JGH Open An open access journal of gastroenterology and hepatology
Open Access
JGHF Journal of Gastroenterology and Hepatology Foundation
doi:10.1002/jgh3.12916

ORIGINAL ARTICLE

The prevalence and treatment outcomes of *Helicobacter pylori* infection in a tertiary hospital in Thailand, 2018–2021

Pakkapon Rattanachaisit,* Chuti Burana,* Aunchalee Jaroenlapnopparat,† Sirikorn Vongseenin,† Supakarn Chaithongrat,† Rungsun Rerknimitr† and Duangporn Werawatganon*

*Department of Physiology, Faculty of Medicine, Chulalongkorn University and Center of Excellence in Alternative and Complementary Medicine for Gastrointestinal and Liver Diseases and †Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Key words
eradication rate, *H. pylori*, treatment regimen, urea breath test.

Accepted for publication 11 May 2023.

Correspondence
Duangporn Werawatganon, Department of Physiology, Faculty of Medicine, Chulalongkorn University and Center of Excellence in Alternative and Complementary Medicine for Gastrointestinal and Liver Diseases, Bangkok, 10330 Thailand.
Email: dr.duangporn@gmail.com; duangporn.t@chula.ac.th

Declaration of conflict of interest: The authors declare no potential conflict of interest.
Author contribution: Duangporn Werawatganon and Rungsun Rerknimitr contributed substantially to the conception and design of this study. Pakkapon Rattanachaisit, Chuti Burana, Aunchalee Jaroenlapnopparat, Sirikorn Vongseenin, Supakarn Chaithongrat, and Duangporn Werawatganon contributed substantially to the acquisition of data, and analyzed and interpreted the data. Pakkapon Rattanachaisit and Duangporn Werawatganon drafted the manuscript, and all the authors contributed substantially to its critical revision. All the authors approved the final version submitted for publication and take responsibility for the statements made in the published article.
Financial support: This work was supported by the Grant of Ratchadaphiseksomphot, Faculty of Medicine, Chulalongkorn University.

Funding support: Ratchadaphiseksomphot, Faculty of Medicine, Chulalongkorn University

Abstract

Background and Aim: *Helicobacter pylori* (HP) infection remains a significant global public health problem. This study aimed to study the prevalence of HP infection and treatment outcomes in Thailand.
Methods: We retrospectively reviewed the results of the urea breath test (UBT) performed at the King Chulalongkorn Memorial Hospital between 2018 and 2021. The prevalence of HP infection was evaluated in dyspeptic patients undergoing UBT screening. In patients with known HP infection, the treatment regimen and the success rate in each patient were recorded.
Results: One-thousand nine-hundred and two patients were included in this study. The prevalence of HP infection in dyspeptic patients was 20.77% (UBT was positive in 65 out of 313 patients). Of the 1589 patients who received the first treatment regimen, 1352 (85.08%) had a negative UBT result. Patients who failed in each treatment regimen were treated with subsequent regimens. The overall success rates for the second, third, and fourth regimens were 69.87% (109 of 156 patients), 53.85% (14 of 26 patients), and 50% (3 of 6 patients), respectively. Univariate logistic regression analysis found that using lansoprazole was associated with failure of treatment with OR = 2.11 (95% CI: 1.14–3.92, $P = 0.018$).
Conclusion: Current primary HP treatment regimens have an eradication rate of >80%. Even though the previous regimens failed, without available antibiotic sensitivity results, the subsequent regimens were successful by at least 50%. In cases of multiple-treatment failure and where antibiotic sensitivity tests were unavailable, continuing to change regimens could provide satisfactory results.

Introduction

Helicobacter pylori (HP) infections are one of the most common chronic bacterial infections in the world that affect global public health.[1] It is the main cause of many gastric diseases such as chronic gastritis, mucosa-associated lymphoid tissue lymphoma, gastroduodenal ulcer, and gastric cancer. The World Health Organization has classified HP as a carcinogen with the strongest known risk factor for non-cardia gastric adenocarcinoma, which is the most prevalent form of gastric cancer.[2,3] HP is one of the main controllable factors that affects the incidence of gastric carcinoma. Therefore, major Gastroenterology Associations recommend the elimination of HP in people with positive tests.[4–7]

In many countries, the prevalence of HP infections has decreased as a result of improved hygiene and eradication methods. However, HP remains an important public health problem worldwide, with more than half of the world's population infected with the organism.[1] Previous studies on the situation of HP in Thailand had found a prevalence range of 27.7–43.6%.[1,8,9] Our objective was to study the most recent prevalence of HP infection in Thailand.

