Chapter 2.

Current evidence from randomized controlled trials of the benefits and harms of population-based *Helicobacter pylori* screen-and-treat strategies for gastric cancer prevention and review of the existing recommendations, consensus reports, and guidelines

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Summary

- Guidelines have generally become more assertive over time in their recommendations for population-based *H. pylori* screen-and-treat strategies.
- Recent guidelines have given divergent recommendations on the appropriateness of population-based *H. pylori* screen-and-treat strategies for gastric cancer prevention.
- In a systematic review of randomized controlled trials of population-based *H. pylori* screen-and-treat strategies, the Working Group identified eight trials, which involved 58 628 participants. The relative risk of gastric cancer in the *H. pylori* eradication arm was 0.64 (95% confidence interval, 0.48–0.84). The number needed to treat to prevent one case of gastric cancer was 228 (95% confidence interval, 158–514).
- *H. pylori* eradication was associated with reduced risk of recurrent gastric adenocarcinoma in patients with *H. pylori* infection (relative risk, 0.52; 95% confidence interval, 0.38–0.71). The number needed to treat was 18 (95% confidence interval, 14–30). This suggests that there is no “point of no return” for the prevention of gastric adenocarcinoma, provided that gastric adenocarcinoma has not already occurred before eradication therapy.
- There was no evidence that *H. pylori* eradication therapy increased the risk of oesophageal cancer or reflux symptoms.

- Population-based *H. pylori* screen-and-treat strategies reduce the incidence of dyspepsia and reduce health-care costs in people allocated to treatment compared with no treatment or placebo.
- More trials are needed in populations at lower risk of gastric cancer.

2.1 Introduction

The Correa hypothesis describes the series of histological changes that are the precursors to gastric adenocarcinoma [1]. The discovery that these changes were strongly associated with a then-new infectious organism, eventually named *H. pylori* [2], led to the possibility that treating this infection could reduce the incidence of gastric cancer. This possibility grew stronger after three seminal observational studies [3–5], which showed that *H. pylori* infection was associated with a strong risk of the future development of gastric adenocarcinoma. These studies and other findings led to *H. pylori* being classified by IARC as carcinogenic to humans (Group 1) [6]. Therefore, *H. pylori* gastritis was recognized as an essential trigger in the oncogenic cascade, which, over a period of decades, leads to gastric cancer in a subset of individuals with *H. pylori* infection [1, 7]. This concept opened the door for gastric cancer to be recognized as a disease with an infectious etiology, and for *H. pylori* eradication to represent a rational strategy for gastric cancer prevention [8]. There are no alternative targets for intervention in the complex interplay of the bacterium with the genetic determinants of the host. Furthermore, dietary interventions were not associated with consistent and substantial benefits for gastric cancer prevention [9]. It was not clear that treating *H. pylori* infection would reduce the incidence of gastric cancer, but about 20 years ago randomized trials and guidelines addressing this topic started to emerge. This chapter explores what these guidelines have concluded over this period, summarizes the evidence from randomized controlled trials (RCTs) that population-based *H. pylori* screen-and-treat strategies may reduce the risk of gastric cancer, and explores the other key harms and benefits of such screen-and-treat strategies.

2.2 Statements from existing guidelines and consensus reports

The landmark event that initiated the development of guidelines on population-based *H. pylori* screen-and-treat strategies was the convening in 2005 of an international working group that summarized and reviewed the available evidence on the relationship of *H. pylori* with gastric cancer and concluded that eradication of the infection had the

potential to prevent the disease. The data supporting this conclusion were obtained from animal experiments, cell biology studies, epidemiological studies, and clinical studies [10]. Guidelines addressing gastric cancer prevention by adopting *H. pylori* test-and-treat strategies soon followed. The first was the Maastricht III Consensus report, published in 2007 [11]. This consensus report evaluated existing evidence for *H. pylori*-related interventions and stated that population-based *H. pylori* screen-and-treat strategies were a promising approach, but the evidence was not sufficient to recommend this for populations, although the panel did recommend this for individuals at high risk of gastric cancer. The Asia–Pacific Consensus Guidelines on Gastric Cancer Prevention, published in 2008, were the first to recommend population-based screening for populations at high risk of gastric cancer [12]. These guidelines recommended against screening low-risk populations.

Since then, the development of guidelines has been a dynamic process, which has been influenced by several studies that have provided more evidence for the role of *H. pylori* eradication in gastric cancer prevention and have led to the extension of the statements and recommendations. Table 2.1 provides an overview of this progress, which is reflected by the key statements and recommendations published in the consensus reports and guidelines from 2007 to 2024.

