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Helicobacter pylori antibiotic resistance: A global challenge in search of solutions

-Management options and perspectives from current guidelines-

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What is already known on this topic

Many countries have reported an increase in *Helicobacter pylori* resistance, leading to significant failure rates of current eradication therapies. Most data on *H. pylori* antibiotic resistance in the community are based on phenotypic testing. Only recently has molecular genotypic testing become more widely available. For this analysis, we conducted a database searchOnly English-language publications published between 2018 and 2024 were included. The search terms used were: “Helicobacter pylori [Title/Abstract]) AND (resistance [Title/Abstract])) OR (resistant[Title/Abstract])) OR (antibiotic susceptibility testing [Title/Abstract])) OR (Metronidazole[Title/Abstract])) OR (Clarithromycin[Title/Abstract])) OR (Levofloxacin[Title/Abstract])) OR (country[Title/Abstract])) NOT (review[Title/Abstract])) NOT (meta-analysis[Title/Abstract]))”.

What this study adds

Our survey updates and extends the global mapping of antibiotic resistance to include data from 6 continents and 31 countries. Results indicate a rapid growth in antibiotic resistance worldwide. Major challenges to *H. pylori* management were identified, including the LIMITED availability of molecular antibiotic susceptibility testing to select individualized treatment regimens and a lack of re-imbursement for these tests. In many countries, adequate empirical therapy is not accessible due to the unavailability of relevant medications (e.g., bismuth).

Antimicrobial resistance rates reported in our survey exceeded the cut-off value of 15% recommended by national and international guidelines for the empirical use of clarithromycin and levofloxacin in 1st and 2nd line eradication regimens.

It is of concern that antibiotic resistance surveillance programs have been implemented in only 5 of 26 countries.

How this study might affect research, practice or policy

We have identified limitations in current strategies to counteract the progressively increasing antibiotic resistance of *H. pylori*.

This should raise awareness among health care officials and authorities of the need to develop appropriate logistics for *H. pylori* resistance testing, provide access to effective and safe drugs for use in *H. pylori* eradication regimens, and seek affordable reimbursement regulations worldwide. It also encourages the establishment of global surveillance programs to monitor antibiotic resistance rates and therapeutic efficacy in the management of *H. pylori*.

Abstract

Background

Helicobacter pylori resistance to antibiotics commonly used in eradication regimens is increasing dramatically in many locations; new strategies are needed to manage this infectious disease.

Objective

This study's aim was to collect and update information on antibiotic resistance (AR) rates in *H. pylori* as well as current strategies for *H. pylori* management, including public health issues, from a global perspective.

Design

An international survey was conducted in 31 countries on 6 continents to address key issues concerning the management of *H. pylori*-related AR. Individual aspects included the prevalence of AR for specific antibiotics, antibiotic susceptibility testing (AST) in different healthcare systems, availability of drugs, reimbursement issues, and strategies for *H. pylori* AR surveillance.

Results

Resistance to the most effective antibiotics used in *H. pylori* eradication regimens is increasing globally, with clarithromycin and levofloxacin resistance exceeding 15% in 24/31 and 18/31 countries respectively. Amoxicillin remains an exception, with resistance rates under 2% in 14/ 31 countries; though African countries have reported amoxicillin resistance rates of over 90%. Bismuth-based treatment regimens are the most effective and are recommended as first-line treatment in several countries. However, more than 1 billion inhabitants worldwide have no access to bismuth-based regimens. PCR-based tests for AR are used in 16/26 countries but are reimbursed in only 4, while NGS-based tests are available, but not reimbursed, in 3 countries. In 22/26 countries only culture-based methods are available (reimbursed in 9/26 countries). AR surveillance programs have only been established in 4 of 26 countries Therefore, in most countries, empirical therapy with the most effective local regimen available locally is practiced.

Conclusion

The dramatic global rise in *H. pylori* antibiotic resistance requires an urgent revision of current management strategies. Possible solutions include AST-based selection of effective treatment regimens, identification of novel combinations of existing drugs, and exploration of novel drugs.

Introduction

The definition of *Helicobacter pylori* gastritis as an infectious disease has been a game changer in the management of *H. pylori* infection [1].

Whereas previously, *H. pylori* eradication therapies were only recommended for specifically defined clinical indications, they are now recommended for all infected individuals, independent of the treatment of symptoms as well as for preventive purposes [2]. However, the widespread use of *H. pylori* eradication therapies has led to an increase in antibiotic resistance (AR) of *H. pylori,* as well as other bacteria, thereby increasing eradication failure rates [3, 4].

The high rates of *H. pylori* resistance to the antibiotics that were previously most effective in eradication regimens mandate the development of new strategies, including intensified regional antibiotic resistance surveillance, individual antibiotic susceptibility testing, and the global implementation of antimicrobial stewardship measures [5, 6, 7, 8, 9, 10].

The antibiotics that have received much attention are clarithromycin, and to a lesser extent, levofloxacin [11]. Both drugs have strong bactericidal activity on susceptible *H. pylori* strains and are key components of current eradication regimens. Back in 2017, the World Health Organization (WHO) flagged *H. pylori* as a high-priority pathogen for antibiotic research due to the dramatic increase in clarithromycin resistance globally [11, 12]. In 2024, "based on evidence and expert consensus", clarithromycin was surprisingly removed from the priority list, despite the continued increase in clarithromycin resistance in most countries [13]. Recent data also suggest that *H. pylori* resistance to levofloxacin is increasing in many regions of the world, posing a further critical problem regarding the selection of effective alternative eradication regimens [14]. In case of high resistance to clarithromycin, the use of levofloxacin is prioritized in first- and second-line eradication therapy, especially in the absence of bismuth [6]. As an exception, in Japan the use of sitafloxacin is recommended [15, 16].

The aim of this study is to update and extend information on global AR rates of *H. pylori* and on current strategies for *H. pylori* management. The survey includes public health aspects, recommendations from national and international guidelines/consensus reports, and suggests recommendations for an optimized management of *H. pylori* against the challenge of AR.

Methods

An international group was assembled that included 24 gastroenterologists and 7 clinical microbiologists from 23 countries with substantial expertise and a relevant publication record in the field of *H. pylori*. General practitioners and family physicians are the essential Health care providers in clinical management of H. pylori infection. However in most countries they are not directly involved in monitoring treatment effectiveness and surveillance of antibiotic resistance. They are responsible for patient care and reach out for guidance in optimized clinical management from guidelines and specialists. For this reason we restricted the invitation to specialists, Gastroenterologists and Microbiologists, with special dedication to *H.pylori* and related diseases to participate in the survey.

We first reviewed data on drug resistance from 2018 to 2023 using a search on PubMed to identify relevant publications via the following search terms: "Helicobacter pylori [Title/Abstract]) AND (resistance [Title/Abstract])) OR (resistant[Title/Abstract])) OR (antibiotic susceptibility testing [Title/Abstract])) OR (Metronidazole[Title/Abstract])) OR (Clarithromycin[Title/Abstract])) OR (Levofloxacin[Title/Abstract])) OR (country[Title/Abstract])) NOT (review[Title/Abstract])) NOT (meta-analysis[Title/Abstract]))". Secondary literature (e.g., review articles and meta-analyses) was excluded from the data collected. Articles were checked for eligibility based on inclusion criteria: AR of *H. pylori* in therapy-naïve adults. Further updates on regional AR of *H. pylori* were provided by experts on the panel.