Treatment of HP should be provided to all infected patients, regardless of symptoms.[7]

The benefits include reduction of the incidence of peptic ulcer disease and gastric cancer and even reduction of the mortality due to gastric cancer.[10] The choice of the first effective eradication treatment is crucial, since the likelihood of success in eliminating the disease decreases with each subsequent treatment attempt.[3]

Owing to changes in bacteria's sensitivity to antibiotics, treatment failure continues to increase with the previous regimen. Untreated HP infection results in complications of persistent HP infection, multiple exposure to antibiotics, high-dose acid suppression, and an economic burden on the health care system.[3] A meta-analysis on the prevalence of antibiotic resistance in HP found that resistance rates to clarithromycin, metronidazole, and levofloxacin were ≥15% in almost all WHO regions. In Southeast Asia, primary clarithromycin resistance is 10% (95% CI: 5–16%), which is similar to that in the Americas (10%; 95% CI: 4–16%).[11] However, data on real-world efficacy in Thailand are still lacking. A previous study showed that the efficacy of the overall regimens was 92.61%, from the data collected during 2013–2018.[8]

The low availability of culture and sensitivity tests has hampered the selection of antibiotic regimens in refractory cases. Therefore, treatment should be based on clinical practice based on prior antibiotic exposure of the patient and local resistance patterns.[7] However, there is not enough local data on the efficacy of eradication based on treatment regimens and duration. This knowledge gap has a significant impact on the treatment choice and, consequently, the best management. Health authorities should periodically conduct sensitivity tests and encourage clinicians to record successes.[5]

Our objective is to investigate the current treatment outcomes of each HP eradication regimen. This will have an impact on clinicians and the authority to decide the appropriate strategies to combat this infection and allocate health care resources.

Methods

Patient characteristics. This study was a retrospective study that reviewed the medical records of adults, 18 years or older, who underwent a urea breath test (UBT) at the Center of Excellence for Gastrointestinal Endoscopy, King Chulalongkorn Memorial Hospital, Chulalongkorn University, Bangkok, Thailand, during 2018–2021.

We included dyspeptic patients who had undergone UBT for the diagnosis of HP infection prior to other diagnostic tests (diagnosis group) and patients who had been treated for HP and had undergone UBT to confirm eradication (treatment group). Patients were excluded if there were missing data on the treatment regimen and UBT results.

Demographic data and clinical characteristics. Data were collected on demographics (age and sex), UBT results, HP treatment regimen (antibiotics, proton pump inhibitors [PPIs], duration), and endoscopic findings. Patients who failed the initial regimen were treated with subsequent regimens until confirmed eradication. We collected all prescribed regimens for each patient. Patients with endoscopy results were divided into two groups: the "success" group and the "failure" group, according to UBT results. These two groups were compared and the factors related to treatment failure were identified.

UBT method. UBT was performed with an infrared spectrophotometer (POConePlus, Otsuka Pharmaceutical, Tokyo, Japan) in all patients included. This test measures the change in the isotope ratio of carbon dioxide ($^{13}CO_2/^{12}CO_2$) contained in exhaled breath. Patients must stop using PPIs for at least 14 days and stop using antibiotics for at least 28 days prior to UBT. Patients must fast for at least 6 h before undergoing the test. Two consecutive breaths were collected. A basal breath sample was collected to measure the baseline CO_2 (^{12}C). The patients were then asked to consume a tablet containing isotopically labeled urea (^{13}C). Orally administered urea is hydrolyzed to ammonia and carbon dioxide by the enzyme urease, which is produced by HP. ^{13}C-labeled CO_2 diffuses into the blood and is excreted by the lungs. CO_2 labeled with this isotope can be detected in the second breath, which was collected 20 min later. An increase in the proportion $^{13}C/^{12}C$ ($\Delta^{13}CO_2$ [‰]) of 2.5 or more indicates HP infection, according to manufacturer's specifications.

