Review of the Second Asia-Pacific Consensus Guidelines for *Helicobacter pylori* Infection

**Introduction**

*Helicobacter pylori* infection is one of the most common human infections worldwide and has an important etiological association with gastroduodenal disease, particularly peptic ulcer disease and gastric malignancies. The first Asia-Pacific *H. pylori* Consensus Guidelines were published in 1998 (1). In the light of new scientific information, these guidelines were updated and published in 2009 (2). They provided an evidence-based management update. *H. pylori* eradication was recommended in peptic ulcer disease, early mucosa-associated lymphoid tissue type lymphoma, a family history of gastric cancer, functional dyspepsia, patients receiving long-term maintenance with a proton pump inhibitor (PPI) for gastroesophageal reflux disease, unexplained iron-deficiency anaemia or idiopathic thrombocytopenic purpura and patients at high risk of ulcers and ulcer-related complications prior to long-term aspirin or non-steroidal anti-inflammatory drug therapy. A population "test and treat" strategy for *H. pylori* infection in communities with a high incidence of gastric cancer was considered to be an effective strategy for gastric cancer prevention. The recommended first-line therapy for *H. pylori* infection in Asia remained PPI-based triple therapy with amoxicillin or metronidazole and clarithromycin for seven days. Bismuth-based quadruple therapy was considered an effective alternative. There appeared to be an increasing rate of resistance to clarithromycin and metronidazole in parts of Asia, leading to reduced efficacy of PPI-based triple therapy. Recommended salvage therapies included: (i) standard triple therapy that has not been previously used; (ii) bismuth-based quadruple therapy; (iii) levofloxacin-based triple therapy; and (iv) rifabutin-based triple therapy. Levofloxacin-based salvage therapy had an overall *H. pylori* eradication rate of 80% and appeared more efficacious than quadruple therapy with less adverse effects. A 10-day regimen was superior to a 7-day regimen.

**Materials and methods**

The Second Asia-Pacific *H. pylori* Consensus Conference was convened to address two issues: (i) the changing epidemiology and indications for the treatment of *H. pylori* infection; and (ii) the treatment of *H. pylori* infection. It was sponsored by the Asia-Pacific Association of Gastroenterology. The Journal of Gastroenterology and Hepatology Foundation provided financial support through an unrestricted educational grant. Eighteen gastroenterologists from the Asia-Pacific region and two external experts were invited to participate because of their expertise in this field. Prior to the conference, relevant areas for discussion were identified and literature was circulated. At the conference, an overview of each area was presented followed by a discussion where existing data were evaluated and critiqued. Thereafter, a statement of recommendation was formulated and the level of evidence and the classification of evidence.
relative to the recommendations were assessed. Formal voting for each statement was undertaken and the acceptance of a statement was based on agreement of at least two-thirds of the votes.

Results
The indications for *H. pylori* eradication are summarised in Table 1. There were altogether 22 statements and these were subdivided under two headings: (i) epidemiology and indications for treatment of *H. pylori* infection; and (ii) treatment of *H. pylori* infection. The statements are summarised in Table 2.

**Epidemiology and indications for treatment of *H. pylori* infection**
The prevalence of *H. pylori* infection appears to be declining in the Asia-Pacific region. In the first Asia-Pacific consensus statements, peptic ulcer disease, non-steroidal anti-inflammatory drug (NSAID) users with a previous peptic ulcer or dyspepsia, gastric mucosa-associated lymphoid tissue type lymphoma (MALToma), atrophic gastritis, post-gastric cancer resection, patients with first-degree relatives with gastric cancer and patients’ wishes were standard indications for *H. pylori* eradication. It was also stated that treatment be offered to patients with dyspepsia (1). The new guidelines expanded the above indications and stated that treatment was indicated for *H. pylori*-associated functional dyspepsia, patients with uninvestigated dyspepsia without alarm symptoms, in NSAID users to reduce the risk of peptic ulcer and upper gastrointestinal (GI) bleeding, in patients at high risk of ulcers and ulcer-related complications prior to starting long-term aspirin therapy, in patients receiving long-term low-dose aspirin therapy and who had a past history of upper GI bleeding and perforation, in gastroesophageal reflux disease requiring long-term proton pump inhibitor (PPI) therapy and in unexplained iron-deficiency anaemia or idiopathic thrombocytopenic purpura. The guidelines highlighted that there was sufficient scientific evidence to recommend *H. pylori* eradication as a strategy for primary prevention of gastric cancer in communities with a high incidence of gastric cancer (2).