The statements and recommendations in the Maastricht IV/Florence Consensus report [13], published in 2012, built on previous consensus groups that strongly recommended community *H. pylori* screen-and-treat strategies for gastric cancer prevention in areas with a substantial disease burden. This consensus report also proposed that screening should involve non-invasive testing for *H. pylori* infection [13]. In the Maastricht V/Florence Consensus report [14], published in 2017, the recommendation for the screen-and-treat approach in individuals with an increased risk of gastric cancer at the population level was enforced and extended by advising that communities at low and intermediate risk of gastric cancer were also included. The implementation of population-based screen-and-treat strategies became recognized as the main challenge, including how to administer *H. pylori* testing, which test to use, and what treatment should be given. Thus, this statement was made: “Public awareness campaigns for prevention of gastric cancer should be encouraged” [14].

Table 2.1. Consensus reports and guidelines on *H. pylori* screen-and-treat strategies for gastric cancer prevention

Consensus report (year) [reference]	Statements and recommendations
Maastricht III Consensus report (2007) [11]	• Eradication of *H. pylori* prevents development of pre-neoplastic changes of the gastric mucosa. • Eradication of *H. pylori* has the potential to reduce the risk of gastric cancer development. The optimal time to eradicate *H. pylori* is before pre-neoplastic conditions (atrophy, intestinal metaplasia) are present, probably in early adulthood. • *H. pylori* eradication for gastric cancer prevention is cost-effective in economic analyses. Feasibility studies are required to further evaluate the benefits and risks of this strategy. • The potential for gastric cancer prevention on a global scale is restricted by currently available treatments. • New treatments are required for a global strategy of *H. pylori* eradication to prevent gastric cancer. • *H. pylori* eradication for gastric cancer prevention in populations at risk should be evaluated and considered.
Asia–Pacific Consensus Guidelines (2008) [12]	• *H. pylori* screening and treatment is recommended for populations at high risk of gastric cancer. • *H. pylori* screening can be effective even in older age groups. • *H. pylori* screening is not recommended for low-risk populations.
Maastricht IV/Florence Consensus report (2012) [13]	• An *H. pylori* screen-and-treat strategy should be explored in communities with a substantial burden of gastric cancer. • *H. pylori* eradication to prevent gastric cancer should be undertaken in populations at high risk. • Validated serological tests for *H. pylori* and markers of atrophy (i.e. pepsinogens) are the best available non-invasive tests to identify individuals at high risk of gastric cancer.
Maastricht V/Florence Consensus report (2017) [14]	• *H. pylori* eradication for gastric cancer prevention is cost-effective in communities with a high risk of gastric cancer. • *H. pylori* eradication offers clinical and economic benefits other than gastric cancer prevention and should be considered in all communities. • A screen-and-treat strategy for *H. pylori* gastritis should be considered in communities with a low to intermediate risk of gastric cancer. • Public awareness campaigns for prevention of gastric cancer should be encouraged.
Bangkok Consensus report (2018) [15]	• Currently, community-based gastric cancer screening by endoscopy is not feasible in most ASEAN countries. • Community screening for *H. pylori* infection by non-invasive tests followed by eradication for gastric cancer prevention can be cost-effective depending on the disease burden in that community.
Taipei Global Consensus report (2020) [16]	• Young individuals would benefit most from *H. pylori* eradication because it cures *H. pylori*-related gastritis, reduces the risk of gastric cancer, and reduces transmission to their children. • The screen-and-treat strategy for *H. pylori* infection is most cost-effective in young adults for gastric cancer prevention in regions with a high incidence of gastric cancer. • The urea breath test or *H. pylori* stool antigen test are the preferred tests for mass screening, but a locally validated serology test may be considered. • Population-wide screening and eradication of *H. pylori* infection should be integrated or included in national health-care priorities to optimize the resources.

Table 2.1. Consensus reports and guidelines on *H. pylori* screen-and-treat strategies for gastric cancer prevention (continued)

Consensus report (year) [reference]	Statements and recommendations
Maastricht VI/Florence Consensus report (2022) [17]	• *H. pylori* eradication offers the chance for gastric cancer prevention at any age in adulthood. The magnitude of the benefit decreases with age. • Asymptomatic individuals older than 50 years are considered vulnerable and at increased risk of gastric cancer. • Screening modalities for gastric cancer prevention (non-invasive or endoscopic) combined with colorectal cancer screening is an opportunity. • Diagnostic tests used to screen *H. pylori* infection for the purpose of gastric cancer prevention should preferably be non-invasive. • If a serological method is used for *H. pylori* detection, a further test (urea breath test or stool antigen test) confirming current infection is required before initiating therapy. • Population-based *H. pylori* test-and-treat strategies provide additional benefits by preventing other gastroduodenal pathologies.
Chinese Consensus report (2022) [18]	• *H. pylori* should be screened and treated among family members living in the same household with patients who have gastric cancer or gastric mucosal pre-neoplastic lesions. • "Family-based *H. pylori* infection control and management" is an essential part of comprehensive *H. pylori* infection prevention and control strategies at the general public and community levels.
ACG Clinical Guideline (2024) [19]	• Broadly applied *H. pylori* screening and eradication for the primary prevention of gastric adenocarcinoma is not currently recommended in the general population in the USA. • Testing and treatment of *H. pylori* infection is appropriate in high-risk patient subgroups and in high-risk populations that involve defined ethnicities. • Serology for screening is not recommended.