Statistical analysis. Baseline characteristics and clinical outcomes were expressed as a proportion and mean ± SD for continuous data. The comparison between the "success" and "failure" groups was carried out using a nonparametric test such as the Chi-squared test or Fisher's exact test for categorical data and the *t*-test for continuous data. $P < 0.05$ was considered for statistical significance. Factors influencing the failure of treatment were analyzed using logistic regression. Statistical analyses were performed using SPSS version 28.0 (Chicago, IL, USA).

Results

HP prevalence. During 2018–2021, 1902 patients underwent UBT at the Center of Excellence for Gastrointestinal Endoscopy. They were divided into two groups: 313 patients in the diagnosis group and 1589 patients in the treatment group. UBT results were positive in 65 patients (20.77%), indicating the prevalence of HP infection in dyspeptic patients.

HP treatment outcome. In the treatment group, the success rate of the first treatment regimen was 85.08% (1352 patients out of 1589 patients had a negative UBT result). The detailed first-line regimens and success rates are shown in Table 1. Triple therapy was the preferred treatment for the majority of patients (1514 patients, 95.28%), while bismuth quadruple therapy was preferred for 3.21% (51 patients) because of penicillin allergy or prior macrolide use.

Patients who had failed the first-line regimen were prescribed other regimens by changing the combination of antibiotics or extending the duration of treatment. We collected data

Table 1 Success rate of initial regimens

	Success (*n*)	Total (*n*)	Success rate (%)
Clarithromycin triple therapy	907	1064	85.24
Levofloxacin triple therapy	381	450	84.67
Bismuth quadruple therapy	44	51	86.27
Sequential therapy	20	24	83.33
Total	1352	1589	85.08

Table 2 Success rate of the second regimens in the patient who failed the initial clarithromycin triple therapy

	Success (*n*)	Total (*n*)	Success rate
Clarithromycin triple therapy[†]	9	17	52.94%
Levofloxacin triple therapy	32	44	72.73%
Bismuth quadruple therapy	29	40	72.50%
Sequential therapy	3	4	75%
Total	73	105	69.52%

[†]Triple therapy was changed to a higher dose of antibiotics or proton pump inhibitors or to a longer duration.

on the subsequent regimens in 156 patients. The overall success rate of the second regimen was 69.87% (109 pateints). The second regimen included clarithromycin triple therapy (67.31%, 105 pateints), levofloxacin triple therapy (25%, 39 patients), bismuth quadruple therapy (6.41%, 10 patients), and sequential therapy (1.28%, 2 patients).

One-hundred and five patients who received standard clarithromycin triple therapy and failed eradication were given second-line treatment. The detailed regimens and success rates are shown in Table 2.

Patients who received levofloxacin triple therapy, bismuth quadruple therapy, and sequential therapy as their initial regimen and remained positive for UBT were given the second-line treatment. The success rates for each combination are shown in Table 3.

There were 26 patients who were classified as "multiple treatment failure", defined by more than two regimens administered. These patients were prescribed the third regimen, even though there was no result on antibiotic susceptibility. The overall success rate of the third regimen was 53.85% (14 out of 26 patients). Six patients received fourth-line treatment with a success rate of 50% (three patients).

Predictor of HP treatment failure. Consecutive clinical data from 1017 patients who received the initial treatment regimen were reviewed, out of a total of 1589 patients in the treatment group. Only patients with complete endoscopic results were included in the selection process. The data collected were demographics (age and sex), UBT results, HP treatment regimen (antibiotics, PPIs, duration), and endoscopic findings. One-hundred and six patients failed the initial treatment. The clinical characteristics between the two groups are shown in Table 4.

Univariate logistic regression analysis found that only lansoprazole use was associated with failure of treatment, with OR = 2.11 (95% CI: 1.14–3.92, $P = 0.018$) (Table 5).