**Treatment of *H. pylori* infection**
The recommended first-line therapy for *H. pylori* infection in Asia remained PPI-based triple therapy with amoxicillin or metronidazole and clarithromycin for 7 days. Bismuth-based quadruple therapy was considered an effective alternative. There appears to be an increasing rate of resistance to clarithromycin and metronidazole in parts of Asia, leading to reduced efficacy of PPI-based triple therapy. Recommended salvage therapies included: (i) standard triple therapy that has not been previously used; (ii) bismuth-based quadruple therapy; (iii) levofloxacin-based triple therapy; and (iv) rifabutin-based triple therapy.

**Discussion**
The discussion will focus on developments in two key areas. In the section on epidemiology and in-

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**Table 1. Indications for *H. pylori* eradication**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Grade of recommendation</th>
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<tbody>
<tr>
<td>1. Peptic ulcer disease</td>
<td>A</td>
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<tr>
<td>2. MALToma</td>
<td>A</td>
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<tr>
<td>3. Atrophic gastritis</td>
<td>B</td>
</tr>
<tr>
<td>4. After gastric cancer resection</td>
<td>B</td>
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<tr>
<td>5. Patients with first-degree relatives with gastric cancer</td>
<td>B</td>
</tr>
<tr>
<td>6. Patients’ wishes (after full consultation with their physicians)</td>
<td>A</td>
</tr>
<tr>
<td>7. Non-ulcer dyspepsia</td>
<td>A</td>
</tr>
<tr>
<td>8. To reduce the risk of peptic ulcer and upper GI bleeding in NSAID-naive users</td>
<td>A</td>
</tr>
<tr>
<td>9. Before starting long-term aspirin therapy for patients at high risk for ulcers and ulcer-related complications</td>
<td>B</td>
</tr>
<tr>
<td>10. Patients receiving long-term low-dose aspirin therapy and who have a past history of upper GI bleeding and perforation</td>
<td>B</td>
</tr>
<tr>
<td>11. Gastroesophageal reflux disease patients requiring long-term PPI</td>
<td>B</td>
</tr>
<tr>
<td>12. As a strategy for gastric cancer prevention in communities with a high incidence of gastric cancer</td>
<td>A</td>
</tr>
<tr>
<td>13. Unexplained iron-deficiency anaemia or idiopathic thrombocytopenic purpura</td>
<td>C</td>
</tr>
</tbody>
</table>

Abbreviations: *H. pylori* = *Helicobacter pylori*, MALToma = mucosa-associated lymphoid tissue type lymphoma, GI = gastrointestinal, NSAID = non-steroidal anti-inflammatory drug, PPI = proton pump inhibitor.
Abbreviations: *H. pylori*= *Helicobacter pylori*, PPI = proton pump inhibitor, NSAID = non-steroidal anti-inflammatory drug, GI = gastrointestinal.

Epidemiology and indications for treatment of *H. pylori* infection

1. The prevalence of *H. pylori* infection has been declining in the Asia-Pacific region.
2. *H. pylori* eradication is indicated for *H. pylori*-positive patients with investigated dyspepsia.
3. In *H. pylori*-positive patients with uninvestigated dyspepsia and with no alarm features, *H. pylori* “test and treat” is an appropriate strategy.
4. Routine “test and treat” for *H. pylori* infection is not recommended for patients with gastroesophageal reflux disease.
5. *H. pylori* testing should be considered in patients receiving long-term maintenance treatment with PPI for gastroesophageal reflux disease.
6. Screen and treat for *H. pylori* infection in communities with a high incidence of gastric cancer is an effective strategy for gastric cancer prevention.
7. In areas with a high prevalence of both *H. pylori* infection and gastric cancer, eliminating *H. pylori* infection through improvements in public health and education will have the greatest impact in reducing the burden of gastric cancer.
8. In NSAID-naïve users, *H. pylori* eradication will reduce the risk of peptic ulcers and upper GI bleeding.
9. In patients receiving long-term NSAIDs who have a past history of peptic ulcer disease or complications of peptic ulcer disease, *H. pylori* eradication alone is not sufficient to prevent ulcer recurrence and/or bleeding.
10. Before starting long-term aspirin therapy for patients at high risk of ulcers and ulcer-related complications, testing for and eradication of *H. pylori* infection are indicated.
11. Treating *H. pylori* infection in patients receiving long-term low-dose aspirin therapy and who have a past history of upper GI bleeding and perforation will reduce the risk of recurrent hemorrhage.
12. *H. pylori* infection should be sought for and treated in patients with unexplained iron-deficiency anaemia and idiopathic thrombocytopenic purpura.
13. Urea breath tests and monoclonal stool antigen tests are accurate and appropriate tests for confirmation of *H. pylori* eradication.
14. Serological tests have a limited role in the management of *H. pylori* infection.