International and National guidelines were scrutinized for statements relevant to *H. pylori* therapy, with a focus on the management of *H. pylori* resistance (see Suppl.).

All experts included in this study responded to questionnaires (see Suppl.) on the real-world conditions of *H. pylori* management in their own countries, including logistics, access to and reimbursement of the AST and antibiotics as well as current or planned national resistance surveillance programs.

Results

The data obtained from the survey and literature research are summarized in Tables 1-4. Table 1 shows the AR to clarithromycin, levofloxacin, metronidazole, amoxicillin, rifampicin, tetracycline, and ciprofloxacin in each continent. Within each continent, there was considerable variation between each country, as shown in Table 2 and Figure 1.

The availability of drugs also varies considerably from country to country. While clarithromycin is universally available, other drugs are more restricted (e.g. bismuth salts are not allowed in Nigeria, Democratic Republic of the Congo, Malaysia, Indonesia, Korea, Japan and Brazil; tetracycline is not allowed in Egypt, South Africa, and Malaysia) (Table 3). Bismuth in a single form or in a fixed formulation is unavailable in 7 of the 26 countries included in the survey. This results in an estimated 1 billion people being denied access to bismuth-containing treatments.

The availability and reimbursement of AST is shown in Table 4. Access to phenotypic AST was limited to 13 of 26 countries, of which only 9 were reimbursed. Molecular testing (PCR) of AR is available and reimbursed in only 4 of the 26 countries. PCR testing is not reimbursed

in 12/26 countries and is not available in 10/ 26 countries. AST based on next generation sequencing (NGS) is in only available in 3 of the 26 countries. None of these three countries have a reimbursement policy for these tests in place.

Only 4/26 (15.3%) of the countries in this survey (Spain, Germany, Japan, Korea) have regular AR surveillance measures in place (data not shown).

Discussion

This survey provides a representative picture of the development of *H. pylori* AR over the past five years. Globally, resistance rates to critical antibiotics used for eradication exceed the most recent data reported in the literature [3, 5, 17, 18]. In this highly dynamic field, the time lag between data collection and publication release may account for this discrepancy.

The magnitude of the increase in AR varies between individual antibiotics used for eradication and also differs widely between continents and countries within each continent.

In Europe, clarithromycin resistance ranges from 12 to 22.4%. The most recent survey from Europe reported an increase of clarithromycin resistance by >10% compared to 10 years ago [18]. In Asia, clarithromycin resistance ranged from 7 to 92.1%. This is a dramatic increase when compared to data released in 2024, which reported a primary clarithromycin resistance rate of 22% [5]. In Africa, clarithromycin resistance rates ranged from 13.6 to 66.7%, but no previous data were available. For comparison, according to our survey, levofloxacin resistance ranged from 13 to 20.3% in Europe, 42.6% in North America, 13.5 to 29% in South America, 20 to 65.7% in Africa, and 3.3 to 65.6% in the Asia-Pacific region. A previous report showed an increase of levofloxacin resistance from 15.8% to 20.3% in treatment-naïve patients in Europe [18]. At the country level, increasing resistance rates are now reported in up to 50% of Asian countries (e.g. Cambodia 50%, China 35%, Vietnam 31.6 – 41.8%, Korea 37%, and Myanmar 33.8%) [17]. Just as clarithromycin resistance cross-reacts with all macrolides, levofloxacin resistance affects all quinolones due to their cross-reactivity in inducing resistance (Tables 1 and 2; Figure 1). The increasing resistance to levofloxacin, which is recommended as the antibiotic of choice for second-line treatment by consensus reports in Europe [6], Asia (except Japan, where sitafloxacin is the recommended 2nd line treatment[19]), and Africa [20, 21], hinders its empirical use and suggests selection should instead be based on AST.

Global resistance rates of amoxicillin vary from 0-97.1% and in most countries do not exceed 1% [5]. Confirmatory studies on amoxicillin resistance in Africa are important. In a recent analysis of time trends in the development of AR in children, amoxicillin resistance was consistently low at 4% [22]. Amoxicillin is an essential component of triple and dual therapy eradication regimens. High-dose PPI therapy in combination with amoxicillin is an effective option for *H. pylori* eradication. Dual therapy can now be augmented by potassium-competitive acid blockers (P-CABs) to provide even stronger acid inhibition [23, 24]. A potential limitation regarding the general recommendations for the use of dual therapies is that emerging amoxicillin resistance is >70% in some countries in Africa [25] and >15% in some countries in Asia (27.2- 50% in Vietnam and 15.9% in Iran) (Tables 1 and 2; Figure 1). Reflecting antimicrobial stewardship measures the reported resistance rates from Africa and some Asian countries need to be confirmed by future studies. In most countries around the world amoxicillin resistance is currently not in focus which is reflected by its excellent efficacy of dual therapies including amoxicillin and P-CABs[26, 27].

Rifabutin resistance is negligible, with a global resistance rate in the range of 0 – 0.2%, so AST is not currently required for this drug [28]. Rifabutin is generally used as a rescue medication, only used as a first-line drug in the United States. Reasons for limiting Rifabutin-containing regimens as rescue therapy only are based on the use of this drug for other critical infections and the risk of severe although rare adverse events (e.g. myelotoxicity).

Nitroimidazoles (e.g., metronidazole) deserve special consideration because of the highest resistance rates worldwide. Chile is likely to be an exception, as furazolidone is predominantly used instead of metronidazole [29, 30, 31]. Nitroimidazoles have a subordinate role in PPI-based triple combinations and are usually preferred in combination with amoxicillin.

However, metronidazole has been used successfully in Bismuth based quadruple therapy (BQT) [32]. Combination with bismuth may synergize with metronidazole and overcome resistance [33]. Real-world data from Europe confirm a therapeutic efficacy of >90% in BQT, independent of metronidazole resistance [3, 34]. Tetracycline is also part of the BQT regimen and has an established resistance of less than 1% [32].

The empirical use of BQT instead of PPI triple is an important strategy to limit further increases in AR and reduce treatment failures. International and several national guidelines

recommend that BQT should be considered as first-line treatment due to the lack of need for considering AR [6, 9, 20, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46].

In many countries, BQT has only recently become available, but it is still not accessible to more than one billion people in the world. BQT is not available in countries such as Nigeria, Malaysia, Indonesia, Republic of Korea, Japan, and Brazil, as shown in Table 3.

In many countries, clarithromycin-based triple therapy is retained as a first-line option. Guidelines have long recommended the empirical use of PPI triple only if clarithromycin resistance is <15% and is properly monitored [5, 9, 17, 47]. However, because, clarithromycin resistance rates are significantly higher than 15% in numerous countries, clarithromycin-based triple should no longer be empirically prescribed [17].

