

SUPPLEMENTARY MATERIALS**Search Strategy**

- 1 exp Helicobacter/ or exp Helicobacter Infections/
- 2 (helicobacter or campylobacter).tw,kw.
- 3 (pylori or pyloridis or HP).tw,kw.
- 4 or/1-3
- 5 exp Stomach Neoplasms/
- 6 exp Lymphoma, B-Cell, Marginal Zone/
- 7 (mucosa associated lymphoid tissue lymphoma or MALT).tw,kw.
- 8 ((stomach or gastric) adj3 (cancer* or carcinoma* or neoplas* or tumor* or tumour* or lymphoma* or adenocarcinoma* or malign*)).tw,kw.
- 9 or/5-8
- 10 4 and 9
- 11 randomized controlled trial.pt.
- 12 controlled clinical trial.pt.
- 13 placebo.ab.
- 14 drug therapy.fs.
- 15 random*.mp.
- 16 trial.ab.
- 17 groups.ab.
- 18 or/11-17
- 19 exp animals/ not humans/
- 20 18 not 19
- 21 10 and 20
- 22 exp Proton Pump Inhibitors/
- 23 proton pump inhibitor*.mp.
- 24 (PPI or PPIs).tw,kw.
- 25 (omeprazole or h 16868 or losec or prilosec or rapinex or zegerid).mp.
- 26 (lansoprazole or lanzoprazole or ag 1749 or agopton or bamalite or lanzor or monolimum or ogast or ogastro or opiren or prevacid or prezal or pro ulco or promeco or takepron or ulpax or zoton).mp.

Ford *et al.*

Page 2 of 10

- 27 (pantoprazole or by 1023 or protium or protonix or skf-96022).mp.
- 28 (esomeprazole or nexium).mp.
- 29 (rabeprazole or aciphex or dexrabeprazole or e 3810 or ly-307640 or pariet).mp.
- 30 (dexlansoprazole or Kapidex or Dexilant or AGN 20194* or AGN20194* or dexrabeprazole).mp.
- 31 (tenatoprazole or CAS 113712-98-4 or STU-Na or TAK-390* or TAK390* or TAK-438 or TAK438 or AZD0865 or "AZD 0865").mp.
- 32 or/22-31
- 33 exp Histamine H2 Antagonists/
- 34 ((histamine or H2 or H-2 or H2R or H 2 R) adj3 (antagonist* or blocker* or blockage* or blockader*)).tw,kw.
- 35 (H2RA or H2RAs or H2-RA or H2RAs).tw,kw.
- 36 (antihistaminic* adj2 (H2 or H-2)).tw,kw.
- 37 (Cimetidine or Tagamet or altramet or biomet or biomet400 or eureceptor or histodil or skf 92334 or skf92334).tw,kw.
- 38 (ranitidine or zantac or ah 19065 or ah19065 or biotidin or ranisen or ranitidine or sostril or zantic).tw,kw.
- 39 (Famotidine or Pepcid or mk 208 or mk208 or ym 11170 or ym11170).tw,kw.
- 40 (Nizatidine or Axid or axid or ly 139037 or ly139037).tw,kw.
- 41 (Roxatidine or Rotane or Zorpe).tw,kw.
- 42 or/33-41
- 43 exp Bismuth/
- 44 exp Amoxicillin/
- 45 exp Clarithromycin/
- 46 exp Nitroimidazoles/
- 47 exp Macrolides/
- 48 (metronidazole or tinidazole or amoxicillin* or amoxycillin*).tw,kw.
- 49 (clarithromycin or azithromycin or roxithromycin).tw,kw.
- 50 (bismuth or nitroimidazole* or macrolide*).tw,kw.
- 51 or/43-50
- 52 32 or 42 or 51
- 53 21 and 52