Discussion

Our group's previous study from 2013 to 2017 had found the prevalence of HP infection in dyspeptic patients as 28.4%. Recent research has shown a decreasing trend, with 20.77% prevalence in symptomatic patients. This finding correlates with the global trend of declining rates, which can be attributed to improved public hygiene standards and urbanization, along with socioeconomic advancements.[12–16]

Front-line treatment strategies in our study show slightly lower efficacy than in the previous study.[8] The overall regimen efficacy is 85.08%, compared to 92.61% from the 2013–2018 data. Bismuth quadruple therapy has the highest eradication rate (86.27%), while clarithromycin triple therapy shows a lower success rate.

Eradication rates are low compared to the 95% threshold required for first-line treatment of sensitive strains. Nevertheless, the results are consistent with the recent European *H. pylori* Management Register (Hp-EuReg) and reflect actual clinical practices. According to a survey of 21 533 infected persons from 27 countries, the overall effectiveness of the modified intention-to-treat (mITT) empirical therapy was 85.6%.[17,18]

The effectiveness of triple therapy with clarithromycin depends on the rate of resistance to clarithromycin. The MaastrichtVI/Florence consensus recommends against triple therapy when the clarithromycin resistance rate exceeds 15%.[7] A survey of five teaching hospitals in Thailand showed that the

Table 3 Success rate of the second regimen in patients who failed each initial regimen

First regimen	Second regimen	Success (*n*)	Total (*n*)	Success rate (%)
Levofloxacin triple therapy ($n = 39$)	Clarithromycin triple therapy	3	7	42.86
	Levofloxacin triple therapy	3	7	42.86
	Bismuth quadruple therapy	18	19	94.74
	Sequential therapy	5	6	83.33
Bismuth quadruple therapy ($n = 10$)	Clarithromycin triple therapy	2	4	50
	Levofloxacin triple therapy	2	4	50
	Bismuth quadruple therapy	0	1	0
	Sequential therapy	1	1	100%
Sequential therapy ($n = 2$)	Levofloxacin triple therapy	2	2	100
Total		36	51	70.59

Table 4 Clinical characteristics of patients who succeded and failed in HP eradication by initial regimen

	Success ($n = 857$)		Failure ($n = 160$)		
Clinical characteristics	*n*	%	*n*	%	*P*-value
Sex (male)	372	43.41	59	36.88	0.13
Age >60 years	535	62.43	108	67.50	0.22
Endoscopic findings					
Esophagitis	245	28.59	46	28.75	0.97
Gastritis	775	90.43	140	87.50	0.26
Gastric ulcer	112	13.07	18	11.25	0.53
Duodenal ulcer	64	7.47	10	6.25	0.59
Esophageal varices	38	4.43	7	4.38	0.97
Gastric varices	4	0.47	1	0.63	0.58
Treatment regimen					
Clarithromycin triple therapy	576	67.21	107	66.88	0.93
Levofloxacin triple therapy	243	28.35	44	27.50	0.83
Bismuth quadruple therapy	28	3.27	4	2.50	0.61
Sequential therapy	10	1.17	5	3.13	0.07
Proton pump inhibitors					
Omeprazole	694	80.98	120	75.00	0.08
Rabeprazole	94	10.97	18	11.25	0.92
Lansoprazole	40	4.67	15	9.38	0.02
Esomeprazole	19	2.22	6	3.75	0.25
Pantoprazole	9	1.05	1	0.63	1
Dexlansoprazole	1	0.12	0	0	1
Duration of treatment					
≤7 days	2	0.23	0	0	1
8–14 days	845	98.60	158	98.75	1
>14 days	10	1.17	2	1.25	1

Table 5 Univariate logistic regression for failure of HP eradication by initial regimen

Clinical Characteristics	OR	95% CI	*P*-value
Sex (male)	0.76	0.54–1.08	0.13
Age >60 years	1.25	0.87–1.79	0.22
Endoscopic findings			
Esophagitis	1.01	0.69–1.46	0.97
Gastritis	0.74	0.44–1.25	0.26
Gastric ulcer	0.84	0.50–1.43	0.53
Duodenal ulcer	0.83	0.42–1.65	0.59
Esophageal varices	0.99	0.43–2.25	0.97
Gastric varices	1.34	0.15–12.08	0.79
Treatment regimen			
Clarithromycin triple therapy	0.99	0.69–1.41	0.93
Levofloxacin triple therapy	0.96	0.66–1.40	0.83
Bismuth quadruple therapy	0.76	0.26–2.20	0.61
Sequential therapy	2.73	0.92–8.10	0.07
Proton pump inhibitors			
Omeprazole	0.71	0.47–1.05	0.08
Rabeprazole	1.03	0.60–1.76	0.92
Lansoprazole	2.11	1.14–3.92	0.02*
Esomeprazole	1.72	0.68–4.37	0.26
Pantoprazole	0.59	0.08–4.71	0.62
Dexlansoprazole	0	0	1
Duration of treatment			
≤7 days	0	0	0.99
8–14 days	0.89	0.20–4.02	0.88
>14 days	1.07	0.23–4.94	0.93