Treatment of *H. pylori* infection

15. In Asia, the currently recommended first-line therapy for *H. pylori* infection is PPI, amoxicillin and clarithromycin for 7 days.
16. There is an increasing rate of resistance to clarithromycin and metronidazole in parts of Asia. This has led to reduced efficacy of PPI-based triple therapy.
17. Fourteen-day triple therapy has a limited advantage over 7-day triple therapy in terms of *H. pylori* eradication rates.
18. Bismuth-based quadruple therapy is an effective alternative first-line therapy for *H. pylori* eradication.
19. There are currently insufficient data to recommend sequential therapy as an alternative first line for *H. pylori* therapy in Asia.
20. Salvage therapy for *H. pylori* eradication includes: (i) standard triple therapy that has not been previously used; (ii) bismuth-based quadruple therapy; (iii) levofloxacin-based triple therapy; (iv) rifabutin-based triple therapy.
21. CYP2C19 polymorphisms may affect *H. pylori* eradication rates in PPI-based triple therapy. The choice of a PPI or increasing the dose is a more practical approach than CYP2C19 genotyping in the clinical setting to overcome CYP2C19 polymorphisms in the context of salvage therapy.
22. Smoking adversely affects the outcome of *H. pylori* eradication therapy.

Epidemiology and indications for treatment of *H. pylori* infection

**Epidemiology**

The statement on the decreasing prevalence of *H. pylori* infection was agreed upon with significant qualification. This was because the Asia-Pacific was a vast and heterogeneous region with a varying prevalence of *H. pylori* infection both between and within countries. In countries undergoing rapid economic development and improvements in standards of living, there was evidence that the prevalence of infection was declining. However, a heterogeneity of infection rates existed even within more developed countries, with well-defined high-risk groups. These groups included the elderly, those who live in poorer conditions, migrants from high prevalence areas, the institutionalised and possibly rural populations in some areas. Despite the decrease in prevalence, large proportions of many adult populations remained infected so the burden of infection manifesting as peptic ulcer disease and gastric cancer will continue to be an important problem across the region for years to come (2).

**Treatment indications**

In the second consensus statement, it was stated unequivocally that *H. pylori* eradication was indicated for *H. pylori*-positive patients with investigated dyspepsia (non-ulcer dyspepsia) as well as...
those with uninvestigated dyspepsia and no alarm features. The evidence included: (i) a small but clinically relevant likelihood of an improvement in symptoms in the short- and long-term (4); (ii) a long-term benefit with regard to reducing risks for subsequent peptic ulcer disease and gastric cancer (3, 5); (iii) a lack of a clinical cost-effective superior alternative treatment; (iv) cost-effectiveness data from a number of different populations (4); and (v) recognition of the rights of the patient and the obligation of the clinician to offer the best treatment option in this setting. It was considered that the decision not to treat H. pylori infection must be an active one rather than the default position. In the case of uninvestigated dyspepsia, a subset of patients may have undiagnosed ulcer disease and eradication of H. pylori infection would be of benefit, while obviating the need for endoscopy. The ongoing dilemma related to the fear of missing gastric cancer was an important issue. It was agreed that previous recommendations for a “cascade” approach remained relevant with thresholds for referral for endoscopy being related to the age of the patient, the prevalence of gastric cancer in the community and the availability of endoscopy. It was further noted that there was no consistent relationship between early gastric cancer and the presence of symptoms and recognition of this underpinned screening programs in some countries, such as Japan and Korea, where the prevalence of gastric cancer was high.

