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Recent advances in *Helicobacter pylori* diagnosis, treatment, and management: a comprehensive review

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Abstract

This review explores recent advancements in the management of *Helicobacter pylori* infection, a widespread bacterial pathogen associated with various gastrointestinal disorders. The paper discusses improved diagnostic techniques, including molecular methods and non-invasive tests, which have enhanced detection accuracy and antibiotic resistance profiling. New treatment strategies, such as individualized therapy based on antimicrobial susceptibility testing (AST) and the use of probiotics as adjunctive therapy, are examined. The review also addresses the challenges of antibiotic resistance, highlighting the importance of surveillance and monitoring strategies. Novel antibiotic combinations and non-antibiotic therapies, including antibiofilm agents, are presented as potential solutions. The paper concludes by discussing post-treatment follow-up, management of persistent infections, and considerations for special patient populations. Future directions in *Helicobacter pylori* management, including emerging technologies and global eradication efforts, are briefly outlined.

Keywords

Helicobacter pylori, gastrointestinal infections, peptic ulcer disease, antibiotic resistance

Introduction

Overview of *Helicobacter pylori* infection

Helicobacter pylori (*H. pylori*) is a gram-negative, spiral-shaped, microaerophilic bacterium that colonises the human stomach, frequently infects early in childhood, and maintains lifelong infection if left untreated [1–3]. Its ability to survive in an acidic gastric environment is due to ammonia production through urease activity and motility, which allows it to penetrate the protective mucous layer [1, 2].

Infection is observed in approximately 50% of the global population [2, 3]. *H. pylori* infection often remains asymptomatic; however, it can also lead to chronic gastritis and greatly enhance peptic ulcer,

mucosa-associated lymphoid tissue (MALT) lymphoma, and gastric adenocarcinoma, which has led the World Health Organization to categorise it as a Group I carcinogen [2].

The pathogenic capacity of the bacterium is primarily fuelled by two principal virulence factors, cytotoxin-associated gene A (*cagA*) and vacuolating cytotoxin gene A (*vacA*) [1]. The *cagA* gene, which is found on the cag pathogenicity island, encodes proteins of a type IV secretion system that injects bacterial effector proteins, such as *cagA*, directly into gastric epithelial cells. This results in dysregulated host signalling, aberrant cellular proliferation, and inflammation, and is also linked to an increased risk of gastric cancer. *vacA*, however, occurs in all strains but has polymorphisms that regulate cytotoxicity. *vacA* toxins induce host cell damage by causing vacuolation, mitochondrial damage, and disruption of antigen presentation and contribute to immune evasion and pathogenicity [1].

Growing evidence also implicates *H. pylori* in extra-gastric conditions, such as cardiovascular, liver, metabolic, and neurodegenerative disorders, although the mechanisms are unknown. An important mediator is the release of outer membrane vesicles (OMVs), which enable the bacterium to disseminate virulence factors at a distance, thereby impacting host tissues outside the gastric environment. OMVs also facilitate bacterial persistence and are considered vaccine carriers; however, immunogenic heterogeneity and safety are issues [2]. Initially thought of as an infection specific to humans, recent studies have isolated not only *H. pylori* but also several other subspecies of *Helicobacter* in cats and dogs.

Treatment of *H. pylori* infection is increasingly hindered by antibiotic resistance. The bacterium now exhibits heterogeneous resistance patterns, including multidrug and heteroresistance, mainly resulting from chromosomal mutations and possibly also affecting the mechanisms of drug transport, biofilm development, and conversion to resting forms [4]. This emerging resistance underscores the pressing need for alternative therapeutic approaches.

Historical perspective on *Helicobacter pylori* management

Warren and Marshall's 1982 identification of *H. pylori* transformed the epidemiology of peptic ulcer disease. By culturing the bacterium successfully and self-administering it to prove causality, Marshall completed Koch's postulates and firmly confirmed *H. pylori* as a pathogen in the gastrointestinal tract [1]. This discovery changed the medical dogma, converting the treatment of ulcers from symptomatic relief to specific antimicrobial intervention, and opening decades of studies on bacterial pathogenesis and eradication.

