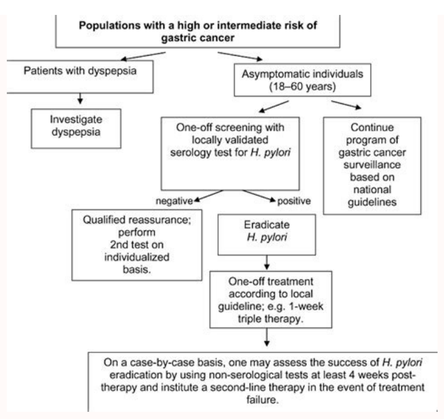
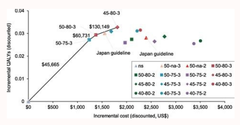
Gastric cancer screening guidelines japan

I'm not robot!



	Reference No	Target age (years)			
		40	45	50	55
%)	16	0.052	0.111	0.248	0.47
	17	0.865	0.865	0.865	0.8€
ıction		0.045	0.096	0.214	0.41
		0.007	0.015	0.033	0.0€
		14 113	6665	2990	155·
	20	4.75	6.03	7.94	9.84
		670	402	237	153
%)	16	0.047	0.074	0.118	0.18
	17	0.865	0.865	0.865	0.8€
ıction		0.041	0.064	0.102	0.15
		0.006	0.010	0.016	0.02
		15 733	10 036	6303	409
	20	4.14	4.72	5.69	6.54
		651	474	359	268



Screening strategies		Lifetime screening outcomes per 1000 individuals					
		GC deaths predicted[a]	GC deaths reduction, %[b]	Number of endoscopies[a]	QALYs gained[b,c]	Total costs ($1000)[c]	ICER ($ per QALY gained)[c,d]
No screening		9.1	0.0	81	0.0	693	–
Current screening guidelines							
50–no stopping age, 3 years		2.3	74.8	14,516	30.1	2247	Dominated
50–no stopping age, 2 years		1.8	80.5	21,379	28.1	3091	Dominated
Alterative screening strategies							
Biennial screening							
Initiation at age 50 years							
50–75, 2 years	3.0	67.3	14,873	25.9	2662	Dominated	
50–80, 2 years	2.5	72.3	16,666	27.4	2798	Dominated	
Initiation at age 45 years							
45–75, 2 years	2.7	70.3	17,237	26.4	3263	Dominated	
45–80, 2 years	2.0	77.9	19,928	28.6	3465	Dominated	
Initiation at age 40 years							
40–75, 2 years	2.5	72.7	20,559	25.5	4064	Dominated	
40–80, 2 years	2.0	77.6	22,358	26.7	4199	Dominated	
Triennial screening							
Initiation at age 50 years							
50–75, 3 years	3.4	63.0	9694	27.2	1934	45,665	
50–80, 3 years	2.8	69.1	11,507	29.4	2066	60,731	
Initiation at age 45 years							
45–75, 3 years	3.0	67.6	11,907	30.9	2380	Dominated	
45–80, 3 years	2.4	73.7	13,660	32.7	2504	130,149	
Initiation at age 40 years							
40–75, 3 years	2.8	69.6	14,101	31.1	2909	Dominated	
40–80, 3 years	2.4	73.4	15,024	31.5	2975	Dominated	

Follow-up period (year)	Sens
1	88.5
1	70.4
1	69.3
1	84.1
2	70.1
1	68.6-
1	56.8

Screening for gastric cancer guidelines. Japanese gastric cancer screening guidelines. Korean gastric cancer screening guidelines.