OR, odds ratio; CI, confidence interval.

clarithromycin resistance rate in Thailand ranges from 5% to 29.20% (median = 13.8%). The current Thai guideline, based on a real-world study, recommends the use of standard triple therapy, which results in an eradication rate of 80%.[6] However, our data report a declining eradication rate, which may reflect increased HP resistance to clarithromycin. Further HP culture and clarithromycin susceptibility testing is needed to prove the current situation. This finding may impact the initial regimen recommended in our country, as clarithromycin-based triple therapy is no longer recommended in most regions of the world.[3]

Although bismuth quadruple therapy shows a higher success rate, the eradication rate is still less than 90%. This may reflect the change in antimicrobial resistance in other antibiotic groups. Further testing of the genetic polymorphisms and the adequacy of pH control, such as gastric pH, may elucidate this changing trend.

Patients with refractory infections are defined by non-serologic HP tests (i.e., a breath-, stool-, or gastroscopy-based test) that are persistently positive and at least 4 weeks after completion of one or more of the current guideline-recommended first-line regimen.[4] The second salvage treatment is mostly empirical. Choices of antibiotics usually depend on previous antibiotic exposure and penicillin allergy.[3] Some clinicians may favor sensitivity-based antibiotic treatment with a customized regimen as directed by susceptibility testing. However, in a real-world setting, there are many challenges in testing antibiotic sensitivity of HP. Studies show that there is little evidence that the selection of sensitivity-based therapies significantly improves the

success rate of HP eradication over the empirically selected second-line therapy.[3,19]

In refractory cases, according to international guidelines,[7,20] it seems obvious to prescribe susceptible antibiotics based on the results of a bacterial culture with susceptibility tests after two failed treatment attempts. However, in practice, the success rate of bacterial culture is much less than 80% to achieve useful results.[21–23] These low success rates outside of a clinical protocol are multifactorial. Since HP is a fastidious organism, delays and errors in the processing and transportation of samples, as well as the recent use of PPIs and antibiotics, can affect the success rate of HP culture. Molecular resistance tests can be a simple and good alternative because they can be performed on formalin-fixed paraffin-embedded gastric biopsy tissue.[3] However, these test methods are not widely available.

Although resistance-test-directed treatment is theoretically superior to empirical treatment, comparative efficacy was demonstrated only in the first or second line of treatment. In multiple-failure cases, there is limited data on the choice of the third and even fourth line of treatment. Our study found that the success rate of empirical third- and fourth-line treatments was 53.85% and 50%, respectively. These findings may indicate the slightly low eradication rates. However, there were only a small number of patients and the options of regimens were limited because of local unavailability, and no other salvage regimens recommended in the guidelines were prescribed, such as triple therapy with rifabutin, high-dose dual therapy, or furazolidone-containing regimens.[4,7] Even with this restricted resource, half of the patients still benefit from the empirical salvage regimen.

The effect of selected predictors on treatment efficacy was determined by logistic regression. From the demographics (age and sex), HP treatment regimen (antibiotics, PPIs, duration), and endoscopic findings, only lansoprazole use was associated with failure of treatment with OR = 2.11 (95% CI: 1.14–3.92, $P = 0.018$).