There are two opposing views concerning the role of AST in the management of *H. pylori* infection. One view is that the choice of treatment regimen should always be based on an individual strain's AST. The opposing position is that the preferred strategy is to choose an effective empirical therapy that is typically unaffected by AR surveilled on a population level. There was general agreement among the experts on the broader use of AST if certain antibiotics are intended to be used. Current recommendations for antibiotic (clarithromycin, levofloxacin) resistance testing vary between guidelines, with some recommending that AST has already been used in the 1st line [6, 35], and others only after treatment failure [20] (see Suppl.) [6]. According to this survey, AST is currently available routinely in only a few countries (Table 2). AST in most countries depends upon successful bacterial culture obtained from gastric biopsies (phenotypic AR testing). In most parts of the world, molecular testing is rarely or not at all available for use in clinical practice [7, 8, 10, 48, 49]). A change towards broader use of molecular AST would benefit the strategy of selecting eradication regimens based on antibiotic resistance because phenotypic culture-based AST is cumbersome and not always successful, and it requires gastric biopsies (and therefore an invasive procedure to obtain these), and specialized microbiological laboratories, resulting in high costs (Table 4). Genotypic AST (PCR- or NGS-based) is more convenient and can be applied to gastric aspirates, gastric biopsies, and, much less invasively stool samples, though further validation is required for the latter [7, 8, 50] Molecular tests are not currently accessible in many parts of the world and are often not reimbursed by national health care systems even when they are available. Access to and reimbursement for molecular tests for clarithromycin and levofloxacin resistance are only currently available in Japan and Chile (Table 4). In addition, time delay for

additional diagnostic measures before initiating treatment and the necessity of additional visits might hamper the broad implementation of AST in general management.

The concept of selecting an effective empirical therapy that is not compromised by AR based on regional AR rates requires AR surveillance programs. To date, only a few countries have national antibiotic resistance/susceptibility registries. Japan, Korea, Spain, and Germany are running joint or individual prospective programs to collect resistance data. In the UK, only isolates following treatment failure are centrally analyzed, but the service was just put on hold due to capacity issues. AR data are often used to draw conclusions from an epidemiological perspective, and these are only available in the selective context of therapy studies or single-center studies [51]. More structured efforts are needed to gain a representative insight into *H. pylori* resistance among the world`s population and the need to implement AST-based treatment recommendations (see Suppl.). The lack of such data prevents adequate recommendations for 1st-line combinations, which is expected to lead to a further reduction in successful eradication rates.

Antimicrobial Stewardship measures need to be consequently included in *H. pylori* management strategies. According to the selected principles of antimicrobial stewardship BQT is the most suitable regimen and thus recommended in first line. The reason for this is that the efficacy of standard BQT with tetracycline and metronidazole is not jeopardized by antibiotic resistance and safety concerns. The contrary holds true for clarithromycin and levofloxacin containing regimens in Triple- and Non- Bismuth -Quadruple therapies and thus they should not be used in first line except when their efficacy can be predicted by a positive AST. However, from the responses in our survey AST is only available in few, mostly specialized centers only and thus their use lacks in practicality[52].

AR data are of crucial importance in laying the foundation for evidence-guided strategies and successful management of *H. pylori* infections. Currently available data on molecular AST are based on small sample numbers and, in addition, there is a lack in comparability of methods used in different settings. The majority of data are still obtained via culture-based methods, but their major complexities in handling and logistics limit broader use. Molecular testing holds greater promise for more widespread implementation [7, 8, 10, 48, 49]).

There are relevant limitations of our survey including incomplete epidemiological data from large parts of the world, heterogenous measures used for AST in different studies and

frequently small cohorts analyzed. It results from our survey that phenotypic testing is still the gold standard for detection of antibiotic resistance and the only one available in most countries. However, there are important limitations for its use as apart from challenges in the management of logistics in the majority of countries (pretherapeutic) testing is not reimbursed.

Molecular testing for AST in most countries is neither available nor reimbursed with the exception in few Asian countries (Korea, Japan). Molecular testing in stool samples although reported from some centers as an attractive way to be included in non -invasive testing of antibiotic resistance is at present insufficiently validated for use in clinical practice and not ready for a general implementation.

Conclusions and future directions

Our study documents high rates of *H. pylori* AR, which are further increasing at pace in many parts of the world. The greatest concerns relate to the use of clarithromycin and levofloxacin, and require urgent revision of current therapeutic strategies. The options are to either select individually effective antibiotics via regular use of AST, or to use empirical therapies that are minimally or not affected by AR. In view of these circumstances, it is unclear why clarithromycin-resistant *H. pylori* was removed from the World Health Organization's list of high-priority organisms [53] for which urgent additional research is needed [54].

Effective antibiotics for first-line treatment and alternatives in case of first-line failure are still missing in certain parts of the world and need to be made universally available. Bismuth-based combinations, which are currently the least influenced by AR, are not yet available in many countries[55, 56, 57]. There is an urgent need for the supply of such therapies to keep eradication effective and to stop further uncontrolled progression of AR. Integrating antimicrobial stewardship measures into *H. pylori* management could reduce antimicrobial resistance, improve patient outcomes, optimize the use of effective antibiotics and lower healthcare costs [53]. There is a need to extend measures for AR surveillance measures which are running only in 4/26 countries surveyed.

In this context, the identification of novel combinations and/or doses of existing drugs or the inclusion of novel drugs in eradication regimens deserves sustained effort. The introduction of new potent acid suppressive agents has already influenced development positively, and the search for novel selective anti-*H. pylori* agents and vaccinations continue to be important goals for the immediate future.

International and national guidelines remain important drivers in setting the basic framework for the management of *H. pylori* infections. However, regional surveillance of AR development and monitoring the efficacy of locally used therapies needs to be an integral part of future guidelines in order to deliver the most appropriate treatment to patients.

The information collected in our survey aims to raise awareness among health care authorities around the world for the establishment of programs for *H. pylori* AR testing and surveillance, to pay attention to the availability of effective and safe drugs in *H. pylori*.

Tables 1 *H. pylori* antibiotic resistance (%) at continental (1) and country (2) level from 2018- 2023 according to literature references and personal data from experts.

	Clarithromycin	Levofloxacin	Metronidazole	Amoxicillin	Rifampicin	Tetracycline	Ciprofloxacin
Africa	13.6 - 66,7	20 – 65.7	62.7- 100	30- 97.1	90	2.9 - 100	17 - 100
North America	16.7 - 19	42.6	29.3 - 35	1.1	<1%	1.7	
South America	14.4 – 31.3	13.5 - 29	54	2.7		0.7	
Asia-Pacific	7.7 – 92.1	3.3 – 65.6	4.2 – 81.7	0 - 50	22.8	0 - 16.1	37
Europe	12 – 22.4	13 - 20.3	17 – 62.4	0 – 3.5	0 – 4.3	0 – 0.5	

Table 2 *H. pylori* antibiotic resistance (%) at continental (1) and country (2) level from 2018- 2023 according to literature references and personal data from experts.