This study aims to assess the effectiveness of a risk-stratified screening approach for gastric cancer in Japan. A second goal of the study is to evaluate cost-effectiveness of gastric cancer screening policies. What is the Tokyo Gastric Cancer Screening Study? The Tokyo Gastric Cancer Screening Study is a long-term follow-up study of gastric cancer screening participants in the Tokyo area. The Study collaborates with the Tokyo Medical Association, local medical associations, and municipal government offices in the Tokyo area. The Study will provide useful data for future gastric cancer screening programs in Japan. Background of the Study Gastric cancer ranks high in both mortality and incidence rates in Japan. The majority of Japanese gastric cancer cases could be attributed to Helicobacter pylori (H. pylori) infection. However, the H. pylori infection rate in Japan is declining. While the current Japanese gastric cancer screening program targets all people above age 50, a more effective and practical screening strategy is needed, focusing on high-risk populations. The risk-stratified screening approach detects serum anti-H. pylori IgG antibody and serum pepsinogen concentration in blood 1 . This screening method categorizes the population into four groups, based on the risk of developing gastric cancer. This method is becoming more popular because it is less invasive. Additionally, H. pylori gastritis diagnosis and treatment have been covered by Japanese health insurance since 2013. However, the risk stratification method was not recommended as the preferred mass screening approach in the most updated Japanese gastric cancer screening guideline, due to limited evidence of its effectiveness. We need more research to clarify whether the risk stratification method decreases the mortality rate of gastric cancer. Baseline survey Study subjects The current research targets those who undergo gastric cancer screening in the Tokyo area. Gastric cancer screening includes radiography, endoscopy, and the risk-stratified method. Study flow Participants agree to join the Study by signing a consent form Screening a) Participants answer a simple lifestyle questionnaire (optional) b) Participants undergo gastric cancer screening Follow-up survey a) A survey will be sent by mail annually for 10 years asking participants about their health (optional) b) Incidence of gastric cancer and cause of death will be identified during the follow-up period For participants Only Japanese version is available. Q & A Only Japanese version is available. For collaborators Under construction Brochure Only Japanese version is available. Inquiry Only Japanese version is available. Contact us Principal Investigator: Dr. Manami Inoue Tokyo Gastric Cancer Screening Study Administrative Office Epidemiology and Prevention Group Center for Public Health Sciences, National Cancer Center Japan Address: 5-1-1 Tsukiji, Chuo-ku, Tokyo, 104-0045 Japan Tel: +81-3-3547-5201 (Ext. 3349) Email: tigan@ml.res.ncc.go.jp References 1. 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. Although the incidence and mortality of gastric cancer have gradually decreased, its burden remains in East Asian countries. Gastric cancer screening has been performed in Japan since 1983, and the introduction of new screening techniques has been eagerly anticipated.To promote evidence-based screening, the Japanese guidelines for gastric cancer screening have been revised based on the new studies.The guidelines for gastric cancer screening have been developed according to a previously established method. To assess evidence regarding the effectiveness of the screening methods, a systematic review was conducted based on an analytic framework including clinical questions aiming at reducing mortality from gastric cancer. The following methods were assessed for gastric cancer screening: upper gastrointestinal series (radiographic screening), gastrointestinal endoscopy (endoscopic screening), Helicobacter pylori antibody test and serum pepsinogen tests. Based on the balance of the benefits and harms of each screening method, recommendations for population-based and opportunistic screenings were formulated.After the Japanese guidelines for gastric cancer screening were published in 2005, several observational studies on radiographic and endoscopic screenings have been reported. Three case–control studies have evaluated mortality reduction from gastric cancer by endoscopic screening. Notably, evidence of the H. pylori antibody and serum pepsinogen tests was insufficient. Although false-positive results, false-negative results, and complications were observed in endoscopic and radiographic screenings, the complication rates were higher in endoscopic screening than in radiographic screening. Overdiagnosis was not estimated directly in both methods.Radiographic and endoscopic screenings for gastric cancer are recommended for population-based and opportunistic screenings. The H. pylori antibody and serum pepsinogen tests are not recommended for population-based screening because of insufficient evidence. Gastric cancer is the second leading cause of death worldwide. About half of the incidence of stomach cancer has been reported in East Asian countries, with the mortality higher than that in other countries (1). In Japan, the