ClinicalEvidence

Helicobacter pylori eradication: gastric cancer prevention

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ABSTRACT

INTRODUCTION: The principal effect of Helicobacter pylori infection is lifelong chronic gastritis, affecting up to 20% of younger adults but 50% to 80% of adults born in resource-rich countries before 1950. METHODS AND OUTCOMES: We conducted a systematic overview, aiming to answer the following clinical question: What are the effects of H pylori eradication treatment on the risk of developing gastric cancer? We searched: Medline, Embase, The Cochrane Library, and other important databases up to July 2014 (BMJ Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). RESULTS: At this update, searching of electronic databases retrieved 208 studies. After deduplication and removal of conference abstracts, 166 records were screened for inclusion in the overview. Appraisal of titles and abstracts led to the exclusion of 124 studies and the further review of 42 full publications. Of the 42 full articles evaluated, one systematic review was added at this update. We performed a GRADE evaluation for two PICO combinations. CONCLUSIONS: In this systematic overview, we categorised the efficacy for one intervention based on information about the effectiveness and safety of H pylori eradication treatment for the prevention of gastric cancer.

QUESTIONS

INTERVENTIONS

EFFECTS OF H PYLORI TREATMENT ON RISK OF GASTRIC CANCER

Likely to be beneficial

Key points

- The principal effect of *Helicobacter pylori* infection is lifelong chronic gastritis, affecting up to 20% of younger adults but 50% to 80% of adults born before 1950 in resource-rich countries.

  H pylori infection can be identified indirectly by the C13 (or C14) urea breath test and stool antigen tests, which are more accurate than serology.

  Transmission and prevalence rates are higher in areas of childhood poverty. Adult re-infection rates are less than 1% a year.

  In people with *H pylori* infection, about 15% will develop a peptic ulcer and 1% will develop gastric cancer during their lifetime.

  Gastric cancer is the fourth most frequent cancer worldwide in men and the fifth in women, although the incidence varies widely among countries.

- For this overview, we evaluated evidence from RCTs and systematic reviews of RCTs. We found one systematic review and meta-analysis showing:

  H pylori eradication treatment is likely to be more effective than placebo or no treatment at reducing the risk of developing gastric cancer within the subsequent 4 to 15 years in healthy *H pylori*-infected individuals (relative risk 0.66; 95% CI 0.46 to 0.95).

  The quality of evidence was low because of methodological limitations of the RCTs (lack of masking, factorial design) and also because of indirectness, as five out of six RCTs were conducted in East Asia, while the sixth RCT was conducted in Central America.

Clinical context

GENERAL BACKGROUND

Gastric cancer is the fourth most frequent cancer worldwide in men and the fifth in women, but the incidence varies widely among countries. A large number of observational studies have shown a consistent association of gastric cancer, especially non-cardia gastric cancer, with *Helicobacter pylori* infection, a chronic infection of the gastric mucosa that affects approximately half of all humans worldwide.

FOCUS OF THE REVIEW

Given the epidemiological association between gastric cancer and *H pylori* infection, it is of major clinical importance to assess through RCTs whether the risk of this malignancy is reduced when the infection is eradicated.

COMMENTS ON EVIDENCE

We found a systematic review and meta-analysis showing that *H pylori* eradication treatment is likely to be more effective than placebo or no treatment at reducing the risk of developing gastric cancer within the subsequent 4 to 15 years in healthy *H pylori*-infected individuals. The quality of evidence was low because of methodological limitations of the RCTs (lack of masking, factorial design), and also because of indirectness, as five out of six RCTs had been conducted in East Asia, while the sixth RCT had been conducted in Central America. In fact, if our population of interest had been healthy *H pylori*-infected individuals who live in East Asia, the quality of evidence for the results would have been moderate (i.e., one level higher).

SEARCH AND APPRAISAL SUMMARY

The update literature search for this overview was carried in July 2014. For more information on the electronic databases searched and criteria applied during assessment of studies for potential relevance to the overview, please see the Methods section. Searching of electronic databases retrieved 208 studies. After deduplication and removal of conference abstracts, 166 records were screened for inclusion in the overview. Appraisal of titles and abstracts led to the exclusion of 124 studies and the further review of 42 full publications. Of the 42 full articles evaluated, one systematic review was added at this update.