Ford *et al.*

Page 3 of 10

- 54 limit 53 to yr="2014 -current"
- 55 exp Helicobacter/ or exp Helicobacter infection/
- 56 (helicobacter or campylobacter).tw,kw.
- 57 (pylori or pyloridis or HP).tw,kw.
- 58 or/55-57
- 59 exp stomach tumor/
- 60 exp marginal zone lymphoma/
- 61 (mucosa associated lymphoid tissue lymphoma or MALT).tw,kw.
- 62 ((stomach or gastric) adj3 (cancer* or carcinoma* or neoplas* or tumor* or tumour* or lymphoma* or adenocarcinoma* or malign*)),tw,kw.
- 63 or/59-62
- 64 58 and 63
- 65 random*.mp.
- 66 placebo*.mp.
- 67 double-blind*.mp.
- 68 clinical trial:.mp.
- 69 blind*.tw.
- 70 or/65-69
- 71 exp animal/ not exp human/
- 72 70 not 71
- 73 64 and 72
- 74 exp proton pump inhibitor/
- 75 proton pump inhibitor*.mp.
- 76 (PPI or PPIs).tw,kw.
- 77 (omeprazole or h 16868 or losec or prilosec or rapinex or zegerid).mp.
- 78 (lansoprazole or lanzoprazole or ag 1749 or agopton or bamalite or lanzor or monolium or ogast or ogastro or opiren or prevacid or prezal or pro ulco or promeco or takepron or ulpax or zoton).mp.
- 79 (pantoprazole or by 1023 or protium or protonix or skf-96022).mp.
- 80 (esomeprazole or nexium).mp.
- 81 (rabeprazole or aciphex or dexrabeprazole or e 3810 or ly-307640 or pariet).mp.