Improved diagnostic techniques

Molecular diagnostic techniques

The advent of sophisticated molecular diagnostics has greatly enhanced the identification and characterisation of *H. pylori*, particularly in clinical situations where conventional diagnostic methods are inconclusive or inadequate. Polymerase chain reaction (PCR) of the 16S rRNA gene has been reported to have better sensitivity in gastric biopsy samples than traditional techniques, providing accurate detection, even in patients with prior exposure to proton pump inhibitors (PPIs) or antibiotics [5]. Real-time PCR (RT-PCR) further improves diagnostic accuracy by detecting not only *H. pylori* DNA, but also the determination of mutations that cause antibiotic resistance, specifically clarithromycin- and levofloxacin-resistant mutations through the 23S rRNA and *gyrA* genes [5].

The most promising innovation over the past few years has been the application of next-generation sequencing (NGS) to clinical microbiology. NGS allows whole-genome *H. pylori* genotyping of formalin-fixed, paraffin-embedded gastric biopsies to detect multiple resistance-determining mutations with high sensitivity. Research has found high correlations between mutation profiles detected via NGS and clinical treatment failures, especially in patients with multiple mutations in various genes [5]. In addition, stool-based molecular tests, such as the Amplidiag® *H. pylori* + *ClariR* assay, have yielded very good performance with sensitivity and specificity of 96.3% and 98.7%, respectively, and for simultaneous detection of infection and clarithromycin resistance [5].

New technologies, such as the RPA-CRISPR-Cas12a-based system, have further opened up the boundaries of molecular diagnostics. This *ureB* gene-targeting system is capable of detecting even 50–100 copies of *H. pylori* DNA, provides results in 40 min, and is perfectly suited for fast, resource-poor, or point-of-care testing settings [6]. Concurrently, MALDI-TOF mass spectrometry, which is more traditionally utilised for microbial identification, has also demonstrated utility for the identification of certain *H. pylori* proteins and resistance enzymes, including beta-lactamases and rRNA methyltransferases, thus contributing to both diagnostic and therapeutic decision-making [6].

Advances in non-invasive testing

Among non-invasive tests, the urea breath test (UBT) continues to be a cornerstone for the diagnosis and post-treatment assessment of *H. pylori* infection. Its excellent accuracy, simplicity, and acceptability have made it an established first-line test in many clinical guidelines [7, 8]. The 13C-UBT, as it is non-radioactive, is best reserved for children and pregnant women, while 14C-UBT, although mildly radioactive, is still commonly used among adult populations owing to its availability and low cost [8, 9]. Accuracy of UBT is affected by several factors, such as recent ingestion of PPIs, antibiotics, or bismuth salts, test meal type, dose of isotope, and cut-offs, which require optimal standardisation for performance [7].

The *H. pylori* stool antigen (HpSA) test is now a useful non-invasive option with high accuracy, particularly in groups not amenable to breath testing. HpSA directly detects *H. pylori* antigens in faeces and can be used for both diagnosis and surveillance after eradication. The conventional ELISA-based faecal antigen tests now share the stage with rapid immunochromatographic assays (ICA) that are sensitive (91.3%) and specific (93.5%) but better adapted to field and low-resource level settings [6]. Assays based on monoclonal antibodies have become the standard replacement for polyclonal versions due to their increased specificity and fewer false positives, and are particularly valuable in patients on long-term antisecretory therapy [9].

The decision to use UBT or HpSA usually depends on regional infrastructure, patient population, and costs. Although UBT is still the best non-invasive test in perfect circumstances, it is less expensive and simpler to perform, especially among children and in rural areas [8]. However, stool sample integrity and handling are important to ensure that the test remains accurate, and local strain variation can affect the performance of the test, highlighting the need for local validation [9].

Imaging advances

Endoscopic imaging techniques have evolved significantly, with a central role in the visualisation and grading of *H. pylori*-associated gastric diseases. Linked colour imaging (LCI) and Blue Laser Imaging (BLI) are new imaging modalities that have proven to be better than conventional white light imaging (WLI). These modalities improve mucosal contrast and help visualise minimal mucosal alterations in *H. pylori* gastritis, atrophy, and intestinal metaplasia [5]. Research has demonstrated that LCI provides sensitivity and specificity rates of 83.8–85.4% and 79.5–99.5%, respectively, for the detection of *H. pylori*-associated gastritis, which is superior to WLI in various settings [5].

Confocal Laser Endomicroscopy (CLE) and Narrow-Band Imaging (NBI) have also been used to identify premalignant lesions and early gastric cancers, especially post-*H. pylori* eradication surveillance [6]. They allow in vivo histological evaluation and enhance the diagnostic yield, particularly when combined with magnifying and image-enhancing technology.