ADDITIONAL INFORMATION

The systematic review cited above found no significant difference between eradication therapy and control in all-cause mortality. The systematic review included subgroup analyses according to the presence or absence of pre-cancerous lesions at baseline, and found no evidence that the eradication therapy had a different effect on the risk of gastric cancer in any of the subgroups (contrary to widely publicised preliminary results of one of the RCTs).

DEFINITION	*Helicobacter pylori* is a gram-negative flagellated spiral bacterium found in the stomach. Infection with *H pylori* is predominantly acquired in childhood. It is the fourth most frequent cancer worldwide in men, and fifth in women, but incidence varies widely among countries. [1] *H pylori* infection is not associated with a specific type of dyspeptic symptom. The organism is associated with lifelong chronic gastritis and may cause other gastroduodenal disorders. [2] A large number of observational studies have shown a consistent association of gastric cancer, especially non-cardia gastric cancer, with *H pylori* infection, a chronic infection of the gastric mucosa that affects approximately half of all humans. [3] [4] **Diagnosis** *H pylori* can be identified indirectly by serology or by the C13 urea breath test. The urea breath test is more accurate than serology, with a sensitivity and specificity greater than 95%, and indicates active infection, whereas serology may lack specificity and cannot be used reliably as a test of active infection. Thus, the urea breath test is the test of choice where prevalence (and hence predictive value of serology) may be low, or where a 'test of cure' is required. In some areas, stool antigen tests that have a similar performance to the urea breath test are now available. [5] **Population** This overview focuses on healthy asymptomatic *H pylori*-positive people throughout.
INCIDENCE/ PREVALENCE	In the developed world, *H pylori* prevalence rates vary with year of birth and social class. Prevalence in many resource-rich countries tends to be much higher (50%–80%) in individuals born before 1950 compared with prevalence (<20%) in individuals born more recently. [6] In many resource-poor countries, the infection has a high prevalence (80%–95%) irrespective of the period of birth. [7] Adult prevalence is believed to represent the persistence of a historically higher rate of infection acquired in childhood, rather than increasing acquisition of infection during life.
AETIOLOGY/ RISK FACTORS	Overcrowded conditions associated with childhood poverty lead to increased transmission and higher prevalence rates. Adult re-infection rates are low — less than 1% a year. [7]
PROGNOSIS	*H pylori* infection is believed to be causally related to the development of duodenal and gastric ulceration, B cell gastric lymphoma, and distal (i.e., non-cardia) gastric cancer. About 15% of people infected with *H pylori* will develop a peptic ulcer, and 1% of people will develop gastric cancer during their lifetime. [8]
AIMS OF INTERVENTION	Reduction of risk of gastric cancer; improvement in quality of life.
OUTCOMES	**Incidence of or mortality from gastric cancer**; **regression of pre-cancerous lesions**; **adverse effects**.
METHODS	**Search strategy** *BMJ Clinical Evidence* search and appraisal date July 2014. Databases used to identify studies for this systematic overview include: Medline 1966 to July 2014, Embase 1980 to July 2014, The Cochrane Database of Systematic Reviews 2014, issue 7 (1966 to date of issue), the Database of Abstracts of Reviews of Effects (DARE), and the Health Technology Assessment (HTA) database. **Inclusion criteria** Study design criteria for inclusion in this systematic overview

