

Law for the Aged, employer medical examination, and personal medical examination. Gastric cancer screening using photofluorography indicated reduction of mortality in meta-analysis including three Japanese case-control studies, but its evidence level is not strong, i.e., equivalent to IVa in MINDS (Medical Information Network Distribution Service) classification. (42) The sensitivity of photofluorography ranged from 60% to 80%, whereas the specificity and true positive rate were 90% and 0.7-2.0%, respectively. In overall results of Japanese cancer screening in 2007, the number of persons who received gastric cancer screening using photofluorography and the number of detected gastric cancers were about 6,390,000 and 5,600, respectively. However, endoscopic examination as close examination found gastric cancer at a different site in the half of screen-detected gastric cancers. True detection rate of early gastric cancer using photofluorography is known to be not so high. Current gastric cancer screening using photofluorography has various well-known problems, such as low consultation rate of close examination and immobilization of participant. Recently, the prevalence rate of *H. pylori* infection in less than 50-year-old Japanese has decreased to less than 40%. (43) Since more than half of participants in gastric cancer screening have low risk of gastric cancer, it is a serious problem that *H. pylori* negative persons have to receive photofluorography every year in terms of radiation exposure. Unnecessary annual invasive screening examinations for *H. pylori* negative population should be avoided. Therefore, it is necessary to reconsider mass screening program of gastric cancer using photofluorography.

ii) Endoscopic examination

Recently, endoscopic screening for gastric cancer has been used gradually according to the spread of transnasal esophagogastroduodenoscopy. (44) Transnasal endoscopy is suitable for gastric cancer screening because of good compliance by participants. (45)(46) Mass screening using endoscopic examination has some problems such as the need for an endoscopist, performance limitation of operation number, sterilization of scope, complication of endoscopy, and low acceptability of participant. Endoscopic examination has been the best for finding early gastric cancer, with a detection ratio of 0.87% in 2004, approximately about 3 to 5 times higher than those of photofluorography. (47) The efficacy of endoscopic screening in term of mortality reduction in Japan has been compared to that of X-ray examination (48): 4,261 residents underwent gastric X-ray examination for gastric cancer screening from 1991 to 1995, and all 7,178 residents underwent endoscopic examination for the same purpose from 1996 to 2003. Following the introduction of endoscopic screening, the age-adjusted gastric cancer mortality rates decreased from 1.04 (95% CI 0.50-1.58) to 0.71 (95% CI 0.33-1.10) for males and from 1.54 (95% CI 0.71-2.38) to 0.62 (95% CI 0.19-1.05) for females. Reduction of gastric cancer mortality was achieved by not only increase in the detection of early cancer using endoscopic screening but also improvement of the treatment including surgery.

### iii) Serum pepsinogen test

Pepsinogen (PG) is precursor for pepsin produced in gastric mucosa, of which 99% is secreted into the gastric lumen and 1% into the blood stream. PG is classified into two biochemically and immunologically different isozymes, namely PG I and PGII. While PG I is produced in chief and mucous neck cell of fundic glands, PG II is secreted from the fundic, pyloric, and proximal duodenal glands. (49)(50) Serum PG level reflects the morphology and function of acid secretory glands and pathological condition of gastric mucosa such as inflammation. (51)-(53) Inflammation of gastric mucosa by *H. pylori* infection elevates serum PG I and PG II levels and decreases PG I/II ratios due to relative high elevation of PG II. Decline of serum PG I levels and PG I/II ratios correlates with the extent of mucosal atrophy in the gastric corpus and gastric acid secretion ability. Stepwise reduction of the PG I/II ratio is closely correlated with the progression from normal gastric mucosa to extensive atrophic gastritis. (54)(55)