ACG, American College of Gastroenterology; ASEAN, Association of Southeast Asian Nations.

The Bangkok Consensus report, published in 2018, stated that endoscopy-based gastric cancer screening was "not feasible" in most countries in the Association of Southeast Asian Nations (ASEAN) but considered non-invasive community screening for *H. pylori* infection followed by eradication to be cost-effective relative to the disease burden in that community [15]. The Taipei Global Consensus report, published in 2020, was the first global and comprehensive consensus report on population-based *H. pylori* screen-and-treat strategies for gastric cancer prevention [16]. In this consensus report, emphasis was placed on how to most effectively implement a population-based *H. pylori* screen-and-treat strategy. The urea breath test or the *H. pylori* stool antigen test (SAT) were the preferred tests, but locally validated serology tests were also considered to be appropriate [16].

The statements of the Maastricht VI/Florence Consensus report, published in 2022, provide the most recent comprehensive update of the evidence in support of *H. pylori*

test-and-treat strategies at the population level [17]. This consensus report also recommended the use of this prevention strategy at the individual level and for specific communities that are at increased risk. The report recommended adopting population-based *H. pylori* screen-and-treat strategies in all communities and suggested that the age group 50–69 years could be targeted at the same time as colorectal cancer screening was offered, in countries in which such programmes are in place [17].

A novel approach to gastric cancer prevention was proposed in the Chinese Consensus report, published in 2022 [18], which focused on family-based *H. pylori* infection testing and treatment as an important strategy to prevent intrafamilial transmission of the infection [20]. This consensus report deals with important considerations for a comprehensive prevention strategy with greater impact at the general public and community levels, particularly in regions with a high prevalence of *H. pylori* infection and a high incidence of gastric cancer.

However, there are other guidelines that do not recommend population-based *H. pylori* screen-and-treat strategies, particularly in areas with a low prevalence of gastric cancer. For example, in the most recent American College of Gastroenterology (ACG) Clinical Guideline, published in 2024, the primary prevention of gastric adenocarcinoma is not currently recommended in the general population in the USA [19].

Table 2.1 gives a summary of these guidelines. The most notable of these is the guideline from the USA on *H. pylori* management [19], which uses the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology [21].

2.3 Evidence from randomized controlled trials for the efficacy of *H. pylori* eradication in *H. pylori*-positive individuals to prevent gastric adenocarcinoma

Recent guidelines have given divergent recommendations on whether population-based *H. pylori* screen-and-treat strategies should be used for gastric cancer prevention. These guidelines have used evidence from systematic reviews and meta-analyses that have examined this issue [22–25]. Overall, in these systematic reviews, the quality of the evidence supporting the efficacy of population-based *H. pylori* screen-and-treat strategies to prevent gastric adenocarcinoma was low. The low grade of the evidence was based on the modest number of gastric cancer events that were observed in the systematic review. Therefore, the Working Group updated this systematic review using the same methodology [24] to evaluate whether any new randomized trials would

change the estimate of effect and/or the quality of the evidence. Searches of MEDLINE (from 1947 to September 2024), Embase and Embase Classic (from 1947 to September 2024), and the Cochrane Central Register of Controlled Trials (CENTRAL) were conducted to identify potential studies. In addition, ClinicalTrials.gov was searched to identify unpublished trials, or supplementary data for potentially eligible studies. Also, conference proceedings (Digestive Disease Week, ACG, United European Gastroenterology Week, and Asian Pacific Digestive Week) from 2001 to 2024 were searched. Finally, a recursive search was performed, using the bibliographies of all obtained articles.

The RCTs that were considered to be eligible examined the effects of at least 7 days of eradication therapy on subsequent occurrence of gastric cancer in *H. pylori*-positive individuals who were otherwise healthy or in *H. pylori*-positive patients with gastric neoplasia, including dysplasia or early gastric cancer, who underwent endoscopic mucosal resection (EMR), compared with placebo or no eradication therapy. Eligible studies were required to have recruited adults (aged ≥ 18 years). In all studies, irrespective of design, a minimum duration of follow-up of 2 years was required, and at least two gastric cancers had to occur during follow-up. All end-points were extracted at the last point of follow-up at which they were reported.

All abstracts identified by the search were independently assessed for eligibility, and the data were extracted by two investigators (Yuhong Yuan and Alexander C. Ford). Any disagreements between the investigators were resolved through arbitration by a third investigator (Paul Moayyedi). There were no language restrictions. When multiple articles were identified for a single study, only the data from the latest publication from each eligible study were extracted. The primary outcome in the RCTs was the effect of *H. pylori* eradication therapy, compared with placebo or no eradication therapy, on subsequent occurrence of gastric cancer. Secondary outcomes in RCTs included the effect of eradication therapy on gastric cancer-related mortality and the effect on all-cause mortality.