Gastric cancer carcinogenesis is a multi-factorial process related to an interaction of host factors, H. pylori infection and environmental factors such as diet. An analysis of 12 case-control studies concluded that H. pylori infection was associated with an odds ratio (OR) of 5.9 for non-cardiac gastric cancer. Based on an average prevalence of H. pylori of 35% in developed countries and 85% in developing countries, this implied that between 65% and 80% of non-cardiac gastric cancers were attributable to H. pylori infection and potentially preventable (6). The potential benefit of H. pylori eradication in reducing the risk of gastric cancer can be considered indirectly from studies that assessed its effect on precancerous lesions and directly from its effect on cancer development. Studies from South America and China, regions with high prevalence rates of H. pylori infection and high incidence rates of gastric cancer, have shown that H. pylori eradication produced a significant increase in the rates of regression for intestinal metaplasia and gastric atrophy, and lowered the risk of progression to intestinal metaplasia (7–11). Uemura et al. provided evidence that H. pylori eradication had a direct impact on gastric cancer occurrence, reducing the risk of metachronous gastric cancer after endoscopic resection (12). A meta-analysis (3) of five randomised placebo-controlled H. pylori eradication trials (9, 13–16) showed that with H. pylori eradication, the pooled relative risk of developing gastric cancer was 0.56 (95% confidence interval [CI]: 0.40–0.8). Modelling data from China suggested screening and treatment of H. pylori infection may be cost-effective (17). Thus, a strategy of H. pylori screening and eradication in high-risk populations was recommended and it was felt that this approach may be considered in intermediate-risk populations, especially in subpopulations at high risk, although it was acknowledged that supporting data were lacking. Finally, screening of low-risk populations was not currently recommended, although even in countries with a relatively low incidence of gastric cancer, modelling suggested that a “screen and treat” strategy may be cost-effective at a level that may even exceed that of breast cancer and cervical cancer screening (18). There was a qualification that the current gastric surveillance programs in populations at high risk of gastric cancer such as in Japan and Korea should be continued.

In the case of NSAID users, H. pylori eradication was previously recommended only in the context of past or current peptic ulcer or dyspepsia. In the updated guidelines, additional statements concerning eradicating H. pylori infection in NSAID and aspirin users were added. In terms of primary prevention of peptic ulcer in NSAID users, randomised, placebo-controlled Asian data demonstrated that eradication therapy prior to NSAID use reduced peptic ulcers and ulcer bleeding significantly, irrespective of whether PPI were given (19). These data were supported by a recent global meta-analysis that confirmed that eradication of H. pylori infection prior to NSAID use significantly reduces the risk of peptic ulceration (20). In terms of the interaction between aspirin and H. pylori, it was clear that the risk of upper GI bleeding in aspirin users was increased by concomitant H. pylori infection (OR: 4.7) or a past history of ulcer disease (OR: 15.2) (21). The value of prophylactic eradication prior to aspirin use in all patients was uncertain, but it was considered reasonable to consider treatment in those with significant risk factors for ulcers or bleeding such as being over 60 years of age, concomitant use of anticoagulants and systemic corticosteroids, and severe co-morbid diseases (22, 23). In addition, a randomised controlled trial showed a marked reduction in recurrent ulcer complications in low-dose aspirin-users following sequential H. pylori eradication therapy and then PPI prophylaxis (24). Based on these data, the recom-
recommended strategy was for *H. pylori* eradication therapy, followed by PPI prophylaxis in high-risk patients.