Artificial intelligence (AI) and machine learning programs have also entered endoscopic diagnoses. Deep learning algorithms developed on LCI images have shown diagnostic accuracy equivalent to that of experienced endoscopists, with sensitivities and specificities of over 90% in identifying *H. pylori*-related changes [5]. These programmes can potentially standardise interpretation, lower inter-observer variability, and assist less experienced clinicians in providing accurate real-time diagnoses.

With advances in imaging, the emergence of AI, high-definition optics, and functional imaging modalities will serve to increase the diagnostic accuracy and clinical value of endoscopy in the treatment of *H. pylori* infection and associated gastric disease.

New treatment strategies

Individualised therapy for *H. pylori* is given priority because of increased antimicrobial resistance and the weaknesses of empirical treatments. Rocha et al. [10] define phenotypic antimicrobial susceptibility testing (AST) methods like agar dilution, broth microdilution, and E-test as the gold standards for culture-based testing, despite being labor-intensive, invasive, and not generally accessible. Genotypic AST, based on PCR and sequencing, allows for quick identification of mutations in genes such as 23S rRNA (clarithromycin), *gyrA* (fluoroquinolones), and *rdxA/frxA* (metronidazole) and can be performed on non-invasive specimens such as stool, promising a wider application. Alihosseini et al. [11] corroborated this by documenting high resistance-associated mutations in Iranian strains, particularly *A2143G* in 23S rRNA and *gyrA* mutations, with solid evidence for regimens tailored on these profiles. Brennan et al. [12] highlighted that molecular diagnostics such as RT-PCR and droplet digital PCR (ddPCR) permit non-invasive stool-based screening and the identification of heteroresistance, making individually tailored treatment possible without requiring endoscopy. Alfaro et al. [13] further stated that while PCR-based clarithromycin testing is now guideline-recommended, the take-up in primary care continues to be poor, although stool-based PCR may help fill gaps in accessibility. Sun et al. [14] found that molecular testing-based personalised treatment has the same or better outcomes as empirical bismuth quadruple therapy (BQT). Sun et al. [14] also observed that host genetic elements such as *CYP2C19* polymorphisms influence the metabolism of PPI and proposed vonoprazan, a potassium-competitive acid blocker (P-CAB), as a more potent acid suppressor that is not influenced by these polymorphisms.

Probiotics as adjunctive therapy

Probiotic administration concomitant with antibiotics has been investigated as a method to decrease treatment-related side effects and possibly increase eradication effectiveness. Alihosseini et al. [11] reported Iranian in vitro research to demonstrate that some *Lactobacillus* species suppress *H. pylori*, implying a local rationale for probiotic therapy. Rocha et al. [10] summarised a number of clinical trials to demonstrate that *Lactobacillus* reuteri administered following triple therapy may prevent adverse effects and slightly improve eradication outcomes, although the effects are inconsistent with those of quadruple therapy. The article further contains meta-analyses favouring probiotics, particularly *Lactobacillus* and *Saccharomyces*, to enhance tolerability and modestly enhance efficacy in triple therapy. Nevertheless, Sun et al. [14] warn that though probiotics are generally well-tolerated, the variability of probiotic strains, dosages, and regimens complicates the formulation of definite clinical recommendations.

Vaccine development

There are no vaccine trials reported in the reviewed articles, but some have addressed immunological barriers. Rocha et al. [10] described how *H. pylori* avoids host immunity through intracellular location, macrophage maturation inhibition, and antigen presentation suppression by VacA and CagA proteins. These are the reasons why a protective immune response is not naturally formed. Sun et al. [14] repeated this by saying that the immune evasion ability of *H. pylori*, coupled with its capacity to be harbored in the gastric mucosa, renders vaccine development particularly difficult.

Management of antibiotic resistance

Surveillance and monitoring strategies

Timely surveillance is the key to effective resistance management. Alihosseini et al. [11] reported on Iran's generalized resistance to several antibiotics, with more than 90% of clarithromycin-resistant isolates possessing the *A2143G* mutation. Rocha et al. [10] reported international WHO data demonstrating rising resistance to clarithromycin, metronidazole, and levofloxacin between 2006 and 2016, highlighting the need to revisit national surveillance programs. Brennan et al. [12] illustrated that molecular stool-based techniques such as PCR and ddPCR are able to identify resistance mutations with speed and are on par with biopsy-derived results, allowing for wider testing. Alfaro et al. [13] observed poor primary care

implementation of resistance testing, despite the Maastricht VI recommendations. Sun et al. [14] expounds that the consistency of stool-based PCR makes it a perfect instrument to enhance diagnostic reach. Sun et al. [14] added that in the absence of surveillance for resistance, treatment options are still empirical and less than optimal.