were systematic reviews and RCTs published in English, at least single-blinded, and containing more than 20 individuals (at least 10 in each arm), of whom more than 80% were followed up. There was no minimum length of follow-up. We excluded all studies described as 'open', 'open label', or not blinded unless blinding was impossible. *BMJ Clinical Evidence* does not necessarily report every study found (e.g., every systematic review). Rather, we report the most recent, relevant, and comprehensive studies identified through an agreed process involving our evidence team, editorial team, and expert contributors. **Evidence evaluation** A systematic literature search was conducted by our evidence team, who then assessed titles and abstracts, and finally selected articles for full text appraisal against inclusion and exclusion criteria agreed *a priori* with our expert contributors. In consultation with the expert contributors, studies were selected for inclusion and all data relevant to this overview extracted into the benefits and harms section of the review. In addition, information that did not meet our pre-defined criteria for inclusion in the benefits and harms section may have been reported in the 'Further information on studies' or 'Comment' sections (see below). **Adverse effects** All serious adverse effects, or those adverse effects reported as statistically significant, were included in the harms section of the overview. Pre-specified adverse effects identified as being clinically important were also reported, even if the results were not statistically significant. Although *BMJ Clinical Evidence* presents data on selected adverse effects reported in included studies, it is not meant to be, and cannot be, a comprehensive list of all adverse effects, contraindications, or interactions of included drugs or interventions. A reliable national or local drug database must be consulted for this information. **Comment and Clinical guide sections** In the Comment section of each intervention, our expert contributors may have provided additional comment and analysis of the evidence, which may include additional studies (over and above those identified via our systematic search) by way of background data or supporting information. As *BMJ Clinical Evidence* does not systematically search for studies reported in the Comment section, we cannot guarantee the completeness of the studies listed there or the robustness of methods. Our expert contributors add clinical context and interpretation to the Clinical guide sections where appropriate. **Structural changes this update** At this update, we have removed the following previously reported questions: What are the effects of *H pylori* eradication treatment in people with a confirmed duodenal ulcer, a confirmed gastric ulcer, confirmed gastro-oesophageal reflux disease (GORD), confirmed non-ulcer dyspepsia, uninvestigated dyspepsia, localised B cell lymphoma of the stomach, and non-steroidal anti-inflammatory drug (NSAID)-related peptic ulcers? What are the effects of *H pylori* eradication treatment for preventing NSAID-related peptic ulcers in people with or without previous ulcers or dyspepsia? Do *H pylori* eradication treatments differ in their effects? **Data and quality** To aid readability of the numerical data in our overviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). *BMJ Clinical Evidence* does not report all methodological details of included studies. Rather, it reports by exception any methodological issue or more general issue that may affect the weight a reader may put on an individual study, or the generalisability of the result. These issues may be reflected in the overall GRADE analysis. We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 8). The categorisation of the quality of the evidence (high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the Clinical Evidence population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com).

QUESTION What are the effects of Helicobacter pylori eradication treatment on the risk of developing gastric cancer?

OPTION HELICOBACTER PYLORI ERADICATION TREATMENT FOR PREVENTION OF GASTRIC CANCER

- For GRADE evaluation of interventions for Helicobacter pylori eradication: gastric cancer prevention, see table, p 8 .
- Our population of interest was healthy asymptomatic people who tested positive for *H pylori*.
- *H pylori* eradication treatment may be more effective at reducing the risk of developing gastric cancer within 4 to 15 years in healthy

  H pylori-infected individuals in East Asia compared with placebo or no treatment.
- *H pylori* eradication treatment may be more effective than no

H pylori eradication treatment at increasing regression of pre-cancerous lesions in people with gastric atrophy. We don't know if it is more effective than no

H pylori eradication treatment at increasing regression of pre-cancerous lesions in people with intestinal metaplasia because the results were of borderline significance.

Benefits and harms

H pylori eradication treatment versus placebo or no treatment for the prevention of gastric cancer in asymptomatic, healthy *H pylori*-infected individuals:

We found one systematic review (search date 2013, 6 RCTs, at least 6497 people), [9] which evaluated eradication treatment compared with control (placebo or no treatment) in asymptomatic, healthy *H pylori*-infected individuals. We also found the full publication of a conference abstract identified by the review and from which data on 10-year follow-up were taken and used in the analysis carried out by the review; the event rates reported in the conference abstract matched those presented in the full publication. [10]

Incidence of or mortality from gastric cancer

H pylori eradication treatment compared with placebo or no treatment *H pylori* eradication treatment may be more effective at reducing the risk of developing gastric cancer within 4–15 years in healthy *H pylori*-infected individuals in East Asia compared with placebo (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Rate of gastric cancer					
[9] Systematic review	People positive for *H pylori infection* and who were otherwise healthy and asymptomatic 6 RCTs in this analysis See Further information on studies	**Occurrence of gastric cancer , 4–15 years** 51/3294 (1.5%) with *H pylori* eradication treatment 76/3203 (2.4%) with control (placebo or no treatment) 6497 people in this analysis	RR 0.66 95% CI 0.46 to 0.95 P = 0.02 The authors of the review note that the effect estimate is heavily influenced by one study	●○○	*H pylori* eradication treatment

Adverse effects

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Adverse effects					
[9] Systematic review	People positive for *H pylori* infection and who were otherwise healthy and asymptomatic Data from 1 RCT	**Adverse effects** with *H pylori* eradication treatment with control (placebo or no treatment) Absolute results not reported	Reported as not statistically significant P value not reported	⟷	Not significant
[9] Systematic review	People positive for *H pylori* infection and who were otherwise healthy and asymptomatic Data from 1 RCT	**Skin rash** 3.1% with *H pylori* eradication treatment 0.1% with control (placebo or no treatment) Absolute numbers not reported	Reported as significant P value not reported	○○○	control (placebo or no treatment)

H pylori eradication treatment versus placebo or no treatment for regression of pre-cancerous lesions:

We found one RCT. [11]

Regression of pre-cancerous lesions

H pylori eradication treatment compared with no treatment H pylori eradication treatment may be more effective than no *H pylori* eradication treatment at increasing regression of pre-cancerous lesions in people with gastric atrophy. We don't know if it is more effective than no *H pylori* eradication treatment at increasing regression of pre-cancerous lesions in people with intestinal metaplasia because the results were of borderline significance (low-quality evidence).