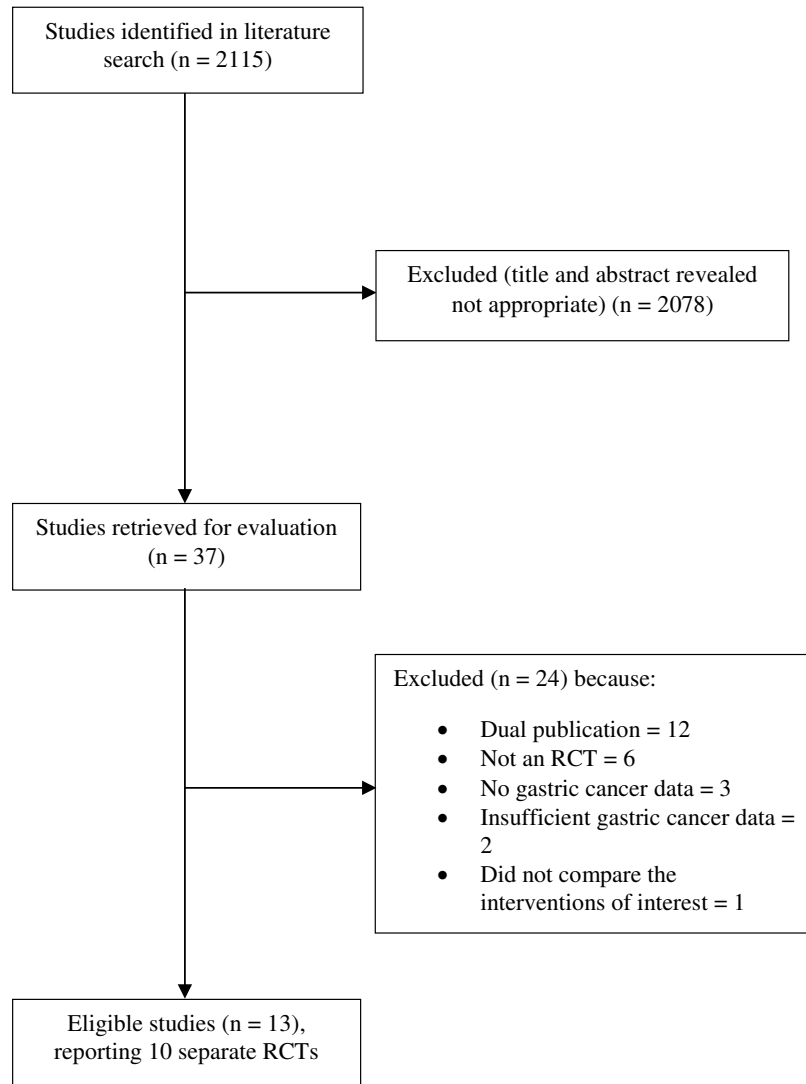
Ford *et al.*

Page 4 of 10

- 82 (dexlansoprazole or Kapidex or Dexilant or AGN 20194* or AGN20194* or dexrabeprazole).mp.
- 83 (tenatoprazole or CAS 113712-98-4 or STU-Na or TAK-390* or TAK390* or TAK-438 or TAK438 or AZD0865 or "AZD 0865").mp.
- 84 or/74-83
- 85 exp histamine H2 receptor antagonist/
- 86 ((histamine or H2 or H-2 or H2R or H 2 R) adj3 (antagonist* or blocker* or blockage* or blockader*)).tw,kw.
- 87 (H2RA or H2RAs or H2-RA or H2RAs).tw,kw.
- 88 (antihistaminic* adj2 (H2 or H-2)).tw,kw.
- 89 (Cimetidine or Tagamet or altramet or biomet or biomet400 or eureceptor or histodil or skf 92334 or skf92334).tw,kw.
- 90 (ranitidine or zantac or ah 19065 or ah19065 or biotidin or ranisen or ranitidine or sostril or zantic).tw,kw.
- 91 (Famotidine or Pepcid or mk 208 or mk208 or ym 11170 or ym11170).tw,kw.
- 92 (Nizatidine or Axid or axid or ly 139037 or ly139037).tw,kw.
- 93 (Roxatidine or Rotane or Zorpe).tw,kw.
- 94 or/85-93
- 95 exp bismuth citrate/ or exp bismuth salt/ or exp bismuth/ or exp bismuth salicylate/ or exp ranitidine bismuth citrate/ or exp colloidal bismuth compound/ or exp bismuth citrate plus metronidazole plus tetracycline/
- 96 exp amoxicillin plus clarithromycin plus lansoprazole/ or exp clarithromycin/ or exp clarithromycin derivative/
- 97 exp amoxicillin/
- 98 exp nitroimidazole/
- 99 exp macrolide/
- 100 (metronidazole or tinidazole or amoxicillin* or amoxycillin*).tw,kw.
- 101 (clarithromycin or azithromycin or roxithromycin).tw,kw.
- 102 (bismuth or nitroimidazole* or macrolide*).tw,kw.
- 103 or/95-102
- 104 84 or 94 or 103
- 105 73 and 104
- 106 limit 105 to yr="2014 -current"

- 107 exp Helicobacter/ or exp Helicobacter Infections/
108 (helicobacter or campylobacter).tw,kw.
109 (pylori or pyloridis or HP).tw,kw.
110 or/107-109
111 exp Stomach Neoplasms/
112 exp Lymphoma, B-Cell, Marginal Zone/
113 (mucosa associated lymphoid tissue lymphoma or MALT).tw,kw.
114 ((stomach or gastric) adj3 (cancer* or carcinoma* or neoplas* or tumor* or tumour* or lymphoma* or adenocarcinoma* or malign*)).tw,kw.
115 or/111-114
116 110 and 115
117 exp Proton Pump Inhibitors/
118 proton pump inhibitor*.mp.
119 (PPI or PPIs).tw,kw.
120 (omeprazole or h 16868 or losec or prilosec or rapinex or zegerid).mp.
121 (lansoprazole or lanzoprazole or ag 1749 or agopton or bamalite or lanzor or monolium or ogast or ogastro or opiren or prevacid or prezal or pro ulco or promeco or takepron or ulpax or zoton).mp.
122 (pantoprazole or by 1023 or protium or protonix or skf-96022).mp.
123 (esomeprazole or nexium).mp.
124 (rabeprazole or aciphex or dexrabeprazole or e 3810 or ly-307640 or pariet).mp.
125 (dexlansoprazole or Kapidex or Dexilant or AGN 20194* or AGN20194* or dexrabeprazole).mp.
126 (tenatoprazole or CAS 113712-98-4 or STU-Na or TAK-390* or TAK390* or TAK-438 or TAK438 or AZD0865 or "AZD 0865").mp.
127 or/117-126
128 exp Histamine H2 Antagonists/
129 ((histamine or H2 or H-2 or H2R or H 2 R) adj3 (antagonist* or blocker* or blockage* or blockader*)).tw,kw.
130 (H2RA or H2RAs or H2-RA or H2RAs).tw,kw.
131 (antihistaminic* adj2 (H2 or H-2)).tw,kw.
132 (Cimetidine or Tagamet or altramet or biomet or biomet400 or eureceptor or histodil or skf 92334 or skf92334).tw,kw. (29599)