reported mortality rates from gastric cancer adjusted according to the world population are 15.4 for men and 5.8 for women (2). Although the incidence of and mortality from gastric cancer have gradually decreased over the years, its burden has remained in East Asian countries. However, in these countries, only Korea and Japan have a national program for gastric cancer screening (3). Thus, gastric cancer screening has played a significant role in reducing mortality from gastric cancer in both countries (4,5).In Japan, gastric cancer screening was conducted in local areas around the 1960s, and since 1983, it has expanded nationwide in accordance with the Health Law for the Aged (6). The previous guidelines for gastric cancer screening (Japanese version) were published in 2005, and there were referred to in the establishment of a national program (6). Although the upper gastrointestinal series with barium meal (i.e., radiographic screening) has been performed as the main method for population-based screening, endoscopic examinations have increased in the clinical settings over the last decade and have been adopted as opportunistic screening. In Korea, endoscopic and radiographic screenings have been introduced since 2000 (4). However, in the previous guidelines, it was only radiographic screening that was recommended based on the results of observational studies mainly conducted in Japan (5). Evidence for endoscopic screening was limited to only one study from China whose results were insufficient to suggest mortality reduction from gastric cancer by endoscopic screening (7). Following the publication of these guidelines, primary studies to evaluate the effectiveness of endoscopic screening for gastric cancer have increased.In the Basic Plan for Cancer Control, the targeted participation rate was 40% (8). However, the participation rate in radiographic screening has seen a decrease to about 10% (9). Therefore, some municipalities have introduced endoscopic screening despite insufficient evidence from the previous guidelines (10,11). As an alternative method for gastric cancer screening, a combined method of the Helicobacter pylori antibody and serum pepsinogen tests has been eagerly anticipated (12).The Japanese guidelines for cancer screening have been developed based on the standardized method since 2003 (6). On the base of the results of new studies that were reported after the publication of the previous guidelines, the effectiveness of new techniques for gastric cancer screening, particularly endoscopic screening, was assessed from the perspective of benefits and harms, and then the guidelines were revised. Methods The gastric cancer screening guidelines were revised using the standardized method which was defined as the development method for the Japanese guidelines for cancer screening (13). The target audiences of the gastric cancer screening guidelines included citizens, health professionals working in cancer screening programs, providers of cancer screening programs and policy makers. The guideline development group collaborated with the systematic review group and then developed the guidelines based on their results (14). The members of both groups were selected from various specialties, which included primary care physicians, gastroenterologists, surgeons, endoscopists, epidemiologists and economists. Specialists for systematic review and guideline development were also included. All members of the systematic review and guideline development groups have declared that they have no conflicts of interest associated with the guidelines for gastric cancer screening. Target screening methods The upper gastrointestinal series with barium meal (radiographic screening), gastrointestinal endoscopy (endoscopic screening), H. pylori antibody test, and serum pepsinogen test were assessed in terms of their effectiveness for gastric cancer screening. Although Korea has provided endoscopic screening for gastric cancer to date, there was insufficient evidence when they first introduced it. In Japan, gastrointestinal endoscopy has been used as a standard examination for gastric diseases and is often used as opportunistic screening. Recently, a combined method of the H. pylori antibody and serum pepsinogen test has been rapidly disseminated over the last decade, and the introduction of this combined method as population-based screening has been greatly anticipated (12). Therefore, the primary topic in the updated version is assessment of the effectiveness of endoscopic screening. The secondary topic is the assessment of the effectiveness of cancer screening using the H. pylori antibody and serum pepsinogen tests. Analytic framework The target population for gastric cancer screening was defined as asymptomatic people with an average risk of gastric cancer. To select appropriate evidence, an analytic framework for gastric cancer screening was developed (Fig. 1). For each stage of the analytic framework, clinical questions (CQs) based on the PICO (population, intervention, comparator and outcome) format were developed. Direct evidence was defined as evidence provided by a study that evaluated the effectiveness of gastric cancer screening for reducing gastric cancer incidence and mortality (Fig. 1, CQ 1). The test accuracy of each screening method was assessed in