The risk of gastric cancer incidence, especially intestinal type, depends on advancement of atrophic gastritis. Serum PG level is considered a useful marker of atrophic gastritis, which is a precancerous change in the stomach. Mass screening of high-risk patients with gastric cancer using the PG method was introduced to detect gastric cancer following endoscopic examination. Positive PG method that are  $PG\ I \leq 70\text{ng/l}$  and  $PG\ I/II\ \text{ratio} \leq 3.0$  indicates high risk of gastric cancer. Prospective cohort studies also confirmed that PG method is useful for assessing gastric cancer risk. (56)-(58) A case-control study on the

effect of gastric cancer screening using the PG method showed the odds ratios for death from gastric cancer among control subjects screened within 1 and 2 years were 0.238 (0.061-0.929) and 0.375 (0.155-0.905), respectively. (59) Gastric cancer screening using the pepsinogen method was suggested to reduce mortality from gastric cancer.

The ABC(D) stratification using both anti-*H. pylori* antibody and serum PG levels allows classification of gastric cancer risk into the following groups based on these levels: Group A is negative for both PG method results and the antibody, Group B is negative for PG method results and positive for the antibody, Group C is positive for both PG method results and the antibody, and Group D that is positive for PG method results and negative for the antibody. With the progression of *H. pylori*-induced gastritis, the risk of gastric cancer increased in a stepwise fashion from Group B (HR=7.13, 95%CI=0.95-53.33) to Group C (HR=14.85, 95%CI=1.96-107.7) and finally to Group D (HR=61.85, 95%CI=5.6-682.64). (60) In another result, Group C had a moderately high hazard ratio of 11.23, while Group D had a markedly higher hazard ratio of 14.81. (61) Therefore, these two groups are considered the most appropriate candidates for gastric cancer screening. Recently, ABC(D) stratification has spread as a new method of gastric cancer screening (Table 5). Because of the high risk of gastric cancer, endoscopic examination is recommended every year for Group D, every two years for Group C, every three years for Group B, and every five years for Group A. (62)

## Strategy of eliminating gastric cancer

According to Asia-Pacific consensus guidelines, a population 'test and treat' strategy for *H. pylori* infection in communities with high incidence of gastric cancer such as Japan and Korea is considered to be an effective strategy for gastric cancer prevention. (63)(64) The Japanese Society for *Helicobacter* Research has published a guideline recommending that *H. pylori* infection be treated with eradication therapy. (65) Strategy of test and treat for *H. pylori* infection is effective at reducing the incidence and mortality of gastric cancer in communities with high incidence of gastric cancer. However, follow-up surveillance for gastric cancers was necessary after successful eradication of *H. pylori*, because the risk of cancer persists for long after cure of *H. pylori*. Therefore, strategy of test, treat and screening that combines primary and secondary prophylaxis is the most important to reach the final goal of eliminating gastric cancer in Japan.

We have proposed a program of risk stratification (ABC stratification) based on the presence of *H. pylori* infection with or without atrophic gastritis followed by targeted interventions. (66) (Figure 1) Those at no risk for gastric cancer (no *H. pylori*, no atrophic gastritis) need no therapy or follow-up. Those at low risk (*H. pylori* infected, non-atrophic gastritis) need only *H. pylori* eradication therapy. The smaller groups at high or very high risk need eradication and cancer surveillance using endoscopic examination. We estimated the costs and the benefits of this strategy markedly reduce the cost of treating gastric cancer in spite of initially increasing national healthcare expenditure. In Japan, about 3 billion

dollars are spent annually on the treatment of gastric cancer. (67) The annual cost will probably exceed 5 billion dollars after 10 years if effective strategy of gastric cancer prevention are not taken. Theoretically, eradication of *H. pylori* in all carriers could prevent about 150 000 deaths from gastric cancer during the subsequent 5 years. (68) The program of gastric cancer prevention is expected to induce reduction in costs consumed by *H. pylori*-related diseases.