Ref (type)	Population	Outcome, Interventions	Results and statistical analysis	Effect size	Favours
Regression of gastric atrophy					
[11] RCT **4-armed trial**	852 people with gastric atrophy or intestinal metaplasia found at screening endoscopy	**Atrophy** with *H pylori* eradication treatment with no *H pylori* eradication treatment Absolute results not reported The four arms evaluated *H pylori* eradication treatment, beta-carotene, ascorbic acid, and placebo	RR 4.8 95% CI 1.6 to 14.2 Result calculated by multivariate modelling	●●○	*H pylori* eradication treatment
Regression of intestinal metaplasia					
[11] RCT **4-armed trial**	852 people with gastric atrophy or intestinal metaplasia found at screening endoscopy	**Intestinal metaplasia** with *H pylori* eradication treatment with no *H pylori* eradication treatment Absolute results not reported The four arms evaluated *H pylori* eradication treatment, beta-carotene, ascorbic acid, and placebo	RR 3.1 95% CI 1.0 to 9.3 Result calculated by multivariate modelling	●●○	*H pylori* eradication treatment

Adverse effects

No data from the following reference on this outcome. [11]

Further information on studies

[9] Of the six identified RCTs, only three were considered to have a low risk of bias. Of the remaining three RCTs, two were open label and one did not describe its methods of randomisation. In addition, some of the trials had a factorial design, which makes it difficult to determine whether the reduction in relative risk of subsequent gastric cancer was due to *H pylori* eradication therapy alone or due to the combination of *H pylori* eradication therapy with co-administered antioxidants or vitamins. Five of the RCTs were carried out in East Asia and, therefore, it would not be appropriate to extrapolate the results of the analysis to populations outside Asia. The review found no significant difference between *H pylori* eradication therapy and control in all-cause mortality (4 RCTs, 5253 people: 192/2639 (7%) with eradication therapy *v* 175/2614 (7%) with control; RR 1.09, 95% CI 0.86 to 1.38).

Comment: Two of the identified RCTs [12] [13] [14] included in the systematic review [9] reported subgroup analyses according to the presence or absence of pre-cancerous lesions at baseline. In one of these RCTs, [12] this subgroup analysis suggested that the risk of gastric cancer was reduced only in people without baseline pre-cancerous lesions (not in patients with pre-cancerous lesions at

baseline), and this has been widely publicised. However, when the systematic review [9] conducted subgroup analyses according to the presence or absence of pre-cancerous lesions at baseline, there was no evidence that the *H pylori* eradication therapy had a different effect on the risk of gastric cancer in any of the subgroups.

We assessed the GRADE for the outcome 'Regression of pre-cancerous lesions', which included Regression of gastric atrophy and Regression of intestinal metaplasia combined under the same outcome. A single GRADE assessment was made of 'low-quality evidence'. However, if we had pre-specified separate outcomes for regression of gastric atrophy and regression of intestinal metaplasia, the GRADE assessment would have been higher quality for Regression of gastric atrophy than it would have been for Regression of intestinal metaplasia.

With regards to the international readership of *BMJ Clinical Evidence*, the findings of the systematic review [9] are even more relevant and more directly generalisable to populations in the developing or developed world with a high prevalence of *H pylori*. As mentioned above, five of the six identified RCTs were conducted in East Asia, while the sixth RCT was conducted in Central America. The quality of evidence for reducing gastric cancer risk with *H pylori* eradication treatment as assessed by GRADE is moderate for populations in East Asian countries, as opposed to low quality of evidence for Western countries. The authors of the systematic review [9] calculated that the number needed to treat in China or Japan is approximately 15 for men and 23 for women, as opposed to 95 and 163, respectively, in the UK.

