically had higher rates of organic pathology (gastric or duodenal ulcer instead of dyspepsia), so they would especially benefit from taking subsequent lines if *H. pylori* infection persists.[29] Until now, no strategies have been developed to improve control of eradication success. Nonetheless, future strategies could focus on men over 55 years, so they showed an increased risk of losing follow-up.

Finally, we acknowledge the following limitations of the study. First, the retrospective design of the study. Second, the absence of data regarding therapeutic adherence, which may not necessarily correlate with post-treatment follow-up. Third, it is not known whether in those patients who discontinue the follow-up, patients voluntarily abandoned surveillance or the gastroenterologist did not indicate the confirmatory test. Fourth, the study was carried out in centers where *H. pylori* infection is an area of research, which could affect the management of the infection by the professional and influence the high rates of eradication confirmation. However, the main strengths of the study were its large sample size, the evaluation of both diagnostic and therapeutic aspects, and the identification of risk factors to guide future research on the optimization of *H. pylori* infection management.

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5 | CONCLUSIONS

Although investigation of *H. pylori* infection by gastroenterologists is rare in absence of a formal indication, endoscopy is commonly used for dyspeptic patients <55 years without red flags and non-invasive tests are still used for dyspeptic patients ≥55 years or presenting alarm signs. Erroneous prescription of quinolones in first-line regimens is decreasing in last years, but clarithromycin is commonly and incorrectly repeated as second-line therapy after first-line failure. In addition, men, patients under 55 years, and patients diagnosed by UBT have an increased risk of discontinuation of clinical surveillance after eradication treatment so strategies to improve follow-up could be directed to this profile of patients.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

