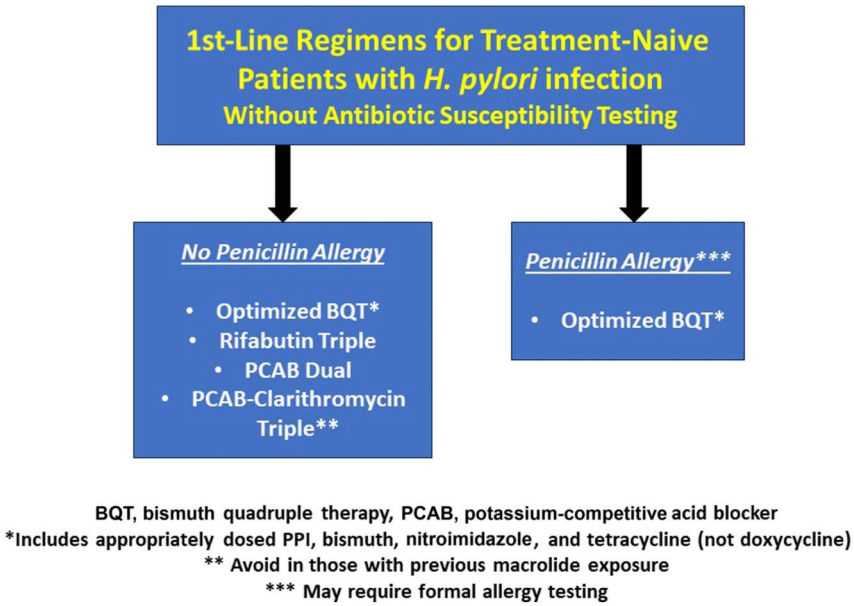

Figure 1. Empiric first-line regimens for treatment-naive patients with *H. pylori* infection (no antibiotic susceptibility testing).

In a nonrandomized, single-center observational study from Brown University, Rhode Island, BQT had the highest eradication rate in routine clinical practice among treatment-naive patients (57). When given for 14 days, it eradicated *H. pylori* infection in 87% of 585 patients. Shortening the duration of BQT to 10 days reduced overall effectiveness to 77% in 135 patients. Furthermore, when doxycycline was used in place of tetracycline, effectiveness fell to 70% when given for 14 days and 67% when given for 10 days—although the numbers of patients receiving doxycycline in place of tetracycline were quite small.

BQT is recommended over PPI-clarithromycin triple therapy, which typically comprises a PPI, clarithromycin, and amoxicillin (or, less often, metronidazole in patients with penicillin allergy) given for 14 days. Eradication rates with PPI-clarithromycin triple therapy have been decreasing over time—due largely to the increasing prevalence of clarithromycin resistance related to the frequent use of macrolide antibiotics in clinical practice. In an RCT conducted in the United States and Europe, the prevalence of clarithromycin resistance was 22.2% (58). In a meta-analysis of studies on *H. pylori* isolates performed in the United States between 2011 and 2021, the pooled prevalence of clarithromycin resistance was 31.5% (59) (Figure 2a). Despite these consistent downward trends, PPI-clarithromycin triple therapy remains the most common first-line *H. pylori* treatment in the United States and elsewhere (60).

RCTs from outside North America that have compared BQT with PPI-clarithromycin triple therapy have generally shown superiority or noninferiority of the former (61–71). However, the dosages of the components of different bismuth quadruple regimens have been inconsistent among trials, as has the duration of treatment. In a network meta-analysis of a range of first-line regimens, BQT was superior to PPI-clarithromycin triple therapy among trials conducted in Western countries (72). One notable advantage of BQT over PPI-clarithromycin triple therapy is that there is no concern for possible clarithromycin resistance and no requirement or role for pretreatment antimicrobial sensitivity testing. In addition, because BQT does not contain amoxicillin, it is an appropriate option for patients with penicillin allergy. Disadvantages of BQT include the large pill burden, relatively high frequency of minor adverse events (particularly gastrointestinal), difficulties with acquisition and cost of tetracycline, and relative contraindications for tetracycline in specific patient groups (e.g., those with photosensitivity and women of childbearing potential). Although minor side effects are common, discontinuation rates because of adverse effects are low. An RCT from Taiwan reported that although >50% of treatment-naive patients with *H. pylori* infection reported at least 1 adverse effect (dark stool, fatigue, nausea, diarrhea, and dizziness all reported by >15%) with BQT, only ~5% discontinued therapy because of adverse effects (73). Similarly low rates of discontinuation because of adverse events with BQT have also been reported from Europe (74). To maximize adherence, patients should be educated on the reason it is important to treat *H. pylori* and the most frequent adverse effects that could occur with treatment.

Recommendation

2. In treatment-naive patients with *H. pylori* infection, rifabutin triple therapy is suggested as a first-line treatment option (conditional recommendation; low quality evidence)

Rifabutin triple therapy consists of a PPI, rifabutin, and amoxicillin. This regimen has traditionally been viewed as an option for treatment-experienced patients with persistent *H. pylori* infection. More recently, this combination has been evaluated in treatment-naive patients. In a meta-analysis of clinical trials that compared rifabutin triple therapy with a variety of other regimens, only a minority were randomized, and only one of the 8 that were randomized was adequately blinded (75). Furthermore, most trials were performed outside of the United States. In the United States, only 1 rifabutin-based triple regimen (Talicia; RedHill Biopharma, Raleigh, NC) is approved by the FDA for the treatment of *H. pylori* infection in adults. It is a fixed-dose combination of omeprazole, rifabutin, and amoxicillin—with