One week of triple therapy using a proton pump inhibitor (PPI) combined with amoxicillin (AMPC) and clarithromycin (CAM) is used as the first-line treatment for eradicating *H. pylori* in Japan. If the first-line treatment is failed, one week of triple therapy including PPI, AMPC, and metronidazole (MNZ) is used as the second-line rescue treatment. Overall eradication rate of first and second-line treatment is currently 97-98 %. Because adverse events are mainly soft stools and diarrhea, the safety of *H. pylori* eradication treatment is proved.

## References

1. Kakizoe T. Chemoprevention of cancer--focusing on clinical trials.. Jpn J Clin Oncol. 2003;33:421-42.
2. Inoue M, Tsugane S. Epidemiology of gastric cancer in Japan. Postgrad Med J. 2005;81:419-24.
3. Hisamichi S, Sugawara N. Mass screening for gastric cancer by X-ray examination. Jpn

J Clin Oncol 1984;11:211-33

4. Fukase K, Kato M, S Kikuchi, 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 Aug 2;372:392-7
5. Tsugane S, Sasazuki S. Diet and the risk of gastric cancer: review of epidemiological evidence. *Gastric Cancer*. 2007;10:75-83.
6. Martin Wiseman. The Second World Cancer Research Fund/American Institute for Cancer Research Expert Report. Food, Nutrition, Physical Activity, and the Prevention of Cancer: A Global Perspective. *Proceedings of the Nutrition Society* 2008; 67, 253–256.
7. Palli D. Epidemiology of gastric cancer.. *Ann Ist Super Sanita*. 1996;32(1):85-99.
8. Kato S, Tsukamoto T, Mizoshita T, Tanaka H, Kumagai T, Ota H, et al. High salt diets dose-dependently promote gastric chemical carcinogenesis in *Helicobacter pylori*-infected Mongolian gerbils associated with a shift in mucin production from glandular to surface mucous cells. *Int J Cancer*. 2006;119:1558-66.
9. Kobayashi M, Tsubono Y, Sasazuki S, Sasaki S, Tsugane S; JPHC Study Group. Vegetables, fruit and risk of gastric cancer in Japan: a 10-year follow-up of the JPHC Study Cohort I. *Int J Cancer*. 2002;102:39-44.
10. Lunet N, Lacerda-Vieira A, Barros H. Fruit and vegetables consumption and gastric

cancer: a systematic review and meta-analysis of cohort studies. *Nutr Cancer*.

2005;53:1-10.

11. Poydock ME, Fardon JC, Gallina D, Ferro V, Heher C. Inhibiting effect of vitamins C and B12 on the mitotic activity of ascites tumors. *Exp Cell Biol*. 1979;47:210-7.
12. Palace VP, Khaper N, Qin Q, Singal PK. Antioxidant potentials of vitamin A and carotenoids and their relevance to heart disease. *Free Radic Biol Med*. 1999; 26:746-61
13. Rousseau EJ, Davison AJ, Dunn B. Protection by beta-carotene and related compounds against oxygen-mediated cytotoxicity and genotoxicity: implications for carcinogenesis and anticarcinogenesis. *Free Radic Biol Med*. 1992; 13:407-33.
14. Wang ZY, Cheng SJ, Zhou ZC, Athar M, Khan WA, Bickers DR. Antimutagenic activity of green tea polyphenols. *Mutat Res* 1989;223:273–85.
15. Xu Y, Ho CT, Amin SG, Han C, Chung FL. Inhibition of tobacco specific nitrosamine-induced lung tumorigenesis in A/J mice by green tea and its major polyphenols as antioxidants. *Cancer Res* 1992;52:3875–9.
16. Abnet CC, Freedman ND, Kamangar F, Leitzmann MF, Hollenbeck AR, Schatzkin A. Non-steroidal anti-inflammatory drugs and risk of gastric and oesophageal adenocarcinomas: results from a cohort study and a meta-analysis. *Br J Cancer*. 2009;100:551-7.
17. Wu CY, Wu MS, Kuo KN, Wang CB, Chen YJ, Lin JT. Effective reduction of gastric cancer risk with regular use of nonsteroidal anti-inflammatory drugs in *Helicobacter*