An adequate inhibition of acid is necessary for the eradication of HP.[24,25] Various PPIs were used in this study, including omeprazole, rabeprazole, lansoprazole, esomeprazole, pantoprazole, and dexlansoprazole. The second generation (esomeprazole, rabeprazole, dexlansoprazole) is probably more effective than the first generation (omeprazole, lansoprazole, pantoprazole), as their metabolism pathways are less dependent on genetic variables of cytochrome P450 (CYP) 2C19. Lansoprazole is mainly metabolized by CYP2C19 and CYP3A4.[26–28] Since our study did not measure the genotype of CYP2C19, the involvement of these genetic polymorphisms in the pharmacokinetic properties of PPIs that result in inadequate acid suppression may cause various treatment outcomes.

Our study has some limitations. First, it is a retrospective study with complex data, which include the pharmacological regimen, the type and doses of antibiotics and PPIs, as well as the duration of treatment. Some other uncontrollable factors are associated with treatment failure, such as nonadherence to treatment, clarithromycin resistance, prior exposure to macrolides, genetic factors, and altered intragastric pH. Second, subgroup analyses for specific salvage regimens were not performed because of the relatively small sample sizes. A prospective study on the success rate of the empirical third-, fourth-, or even fifth-line regimen in patients who cannot obtain antibiotic sensitivity testing done because of technical or financial issues may fill the gap in the real-world situation. Third, the prevalence rate of HP in dyspeptic patients in this study is based on data from a single institution. This might have introduced selection bias and limited the representativeness of the sample for the wider population of dyspeptic patients in Thailand. It is possible that important differences exist between dyspeptic patients referred for UBT as the first investigation *versus* those referred for gastroscopy, which could affect the results.

Conclusions

Current primary HP treatment regimens remain with an eradication rate of >80%. Even though the previous regimens failed, without the availability of antibiotic sensitivity results, the subsequent regimens were successful by at least 50%. In case of multiple-treatment failure and unavailability of antibiotic sensitivity testing, continuing to change regimens could provide satisfactory results.

Data availability statement. All data generated or analyzed during this study are included in this published article.

References

1 Hooi JKY, Lai WY, Ng WK *et al*. Global prevalence of *Helicobacter pylori* infection: systematic review and meta-analysis. *Gastroenterology*. 2017; **153**: 420–9.
2 Moss SF. The clinical evidence linking *Helicobacter pylori* to gastric cancer. *Cell. Mol. Gastroenterol. Hepatol.* 2017; **3**: 183–91.
3 Shah SC, Iyer PG, Moss SF. AGA clinical practice update on the management of refractory *Helicobacter pylori* infection: expert review. *Gastroenterology*. 2021; **160**: 1831–41.
4 Chey WD, Leontiadis GI, Howden CW, Moss SF. ACG clinical guideline: treatment of *Helicobacter pylori* infection. *Off. J. Am. College Gastroenterol.* 2017; **112**: 212–39.
5 Fallone CA, Chiba N, van Zanten SV *et al*. The toronto consensus for the treatment of *Helicobacter pylori* infection in adults. *Gastroenterology*. 2016; **151**: 51–69.e14.
6 Mahachai V, Vilaichone R-K, Pittayanon R *et al*. Thailand consensus on *Helicobacter pylori* treatment 2015. *Asian Pac. J. Cancer Prev.* 2016; **17**: 2351–60.
7 Malfertheiner P, Megraud F, Rokkas T *et al*. Management of *Helicobacter pylori* infection: the Maastricht VI/Florence consensus report. *Gut*. 2022; **71**: 1724–62.
8 Shoosanglertwijit R, Kamrat N, Werawatganon D, Chatsuwan T, Chaithongrat S, Rerknimitr R. Real-world data of *Helicobacter pylori* prevalence, eradication regimens, and antibiotic resistance in Thailand, 2013–2018. *JGH Open*. 2020; **4**: 49–53.
9 Suchartlikitwong S, Lapumnuaypol K, Werawatganon D. Prevalence of antibiotic-resistant *Helicobacter pylori* and the effect on standard treatment. *Thai. J. Gastroenterol.* 2014; **15**: 166–8.
10 Ford AC, Yuan Y, Moayyedi P. *Helicobacter pylori* eradication therapy to prevent gastric cancer: systematic review and meta-analysis. *Gut*. 2020; **69**: 2113–21.
11 Savoldi A, Carrara E, Graham DY, Conti M, Tacconelli E. Prevalence of antibiotic resistance in *Helicobacter pylori*: a systematic Review and meta-analysis in World Health Organization Regions. *Gastroenterology*. 2018; **155**: 1372–82.e17.
12 Ren S, Cai P, Liu Y *et al*. Prevalence of *Helicobacter pylori* infection in China: a systematic review and meta-analysis. *J. Gastroenterol. Hepatol.* 2022; **37**: 464–70.