**Treatment of *H. pylori* infection**

**First-line *H. pylori* eradication regimens**

Observational studies suggested an increasing rate of resistance to clarithromycin and metronidazole in parts of Asia (2, 25). This may result in reduced efficacy of PPI-based triple therapy (2). Due to concerns about standard treatment regimens becoming less effective, the Consensus Group specifically examined the choice of first-line therapy in Asia based on published data. After much deliberation, the recommended first-line therapy for *H. pylori* infection remained PPI, amoxicillin and clarithromycin; (ii) omeprazole/metronidazole/clarithromycin; and (iii) esomeprazole/amoxicillin/clarithromycin; (i) omeprazole/levofloxacin/amoxicillin; (ii) omeprazole/metronidazole/clarithromycin (PP: 80.8%; ITT: 75%) and esomeprazole/metronidazole/clarithromycin (PP: 77.4%; ITT: 72%) treatment regimens (34). Molina-Infante et al. analysed four 10-day therapeutic regimens: (i) omeprazole/clarithromycin/amoxicillin; (ii) omeprazole/levofloxacin/amoxicillin; (iii) omeprazole/amoxicillin/clarithromycin for 5 days, followed by omeprazole/clarithromycin/metronidazole for 5 days; and (iv) omeprazole/amoxicillin for 5 days, followed by omeprazole/levofloxacin/metronidazole for 5 days. The efficacy of levofloxacin-based triple therapy (PP: 82.6%; ITT: 80.8%) and sequential therapies (PP: 80.8–85.2%; ITT: 76.5–82.5%) was found to be significantly higher than standard triple using omeprazole/clarithromycin/amoxicillin (PP: 66%; ITT: 64%). The low efficacy of standard triple therapy was expected because the study was conducted in a setting where there was high clarithromycin resistance. However, even the more effective therapies still had a 20% failure rate (35). Erçin et al. compared 1-week and 2-week levofloxacin-based triple therapy (lansoprazole/levofloxacin/amoxicillin) and found that 2-week therapy was superior. However, in this study, the eradication rate of 1-week therapy was unusually low at 34.15%, while that for 2-week therapy was also low at 72.2% (36). The overall low success rates may well reflect the high prevalence of quinolone resistance in that region. In contrast to the studies by Nista et al. (34) and Molina-Infante et al. (35), no difference was found in two other studies. Cheng et al. compared the efficacy of 1-week standard triple therapy (lansoprazole/amoxicillin/clarithromycin) with 1-week levofloxacin-based triple therapy (lansoprazole/amoxicillin/levofloxacin) and found no significant difference in eradication rates (PP: 82.4% vs. 83.0%; ITT: 74.5% vs. 78.2%) (37). Castro–Fernández et al. compared 10-day levofloxacin–based triple therapy (PPI/amoxicillin/levofloxacin) with a historical control group prescribed 10-day standard triple therapy (PPI/amoxicillin/clarithromycin). Eradication rates were similar in both groups (PP: 74.6% vs. 75.5%) (38). Conversely, Liou et al. showed that standard triple therapy was superior to levofloxacin–based therapy as a first-line treatment. Patients were randomised to two 1-week triple therapies: (i) levofloxacin/amoxicillin/lansoprazole; and (ii) clarithromycin/amoxicillin/lansoprazole. Patients who failed to achieve eradication were retreated with the rescue regimen in a crossover manner for 10 days. As a first-line therapy, standard triple therapy showed significantly higher eradication
rates than levofloxacin-based triple therapy (PP: 87.4% vs. 80.1%; ITT: 83.7% vs. 74.2%). When used as second-line therapy, the results of standard therapy appeared poorer than levofloxacin-based therapy (PP: 61.5% vs. 80.0%; ITT: 60.0% vs. 76.9%) but the difference was not statistically significant. Subanalysis revealed lower eradication rates in the presence of antibiotic resistance. It was concluded that the strategy of using standard triple therapy as the initial treatment and levofloxacin-based therapy as the rescue regimen achieved higher eradication rates than the reverse sequence (39). These differences in outcomes possibly reflected differences in antibiotic resistance patterns between geographic regions.