- 133 (ranitidine or zantac or ah 19065 or ah19065 or biotidin or ranisen or ranitidine or sostril or zantic).tw,kw. (18923)
- 134 (Famotidine or Pepcid or mk 208 or mk208 or ym 11170 or ym11170).tw,kw. (6434)
- 135 (Nizatidine or Axid or axid or ly 139037 or ly139037).tw,kw. (1486)
- 136 (Roxatidine or Rotane or Zorpe).tw,kw. (539)
- 137 or/128-136 (113607)
- 138 exp Bismuth/ (14709)
- 139 exp Amoxicillin/ (75342)
- 140 exp Clarithromycin/ (43950)
- 141 exp Nitroimidazoles/ (185955)
- 142 exp Macrolides/ (410384)
- 143 (metronidazole or tinidazole or amoxicillin* or amoxycillin*).tw,kw. (83908)
- 144 (clarithromycin or azithromycin or roxithromycin).tw,kw. (47498)
- 145 (bismuth or nitroimidazole* or macrolide*).tw,kw. (63917)
- 146 or/138-145 (663543)
- 147 127 or 137 or 146 (869698)
- 148 116 and 147 (5522)

Supplementary Figure 1. Flow Diagram of Assessment of Studies Identified in the Systematic Review.

Supplementary Table 1. Eligibility Criteria.

Randomised controlled trials.
Healthy <i>H. pylori</i> -positive adults or <i>H. pylori</i> -positive adults with gastric neoplasia, including dysplasia or early gastric cancer, undergoing endoscopic mucosal resection (participants aged ≥ 18 years).
Compared a recognised <i>H. pylori</i> eradication regimen* with placebo or no treatment.
Minimum duration of therapy of 7 days.
Minimum follow-up duration of 2 years.
Dichotomous assessment of effect on incidence of gastric cancer.†
At least two gastric cancers occurring during follow-up.

*Proton pump inhibitor (PPI) dual therapy (PPI plus either amoxicillin or clarithromycin);

PPI triple therapy (PPI plus any two of the following: amoxicillin, macrolide, 5-nitroimidazole); histamine₂-receptor antagonist triple therapy (histamine₂-receptor antagonist plus any two of the following: amoxicillin, macrolide, 5-nitroimidazole); bismuth triple therapy (bismuth salt and 5-nitroimidazole with either amoxicillin, or tetracycline); bismuth quadruple therapy (as bismuth triple therapy, but with the addition of a PPI); ranitidine bismuth citrate dual therapy (ranitidine bismuth citrate plus either amoxicillin or clarithromycin); ranitidine bismuth citrate triple therapy (ranitidine bismuth citrate plus any two of the following: amoxicillin, macrolide, 5-nitroimidazole); clarithromycin monotherapy.

†Defined as any gastric adenocarcinoma, including intestinal (differentiated) or diffuse (undifferentiated) type or without specified histology.

Supplementary Table 2.

Study	Method of Generation of Randomisation Schedule	Method of Concealment of Treatment Allocation	Blinding	Evidence of Incomplete Outcomes Data	Evidence of Selective Reporting of Outcomes
Correa 2000 [1] and Correa 2001 [2]	Low	Low	High	Unclear	Unclear
Leung 2004 [3] and Zhou 2014 [4]	Low	Low	Low	High	Unclear
Wong 2004 [5]	Low	Low	Low	Low	Low
Saito 2005 [6]	Unclear	Unclear	Unclear	Unclear	Unclear
Ma 2012 [7] and Li 2019 [8]	Low	Low	Low	Low	Low
Wong 2012 [9]	Low	Low	Low	Low	Low
Choi 2020 [10]	Low	Low	Low	Low	Low
Fukase 2008 [11]	Low	Unclear	High	Low	Low
Choi 2018a [12]	Low	Unclear	High	Low	Low
Choi 2018b [13]	Low	Low	Low	Unclear	Low