13 Sjomina O, Pavlova J, Niv Y, Leja M. Epidemiology of *Helicobacter pylori* infection. *Helicobacter*. 2018; **23**: e12514.
14 Sonnenberg A. Epidemiology of *Helicobacter pylori*. *Aliment. Pharmacol. Ther.* 2022; **55**: S1–S13.
15 Genta RM, Turner KO, Sonnenberg A. Demographic and socioeconomic influences on *Helicobacter pylori* gastritis and its preneoplastic lesions amongst US residents. *Aliment. Pharmacol. Ther.* 2017; **46**: 322–30.
16 Sonnenberg A, Turner KO, Genta RM. Low prevalence of *Helicobacter pylori*-positive peptic ulcers in private outpatient endoscopy centers in the United States. *Am. J. Gastroenterol.* 2020; **115**: 244–50.
17 Graham DY. Efficient identification and evaluation of effective *Helicobacter pylori* therapies. *Clin. Gastroenterol. Hepatol.* 2009; **7**: 145–8.
18 Nyssen OP, Bordin D, Tepes B *et al*. European Registry on *Helicobacter pylori* management (Hp-EuReg): patterns and trends in first-line empirical eradication prescription and outcomes of 5 years and 21 533 patients. *Gut*. 2021; **70**: 40–54.
19 Liou J-M, Chen P-Y, Luo J-C *et al*. Efficacies of genotypic resistance-guided vs empirical therapy for refractory *Helicobacter pylori* infection. *Gastroenterology*. 2018; **155**: 1109–19.
20 Mahachai V, Vilaichone RK, Pittayanon R *et al*. Helicobacter pylori management in ASEAN: The Bangkok consensus report. *J. Gastroenterol. Hepatol.* 2018; **33**: 37–56.
21 Smith SM, O'Morain C, McNamara D. Antimicrobial susceptibility testing for *Helicobacter pylori* in times of increasing antibiotic resistance. *World J. Gastroenterol.* 2014; **20**: 9912–21.
22 Choi JH, Yang YJ, Bang CS, Lee JJ, Baik GH. Current status of the third-line *Helicobacter pylori* eradication. *Gastroenterol. Res. Pract.* 2018; **2018**: 6523653.
23 de Brito BB, da Silva FAF, Soares AS *et al*. Pathogenesis and clinical management of *Helicobacter pylori* gastric infection. *World J. Gastroenterol.* 2019; **25**: 5578–89.
24 Gao W, Zhang X, Yin Y, Yu S, Wang L. Different dose of new generation proton pump inhibitors for the treatment of *Helicobacter pylori* infection: a meta-analysis. *Int. J. Immunopathol. Pharmacol.* 2021; **35**: 20587384211030397.
25 Ierardi E, Losurdo G, Fortezza RF, Principi M, Barone M, Leo AD. Optimizing proton pump inhibitors in *Helicobacter pylori* treatment: Old and new tricks to improve effectiveness. *World J. Gastroenterol.* 2019; **25**: 5097–104.
26 McNicholl AG, Linares PM, Nyssen OP, Calvet X, Gisbert JP. Meta-analysis: esomeprazole or rabeprazole vs. first-generation pump inhibitors in the treatment of *Helicobacter pylori* infection. *Aliment. Pharmacol. Ther.* 2012; **36**: 414–25.
27 Villoria A, Garcia P, Calvet X, Gisbert JP, Vergara M. Meta-analysis: high-dose proton pump inhibitors vs. standard dose in triple therapy for *Helicobacter pylori* eradication. *Aliment. Pharmacol. Ther.* 2008; **28**: 868–77.
28 Murakami K, Sato R, Okimoto T *et al*. Eradication rates of clarithromycin-resistant *Helicobacter pylori* using either rabeprazole or lansoprazole plus amoxicillin and clarithromycin. *Aliment. Pharmacol. Ther.* 2002; **16**: 1933–8.