	Clarithromycin	Levofloxacin	Metronidazole	Amoxicillin	Rifampicin	Tetracycline	Ciprofloxacin
Africa							
Egypt [58, 59, 60]	40 – 52.8	20	100	81.9 - 95	90	25 – 37.5	17 – 41.7
South Africa	No current data	No current data	No current data	No current data	No current data	No current data	No current data
Nigeria [61, 62]	25	nd	100	30 – 90.8	nd	13 - 100	100
Tanzania [63]	28.7	58.8	nd	nd	nd	nd	nd
Morocco [64]	14	nd	62.7	nd	nd	nd	nd
Cameroon [65]	13.6	nd	97.9	97.1	nd	2.9	nd
DRC [66, 67]	23.5	65.7	90.2	34.3	nd	4	nd
Zambia [68]	28	nd	nd	nd	nd	nd	nd
Ethiopia [69]	66.7	nd	91.7	91.7	nd	37.5	66.7
North America							
Canada [70]	19	nd	35	nd	nd	nd	nd
United States [71]	16.7	42.6	29.3	1.1	Nd	1.7	nd
Mexico [72, 73]	12 – 32.2	18.5	58	1.8	nd	nd	nd
South America							
Brazil *[74, 75]*	14.4 – 16,9	13.5	54	nd	nd	nd	nd
Chile [76] [77]	26 – 31.3	29	2.7	2.7	nd	0.7	nd
Asia Pacific							
Australia	no current data	no current data	no current data	no current data	no current data	no current data	no current data
Cambodia [78]	27,8	50	78,6	0	nd	0	nd
China [79]	34	35	78	3	nd	2	nd
Iran [22, 80, 81]	20,1	17,7	57,9	15,9	21,3	12,2	22,6
Japan [82, 83]	35,5	nd	4,2	2,7	nd	nd	nd
Korea [84]	17,8	37	29,5	9,5	nd	0	37
Malaysia [85]	14,8	3,3	nd	0	nd	nd	nd
Myanmar [86]	7,7	33,8	80	4,6	nd	0	nd
Singapore [87]	13,7 - 16,6	16,6 -16,9	nd	7 – 7,2	nd	0	nd
Thailand [88]	15.6	nd	34.1	0	nd	0	nd

Vietnam [89, 90]	61.8 – 92.1	31.6 – 41,8	14.5 – 76,3	27.2 - 50	nd	0	nd
India [91, 92, 93]	8.7 - 45	11.5 – 65.6	27.2 – 81.7	0 - 24	nd	0 – 5.3	nd
Europe							
France [94]	20.9 - 23	17.6 – 18.1	58;6 – 47.5	0 - 0	0.9 – 0.7	0 - 0	nd
Germany [95]	17.4	20.3	17.4	0	4.3	0	nd
Italy [96, 97, 98]	37.8	19.2 – 25.6	16.4 - 33.6	1.6	nd	0	nd
Spain [51, 99, 100, 101, 102]	12 – 15 adults 45 – 53 children	13 - 17 adults 7.9 children	24 – 32 adults 6.3 – 16 children	0 – 3.5 adults 1 – 2 children	nd	0 – 0.5 adults nd children	nd
United Kingdom	No current data	No current data	No current data	No current data	No current data	No current data	No current data

Table 3 **Availability of antibiotics and acid suppressants used in *Helicobacter pylori* eradication regimens in various countries. (A) available and reimbursed, (B) available and not reimbursed, and (C) not available**

Countries in Africa	**Egypt**	**South Africa**	**Nigeria**	**Democratic Republic of Congo**			
Antibiotics and acid suppressants available/ treatment regimens							
PPIs	A	A	A	B			
PCABs	A	C	C	C			
Clarithromycin	A	C	A	B			
Amoxicillin	A	A	A	B			
Metronidazole	A	A	A	B			
Tetracycline	C	C	A	B			
Levofloxacin	A	A	A	B			
Tinidazole	A	C	B	B			
Bismuth	A	A	C	B			
Rifabutin	C	C	C	C			
Countries in Asia Pacific	**Vietnam**	**Singapore**	**Thailand**	**Malaysia**	**Cambodia**	**Indonesia**	**Myanmar**
Antibiotics and acid suppressants available/ treatment regimens							
PPIs	A	A	A	A	A	A	B
PCABs	C	A	A/B depending on reimbursement scheme	A	B	B	C
Clarithromycin	A	A	A	A	A	B	B
Amoxicillin	A	A	A	A	A	A	B
Metronidazole	A	A	A	A	A	A	B
Tetracycline	B	A	A	C	A	A	B
Levofloxacin	A	A	A	B	A	A	B
Tinidazole	A	C	A	C	A	C	B
Bismuth	A	A	A/B depending on reimbursement scheme	C	B	C	B
Rifabutin	C	B	C	B	C	B	C
Countries Asia Pacific (continued)	**China**	**Korea**	**Japan**	**Iran**	**Australia**		
Antibiotics and acid suppressants available/ treatment regimens							
PPIs	A	A	A	A	A		
PCABs	A	A	A	C	C		
Clarithromycin	A	A	A	B	A		
Amoxicillin	A	A	A	A	A		
Metronidazole	A	A	A	A	A		
Tetracycline	B	A	B	A	A		
Levofloxacin	A	A	B	B	A		
Tinidazole	B	C	B	C	C		
Bismuth	A	C	C	A	B		
Rifabutin	B	A	B	C	A		
Countries in Europe	**France**	**Germany**	**Italy**	**Spain**	**United Kingdom**		
Antibiotics and acid suppressants available/ treatment regimens							
PPIs	A	A	A	A	A		
PCABs	C	C	C	C	C		
Clarithromycin	A	A	A	A	A		
Amoxicillin	A	A	A	A	A		
Metronidazole	A	A	A	A	A		
Tetracycline	A	A	A	A	A		
Levofloxacin	A	A	A	A	A		
Tinidazole	A	C	A	A	A		
Bismuth	A	A	A	A	A		
Rifabutin	A	A	A	A	A		
Countries in North America	**Canada**	**United States**					
Antibiotics and acid suppressants available/ treatment regimens							
PPIs	A	A					
PCABs	C	A					
Clarithromycin	A	A					
Amoxicillin	A	A					
Metronidazole	A	A					
Tetracycline	A	A					
Levofloxacin	A	A					
Tinidazole	A	A					
Bismuth	A	A					
Rifabutin	A	A					
Countries in South America	**Brazil**	**Chile**	**Mexico**				
Antibiotics and acid suppressants available/ treatment regimens							
PPIs	A	A	A				
PCABs	B	C	A				
Clarithromycin	A	A	A				
Amoxicillin	A	A	A				
Metronidazole	A	A	A				
Tetracycline	A	A	A				
Levofloxacin	A	A	A				
Tinidazole	A	C	A				
Bismuth	C	A	A				
Rifabutin	C	B	C				

Table 4 Reimbursement and availability for different methods of Antibiotic Susceptibility Testing according to health policies in various countries

Countries in Africa	**Egypt**	**South Africa**	**Nigeria**	**Democratic Republic Congo**			
Antibiotic Susceptibility Testing availability and reimbursement							
Culture based	B	B	B	B			
PCR- based	C***	C***	B	C***			
NGS- based	C***	C***	C***	C***			
Countries in Asia Pacific	**Vietnam**	**Singapore**	**Thailand**	**Malaysia**	**Cambodia**	**Indonesia**	**Myanma**
Culture based	B	B	B	B	C	B	B
PCR- based	C***	B	B	B	C***	B	B
NGS- based	C***	C***	C***	C***	C***	C***	C***
Countries in Asia Pacific (continued)	**China**	**Korea**	**Japan**	**Iran**	**Australia**		
Culture based	B	C	B	C	A		
PCR- based	B	A	A*	C***	C***		
NGS- based	C***	C***	C***	C***	C***		
Countries in Europe	**France**	**Germany**	**Italy**	**Spain**	**United Kingdom**		
Culture based	A	A	A	A	A		
PCR- based	A	B	B	A	C***		
NGS- based	B	C***	C***	C***	C***		
Countries in North America	**Canada**	**United States**	**Mexico**				
Culture based	A	A	B				
PCR- based	B	B	B				
NGS- based	B	B	C***				
Countries in South America	**Brazil**	**Chile**					
Culture based	C	A**					
PCR- based	C	C					
NGS- based	C***	C***					

(A) available and reimbursed, (B) available but not reimbursed, and (C) not available *restricted to Clarithromycin, **restricted to Metronidazole, *** not available does not exclude the availability of technologies in countries (e.g., reference centers or scientific laboratories) but not available for use in clinical practice.