The risk of bias was evaluated at the study level by two independent reviewers (Alexander C. Ford and Paul Moayyedi) using the Cochrane risk-of-bias tool for randomized trials [26]. Disagreements were resolved through arbitration by a third investigator (Yuhong Yuan). Data were pooled using a random-effects model [27] to give a more conservative estimate of the effect of *H. pylori* eradication therapy on future incidence of gastric cancer, allowing for heterogeneity between studies. Heterogeneity

was assessed using both the χ^2 test, with $P < 0.10$ used to define a significant degree of heterogeneity, and the I^2 statistic [28]. The effective sample size of any cluster-randomized trial in the data synthesis was reduced using the method described by Rao et al. [29]. The quality of the evidence was rated using the GRADE methodology, which evaluates the quality of the evidence in terms of risk of bias, inconsistency, directness of the evidence, precision of the data, and evidence of publication bias [30].

A total of 13 articles [31–43] were identified, which reported on eight separate RCTs comparing *H. pylori* eradication therapy [32] with placebo or no eradication therapy in 58 628 healthy *H. pylori*-positive individuals. Since the last systematic review on this topic [24], the number of *H. pylori*-positive participants included in RCTs had increased from 8323 to 58 628. *H. pylori* eradication was defined as any recognized dual, triple, or quadruple therapy regimen [17]. One RCT [44] was excluded because it randomized participants who had received the faecal immunochemical test (FIT) for colorectal cancer screening to either also receiving or not receiving a SAT. All individuals with a positive SAT result were offered treatment, and the gastric cancer rates in the screened arm were compared with those in the unscreened arm. Because the gastric cancer rates in individuals with *H. pylori* infection in the unscreened arm could not be determined, an *H. pylori*-positive population could not be evaluated [44]. All RCTs recruited healthy people from the community who did not have gastric neoplasia at baseline, except for one RCT in the Republic of Korea, which recruited healthy first-degree relatives of patients with gastric cancer [42]. All studies were conducted in East Asia, except for one study that recruited a population at high risk of gastric cancer in Colombia [34]. In the identified RCTs in healthy populations, the longest duration of follow-up was 26.5 years [37] and the shortest duration of follow-up was ≥ 4 years [43].

Overall, 258 (0.87%) gastric cancers occurred in 29 782 individuals with *H. pylori* infection who received eradication therapy, compared with 351 (1.2%) gastric cancers in 28 846 individuals who received placebo or no eradication therapy. The relative risk of subsequent occurrence of gastric cancer with eradication therapy versus placebo or no eradication therapy was 0.64 (95% confidence interval [CI], 0.48–0.84), with some heterogeneity between studies ($I^2 = 35\%$; $P = 0.15$) (Fig. 2.1). The number needed to treat (NNT) to prevent one case of gastric cancer was 228 (95% CI, 158–514). When the analysis was restricted to trials with a low risk of bias, the risk estimate did not change (relative risk [RR], 0.54; 95% CI, 0.41–0.72; $I^2 = 0\%$; $P = 0.43$). Note that the results from one recent well-conducted RCT were excluded from the analyses; this trial

considered *H. pylori* screening and treatment as a total strategy (rather than focusing only on participants with *H. pylori* infection), and the results of the trial were largely negative [44], which is probably related to a lack of power. The initial proportion of participants who were randomized seemed to be large (120 000 in each group), but only 26% received any screening (FIT with or without SAT). Fewer than 40% of the participants in the testing arm had *H. pylori* infection, and only about 70% were offered therapy. In retrospect, this amount of attrition meant that the trial was underpowered. In a post hoc analysis, *H. pylori* screening was associated with a lower gastric cancer incidence (but not mortality) when adjusting for patient characteristics, compared with FIT alone [44].