New antibiotic combinations

Since routine triple therapy is becoming increasingly ineffective, other regimens have taken precedence. Alihosseini et al. [11] documented very high Iranian patient resistance, rendering clarithromycin-containing regimens largely ineffective. Rocha et al. [10] advocated BQT across the board because of its strong efficacy even in high-resistance regions and presented newer options such as vonoprazan-amoxicillin dual therapy, rifabutin regimens, and levofloxacin-bismuth therapy. The paper references a number of trials where vonoprazan-based regimens had similar or superior eradication rates compared to PPI-based quadruple therapies with fewer side effects.

Non-antibiotic therapies

Antibiofilm agents

H. pylori biofilm formation is a significant hindrance to its successful treatment. Alihosseini et al. [11] stated that biofilms play a role in antimicrobial resistance and that their treatment is central to optimizing outcomes. Rocha et al. [10] reported antibiofilm agents such as Pistacia vera oleoresin, Armeniaspirol A, and Casearia sylvestris, which have reported anti-biofilm and antimicrobial activities in vitro and animal models. The article also mentioned new nanomaterials such as rhamnolipids, berberine nanoparticles, and silver ultra-nanoclusters for biofilm disruption. *N*-acetylcysteine, the sole agent used in clinical trials, has demonstrated potential for improving antibiotic penetration through mucus viscosity reduction.

Host and pharmacologic strategies

Genetic variations that influence drug metabolism may alter treatment responses. Sun et al. [14] emphasized the involvement of *CYP2C19* polymorphism in PPI metabolism. Rocha et al. [10] pointed out that vonoprazan has a unique benefit in that it does not utilise the *CYP2C19* pathway, yielding greater acid suppression in all metaboliser phenotypes.

Post-treatment follow-up and management

Confirmation of *Helicobacter pylori* eradication

Assessing the success of *H. pylori* eradication therapy is a critical step in clinical management and requires reliable diagnostic techniques that distinguish persistent infection from post-treatment resolution [1, 4, 5]. The following methods are currently employed for this purpose.

Non-invasive testing modalities

Among the available approaches, non-invasive tests are preferred because of their accessibility, cost-effectiveness, and diagnostic accuracy [5, 6].

- **UBT:** Widely considered the gold standard, UBT detects urease activity exclusive to *H. pylori*. It has high sensitivity and specificity, and is suitable for routine post-treatment confirmation [7, 8]. Testing should be performed at least 4 weeks after completion of antibiotic therapy and 2 weeks after discontinuation of PPIs to mitigate false-negative results [15, 16].
- **Stool antigen test (SAT):** This assay identifies *H. pylori* antigens in fecal samples and yields diagnostic performance comparable to UBT [5, 9, 17]. It is particularly useful in pediatric settings, where breath testing is impractical [17]. Similar to UBT, it should be administered after an appropriate washout period [15].
- **Serologic testing:** Though widely used, antibody detection via serology is not recommended for confirming eradication [5, 14]. Persistent IgG antibodies may remain long after bacterial clearance, rendering this modality unreliable [14, 16].

Invasive diagnostic methods

Biopsy-based confirmation methods may be utilised when endoscopy is clinically indicated, especially in cases of refractory symptoms or complications [4, 10].

- **Histological examination:** Gastric biopsies can reveal residual *H. pylori* infections [5, 14]. Histology provides visual evidence but may be limited by post-treatment bacterial density [5].
- **Rapid urease test (RUT):** This assesses urease activity in the gastric tissue [7, 12]. It is less sensitive in the post-treatment setting because of the reduced bacterial burden [12, 14].
- **Culture and antibiotic susceptibility testing:** In patients with persistent infection following multiple eradication attempts, culture offers both confirmation and an opportunity for tailored antimicrobial therapy [4, 10, 12, 18].

Summary of testing strategies

A summary of various investigations for the purpose of testing for *H. pylori* is provided below in Table 1.

Table 1. Summary of investigation modalities for *Helicobacter pylori*.