- pylori-infected patients. *J Clin Oncol*. 2010;28:2952-7.
18. Yanaoka K, Oka M, Yoshimura N, Deguchi H, Mukoubayashi C, Enomoto S, et al. Preventive effects of etodolac, a selective cyclooxygenase-2 inhibitor, on cancer development in extensive metaplastic gastritis, a *Helicobacter pylori*-negative precancerous lesion. *Int J Cancer*. 2010;126:1467-73.
19. Kato M, Asaka M. Recent knowledge of the relationship between *Helicobacter pylori* and gastric cancer and recent progress of gastroendoscopic diagnosis and treatment for gastric cancer. *Jpn J Clin Oncol* 2010;40:828–837
20. Shimizu N, Ikehara Y, Inada K, Nakanishi H, Tsukamoto T, Nozaki K, et al. Eradication diminishes enhancing effects of *Helicobacter pylori* infection on glandular stomach carcinogenesis in Mongolian gerbils. *Cancer Res*. 2000 15;60:1512-4.
21. Nozaki K, Shimizu N, Ikehara Y, Inoue M, Tsukamoto T, Inada K, et al. Effect of early eradication on *Helicobacter pylori*-related gastric carcinogenesis in Mongolian gerbils. *Cancer Sci* 2003;94:235-9.
22. Take S, Mizuno M, Ishiki K, Baseline gastric mucosal atrophy is a risk factor associated with the development of gastric cancer after *Helicobacter pylori* eradication therapy in patients with peptic ulcer diseases. *J Gastroenterol*. 2007;42 Suppl 17:21-7.
23. Takenaka R, Okada H, Kato J, Makidono C, Hori S, Kawahara Y, et al. *Helicobacter pylori* eradication reduced the incidence of gastric cancer, especially of the intestinal type. *Aliment Pharmacol Ther* 2007;25:805-12.

24. Ogura K, Hirata Y, Yanai A, Shibata W, Ohmae T, Mitsuno Y, et al. The effect of *Helicobacter pylori* eradication on reducing the incidence of gastric cancer. *J Clin Gastroenterol* 2008;42:279-83.
25. Yanaoka K, Oka M, Ohata H, Yanaoka K, Oka M, Ohata H, Eradication of *Helicobacter pylori* prevents cancer development in subjects with mild gastric atrophy identified by serum pepsinogen levels. *Int J Cancer*. 2009;125:2697-703..
26. Mabe K, Takahashi M, Oizumi H, Tsukuma H, Shibata A, Fukase K, et al, Does *Helicobacter pylori* eradication therapy for peptic ulcer prevent gastric cancer? *World J Gastroenterol*. 2009;15: 4290-7.
27. Wu CY, Kuo KN, Wu MS, Chen YJ, Wang CB, Lin JT. Early *Helicobacter pylori* eradication decreases risk of gastric cancer in patients with peptic ulcer disease. *Gastroenterology*. 2009;137:1641-8
28. Wong BC, Lam SK, Wong WM, Chen JS, Zheng TT, Feng RE, 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;291:187-94.
29. Fuccio L, Zagari RM, Eusebi LH, Laterza L, Cennamo V, Ceroni L, et al. Meta-analysis: can *Helicobacter pylori* eradication treatment reduce the risk for gastric cancer? *Ann Intern Med*. 2009;151:121-8
30. Correa P, Fontham ET, 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.
31. You WC, Brown LM, Zhang L, Li JY, Jin ML, Chang YS, et al. Randomized double-blind factorial trial of three treatments to reduce the prevalence of precancerous gastric lesions. J Natl Cancer Inst. 2006;98:974-83.
32. Saito D, Boku N, Fujioka T, Fukuda Y. Impact of *H. pylori* eradication on gastric cancer prevention: endoscopic results of the Japanese Intervention Trial (JITHP-Study). A randomized multi-center trial. [Abstract]. Gastroenterology. 2005;128:A4.
33. Zhou L. Ten-year follow-up study on the incidence of gastric cancer and the pathological changes of gastric mucosa after *H. pylori* eradication in China [Abstract]. Gastroenterology. 2008;134:A233.
34. Ford AC, Moayyedi P. Redundant data in the meta-analysis on *Helicobacter pylori* eradication. Ann Intern Med. 2009;151:513; author reply 513-4.
35. Maehata Y, Nakamura S, Fujisawa K, Fujisawa K, Esaki M, Moriyama T, Asano K, et al. Long-term effect of *Helicobacter pylori* eradication on the development of metachronous gastric cancer after endoscopic resection of early gastric cancer. Gastrointest Endosc. 2012;75:39-46.
36. Kato M, Asaka M, Ono S, Nakagawa M, Nakagawa S, Shimizu Y, et al. Eradication of *Helicobacter pylori* for Primary Gastric Cancer and Secondary Gastric Cancer after EMR. J Gastroenterol. 2007; 42 Suppl 17:16-20.
37. Asaka M, Kato M, Graham DY: Prevention of gastric cancer by *Helicobacter pylori*