Conflicts of interest

All authors declare no conflicts of interest.

Ethics statement

For this study no human participants or animal experiments where performed. All data used were collected through a survey or extracted from published manuscripts.

REFERENCES

1 Sugano K, Tack J, Kuipers EJ, Graham DY, El-Omar EM, Miura S*, et al.* Kyoto global consensus report on Helicobacter pylori gastritis. Gut 2015;**64**:1353-67.

2 Malfertheiner P, Megraud F, O'Morain CA, Gisbert JP, Kuipers EJ, Axon AT*, et al.* Management of Helicobacter pylori infection-the Maastricht V/Florence Consensus Report. Gut 2017;**66**:6-30.

3 Bujanda L, Nyssen OP, Ramos J, Bordin DS, Tepes B, Perez-Aisa A*, et al.* Effectiveness of Helicobacter pylori Treatments According to Antibiotic Resistance. Am J Gastroenterol 2024;**119**:646-54.

4 Tshibangu-Kabamba E, Yamaoka Y. Helicobacter pylori infection and antibiotic resistance - from biology to clinical implications. Nat Rev Gastroenterol Hepatol 2021;**18**:613-29.

5 Megraud F, Graham DY, Howden CW, Trevino E, Weissfeld A, Hunt B*, et al.* Rates of Antimicrobial Resistance in Helicobacter pylori Isolates From Clinical Trial Patients Across the US and Europe. Am J Gastroenterol 2023;**118**:269-75.

6 Malfertheiner P, Megraud F, Rokkas T, Gisbert JP, Liou JM, Schulz C*, et al.* Management of Helicobacter pylori infection: the Maastricht VI/Florence consensus report. Gut 2022.

7 Moss SF, Dang LP, Chua D, Sobrado J, Zhou Y, Graham DY. Comparable Results of Helicobacter pylori Antibiotic Resistance Testing of Stools vs Gastric Biopsies Using Next-Generation Sequencing. Gastroenterology 2022;**162**:2095-7 e2.

8 Moss SF, Shah SC, Tan MC, El-Serag HB. Evolving Concepts in Helicobacter pylori Management. Gastroenterology 2024;**166**:267-83.

9 Katelaris P, Hunt R, Bazzoli F, Cohen H, Fock KM, Gemilyan M*, et al.* Helicobacter pylori World Gastroenterology Organization Global Guideline. J Clin Gastroenterol 2023;**57**:111-26.

10 Fallone CA, Moss SF, Malfertheiner P. Reconciliation of Recent Helicobacter pylori Treatment Guidelines in a Time of Increasing Resistance to Antibiotics. Gastroenterology 2019;**157**:44-53.

11 Tacconelli E, Carrara E, Savoldi A, Harbarth S, Mendelson M, Monnet DL*, et al.* Discovery, research, and development of new antibiotics: the WHO priority list of antibiotic-resistant bacteria and tuberculosis. Lancet Infect Dis 2018;**18**:318-27.

12 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.

13 https://www.who.int/publications/i/item/9789240093461. 2024.

14 Megraud F. Antibiotic Resistance Is the Key Element in Treatment of Helicobacter pylori Infection. Gastroenterology 2018;**155**:1300-2.

15 Matsuzaki J, Suzuki H, Nishizawa T, Hirata K, Tsugawa H, Saito Y*, et al.* Efficacy of sitafloxacin-based rescue therapy for Helicobacter pylori after failures of first- and second-line therapies. Antimicrob Agents Chemother 2012;**56**:1643-5.

16 Sue S, Shibata W, Sasaki T, Kaneko H, Irie K, Kondo M*, et al.* Randomized trial of vonoprazan-based versus proton-pump inhibitor-based third-line triple therapy with sitafloxacin for Helicobacter pylori. J Gastroenterol Hepatol 2019;**34**:686-92.

17 Hong TC, El-Omar EM, Kuo YT, Wu JY, Chen MJ, Chen CC*, et al.* Primary antibiotic resistance of Helicobacter pylori in the Asia-Pacific region between 1990 and 2022: an updated systematic review and meta-analysis. Lancet Gastroenterol Hepatol 2024;**9**:56-67.

18 Megraud F, Bruyndonckx R, Coenen S, Wittkop L, Huang TD, Hoebeke M*, et al.* Helicobacter pylori resistance to antibiotics in Europe in 2018 and its relationship to antibiotic consumption in the community. Gut 2021;**70**:1815-22.

19 Otani K, Hang DV, Pittayanon R, Liu H, Chuah KH, Hsiang J*, et al.* Asia-Pacific Survey on the Management of Helicobacter pylori Infection. J Gastroenterol Hepatol 2024.

20 Smith SI, Schulz C, Ugiagbe R, Ndip R, Dieye Y, Leja M*, et al.* Helicobacter pylori Diagnosis and Treatment in Africa: The First Lagos Consensus Statement of the African Helicobacter and Microbiota Study Group. Dig Dis 2024;**42**:240-56.

21 Liou JM, Jiang XT, Chen CC, Luo JC, Bair MJ, Chen PY*, et al.* Second-line levofloxacin-based quadruple therapy versus bismuth-based quadruple therapy for Helicobacter pylori eradication and long-term changes to the gut microbiota and antibiotic resistome: a multicentre, open-label, randomised controlled trial. Lancet Gastroenterol Hepatol 2023;**8**:228-41.

22 Salahi-Niri A, Nabavi-Rad A, Monaghan TM, Rokkas T, Doulberis M, Sadeghi A*, et al.* Global prevalence of Helicobacter pylori antibiotic resistance among children in the world health organization regions between 2000 and 2023: a systematic review and meta-analysis. BMC Med 2024;**22**:598.

23 Hu Y, Zhang ZY, Wang F, Zhuang K, Xu X, Liu DS*, et al.* Effects of amoxicillin dosage on cure rate, gut microbiota, and antibiotic resistome in vonoprazan and amoxicillin dual therapy for Helicobacter pylori: a multicentre, open-label, non-inferiority randomised controlled trial. Lancet Microbe 2024:100975.

24 Jiang Y, Zhang R, Fang Y, Zhao R, Fu Y, Ren P*, et al.* P-CAB versus PPI in the eradication of Helicobacter pylori: a systematic review and network meta-analysis. Therap Adv Gastroenterol 2024;**17**:17562848241241223.