Method	Recommended for eradication confirmation	Key considerations
UBT	Yes	Most accurate; avoid PPIs before testing [7, 8, 15, 16]
Stool antigen test	Yes	Good alternative: timing is critical [5, 9, 17]
Serologic testing	No	Cannot distinguish current from past infection [5]
Histology/RUT	Conditional	Use only if endoscopy is indicated [4, 5, 12]
Culture & sensitivity	Selective	For treatment-resistant cases [4, 10, 12, 18]

PPIs: proton pump inhibitors; RUT: rapid urease test; UBT: urea breath test.

Accurate confirmation of eradication is essential not only for ensuring symptom resolution but also for preventing complications such as peptic ulcer recurrence or gastric malignancy [4, 15, 16]. Clinicians should select the most appropriate modality based on clinical context, prior treatment history, and resource availability [4, 15, 16, 18].

Management of persistent and resistant infections

Resistance to the key antibiotics metronidazole and clarithromycin has emerged as a significant obstacle in the effective treatment of *H. pylori* infection [4, 10, 11, 18]. While metronidazole resistance ranges from 10% to 80%, clarithromycin resistance typically falls between 2% and 10%, although cases of secondary resistance have been reported to reach as high as 58% following failed therapy [4, 10, 18]. These resistance patterns directly affect the efficacy of standard eradication therapies. When metronidazole resistance is present, the efficacy of PPI-based triple therapy may decrease by nearly 50% [4, 10, 15, 19]. Similarly, clarithromycin resistance may lead to a 56–58% decline in treatment success with both PPI triple and ranitidine bismuth citrate (RBC) dual therapies [4, 10, 15, 19].

Resistance development is typically mediated by bacterial mutations, efflux pump mechanisms, and biofilm formation [4, 10, 12, 18].

Eradication failures present a substantial clinical challenge and are often attributed to resistance to antibiotics used in the initial therapy [4, 10, 11, 18]. Notably, some *H. pylori* strains exhibit dual resistance to both metronidazole and clarithromycin, which severely limits treatment options [4, 10, 11, 18]. In such cases, culturing the organism and conducting susceptibility testing are strongly recommended to guide targeted therapies [4, 10, 12, 18].

The selection of second-line or “rescue” therapy remains ambiguous, with generally lower success rates than first-line regimens [10, 11, 15, 16]. Quadruple and extended PPI triple therapies have achieved moderate efficacy in treatment failure [10, 11, 15, 19]. Importantly, antibiotics used in the initial regimen should be avoided to prevent further resistance [4, 10]. Quadruple therapy is particularly effective if clarithromycin, rather than metronidazole, is used initially [10, 15].

High-dose PPI-amoxicillin dual therapy administered over 10–14 days has shown promise [10, 11, 16]. Likewise, RBC triple therapies have demonstrated preliminary success, although further evidence is required to confirm their utility [19]. Emerging antibiotics, such as rifabutin, have also yielded positive outcomes when combined with PPI and amoxicillin or RBC and amoxicillin [10, 11, 20].

Treatment failure warrants a multi-faceted response [10, 11, 15]. Optimising patient adherence is critical and can be supported through strategies such as medication cards, packaging enhancements, and nurse-led follow-up communication [10, 11, 15]. However, the most influential intervention often involves clear patient education regarding drug regimens and the expected side effects [10, 11, 15].

Long-term monitoring strategies in special populations: elderly and immunocompromised patients

The management of *H. pylori* infection in elderly and immunocompromised individuals presents unique clinical challenges due to altered physiology, polypharmacy, and increased susceptibility to adverse outcomes [15, 21–24]. Long-term monitoring of these populations is essential to ensure therapeutic efficacy, minimise complications, and guide individualised care [15, 21, 22].

Elderly patients

Aging is associated with immunosenescence, reduced gastric mucosal defence, and an increased prevalence of comorbidities, all of which complicate *H. pylori* eradication and follow-up [15, 21–24]. Although eradication regimens are generally similar to those used for younger adults, elderly patients require tailored strategies that account for frailty, renal function, and drug interactions [15, 21, 23].

Key monitoring strategies include the following:

- Post-treatment confirmation using non-invasive methods, such as the UBT or SAT, with timing adjusted to avoid false negatives due to PPI use or delayed gastric emptying [5, 7, 9, 15, 17].
- Periodic reassessment for recurrence or reinfection, particularly in patients with persistent dyspeptic symptoms or a history of peptic ulcer disease [15, 16, 21].
- Surveillance endoscopy is performed in individuals with atrophic gastritis or intestinal metaplasia to monitor the progression of gastric neoplasia [15, 21, 22].
- Medication review to avoid polypharmacy-related adverse effects and ensure adherence to eradication regimens [15, 21, 23].