REFERENCES

- 1 Correa P, Fontham ETH, Bravo JC, Bravo LE, Ruiz B, Zarama G, *et al.* Chemoprevention of gastric dysplasia: Randomized trial of antioxidant supplements and anti-*Helicobacter pylori* therapy. *J Natl Cancer Inst* 2000;**92**:1881-8.
- 2 Correa P, Fontham ETH, Bravo JC, Bravo LE, Ruiz B, Zarama G, *et al.* Chemoprevention of gastric dysplasia: Randomized trial of antioxidant supplements and anti-*Helicobacter pylori* therapy. Reply. *J Natl Cancer Inst* 2001;**93**:559-60.
- 3 Leung WK, Lin SR, Ching JYL, To KF, Ng EKW, Chan FKL, *et al.* Factors predicting progression of gastric intestinal metaplasia: Results of a randomised trial on *Helicobacter pylori* eradication. *Gut* 2004;**53**:1244-9.
- 4 Zhou L, Lin S, Ding S, Huang X, Jin Z, Cui R, *et al.* Relationship of *Helicobacter pylori* eradication with gastric cancer and gastric mucosal histological changes: A 10-year follow-up study. *Chin Med J* 2014;**127**:1454-8.
- 5 Wong BCY, Lam SK, Wong WM, Chen JS, Zheng TT, Feng RE, *et al.* *Helicobacter pylori* eradication to prevent gastric cancer in a high-risk region of China: A randomized controlled trial. *JAMA* 2004;**291**:187-94.
- 6 Saito D, Boku N, Fujioka T, Fukuda Y, Matsushima Y, Sakaki N, *et al.* Impact of *H. pylori* eradication on gastric cancer prevention: Endoscopic results of the Japanese intervention trial (JITHP-Study): A randomized multi-center trial. *Gastroenterology* 2005;**128** (suppl 2):A4.
- 7 Ma JL, Zhang L, Brown LM, Li JY, Shen L, Pan KF, *et al.* Fifteen-year effects of *Helicobacter pylori*, garlic, and vitamin treatments on gastric cancer incidence and mortality. *J Natl Cancer Inst* 2012;**104**:488-92.
- 8 Li WQ, Zhang JY, Ma JL, Li ZX, Zhang L, Zhang Y, *et al.* Effects of *Helicobacter pylori* treatment and vitamin and garlic supplementation on gastric cancer incidence and mortality: Follow-up of a randomized intervention trial. *BMJ* 2019;**366**:15016.
- 9 Wong BCY, Zhang L, Ma JL, Pan KF, Li JY, Shen L, *et al.* Effects of selective COX-2 inhibition and *Helicobacter pylori* eradication on precancerous gastric lesions. *Gut* 2012;**61**:812-8.
- 10 Choi IJ, Kim CG, Lee JY, Kim Y-I, Kook M-C, Park B, *et al.* Family history of gastric cancer and *Helicobacter pylori* treatment. *New England Journal of Medicine* 2020;**382**:427-36.
- 11 Fukase K, Kato M, Kikuchi S, Inoue K, Uemura N, Okamoto S, *et al.* Effect of eradication of *Helicobacter pylori* on incidence of metachronous gastric carcinoma after endoscopic resection of early gastric cancer: An open-label, randomised controlled trial. *Lancet* 2008;**372**:392-7.
- 12 Choi JM, Kim SG, Choi J, Park JY, Oh S, Yang HJ, *et al.* Effects of *Helicobacter pylori* eradication for metachronous gastric cancer prevention: A randomized controlled trial. *Gastrointest Endosc* 2018;**88**:475-85.e2.
- 13 Choi IJ, Kook MC, Kim YI, Cho SJ, Lee JY, Kim CG, *et al.* *Helicobacter pylori* therapy for the prevention of metachronous gastric cancer. *N Engl J Med* 2018;**378**:1085-95.