Recently, there has been much interest in the use of a 10-day sequential therapy which consists of 5 days of treatment with a PPI and one antibiotic (usually amoxicillin), followed by a 5-day treatment with the PPI and two other antibiotics (usually clarithromycin and a 5-nitroimidazole). The rationale for this approach was that amoxicillin could weaken the bacterial cell wall in the initial phase of treatment, and prevent the development of drug efflux channels that inhibit clarithromycin from binding to ribosomes and thus help to improve the efficacy of clarithromycin in the second phase of treatment. In fact, an initial meta-analysis calculated an eradication rate of 93.4% for sequential therapy and 76.9% for standard triple therapy (40). However, during the Consensus Group meeting, it was felt to be premature to recommend the use of sequential therapy as an alternative first line for H. pylori therapy in Asia due to a lack of multicentre, multi-region randomised trials since most studies had been conducted in Europe. Since the publication of the consensus statement, additional data have been published. A retrospective study from Korea evaluated 98 patients with proven H. pylori infection given a 10-day sequential therapy (20 mg rabeprazole, and 1 g amoxicillin, twice daily for the first 5 days, followed by 20 mg rabeprazole, 500 mg clarithromycin, and 500 mg metronidazole, twice daily for the remaining 5 days). The eradication rate of sequential therapy was 91.8% by ITT analysis (41). In another recent study from Thailand, 115 patients with dyspepsia or peptic ulcer underwent a 10-day sequential regimen, which consisted of lansoprazole (30 mg) plus amoxicillin (1 g) twice daily for 5 days, then lansoprazole (30 mg) with metronidazole (500 mg) twice daily, and clarithromycin (1,000 mg) once daily for another 5 consecutive days. Successful eradication was achieved in 95% (42). A randomised study from Taiwan compared sequential therapy with concomitant administration of all 4 drugs (concomitant therapy). A total of 232 H. pylori-infected patients were given 10 days of sequential (n = 115) or concomitant (n = 117) therapy. ITT analysis demonstrated similar eradication rates for sequential (92.3%) and concomitant therapy (93.0%). Importantly, it was found that dual resistance did not influence the level of eradication in the concomitant group, but significantly affected that of the sequential therapy group. It was concluded that either sequential or concomitant therapy with a PPI, amoxicillin, clarithromycin and an imidazole agent were equally effective, and that concomitant therapy may be more suitable for patients with dual resistance to antibiotics (43).

**Second-line H. pylori eradication regimens**

The guidelines acknowledged a lack of well-powered multicentre randomised trials of salvage therapies and a paucity of direct comparisons between salvage options. Nonetheless, based on published data, the following options were recommended.

An option after first-line eradication failure was to use a standard triple therapy that contained an antibiotic that had not been used previously. In Japan, for instance, where the prevalence of metronidazole resistance is low, in the event of failure of PPI, amoxicillin and clarithromycin triple therapy, the use of PPI, amoxicillin and metronidazole triple therapy was a viable alternative, with ITT eradication rates of 87.5% (without susceptibility testing) or 93.5% with susceptibility testing (44). Similar results were reported in another Japanese multicentre study using this strategy (45).

Bismuth-based quadruple therapy remained useful as a second-line therapy after failure of PPI-based triple therapy. Ang et al. evaluated quadruple therapy (PPI/bismuth/tetracycline/metronidazole) as salvage therapy after failed triple therapy (PPI/amoxicillin/clarithromycin). The eradication rate was 82.2% by PP and 69.8% by ITT (46). In another study that evaluated quadruple therapy (PPI/bismuth/tetracycline/metronidazole) as either first-line or salvage therapy, the eradication rate was 98% by PP and 95% by ITT (47). Lin et al. evaluated quadruple therapy (PPI/bismuth/amoxicillin/clarithromycin) after unsuccessful bismuth-based triple therapy (bismuth/metronidazole/tetracycline) and reported successful eradication in 83% (48). A recent study compared 7-day triple therapy (PPI/amoxicillin/clarithromycin) with 7- and 10-day quadruple therapy (PPI/bismuth/metronidazole/tetracycline). The eradication rates were significantly lower with triple therapy compared to 10-day quadruple therapy (PP: 75% vs. 91%; ITT: 73% vs. 89%) (49).
The efficacy of salvage therapy with levofloxacin-based triple therapy compared with quadruple therapy was addressed in a recent meta-analysis of 14 studies. All but four studies prescribed levofloxacin at doses of 250 mg twice daily or 500 mg once daily. In two studies, higher doses of levofloxacin (500 mg twice daily) were given. Most of the studies combined a PPI and amoxicillin with levofloxacin, and only three studies used azithromycin, rifabutin or furazolidone instead of amoxicillin. The overall *H. pylori* eradication rate with levofloxacin-based regimens was 80% (95% CI: 77–82). When administered for 7 days, the rate was 73% (95% CI: 68–79) compared to 81% (95% CI: 78–84) when 10-day regimens were used ($p < 0.01$). Levofloxacin-based triple regimens had significantly higher eradication rates (81%; 95% CI: 78–85) compared to quadruple therapy (70%; 95% CI: 66–74). When only more rigorous studies were considered, the advantage of the levofloxacin regimen over the quadruple regimen increased further (88% [95% CI: 84–92] vs. 64% [95% CI: 58–70]; OR: 4.11 [95% CI: 1.89–8.95]). Adverse effects were less with levofloxacin therapy (19% vs. 44%; OR: 0.27 [95% CI: 0.16–0.46]) (50). A concern associated with the use of levofloxacin-based therapy, similar to that of standard triple therapy, is the local resistance rate. A recent study in Asia found a resistance rate of 11% for levofloxacin; dual resistance to levofloxacin and clarithromycin was observed in 1% (25).