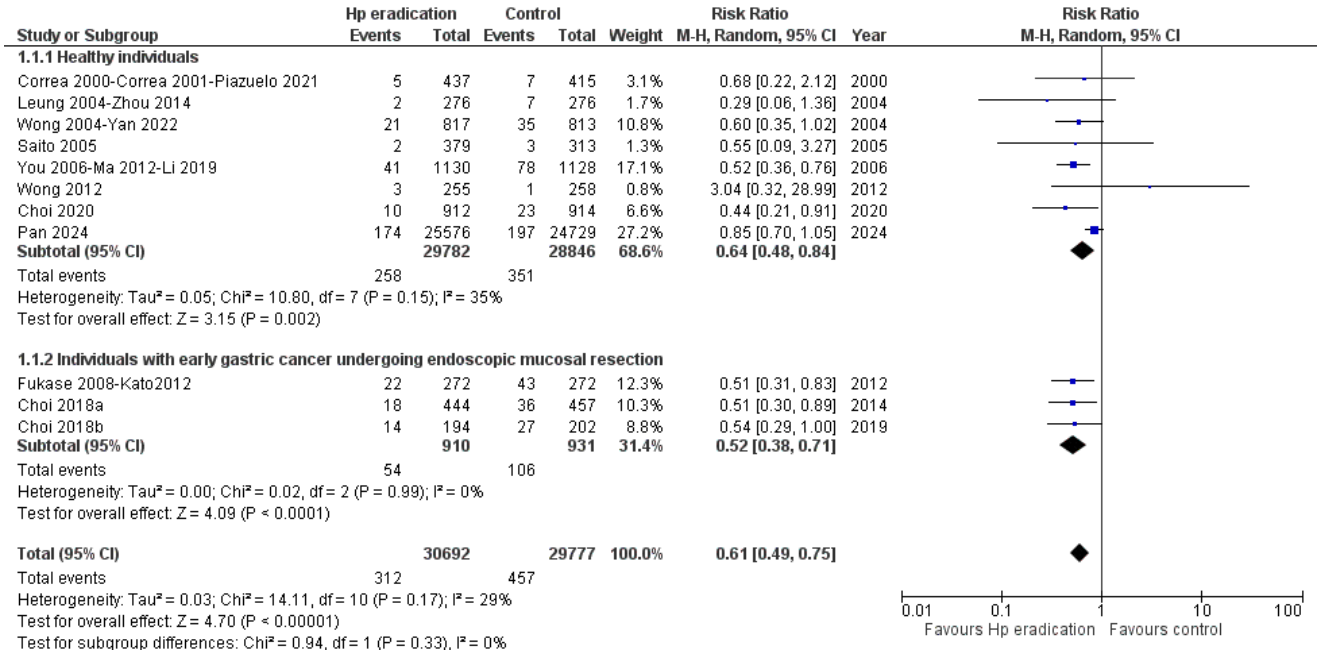

Fig. 2.1. Meta-analysis of population trials evaluating gastric cancer incidence in participants with *H. pylori* infection randomized to eradication therapy versus controls. CI, confidence interval; df, degrees of freedom; Hp, *H. pylori*; M-H, Mantel–Haenszel. Reproduced from Ford et al. (2025) [45].

There were five RCTs conducted in healthy *H. pylori*-positive individuals, which provided data on mortality from gastric cancer in 56 606 individuals [32, 35, 36, 40, 42]. The duration of follow-up in these five trials ranged from 9.2 years to 26.5 years. Overall, there were 124 (0.43%) deaths from gastric cancer in 28 730 individuals with *H. pylori* infection who were randomized to eradication therapy, compared with 156 (0.56%)

deaths from gastric cancer in 27 876 participants who were allocated to placebo or no eradication therapy. The relative risk of death from gastric cancer with eradication therapy compared with placebo or no eradication therapy was 0.78 (95% CI, 0.62–0.98) (Fig. 2.2), with no heterogeneity between studies (I^2 = 0%; P = 0.65). The NNT to prevent one gastric cancer death was 812 (95% CI, 470–8935).

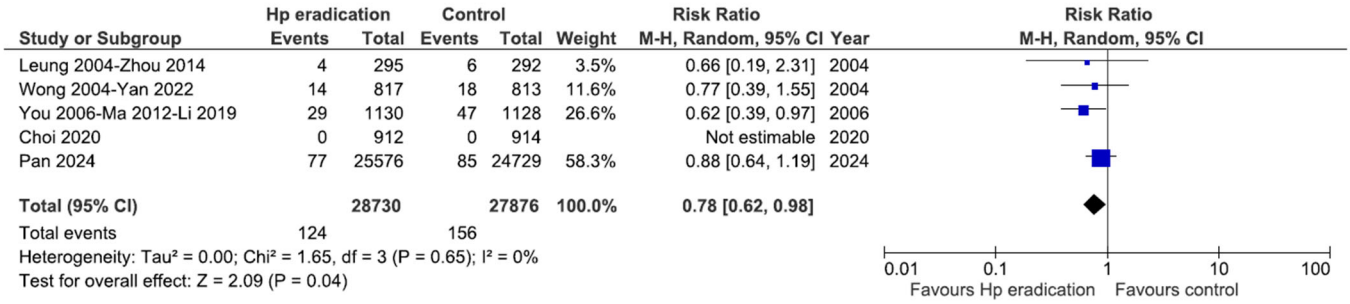

Fig. 2.2. Meta-analysis of population trials evaluating gastric cancer mortality in participants with *H. pylori* infection randomized to eradication therapy versus controls. CI, confidence interval; df, degrees of freedom; Hp, *H. pylori*; M-H, Mantel–Haenszel. Reproduced from Ford et al. (2025) [45]. © 2025 by the AGA Institute. Article available under the Creative Commons CC BY 4.0.