It should be noted that the true efficacy of *H pylori* eradication treatment with regards to gastric cancer risk reduction may have been higher than the observed efficacy in the six RCTs because of two specific biases that would tend to reduce the observed efficacy. First, results were reported per intention to treat (according to whether *H pylori* eradication treatment was administered or not, rather than according to whether *H pylori* eradication was actually achieved or not). This means that patients in whom the treatment failed to eradicate the infection (whose gastric cancer risk was, therefore, unlikely to have changed) were counted in the '*H pylori* eradication treatment' group. This 'misclassification bias' would tend to dilute the beneficial effect of the treatment with regards to the reduction of gastric cancer risk. The effect of this bias on the results was further strengthened by the fact that the eradication regimens used by some studies (PPI plus standard dose amoxicillin for 2 weeks, or bismuth subsalicylate with amoxicillin and metronidazole without acid suppression for 2 weeks) were unlikely to achieve high eradication rates. Second, none of the six RCTs reported the incidence of distal (non-cardia) gastric cancers separately from proximal (cardia) gastric cancers. Current epidemiological evidence suggests that *H pylori* infection is associated with distal gastric cancers, not proximal gastric cancers. Therefore, we would expect that the beneficial effect of *H pylori* treatment on gastric cancer risk to be limited in — or be stronger for — distal gastric cancers. By pooling all gastric cancers together, any beneficial effect of *H pylori* treatment is likely to have been diluted.

We found one systematic review of nested case control studies (search date 1999; 12 studies, 1228 cases, 3406 controls). [15] The review found that overall there was a significant association between *H pylori* infection and the subsequent development of gastric cancer (OR 2.36, 95% CI 1.98 to 2.81). The review found no significant association between *H pylori* and cardia cancer (OR 0.99, 95% CI 0.72 to 1.35). It did find a significant association for non-cardia (distal) cancer (OR 2.97, 95% CI 2.34 to 3.77). The review also found a strong interaction with age and time from sample collection. *H pylori* does not colonise areas of cancer, intestinal metaplasia, or atrophy, and antibodies may be lost with increasing age. Prospective studies with a short time period between the collection of the serum sample and the development of the cancer, or retrospective studies, may underestimate the association. The review found a significant association between *H pylori* and non-cardia cancer, where the time from sampling to cancer was more than 10 years (OR 5.93, 95% CI 3.41 to 10.3). [15]

Clinical guide

H pylori screening (by serology) and treatment for healthy people for prevention of gastric cancer in high-risk populations has been recommended by the 2008 Asia-Pacific guidelines on gastric cancer prevention. [16] No Western clinical practice guidelines have made such a recommendation as yet, although the Maastricht IV Consensus report by the European Helicobacter Study Group recommended that "a screen-and-treat strategy of *H pylori* should be explored in communities with a significant burden of gastric cancer", not only in Asia but also "in other high-risk areas around the world, including Europe". [5] Furthermore, the lead authors of the 2008 Asia-Pacific guidelines have pointed out that the search-and-treat recommendations "may apply to subpopulations with high background rates of *H pylori* in Western countries, for example, in immigrant groups in the US". [17]

GLOSSARY

Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

SUBSTANTIVE CHANGES

***Helicobacter pylori* eradication treatment for prevention of gastric cancer** One systematic review [9] added. Categorisation changed from 'unknown effectiveness' to 'likely to be beneficial'.