25 Jaka H, Rhee JA, Ostlundh L, Smart L, Peck R, Mueller A*, et al.* The magnitude of antibiotic resistance to Helicobacter pylori in Africa and identified mutations which confer resistance to antibiotics: systematic review and meta-analysis. BMC Infect Dis 2018;**18**:193.

26 Hu J, Mei H, Su NY, Sun WJ, Zhang DK, Fan LL*, et al.* Eradication rates of Helicobacter pylori in treatment-naive patients following 14-day vonoprazan-amoxicillin dual therapy: A multicenter randomized controlled trial in China. Helicobacter 2023;**28**:e12970.

27 Du RC, Hu YX, Ouyang Y, Ling LX, Xu JY, Sa R*, et al.* Vonoprazan and amoxicillin dual therapy as the first-line treatment of Helicobacter pylori infection: A systematic review and meta-analysis. Helicobacter 2024;**29**:e13039.

28 Gisbert JP. Rifabutin for the Treatment of Helicobacter Pylori Infection: A Review. Pathogens 2020;**10**.

29 Camargo MC, Garcia A, Riquelme A, Otero W, Camargo CA, Hernandez-Garcia T*, et al.* The problem of Helicobacter pylori resistance to antibiotics: a systematic review in Latin America. Am J Gastroenterol 2014;**109**:485-95.

30 Reyes D, Ortiz J, Fuentes-Lopez E, Budnik S, Gandara V, Gallardo A*, et al.* Quadruple therapies are superior to standard triple therapy for Helicobacter pylori first-line eradication in Chile. Gastroenterol Hepatol 2022;**45**:515-23.

31 Parra-Sepulveda C, Merino JS, Saez-Carrillo K, Gonzalez C, Garcia-Cancino A. Antibiotic Resistance Surveillance of Helicobacter Pylori at the Biobio Region (Chile) in a Decade. Arq Gastroenterol 2019;**56**:361-6.

32 Nyssen OP, Bordin D, Tepes B, Perez-Aisa A, Vaira D, Caldas M*, 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.

33 Malfertheiner P, Bazzoli F, Delchier JC, Celinski K, Giguere M, Riviere M*, et al.* Helicobacter pylori eradication with a capsule containing bismuth subcitrate potassium, metronidazole, and tetracycline given with omeprazole versus clarithromycin-based triple therapy: a randomised, open-label, non-inferiority, phase 3 trial. Lancet 2011;**377**:905-13.

34 Nyssen OP, Perez-Aisa A, Castro-Fernandez M, Pellicano R, Huguet JM, Rodrigo L*, et al.* European Registry on Helicobacter pylori management: Single-capsule bismuth quadruple therapy is effective in real-world clinical practice. United European Gastroenterol J 2021;**9**:38-46.

35 Autoren, Collaborators. [Not Available]. Z Gastroenterol 2023;**61**:544-606.

36 Liu WZ, Xie Y, Lu H, Cheng H, Zeng ZR, Zhou LY*, et al.* Fifth Chinese National Consensus Report on the management of Helicobacter pylori infection. Helicobacter 2018;**23**:e12475.

37 Rasschaert G, Ntounda R. 2023 Belgian consensus on Helicobacter pylori treatment, yet another (Belgian) guideline. Acta Gastroenterol Belg 2023;**86**:581.

38 Zhou L, Lu H, Song Z, Lyu B, Chen Y, Wang J*, et al.* 2022 Chinese national clinical practice guideline on Helicobacter pylori eradication treatment. Chin Med J (Engl) 20 22;**135**:2899-910.

39 Alsohaibani F, Peedikayil M, Alshahrani A, Somily A, Alsulaiman R, Azzam N*, et al.* Practice guidelines for the management of Helicobacter pylori infection: The Saudi H. pylori Working Group recommendations. Saudi J Gastroenterol 2023;**29**:326-46.

40 Chey WD, Howden CW, Moss SF, Morgan DR, Greer KB, Grover S*, et al.* ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. Am J Gastroenterol 2024;**119**:1730-53.

41 Coelho LGV, Marinho JR, Genta R, Ribeiro LT, Passos M, Zaterka S*, et al.* Ivth Brazilian Consensus Conference on Helicobacter Pylori Infection. Arq Gastroenterol 2018;**55**:97-121.

42 Fallone CA, Chiba N, van Zanten SV, Fischbach L, Gisbert JP, Hunt RH*, et al.* The Toronto Consensus for the Treatment of Helicobacter pylori Infection in Adults. Gastroenterology 2016;**151**:51-69 e14.

43 Gisbert JP, Alcedo J, Amador J, Bujanda L, Calvet X, Castro-Fernandez M*, et al.* V Spanish Consensus Conference on Helicobacter pylori infection treatment. Gastroenterol Hepatol 2022;**45**:392-417.

44 Leung WK, Cheung KS, Sham PCO, Tang RSY, Loo CK, Hsu ASJ*, et al.* Consensus recommendations for the screening, diagnosis, and management of Helicobacter pylori infection in Hong Kong. Hong Kong Med J 2023;**29**:532-41.

45 Quach DT, Mai BH, Tran MK, Dao LV, Tran HV, Vu KT*, et al.* Vietnam Association of Gastroenterology (VNAGE) consensus on the management of Helicobacter pylori infection. Front Med (Lausanne) 2022;**9**:1065045.

46 Jaron K, Pietrzak A, Daniluk J, Adrych K, Gasiorowska A, Skrzydlo-Radomanska B*, et al.* Diagnostic and therapeutic recommendations on Helicobacter pylori infection.

Recommendations of the Working Group of the Polish Society of Gastroenterology. Prz Gastroenterol 2023;**18**:225-48.

47 Malfertheiner P, Megraud F, Rokkas T, Gisbert JP. Empiric use of standard triple therapy in Helicobacter pylori eradication does not require readjustment in the clarithromycin resistance cut-off point. Gut 2024;**73**:708-9.

48 Vasapolli R, Ailloud F, Spiessberger B, Malfertheiner P, Suerbaum S, Schulz C. Real-Time Assessment of H. pylori Infection to Guide Molecular Antibiotic Resistance Testing: A Combined Endoscopy-Gastric Juice Analysis Approach. Aliment Pharmacol Ther 2024.

49 Hulten KG, Genta RM, Kalfus IN, Zhou Y, Zhang H, Graham DY. Comparison of Culture With Antibiogram to Next-Generation Sequencing Using Bacterial Isolates and Formalin-Fixed, Paraffin-Embedded Gastric Biopsies. Gastroenterology 2021;**161**:1433-42 e2.

50 Fan CJ, Li Z, Zhai LL, Wang H, Zhao XL, Xie DL*, et al.* Diagnostic accuracy of a real-time PCR assay for detection of Helicobacter pylori and resistance to clarithromycin and levofloxacin directly from stool. Eur Rev Med Pharmacol Sci 2024;**28**:3836-40.

51Bujanda L, Nyssen OP, Vaira D, Saracino IM, Fiorini G, Lerang F*, et al.* Antibiotic Resistance Prevalence and Trends in Patients Infected with Helicobacter pylori in the Period 2013-2020: Results of the European Registry on H. pylori Management (Hp-EuReg). Antibiotics (Basel) 2021;**10**.

52 Goebel MC, Trautner BW, Grigoryan L. The Five Ds of Outpatient Antibiotic Stewardship for Urinary Tract Infections. Clin Microbiol Rev 2021;**34**:e0000320.