Rifabutin is derived from rifampicin and is used in rescue treatment of tuberculosis. Rifabutin-based triple therapy has been found to be a useful salvage therapy for *H. pylori* infection. However, it is not as frequently used as other salvage therapies. It carries a small risk of neutropenia, and is also not readily available in several countries. A 10-day rifabutin triple therapy (pan- toprazole/amoxicillin/rifabutin [either 150 or 300 mg]) compared with quadruple therapy (pan- toprazole/bismuth/metronidazole/tetracycline) revealed a higher eradication rate in the rifabutin 300-mg group (86.6% vs. 66.6%) (51). Results of case series of rifabutin triple therapy have shown eradication rates of 76–86% and 72% by PP and ITT, respectively (52, 53). Conversely, a comparison of second-line treatment using either 1-week rifabutin triple therapy (omeprazole/amoxicillin/rifabutin) or 1-week quadruple therapy (omeprazole/bismuth/tetracycline/metronidazole) favoured the quadruple therapy (PP: 77.1% vs. 46.5%; ITT: 70.4% vs. 44.4%) (54). A comparison of a 10-day levofloxacin-based triple therapy (PPI/amoxicillin/levofloxacin) with rifabutin-based triple therapy (PPI/amoxicillin/rifabutin) in patients who had previously failed standard triple therapy and second-line quadruple therapy favoured levofloxacin-based triple therapy (PP: 45% vs. 81%; ITT: 45% vs. 85%) (55). The *H. pylori* eradication therapies are summarised in Table 3.

### Conclusions

Standard triple therapy remains effective as first-line treatment for *H. pylori* infection in Asia. Quadruple therapy had been most extensively used as a salvage therapy. Other treatment options for salvage therapy included standard triple therapy that has not been previously used, levofloxacin-based triple therapy and rifabutin-based triple therapy. The choice of salvage therapy depended on factors such as the local pattern of antibiotic resistance, drug availability, previous treatment, and perhaps the local prevalence of tuberculosis in the context of rifabutin use (2).

### Table 3. *H. pylori* eradication therapies

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<tr>
<th>Therapy Type</th>
<th>Duration</th>
<th>Regimen</th>
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<tr>
<td>Standard PPI-based triple therapy: 7–14 days</td>
<td>7–14 days</td>
<td>PPI, amoxicillin 1 g, clarithromycin 500 mg b.i.d.</td>
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<tr>
<td></td>
<td></td>
<td>PPI, metronidazole 400 mg, clarithromycin 500 mg b.i.d.</td>
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<tr>
<td></td>
<td></td>
<td>PPI, amoxicillin 1 g, metronidazole 400 mg b.i.d.</td>
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<tr>
<td>Quadruple therapy: 7–14 days</td>
<td>7–14 days</td>
<td>PPI b.i.d., bismuth 240 mg b.i.d., metronidazole 400 mg b.i.d. or t.i.d., tetracycline 500 mg q.i.d.</td>
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<tr>
<td>Levofloxacin-based triple therapy: 10 days</td>
<td>10 days</td>
<td>PPI, levofloxacin 250 mg (or 500 mg), amoxicillin 1 g b.i.d.</td>
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<tr>
<td>Rifabutin-based triple therapy: 7–10 days</td>
<td>7–10 days</td>
<td>PPI, rifabutin 150 mg, amoxicillin 1 g b.i.d.</td>
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Abbreviations: *H. pylori* = *Helicobacter pylori*, PPI = proton pump inhibitor, b.i.d. = twice daily, t.i.d. = three times daily, q.i.d. = four times daily.
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