There were five RCTs that reported all-cause mortality in 7079 healthy *H. pylori*-positive individuals [34, 36, 37, 40, 42]. The duration of follow-up in these five trials ranged from 5 years to 26.5 years. In total, 420 (11.8%) of 3551 individuals with *H. pylori* infection who received eradication therapy had died by the last point of follow-up, compared with 426 (12.1%) of 3528 individuals who received placebo or no eradication therapy. The relative risk of death from any cause at the last point of follow-up with eradication therapy compared with placebo or no eradication therapy was 0.98 (95% CI, 0.87–1.11) (Fig. 2.3), with no heterogeneity between studies (I^2 = 0%; P = 0.49).

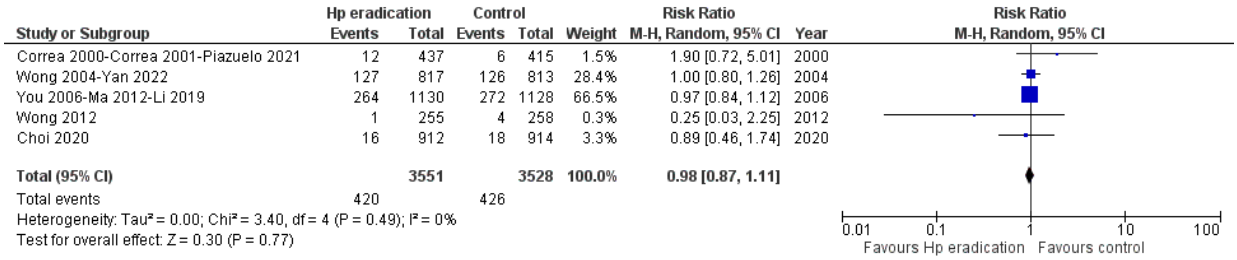

Fig. 2.3. All-cause mortality for randomized controlled trials evaluating *H. pylori* eradication therapy versus placebo or no treatment. CI, confidence interval; df, degrees of freedom; Hp, *H. pylori*; M-H, Mantel–Haenszel. Reproduced from Ford et al. (2025) [45]. © 2025 by the AGA Institute. Article available under the Creative Commons CC BY 4.0.

Some authors have recommended treating the young adult population because there may be a “point of no return”, at which pre-neoplastic changes are too advanced for *H. pylori* eradication to be effective at reducing the risk of gastric adenocarcinoma [46]. To answer this question, studies were identified in which patients with early gastric adenocarcinoma had been treated with EMR and then the patients with *H. pylori* infection were randomized to eradication therapy or placebo or no eradication therapy and were followed up to determine the recurrence of new cancer. Three RCTs [47–49] compared *H. pylori* eradication therapy with placebo or no eradication therapy in 1841 *H. pylori*-positive patients in this group. There were 54 (5.9%) recurrent gastric cancers in 910 patients who were randomized to eradication therapy, compared with 106 (11.4%) recurrent gastric cancers in 931 patients who were received placebo or no eradication therapy (RR, 0.52; 95% CI, 0.38–0.71; $I^2 = 0\%$; $P = 0.99$) (Fig. 2.1). The NNT was 18 (95% CI, 14–30). Minor heterogeneity was observed between the effect in the general population compared with those treated with EMR for early gastric cancer (subgroup heterogeneity, $P = 0.17$; $I^2 = 29\%$), suggesting from a statistical point of view that there was little evidence that the response to eradication therapy was worse in the group with early gastric cancer who were treated with EMR. The overall pooled effect for incidence of new gastric cancer was a relative risk of 0.61 (95% CI, 0.49–0.75) (Fig. 2.1). This is evidence that there is no “point of no return” for receiving *H. pylori* eradication therapy, provided that gastric cancer has not already developed.

Most studies reported adverse events associated with receiving *H. pylori* eradication therapy compared with placebo or no eradication therapy [31, 33–42, 44]. There were increased short-term adverse events associated with antibiotic use, but no severe or

long-term adverse events were reported. These data were not pooled because different antibiotic regimens were used that have different adverse event profiles, such as diarrhoea, altered taste, and nausea.

Overall, the GRADE quality of evidence that population-based *H. pylori* screen-and-treat strategies reduce the incidence of gastric adenocarcinoma is now moderate; the level of evidence was downgraded because of some modest heterogeneity between studies. There had previously been some concerns about imprecision, but the new trial data mean that this is no longer an issue.

2.4 Evidence from randomized trials for other harms and benefits of population-based *H. pylori* screen-and-treat strategies

H. pylori organisms have infected humans for many thousands of years [50]. It is reasonable to hypothesize that over this time mutualism may have evolved and the infection may confer some benefits to humans [51]. *H. pylori* infection has been inversely associated with gastro-oesophageal reflux symptoms and erosive oesophagitis [52], which reduce quality of life [53]. Gastro-oesophageal reflux symptoms have been associated with oesophageal adenocarcinoma [54], and having *H. pylori* infection has also been associated with a reduced risk of developing this malignancy [55]. Both gastro-oesophageal reflux and oesophageal adenocarcinoma are associated with affluent living conditions [56], and *H. pylori* infection is inversely associated with socioeconomic status [57]. Therefore, the apparent protective effect of *H. pylori* may relate to residual confounding by social class or other unmeasured confounding factors. Furthermore, in a recent large cohort study, *H. pylori* eradication was not associated with an increased risk of subsequent oesophageal adenocarcinoma [58].