1. Hooi JKY, Lai WY, Ng WK, et al. Global prevalence of *Helicobacter pylori* infection: systematic review and meta-analysis. *Gastroenterology*. 2017;153(2):420-429. doi:10.1053/j.gastro.2017.04.022
2. Kadkhodaei S, Siavoshi F, Akbari NK. Mucoid and coccoid *Helicobacter pylori* with fast growth and antibiotic resistance. *Helicobacter*. 2020;25(2):e12678. doi:10.1111/hel.12678
3. Eusebi LH, Zagari RM, Bazzoli F. Epidemiology of *Helicobacter pylori* infection. *Helicobacter*. 2014;19(Suppl 1):1-5. doi:10.1111/hel.12165
4. De Martel C, Georges D, Bray F, Ferlay J, Clifford GM. Global burden of cancer attributable to infections in 2018: a worldwide incidence analysis. *Lancet Glob Health*. 2020;8(2):e180-e190. doi:10.1016/S2214-109X(19)30488-7
5. De Brito BB, Da Silva FAF, Soares AS, et al. Pathogenesis and clinical management of *Helicobacter pylori* gastric infection. *World J Gastroenterol*. 2019;25(37):5578-5589. doi:10.3748/wjg.v25.i37.5578
6. O'Connor A, O'Morain CA, Ford AC. Population screening and treatment of *Helicobacter pylori* infection. *Nat Rev Gastroenterol Hepatol*. 2017;14(4):230-240. doi:10.1038/nrgastro.2016.195
7. Gisbert JP, Calvet X, Bermejo F, et al. III Spanish consensus conference on *Helicobacter pylori* infection. *Gastroenterol Hepatol*. 2013;36:340-374. doi:10.1016/j.gastrohep.2013.01.011
8. McColl KEL, Murray LS, Gillen D, et al. Randomised trial of endoscopy with testing for *Helicobacter pylori* compared with non-invasive *H. pylori* testing alone in the management of dyspepsia. *BMJ*. 2002;324:999-1002. doi:10.1136/bmj.324.7344.999
9. McNicholl AG, Calvo XC, Molina-Infante J, Gisbert JP. *Diagnóstico y Tratamiento de la Infección por Helicobacter pylori*. 2nd ed. IMC; 2021 https://www.aegastrum-semfyc.es/require/archivos/infeccion-helicobacter-pylori.pdf
10. Megraud F, Bruyndonckx R, Coenen S, et al. *Helicobacter pylori* resistance to antibiotics in Europe in 2018 and its relationship to antibiotic consumption in the community. *Gut*. 2021;70:1815-1822. doi:10.1136/gutjnl-2021-324032
11. Wang Y-H, Li Z, Wang L, et al. A systematic review and meta-analysis of genotypic methods for detecting antibiotic resistance in *Helicobacter pylori*. *Helicobacter*. 2018;23:e12467. doi:10.1111/hel.12467
12. Malfertheiner P, Megraud F, Rokkas T, et al. Management of *Helicobacter pylori* infection: the Maastricht VI/Florence consensus report. *Gut*. 2017;66(1):6-30. doi:10.1136/gutjnl-2016-312288
13. Gisbert JP, Alcedo J, Amador J, et al. V Spanish consensus conference on *Helicobacter pylori* infection treatment. *Gastroenterol Hepatol*. 2022;45(5):392-417. doi:10.1016/j.gastrohep.2021.07.011
14. Tran PT, Antonelli PJ, Hincapie-Castillo JM, Winterstein AG. Association of US Food and Drug Administration removal of indications for use of Oral quinolones with prescribing trends. *JAMA Intern Med*. 2021;181(6):808-816. doi:10.1001/jamainternmed.2021.1154
15. *Disabling and Potentially Permanent Side Effects Lead to Suspension or Restrictions of Quinolone and Fluoroquinolone Antibiotics*. European Medicines Agency (EMA); 2019.
16. Malfertheiner P, Megraud F, O'Morain CA, et al. Management of *Helicobacter pylori* infection–the Maastricht IV/Florence consensus report. *Gut*. 2012;61(5):646-664. doi:10.1136/gutjnl-2012-302084
17. Laredo V, Sostres C, Alfaro E, Arroyo MT, Lanas A. Management of *Helicobacter pylori* infection at the primary care level. The implementation of specific counseling improves eradication rates. *Helicobacter*. 2019;24(3):e12586. doi:10.1111/hel.12586
18. Moayyedi P, Lacy BE, Andrews CN, Enns RA, Howden CW, Vakil N. ACG and CAG clinical guideline: management of dyspepsia. *Am J Gastroenterol*. 2017;112(7):988-1013. doi:10.1038/ajg.2017.154
19. Black CJ, Paine PA, Anurag A, et al. British Society of Gastroenterology guidelines on the management of functional dyspepsia. *Gut*. 2022;71(9):1697-1723. doi:10.1136/gutjnl-2022-327737
20. Halasz JB, Burak KW, Dowling SK, et al. Do low-risk patients with dyspepsia need a gastroscopy? Use of gastroscopy for otherwise healthy patients with dyspepsia. *J Can Assoc Gastroenterol*. 2021;5(1):32-38. doi:10.1093/jcag/gwab017
21. Ching HL, Hale MF, Sidhu R, McAlindon ME. Reassessing the value of gastroscopy for the investigation of dyspepsia. *Frontline Gastroenterol*. 2018;9(1):62-66. doi:10.1136/flgastro-2017-100838
22. Vakil N, Moayyedi P, Fennerty MB, Talley NJ. Limited value of alarm features in the diagnosis of upper gastrointestinal malignancy: systematic review and meta-analysis. *Gastroenterology*. 2006;131(2):390-401. doi:10.1053/j.gastro.2006.04.029
23. Gisbert JP, Calvet Calvo X, Ferrándiz Santos J, Mascort Roca JJ, Alonso-Coello P, Marzo CM. Manejo del paciente con dispepsia. Guía de práctica clínica. Actualización 2012. *Resumen Ejecutivo*. 2012;44(12):728-733. doi:10.1016/j.aprim.2012.07.008
24. Ariño Perez I, Martinez-Dominguez SJ, Alfaro Almajano E, Carrera-Lasfuentes P, Lanas A. Management of *Helicobacter pylori* infection and effectiveness rates in daily clinical practice in Spain: 2010-2019. *Antibiotics*. 2022;11(5):698. doi:10.3390/antibiotics11050698
25. Nyssen OP, Vaira D, Tepes B, et al. Room for improvement in the treatment of *Helicobacter pylori* infection: lessons from the European registry on *H. pylori* management (Hp-EuReg). *J Clin Gastroenterol*. 2022;56(2):e98-e108. doi:10.1097/MCG.0000000000001482
26. Li H, Liang X, Chen Q, Zhang W, Lu H. Inappropiate treatment in *Helicobacter pylori* eradication failure: a retrospective study. *Scand J Gastroenterol*. 2018;53(2):130.3-130.133. doi:10.1080/00365521.2017.1413132
27. Ribaldone DG, Astegiano M, Pellicano R. *Helicobacter pylori* eradication: poor medical compliance from east to west of the world.

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Scand J Gastroenterol. 2018;53 /3:265. doi:10.1080/00365521.2018.1433231
28. Kumar S, Metz DC, Kaplan DE, Goldberg DS. Low rates of retesting for eradication of *Helicobacter pylori* infection after treatment in the Veterans Health Administration. *Clin Gastroenterol Hepatol*. 2021;19(2):305-313. doi:10.1016/j.cgh.2020.03.059
29. Sharara A. Confirmatory testing for eradication of *Helicobacter pylori*: challenges and opportunities. *Clin Gastroenterol Hepatol*. 2021;19(2):232-234. doi:10.1016/j.cgh.2020.05.051

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