53 https://iris.who.int/bitstream/handle/10665/329404/9789241515481-eng.pdf. 2019.

54 Hasso-Agopsowicz M, Hwang A, Hollm-Delgado MG, Umbelino-Walker I, Karron RA, Rao R*, et al.* Identifying WHO global priority endemic pathogens for vaccine research and development (R&D) using multi-criteria decision analysis (MCDA): an objective of the Immunization Agenda 2030. EBioMedicine 2024;**110**:105424.

55 Malfertheiner P. Infection: Bismuth improves PPI-based triple therapy for H. pylori eradication. Nat Rev Gastroenterol Hepatol 2010;**7**:538-9.

56 Han Z, Li Y, Kong Q, Liu J, Wang J, Wan M*, et al.* Efficacy of bismuth for antibiotic-resistant Helicobacter pylori strains eradication: A systematic review and meta-analysis. Helicobacter 2022;**27**:e12930.

57 Hsu PI, Tsai FW, Kao SS, Hsu WH, Cheng JS, Peng NJ*, et al.* Ten-Day Quadruple Therapy Comprising Proton Pump Inhibitor, Bismuth, Tetracycline, and Levofloxacin is More Effective than Standard Levofloxacin Triple Therapy in the Second-Line Treatment of Helicobacter pylori Infection: A Randomized Controlled Trial. Am J Gastroenterol 2017;**112**:1374-81.

58 Asaad AM, El-Azab G, Abdelsameea E, Elbahr O, Kamal A, Abdel-Samiee M*, et al.* Susceptibility patterns and virulence genotypes of Helicobacter pylori affecting eradication therapy outcomes among Egyptian patients with gastroduodenal diseases. World J Gastroenterol 2023;**29**:2950-60.

59 Metwally M, Ragab R, Abdel Hamid HS, Emara N, Elkholy H. Helicobacter pylori Antibiotic Resistance in Egypt: A Single-Center Study. Infect Drug Resist 2022;**15**:5905-13.

60 Al-Eraky DM, Helmy OM, Ragab YM, Abdul-Khalek Z, El-Seidi EA, Ramadan MA. Prevalence of CagA and antimicrobial sensitivity of H. pylori isolates of patients with gastric cancer in Egypt. Infect Agent Cancer 2018;**13**:24.

61 Palamides P, Jolaiya T, Idowu A, Loell E, Onyekwere C, Ugiagbe R*, et al.* Helicobacter pylori patient isolates from South Africa and Nigeria differ in virulence factor pathogenicity profile and associated gastric disease outcome. Sci Rep 2020;**10**:11409.

62 Bello AK, Borodo MM, Yakasai AM, Tukur AD. Helicobacter pylori antibiotic sensitivity pattern in dyspeptic patients in Kano, Nigeria. S Afr J Infect Dis 2019;**34**:125.

63 Jaka H, Ruttgerodt N, Bohne W, Mueller A, Gross U, Kasang C*, et al.* Helicobacter pylori Mutations Conferring Resistance to Fluoroquinolones and Clarithromycin among Dyspeptic Patients Attending a Tertiary Hospital, Tanzania. Can J Gastroenterol Hepatol 2019;**2019**:8481375.

64 Essaidi I, Bounder G, Jouimyi RM, Boura H, Elyounsi I, Kheir FZ*, et al.* Comparative Study of Helicobacter Pylori Resistance to Clarithromycin and Metronidazole and Its Association with Epidemiological Factors in A Moroccan Population. Asian Pac J Cancer Prev 2022;**23**:2755-61.

65 Kouitcheu Mabeku LB, Eyoum Bille B, Tepap Zemnou C, Tali Nguefack LD, Leundji H. Broad spectrum resistance in Helicobacter pylori isolated from gastric biopsies of patients with dyspepsia in Cameroon and efflux-mediated multiresistance detection in MDR isolates. BMC Infect Dis 2019;**19**:880.

66 Kabamba ET-. Personal communication. wwwww

67Tshibangu-Kabamba E, Ngoma-Kisoko PJ, Tuan VP, Matsumoto T, Akada J, Kido Y*, et al.* Next-Generation Sequencing of the Whole Bacterial Genome for Tracking Molecular Insight into the Broad-Spectrum Antimicrobial Resistance of Helicobacter pylori Clinical Isolates from the Democratic Republic of Congo. Microorganisms 2020;**8**.

68 Kebotsamang T, Munkombwe D, Bwalya L, Kelly P, Kayamba V. Prevalence of Clarithromycin-Resistant Helicobacter pylori Strains in Zambia: A Sub-Saharan African Country. Dig Dis 2024;**42**:154-60.

69 Erkihun M, Chanie DN, Siraj YA. Antimicrobial-Resistance Profile of Helicobacter pylori, Obtained from Endoscopic Patients in Bahir Dar, North West Ethiopia. Can J Infect Dis Med Microbiol 2023;**2023**:7326288.

70 Lauren Lindsey DQ, Taylor Cromarty, Ali Assi, Sander Veldhuyzen van Zanten, Karen Goodman. Antibiotic susceptibility of Helicobacter pylori in Arctic Canadian Indigenous communities. International Journal of Epidemiology 2021;**50**.

71 Ho JJC, Navarro M, Sawyer K, Elfanagely Y, Moss SF. Helicobacter pylori Antibiotic Resistance in the United States Between 2011 and 2021: A Systematic Review and Meta-Analysis. Am J Gastroenterol 2022;**117**:1221-30.

72 Camorlinga-Ponce M, Gomez-Delgado A, Aguilar-Zamora E, Torres RC, Giono-Cerezo S, Escobar-Ogaz A*, et al.* Phenotypic and Genotypic Antibiotic Resistance Patterns in

Helicobacter pylori Strains From Ethnically Diverse Population in Mexico. Front Cell Infect Microbiol 2020;**10**:539115.

73 Alarcon-Millan J, Bonilla-Delgado J, Fernandez-Tilapa G, Nieto-Velazquez NG, Sierra-Martinez M, Alvarado-Castro VM*, et al.* Helicobacter pylori Virulence Factors and Clarithromycin Resistance-Associated Mutations in Mexican Patients. Pathogens 2023;**12**.

74 Benigno T, Ribeiro Junior HL, Azevedo OGR, Pinheiro RF, Oliveira RTG, Maciel FS*, et al.* Clarithromycin-resistant H. pylori primary strains and virulence genotypes in the Northeastern region of Brazil. Rev Inst Med Trop Sao Paulo 2022;**64**:e47.

75 Sanches BS, Martins GM, Lima K, Cota B, Moretzsohn LD, Ribeiro LT*, et al.* Detection of Helicobacter pylori resistance to clarithromycin and fluoroquinolones in Brazil: A national survey. World J Gastroenterol 2016;**22**:7587-94.

76 Arenas A, Serrano C, Quinones L, Harris P, Sandoval M, Lavanderos M*, et al.* High prevalence of clarithromycin resistance and effect on Helicobacter pylori eradication in a population from Santiago, Chile: cohort study and meta-analysis. Sci Rep 2019;**9**:20070.