Emerging evidence supports the use of susceptibility-guided therapy and extended-duration regimens to improve eradication rates in older adults [10, 15, 21, 22].

Immunocompromised patients

In immunocompromised populations, such as those with HIV/AIDS, organ transplant recipients, or individuals undergoing chemotherapy, *H. pylori* infection may present atypically and carry a higher risk of complications, including bleeding, perforation, and poor mucosal healing [24–26].

Monitoring strategies should include the following:

- Enhanced diagnostic vigilance, as conventional tests may yield false negatives due to altered immune responses or concurrent infections [5, 14, 24, 25].
- Culture and sensitivity testing following treatment failure to guide second-line therapy and to avoid resistance-driven recurrence [4, 10, 12, 18, 25].
- Close follow-up for adverse drug interactions, especially between PPIs, antibiotics, and immunosuppressive agents [15, 24, 25].
- Multidisciplinary coordination involves gastroenterologists, infectious disease specialists, and transplant teams to optimise care [15, 24, 25].

Given the increased risk of opportunistic infections and impaired tissue repair, long-term monitoring should include nutritional assessment, surveillance for secondary infections, and consideration of prophylactic strategies where appropriate [24–26].

Future directions and challenges in the management of *Helicobacter pylori* infection

Despite decades of research and therapeutic advancements, the global burden of *H. pylori* infection remains substantial, particularly owing to rising antibiotic resistance, diagnostic limitations, and the absence of a universally effective eradication strategy [4, 10, 15, 18, 25, 26]. Addressing these challenges requires a multifaceted approach that integrates novel technologies, personalised medicine, and global surveillance [10, 15, 18, 25].

Combating antibiotic resistance

Antibiotic resistance is the foremost obstacle in *H. pylori* management [4, 10, 18, 25]. Resistance to clarithromycin, metronidazole, and levofloxacin has reached critical thresholds in many regions, thereby compromising the efficacy of standard triple and quadruple therapies [4, 10, 15, 18]. Future strategies must prioritise:

- Susceptibility-guided therapy using molecular diagnostics or culture-based methods [4, 10, 12, 18].
- Development of novel antimicrobial and non-antibiotic therapies, including antimicrobial peptides, bacteriophage-based treatments, and biofilm-disrupting agents [10, 20, 26, 27].
- Global surveillance programs to monitor resistance patterns and inform regional treatment guidelines [4, 10, 18, 25].

Advancing diagnostic technologies

An accurate and timely diagnosis is essential for effective treatment [5, 6, 14, 25]. Emerging technologies such as:

- Biosensors, nano-diagnostics, and AI-assisted platforms offer promise for rapid, non-invasive, point-of-care detection [20, 25, 26].
- Genomic profiling of *H. pylori* strains may enable prediction of virulence and resistance traits, and guide personalised therapy [12, 18, 25].

However, widespread implementation is hindered by cost, infrastructure limitations, and lack of standardisation [25, 26].

Vaccine Development

Prophylactic vaccines against *H. pylori* are of critical unmet need [25, 26]. Challenges include:

- Strain variability and immune evasion mechanisms are complicating antigen selection [25, 26].
- Limited efficacy in clinical trials and lack of long-term protection [25, 26].
- Regulatory and funding barriers are slowing translational progress [25, 26].

Continued investment in immunological research and global collaboration is essential [25, 26].

Integration of probiotics and microbiome modulation

The adjunctive use of probiotics has shown potential to enhance eradication rates and reduce therapy-related side effects [26, 27]. Future research should focus on:

- Standardising probiotic strains, dosages, and treatment durations [26, 27].
- Exploring microbiome-targeted therapies to restore gastric and intestinal homeostasis post-eradication [26, 27].

Personalised and precision medicine

The heterogeneity of *H. pylori* infection necessitates individualised treatment approaches [15, 18, 25]. Incorporating:

- Host genetic factors, microbiome composition, and local resistance data in planning [15, 18, 25].
- AI-driven decision support systems to optimise regimen selection and predict treatment outcomes [20, 25].

Public health and implementation challenges

Effective management also depends on:

- Improving access to diagnostics and treatment in low-resource settings [15, 25].
- Educating healthcare providers and patients on adherence and resistance prevention [15, 25].
- Establishing international consensus guidelines reflecting regional epidemiology and resources [15, 25].