REFERENCES

1. Torre LA, Bray F, Siegel RL, et al. Global cancer statistics, 2012. *CA Cancer J Clin* 2015;65:87–108.[PubMed]
2. Nguyen TN, Barkun AN, Fallone CA. Host determinants of *Helicobacter pylori* infection and its clinical outcome. *Helicobacter* 1999;4:185–197. [PubMed]
3. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Schistosomes, liver flukes and Helicobacter pylori. *IARC Monogr Eval Carcinog Risks Hum* 1994;61:1–241.[PubMed]
4. Parsonnet J. The incidence of Helicobacter pylori infection. *Aliment Pharmacol Ther* 1995;9(Suppl. 2):45–51.[PubMed]
5. Malfertheiner P, Megraud F, O'Morain CA, et al; European Helicobacter Study Group. Management of Helicobacter pylori infection – the Maastricht IV/ Florence Consensus Report. *Gut* 2012;61:646–664.[PubMed]
6. Harvey RF, Spence RW, Lane JA, et al. Relationship between the birth cohort pattern of *Helicobacter pylori* infection and the epidemiology of duodenal ulcer. *QJM* 2002;95:519–525. [PubMed]
7. Axon AT. *Helicobacter pylori* infection. *J Antimicrob Chemother* 1993;32(suppl A):61–68.[PubMed]
8. Graham DY. Can therapy ever be denied for *Helicobacter pylori* infection? *Gastroenterology* 1997;113(6 Suppl):S113–S117.[PubMed]
9. Ford AC, Forman D, Hunt RH, et al. Helicobacter pylori eradication therapy to prevent gastric cancer in healthy asymptomatic infected individuals: systematic review and meta-analysis of randomised controlled trials. *BMJ* 2014;348:g3174.[PubMed]
10. Zhou L, Lin S, Ding S, et al. Relationship of Helicobacter pylori eradication with gastric cancer and gastric mucosal histological changes: A 10-year follow-up study. *Chin Med J (Engl)* 2014;127:1454–1458.[PubMed]
11. Correa P, Fontham ET, Bravo JC, et al. Chemoprevention of gastric dysplasia: randomized trial of antioxidant supplements and anti-*Helicobacter pylori* therapy. *J Natl Cancer Inst* 2000;92:1881–1888.[PubMed]
12. Wong BC, Lam SK, Wong WM, et al; China Gastric Cancer Study Group. *Helicobacter pylori* eradication to prevent gastric cancer in a high-risk region of China: a randomized controlled trial. *JAMA* 2004;291:187–194.[PubMed]
13. You W, Brown LM, Zhang L, et al. Randomized double-blind factorial trial of three treatments to reduce the prevalence of precancerous gastric lesions. *J Natl Cancer Inst* 2006;98:974–983.[PubMed]
14. Ma JL, Zhang L, Brown LM, et al. Fifteen-year effects of *Helicobacter pylori*, garlic, and vitamin treatments on gastric cancer incidence and mortality. *J Natl Cancer Inst* 2012;104:488–492.[PubMed]
15. Helicobacter and Cancer Collaborative Group. Gastric cancer and *Helicobacter pylori:* a combined analysis of 12 case control studies nested within prospective cohorts. *Gut* 2001;49:347–353.[PubMed]
16. Fock KM, Talley NJ, Moayyedi P, et al; Asia-Pacific Gastric Cancer Consensus Conference. Asia-Pacific consensus guidelines on gastric cancer prevention. *J Gastroenterol Hepatol* 2008;23:351–365.[PubMed]
17. Talley NJ, Fock KM, Moayyedi P. Gastric Cancer Consensus conference recommends Helicobacter pylori screening and treatment in asymptomatic persons from high-risk populations to prevent gastric cancer. *Am J Gastroenterol* 2008;103:510–514.[PubMed]

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Disclaimer

GRADE **Evaluation of interventions for Helicobacter pylori eradication: gastric cancer prevention.**

Important outcomes			Incidence of or mortality from gastric cancer, Regression of pre-cancerous lesions						
Studies (Participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consistency**	**Directness**	**Effect size**	**GRADE**	**Comment**
What are the effects of Helicobacter pylori eradication treatment on the risk of developing gastric cancer?									
6 (6497) [9]	Incidence of or mortality from gastric cancer	*H pylori* eradication treatment versus placebo or no treatment for the prevention of gastric cancer in asymptomatic, healthy *H pylori*-infected individuals	4	–1	0	–1	0	Low	Quality point deducted for methodological limitations of RCTs included in the analysis (lack of masking, factorial design); directness point deducted for generalisability (of the 6 RCTs, 5 were carried out in East Asia and 1 in Central America; eradication regimen used varied across studies)
1 (852) [11]	Regression of pre-cancerous lesions	*H pylori* eradication treatment versus placebo or no treatment for regression of pre-cancerous lesions	4	–1	0	–1	0	Low	Quality point deducted for methodological limitations (incomplete reporting of results, factorial design); directness point deducted for generalisability (the study was conducted in Colombia)

We initially allocate 4 points to evidence from RCTs, and 2 points to evidence from observational studies. To attain the final GRADE score for a given comparison, points are deducted or added from this initial score based on preset criteria relating to the categories of quality, directness, consistency, and effect size. Quality: based on issues affecting methodological rigour (e.g., incomplete reporting of results, quasi-randomisation, sparse data [<200 people in the analysis]). Consistency: based on similarity of results across studies. Directness: based on generalisability of population or outcomes. Effect size: based on magnitude of effect as measured by statistics such as relative risk, odds ratio, or hazard ratio.