Population-based *H. pylori* screen-and-treat strategies may have other benefits. RCTs have reported that treatment of *H. pylori* infection reduces the incidence of both gastric ulcer and duodenal ulcer [59]. A systematic review has also reported that *H. pylori* eradication therapy has a modest impact in reducing symptoms of functional dyspepsia in individuals with *H. pylori* infection [60]. Therefore, it is possible that a population-based *H. pylori* screen-and-treat programme could reduce peptic ulcer disease, dyspepsia symptoms, and dyspepsia-related clinician consultations, in addition to reducing gastric adenocarcinoma. This could help offset the cost of such a programme. Therefore, the potential harms and benefits of the programme in

population-based randomized trials of *H. pylori* screen-and-treat strategies were evaluated.

H. pylori *eradication and risk of oesophageal cancer*

In the meta-analyses described above, three RCTs reported on oesophageal cancer [32, 37, 40]. The duration of follow-up in these trials ranged from 11.8 years and 26.5 years. Overall, there were 56 oesophageal cancers in 27 523 individuals allocated to *H. pylori* eradication arms, compared with 49 oesophageal cancers in 26 670 individuals allocated to control arms (RR, 1.12; 95% CI, 0.76–1.64), with little heterogeneity between trials ($P = 0.85$; $I^2 = 0\%$) (Fig. 2.4). These trials did not report on the histology of oesophageal cancers, but given that all these trials were carried out in Asia it is probable that most were squamous cell carcinomas. There is no evidence from these trials that a population-based *H. pylori* screen-and-treat strategy leads to an increase in oesophageal adenocarcinoma.

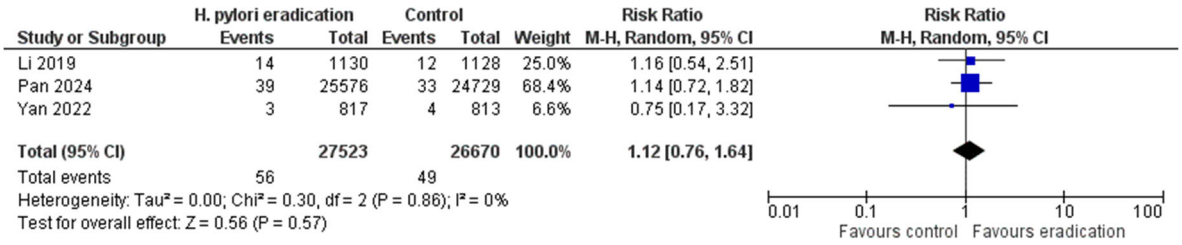

Fig. 2.4. Meta-analysis of population trials evaluating oesophageal cancer incidence in participants with *H. pylori* infection randomized to eradication therapy versus controls. M-H, Mantel–Haenszel.

H. pylori *eradication and risk of gastro-oesophageal reflux symptoms*

Population-based RCTs that reported on gastric adenocarcinoma did not describe reflux or dyspepsia symptoms in their populations. Three trials did evaluate this outcome: two in the United Kingdom [61, 62] and in from Denmark [63]. The trial in Denmark [63] was excluded because it randomized populations to receive screening or not receive screening. Because all participants with *H. pylori* infection in the screening arm were offered eradication therapy and there are no data on *H. pylori* infection status in unscreened participants, data on dyspepsia or reflux are inconclusive. In the other two RCTs [61, 62], 369 (18.9%) of the 1948 participants who were allocated to eradication therapy had heartburn at 2 years, compared with 411 (21.3%) of the 1934 participants in the control group, using the intention-to-treat approach (RR, 0.89; 95% CI, 0.77–1.04)

(Fig. 2.5). About 20% of participants in both trials were lost to follow-up at 2 years and were assumed to not have reflux at 2 years in the intention-to-treat analysis. The corresponding data for all evaluable patients were that 369 (23.2%) of the 1593 participants who were allocated to eradication therapy had heartburn at 2 years, compared with 411 (26.0%) of the 1581 participants in the control group (RR, 0.90; 95% CI, 0.75–1.07). Therefore, there was no signal suggesting that people who had been allocated to *H. pylori* eradication had more heartburn than controls after 2 years of follow-up.