eradication. Intern. Med. 2010;49, 633-6

38. Isobe Y, Nashimoto A, Akazawa K, Oda I, Hayashi K, Miyashiro I, et al. Gastric cancer treatment in Japan: 2008 annual report of the JGCA nationwide registry. Gastric Cancer. 2011;14:301-16.

39. Hamashima C, Saito H, Nakayama T, Nakayama T, Sobue T. The standardized development method of the Japanese guidelines for cancer screening. Jpn J Clin Oncol. 2008;38:288-95.

40. Hamashima C, Shibuya D, Yamazaki H, Inoue K, Fukao A, Saito H, et al. The Japanese guidelines for gastric cancer screening. Jpn J Clin Oncol 2008;38:259-267

41. Asaka M, Kato M, Graham DY. Strategy for eliminating gastric cancer in Japan. Helicobacter. 2010;15:486-90.

42. Asaka M, Kato M, Takahashi S, Fukuda Y, Sugiyama T, Ota H, et al. Japanese Society for Helicobacter Research. Guidelines for the management of Helicobacter pylori infection in Japan: 2009 revised edition. Helicobacter. 2010;15:1-20.

43. Nakajima S, Nishiyama Y, Yamaoka M, Yasuoka T, Cho E. Changes in the prevalence of Helicobacter pylori infection and gastrointestinal diseases in the past 17 years. J Gastroenterol Hepatol. 2010;25:S99-S110.

44. Hayashi Y, Yamamoto Y, Suganuma T, Okada K, Nego M, Imada S, et al. Comparison of the diagnostic utility of the ultrathin endoscope and the conventional endoscope in early gastric cancer screening. Dig Endosc. 2009;21:116-21.

45. Yagi J, Adachi K, Arima N, Tanaka S, Ose T, Azumi T, et al. A prospective randomized comparative study on the safety and tolerability of transnasal esophagogastroduodenoscopy. *Endoscopy*. 2005;37:1226-31.
46. Murata A, Akahoshi K, Sumida Y, Yamamoto H, Nakamura K, Nawata H. Prospective randomized trial of transnasal versus peroral endoscopy using an ultrathin videoendoscope in unsedated patients. *J Gastroenterol Hepatol*. 2007;22:482-5.
47. Tashiro A, Sano M, Kinameri K, Fujita K, Takeuchi Y. Comparing mass screening techniques for gastric cancer in Japan. *World J Gastroenterol*. 2006 14;12:4873-4.
48. Matsumoto S, Yamasaki K, Tsuji K, Shirahama S. Results of mass endoscopic examination for gastric cancer in Kamigoto Hospital, Nagasaki Prefecture. *World J Gastroenterol*. 2007 28;13:4316-20.
49. Samloff IM. Cellular localization of group I pepsinogens in human gastric mucosa by immunofluorescence. *Gastroenterology* 1971; 61:185-8.
50. Samloff IM, Liebman WM. Cellular localization of the group II pepsinogens in human stomach and duodenum by immunofluorescence. *Gastroenterology* 1973; 65:36-42
51. Sipponen P, Samloff IM, Saukkonen M, Varis K. Serum pepsinogens I and II and gastric mucosal histology after partial gastrectomy. *Gut* 1985;26:1179-1182
52. Samloff IM, Stemmermann GN, Heilbrum LK, Nomura A. Elevated serum pepsinogen I and II levels differ as risk factors for duodenal ulcer and gastric ulcer. *Gastroenterology* 1986;90:570-576