77 Gonzalez-Hormazabal P, Arenas A, Serrano C, Pizarro M, Fuentes-Lopez E, Arnold J*, et al.* Prevalence of Helicobacter pylori Antimicrobial Resistance Among Chilean Patients. Arch Med Res 2021;**52**:529-34.

78 Aumpan N, Vilaichone RK, Gamnarai P, Sanglutong L, Ratanachu-Ek T, Mahachai V*, et al.* Prevalence and Antibiotic Resistance Patterns of Helicobacter pylori Infection in Koh Kong, Cambodia. Asian Pac J Cancer Prev 2020;**21**:1409-13.

79 Chen J, Li P, Huang Y, Guo Y, Ding Z, Lu H. Primary Antibiotic Resistance of Helicobacter pylori in Different Regions of China: A Systematic Review and Meta-Analysis. Pathogens 2022;**11**.

80 Khademi F, Sahebkar A. An Updated Systematic Review and Meta-Analysis on the Helicobacter pylori Antibiotic Resistance in Iran (2010-2020). Microb Drug Resist 2020;**26**:1186-94.

81Sholeh M, Maleki F, Krutova M, Bavari S, Golmoradi R, Sadeghifard N*, et al.* The increasing antimicrobial resistance of Helicobacter pylori in Iran: A systematic review and meta-analysis. Helicobacter 2020;**25**:e12730.

82Sugano K. Personal communication.wwww

83Okimoto T, Ando T, Sasaki M, Ono S, Kobayashi I, Shibayama K*, et al.* Antimicrobial-resistant Helicobacter pylori in Japan: Report of nationwide surveillance for 2018-2020. Helicobacter 2024;**29**:e13028.

84 Lee JH, Ahn JY, Choi KD, Jung HY, Kim JM, Baik GH*, et al.* Nationwide antibiotic resistance mapping of Helicobacter pylori in Korea: A prospective multicenter study. Helicobacter 2019;**24**:e12592.

85 Puah SM, Goh KL, Ng HK, Chua KH. Current status of Helicobacter pylori resistance to Clarithromycin and Levofloxacin in Malaysia-findings from a molecular based study. PeerJ 2021;**9**:e11518.

86 Subsomwong P, Doohan D, Fauzia KA, Akada J, Matsumoto T, Yee TT*, et al.* Next-Generation Sequencing-Based Study of Helicobacter pylori Isolates from Myanmar and Their Susceptibility to Antibiotics. Microorganisms 2022;**10**.

87 Ang D, Koo SH, Chan YH, Tan TY, Soon GH, Tan CK*, et al.* Clinical trial: seven-day vonoprazan- versus 14-day proton pump inhibitor-based triple therapy for first-line Helicobacter pylori eradication. Aliment Pharmacol Ther 2022;**56**:436-49.

88 Poonyam P, Chotivitayatarakorn P, Vilaichone RK. High Effective of 14-Day High-Dose PPI- Bismuth-Containing Quadruple Therapy with Probiotics Supplement for Helicobacter Pylori Eradication: A Double Blinded-Randomized Placebo-Controlled Study. Asian Pac J Cancer Prev 2019;**20**:2859-64.

89 Van Thieu H, Duc NM, Nghi BTD, Van Bach N, Khoi HH, Tien VNT*, et al.* Antimicrobial Resistance and the Successful Eradication of Helicobacter pylori-Induced Gastroduodenal Ulcers in Vietnamese Children. Med Arch 2021;**75**:112-5.

90 Tran TT, Nguyen AT, Quach DT, Pham DT, Cao NM, Nguyen UT*, et al.* Emergence of amoxicillin resistance and identification of novel mutations of the pbp1A gene in Helicobacter pylori in Vietnam. BMC Microbiol 2022;**22**:41.

91 Arfi S, Sharma P, Kumar M, Mehra S, Das K, Das R*, et al.* Antibiotic susceptibility pattern of Helicobacter pylori against eight antibiotics: A study from North India. Helicobacter 2024;**29**:e13093.

92 Datta S, Khyriem AB, Lynrah KG, Marbaniang E, Topno N. Antimicrobial resistance pattern of Helicobacter pylori in patients evaluated for dyspeptic symptoms in North-Eastern India with focus on detection of clarithromycin resistance conferring point mutations A2143G and A2142G within bacterial 23S rRNA gene. Indian J Med Microbiol 2024;**50**:100652.

93 Dutta S, Jain S, Das K, Verma P, Som A, Das R. Primary antibiotic resistance of Helicobacter pylori in India over the past two decades: A systematic review. Helicobacter 2024;**29**:e13057.

94 2025.wwwwwww

95 L.Macke RV, ,U.Lang, K.M.Bronny,, K. Lundra,, T. Burrell,, C. Werner,, N. Conzelmann, B. Heidrich,, K. Finger KU, A. Hapfelmeier,, M. Vieth1, B. Spießberger, S. Suerbaum, M. Gerhard, C. Schulz. HelicoPTER – lokale Prävalenz, Therapieerfolg und Antibiotikaresistenz der Helicobacter pylori- Infektion in Deutschland. Z Gastroenterol 2023;**61**:e366.

96 Saracino IM, Fiorini G, Zullo A, Pavoni M, Saccomanno L, Vaira D. Trends in Primary Antibiotic Resistance in H. pylori Strains Isolated in Italy between 2009 and 2019. Antibiotics (Basel) 2020;**9**.

97 Losurdo G, Giorgio F, Pricci M, Girardi B, Russo F, Riezzo G*, et al.* Helicobacter pylori Primary and Secondary Genotypic Resistance to Clarithromycin and Levofloxacin Detection in Stools: A 4-Year Scenario in Southern Italy. Antibiotics (Basel) 2020;**9**.

98 Palmitessa V, Monno R, Panarese A, Cuppone R, Burattini O, Marangi S*, et al.* Evaluation of Antibiotic Resistance of Helicobacter pylori Strains Isolated in Bari, Southern

Italy, in 2017-2018 by Phenotypic and Genotyping Methods. Microb Drug Resist 2020;**26**:909-17.

99 Fernandez-Reyes M, Tamayo E, Rojas-Rengifo D, Fischer W, Carrasco-Garcia E, Alonso M*, et al.* Helicobacter pylori pathogenicity and primary antimicrobial resistance in Northern Spain. Eur J Clin Invest 2019;**49**:e13150.

100 Botija G, Garcia Rodriguez C, Recio Linares A, Campelo Gutierrez C, Perez-Fernandez E, Barrio Merino A. [Antibiotic resistances and eradication rates in Helicobacter pylori infection]. An Pediatr (Engl Ed) 2020.

101 Gallardo Padilla M, Leon Falconi JL, Sanchez-Nebreda Arias R, Gomez Santos C, Munoz Egea MDC, Orden Izquierdo E. Impact of the use of molecular techniques (PCR) on detection and eradication success against Helicobacter pylori. An Pediatr (Engl Ed) 2022;**96**:190-5.

102 Mormeneo Bayo S, Belles Belles A, Vazquez Gomez D, Planella de Rubinat M, Bayas Pastor DC, Morales Portillo A*, et al.* Antibiotic Susceptibility and Clarithromycin Resistance Determinants in Helicobacter pylori in the Northeast of Spain: A One-Year Prospective Study. Antibiotics (Basel) 2023;**12**.