Zoonotic transmission of *Helicobacter pylori*

The zoonotic potential of *H. pylori* has been a topic of interest as well as curiosity among researchers, particularly due to its well-established role in gastroenterological pathologies. Although historically being considered a pathogen specific to humans, recently emerging evidence suggests that domestic animals, especially cats and dogs, might serve as reservoirs or incidental hosts.

Akcakavak et al. [28] used RT-PCR and histopathological analysis to detect *H. pylori*, *H. helimannii*, and *H. felis* in the gastric and hepatic tissues of dogs. These dogs were from various backgrounds, ranging from stray to sheltered animals. It was found that *H. pylori* DNA existed in several gastric samples, either alone or in co-infection with other *Helicobacter* species, which is suggestive of dogs harbouring this organism under certain conditions [28].

A similar study was done in parallel on cats. Tuzcu et al. [29] demonstrated the presence of *H. helimanni* in both stomach and liver tissues of cats using similar molecular and histologic techniques. The shared ecology of *Helicobacter* species among companion animals underscores the plausibility of cross-species transmission.

Gökalp et al. [30] tested shelter dogs for the presence of *Helicobacter* species by collecting faecal samples for antigen testing and ELISA. Positive test cases were treated with triple therapy. This resulted in further blurring of lines between veterinary and human clinical approaches. It also demonstrated raised inflammatory markers in infected dogs, similar to the immunopathology responses seen in human hosts [30].

Overall, these findings suggest complex and multifactorial phenomena of direct zoonotic transmission of *H. pylori*. Close animal contact remains the most likely mode of transmission.

Conclusions

The way we manage *H. pylori* infection has changed a lot. This is because we have better ways to diagnose it, treat it, and understand how it resists antibiotics [4, 10, 15, 18, 25, 26]. New methods like PCR and NGS help us find *H. pylori* and test which antibiotics work faster and more accurately [4, 10, 12, 18]. Non-invasive tests, like the UBT and stool tests, are still important for diagnosing and checking if treatment worked [5, 7, 9, 15, 17].

More *H. pylori* strains are resisting antibiotics, so we now focus on personalized treatments [4, 10, 15, 18]. Treatments based on specific tests for antibiotic resistance are showing better results [4, 10, 11, 15, 18]. In areas with high resistance, BQT and vonoprazan-based treatments work well instead of the usual triple therapy [10, 15, 18, 25]. Adding probiotics can help reduce side effects and slightly improve treatment success, but more research is needed to understand their role [26, 27].

New ideas, like antibiofilm agents and non-antibiotic treatments, are being tested to tackle biofilm formation and resistance [10, 20, 26, 27]. Globally, we need better tracking of antibiotic resistance, more use of treatments based on resistance tests, and to fix healthcare access issues [4, 10, 15, 18, 25]. Future *H. pylori* management may use new technologies like AI to improve diagnosis and treatment choices [20, 25]. Also, combining *H. pylori* treatment with stomach cancer prevention is a promising research area [15, 21, 25, 26].

In summary, we have made progress in managing *H. pylori*, but we need more research and innovation to handle antibiotic resistance and improve treatments [4, 10, 15, 18, 25, 26]. The field is active, with ongoing work to improve diagnosis, create new treatments, and use evidence-based strategies worldwide [4, 10, 15, 18, 25, 26].

Abbreviations

AI: artificial intelligence

AST: antimicrobial susceptibility testing

BQT: bismuth quadruple therapy

cagA: cytotoxin-associated gene A

ddPCR: droplet digital polymerase chain reaction

H. pylori: *Helicobacter pylori*

HpSA: *Helicobacter pylori* stool antigen

LCI: linked colour imaging

NGS: next-generation sequencing

OMVs: outer membrane vesicles

PCR: polymerase chain reaction

PPIs: proton pump inhibitor

RBC: ranitidine bismuth citrate

RT-PCR: real-time polymerase chain reaction

SAT: stool antigen test

UBT: urea breath test

vacA: vacuolating cytotoxin gene A

WLI: white light imaging

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SD: Conceptualization, Resources, Writing—original draft, Writing—review & editing. AR: Conceptualization, Resources, Writing—original draft, Writing—review & editing. Both authors read and approved the submitted version.

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The authors declare that there are no conflicts of interest.

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