53. Miki K, Ichinose M, Shimizu A, Huang SC, Oka H, Furihata C, et al. Serum pepsinogens as a screening test of extensive chronic gastritis. *Gastroentrol Jpn* 1987;22: 133-141
54. Borch K, Axelsson CK, Halgreen H, Damkjaer N, Ledin T, Szesci PB. The ratio of pepsinogen A to pepsinogen C: a sensitive test for atrophic gastritis. *Scand J Gastroenterol* 1989;24:870-6
55. Asaka M, Kato M, Kudo M, Katagiri M, Nishikawa K, Yoshida J, et al. Relationship between *Helicobacter pylori* infection, atrophic gastritis and gastric carcinoma in a Japanese population.. *Eur J Gastroenterol Hepatol*. 1995;7 Suppl 1:S7-10.
56. Watabe H, Mitsushima T, Yamaji Y, Okamoto M, Wada R, Kokubo T, et al. Predicting the development of gastric cancer from combining *Helicobacter pylori* antibodies and serum pepsinogen status: a prospective endoscopic cohort study. *Gut* 2005; 54:764-8
57. Oishi Y, Kiyohara Y, Kubo M, Tanaka K, Tanizaki Y, Ninomiya T, et al. The serum pepsinogen test as a predictor of gastric cancer: the Hisayama study. *Am J Epidemiol*. 2006.163:629-37
58. Yanaoka K, Oka M, Mukoubayashi C, Yoshimura N, Enomoto S, Iguchi M, Magari H, et al. Cancer high-risk subjects identified by serum pepsinogen tests: outcomes after 10-year follow-up in asymptomatic middle-aged males. *Cancer Epidemiol Biomarkers Prev* 2008;17:838-45
59. Yoshihara M, Hiyama T, Yoshida S, Ito M, Tanaka S, Watanabe Y, et al. Reduction in

gastric cancer mortality by screening based on serum pepsinogen concentration: a case-control study. *Scand J Gastroenterol* 2007;42:760-764

60. Ohata H, Kitauchi S, Yoshimura N, Mugitani K, Iwane M, Nakamura H, et al. Progression of chronic atrophic gastritis associated with *Helicobacter pylori* infection increases risk of gastric cancer. *Int J Cancer*. 2004;109:138-43.
61. Mizuno S, Miki I, Ishida T, Yoshida M, Onoyama M, Azuma T, et al. Prescreening of a high-risk group for gastric cancer by serologically determined *Helicobacter pylori* infection and atrophic gastritis. *Dig Dis Sci*. 2010;55:3132-7.
62. Miki K. Gastric cancer screening by combined assay for serum anti-*Helicobacter pylori* IgG antibody and serum pepsinogen levels - "ABC method". *Proc Jpn Acad Ser B Phys Biol Sci*. 2011;87(7):405-14.
63. Fock KM, Talley N, Moayyedi P, Hunt R, Azuma T, Sugano K, et al. Asia-Pacific consensus guidelines on gastric cancer prevention. *J Gastroenterol Hepatol*. 2008;23:351-65
64. Fock KM, Katelaris P, Sugano K, Ang TL, Hunt R, Talley NJ, et al. Second Asia-Pacific Consensus Guidelines for *Helicobacter pylori* infection. *J Gastroenterol Hepatol*. 2009;24:1587-600
65. Asaka M, Kato M, Takahashi S, Fukuda Y, Sugiyama T, Ota H, et al. Japanese Society for *Helicobacter* Research. Guidelines for the management of *Helicobacter pylori* infection in Japan: 2009 revised edition. *Helicobacter*. 2010;15:1-20