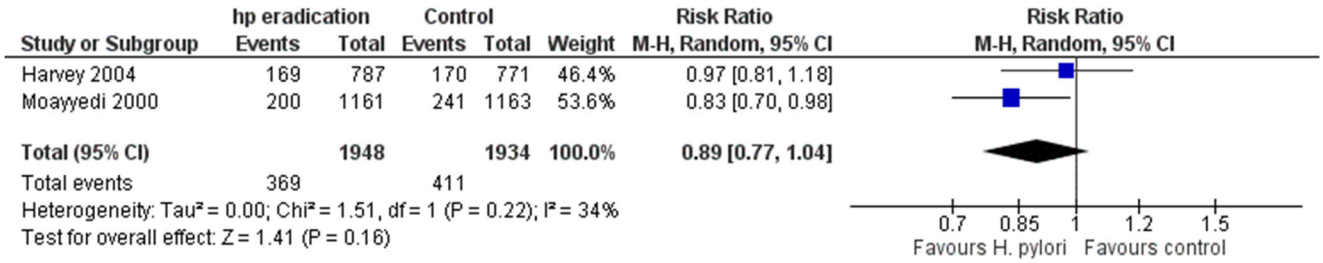

Fig. 2.5. Meta-analysis of population trials evaluating the prevalence of reflux symptoms in participants with *H. pylori* infection randomized to eradication therapy versus controls. CI, confidence interval; df, degrees of freedom; M-H, Mantel–Haenszel.

H. pylori *eradication and reduction of dyspepsia and peptic ulcer in population screening*

There were two RCTs [61, 64] that evaluated dyspepsia as an outcome after 2 years of follow-up. In total, 415 (21.3%) of the 1948 participants allocated to eradication therapy had dyspepsia at 2 years, compared with 500 (25.6%) of the 1934 participants in the control group, using the intention-to-treat approach (RR, 0.82; 95% CI, 0.74–0.92) (Fig. 2.6). About 20% of participants in both trials were lost to follow-up at 2 years and were assumed to not have dyspepsia at 2 years in the intention-to-treat analysis. The corresponding data for all evaluable patients were that 415 (25.7%) of the 1616 participants allocated to eradication therapy had dyspepsia at 2 years, compared with 500 (26.0%) of the 1582 participants in the control group, using the all-evaluable-participant approach (RR, 0.81; 95% CI, 0.73–0.91). One trial [61] reported that peptic ulcer disease was recorded in 4 participants who were allocated to *H. pylori* eradication therapy, compared with 13 participants in the placebo group, which is a statistically

significant reduction ($P = 0.04$). One trial in the United Kingdom [65] found that dyspepsia consultations were reduced by 35% over 2 years in those allocated to *H. pylori* eradication therapy and that this benefit persisted for 7 years [66], although the other trial in the United Kingdom [67] suggested that cost savings occurred after 10 years of follow-up. It is probable that a population-based *H. pylori* screen-and-treat programme would reduce the prevalence of dyspepsia in the community, and the resulting health-care cost savings could partly offset the cost of the programme.

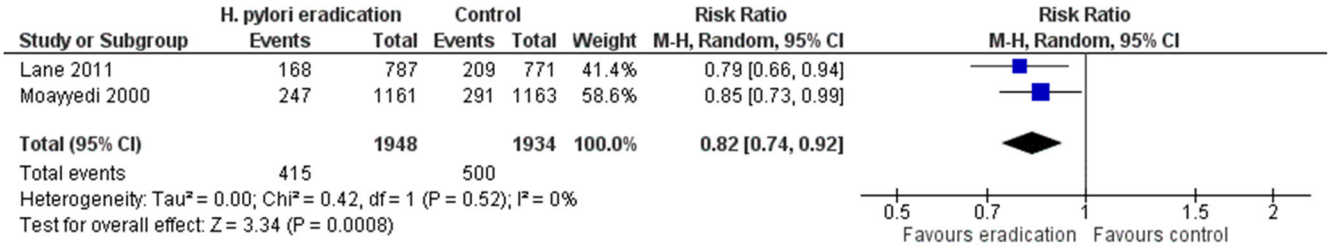

Fig. 2.6. Meta-analysis of population trials evaluating the prevalence of dyspepsia symptoms in participants with *H. pylori* infection randomized to eradication therapy versus controls. CI, confidence interval; df, degrees of freedom; M-H, Mantel–Haenszel.

2.5 Conclusions

There is now moderate-quality evidence that population-based *H. pylori* screen-and-treat strategies reduce the incidence of gastric adenocarcinoma. There are no data from countries in Europe and North America, and results from such trials are eagerly awaited. The NNTs described in this chapter, from meta-analyses of RCTs, are all from high-risk countries, and the NNTs will be much higher for low-risk countries. There is no evidence that these programmes increase the incidence of gastro-oesophageal reflux symptoms or oesophageal cancer. There is evidence that such programmes reduce the prevalence of dyspepsia in the community and reduce the associated health-care costs. If countries adopt population-based *H. pylori* screen-and-treat strategies, it will be important to assess the possible harms, because the data to date are not conclusive.

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