66. Asaka M, Kato M, Graham DY: Strategy for eliminating gastric cancer in Japan. *Helicobacter* 2010; 15, 486-90,
67. Koinuma N, Ogata T, Misawa J. Pharmacoeconomic assessment of gastric cancer treatment (In Japanese). *Nippon Rinsho* 2008;66:639-52.
68. Asaka M. Extermination of gastric cancer from Japan (In Japanese). *Nippon Shokakibyo Gakkai Zasshi* 2010;107: 359-64.



Table 1. Japanese cohort studies  
of *H. pylori* eradication and gastric cancer development

Author	Year	n Disease	Group	Follow (yrs)	Incident rate of GCA(%)	Incident rate per year(%)	Significance (per protocol)
Take	2005	1342	C	3.4	4/176 (2.3)	0.68	P<0.01
		GU/DU	E	3.4	8/944 (0.8)	0.24	
Takenaka	2007	1807	C	2.9	5/288 (1.7)	0.59	P<0.05
		GU/DU	E	3.3	6/1519 (0.4)	0.12	
Ogura	2008	708	C	3.1	13/304 (4.3)	1.40	P<0.01
		GU/DU	E	3.2	6/404 (1.5)	0.47	
Yanaoka	2009	4141	C	9.3	55/3658 (1.5)	0.16	n.s
		Healthy	E	9.3	5/473 (1.1)	0.12	
Mabe	2009	4133	C	5.2	9/352 (2.6)	0.50	P<0.05
		GU/DU	E	5.6	47/3781 (1.2)	0.21	

GU: Gastric ulcer DU: duodenal ulcer C: Control E: Eradication GCA: gastric cancer

Table 2 Randomized controlled studies of *H. pylori* eradication and gastric cancer development

Author	Year	n Disease	Follow (yrs)	Group	Incident rate of GCA(%)	Incident rate per year(%)	Significance
Correa	2000	967	6	C	2/485 (0.4)	0.07	n.s.
		Healthy		E	3/491 (0.6)		
Wong	2004	1807	7.5	C	11/813 (1.4)	0.18	n.s.
		Healthy		E	7/817 (0.9)		
You	2006	2258	7.3	C	27/1128 (2.4)	0.33	n.s.
		Healthy		E	19/1130 (1.7)		
Saito	2005	692	4	C	3/313 (1.0)	0.24	n.s.
		Healthy		E	2/379 (0.5)		
Zhou	2008	552	8	C	7/276 (2.5)	0.32	n.s.
		Healthy		E	2/276 (0.7)		
Fukase	2008	505	3	C	24/255 (9.4)	3.1	P<0.01
		Resected GCA		E	9/250 (3.6)		

Table 3 Incidence rate of gastric cancer and sample size

	Primary Gastric cancer	Metachronous Gastric cancer
Subjects	<i>H. pylori</i> positive	<i>H. pylori</i> positive After endoscopic resection of primary cancer
Incident rate/year		
Control group	0.2-0.4%	3-5%
Eradication group	0.1-0.2%	1-2%
Sample size	10000	500
Follow-up period	10 yrs	3 yrs

Table 4 Method of gastric cancer screening

	Photofluography	Endoscopy	Pepsinogen
Indication	Population-based	Opportunistic	Population-based
Secondary Screening	Endoscopy	Not necessary	Endoscopy
Participants	About 6390,000	About 210,000	About 500,000
Detection rate of gastric cancer	0.088%	0.30%	0.44%
Evidence of mortality reduction	Case-control study Meta-analysis	Case-control study	Case-control study
Level of evidence (Minds)	Evidence level IVa	Evidence level IVa	Evidence level IVa