Fig. 1, CQ 2. Information on harms was obtained in Fig. 1, CQ 3. As the assessment focused on the effectiveness on new screening techniques in the updated version, evaluation studies of diagnostic examinations and treatments were excluded (Fig. 1, CQ 4–7). Open in new tabDownload slideAnalytic framework and key questions for gastric cancer screening. The numbers in the analytic framework refer to the following clinical questions. CQ 1. Compared with no screening (or other screening strategies), is there direct evidence that the mortality from gastric cancer is reduced with the following screening methods? (a) Upper gastrointestinal series (UGI), (b) gastrointestinal endoscopy (GFS), (c) serum pepsinogen test (PG) Helicobacter pylori antibody (HP), (d) Helicobacter pylori antibody (HP), (e) A combined method of Helicobacter pylori antibody and serum pepsinogen test (HP + PG). CQ 2. Can the screening test accurately detect gastric cancer? What are the sensitivity and specificity of the screening test? CQ 3. What are the potential harms of the screening tests, and how often do they occur? CQ 4. Can the diagnostic test accurately diagnose gastric cancers? CQ 5. What are the potential harms of the diagnostic examination, and how often do they occur? CQ 6. For gastric cancer patients, how are the efficacy and effectiveness of the treatment? CQ 7. What are the potential harms of gastric cancers treatment, and how often do they occur?. Systematic literature review Members of the systematic review group individually conducted a systematic review according to the CQs on the analytic framework. PubMed, Cochrane Central, Web of Science, and Igaku-Cyuo zasshi were searched from January 2000 to September 2013 (Fig. 2). The searches were limited to English-language or Japanese-language publications. For CQ1 studies, search terms such as 'gastric cancer', 'cancer screening' 'upper gastrointestinal series', 'gastrointestinal endoscopy', 'Helicobacter pylori antibody', 'serum pepsinogen test' and 'mortality reduction' were used. The keywords 'sensitivity' and 'specificity' were added for CQ2 studies. Articles related to CQ3 studies, which included overdiagnosis, false-positive cases, and complications of radiographic and endoscopic screenings, were also identified using the same search engines. As information on complications was limited, a literature search of related studies conducted in Japan was performed until the end of 2014. Additional references recommended by experts were identified and included as needed. Open in new tabDownload slideFlowchart of literature search. Members of the systematic review group individually conducted a systematic review according to the clinical questions (CQs) on the analytic framework. PubMed, Cochrane Central, Web of Science and Igaku-Cyuo zasshi were searched from January 2000 to September 2013.The inclusion criterion for article selection was basically original articles published after peer review (13). For the updated version, we collected articles with information on primary studies that evaluated mortality reduction from gastric cancer by screening. Although such articles are so-called 'Gray Papers', they were included in the updated version because primary studies related to gastric cancer screening were limited. If the article was not published in a peer-reviewed journal, additional information was directly collected from the authors. If the article was published in a peer-reviewed journal, it was reassessed based on the results.The study design and outcome were defined differently according to the CQs. The common exclusion criteria among all the screening methods were as follows: (1) no abstract, (2) the target screening group is composed of symptomatic persons (patients), (3) guidelines, evidence reports, or reviews, (4) official statistics, letters and personal communications, and (5) articles which cited in the previous Japanese guidelines for gastric cancer screening. Modeling studies including economic evaluation were excluded for assessment of the studies.To select appropriate evidence for our clinical questions, a two-stage review process was performed: the title and abstract were initially checked and then potential papers were subsequently reviewed (13). To select appropriate evidence, a systematic review of the retrieved articles was conducted using the standard checklist according to the study design, and the quality of the studies was defined. If the decision regarding the review of full papers was inconsistent, the appropriateness of these studies was carefully discussed. Finally, adequate studies were selected for evaluation of gastric cancer screening.Evidence for each screening method was summarized in an evidence table based on the CQs. The body of evidence for each screening modality was determined according to the level of evidence, which was defined on the basis of the study design, quality and consistency among study results (13). Finally, the level of evidence for studies evaluating mortality reduction from gastric cancer was decided according to the criteria defined in the guideline development method (13). Net benefit assessment To compare the benefits and harms of each screening method, the number needed to screen (NNS) and number needed for recall (NNR) were calculated on the basis of studies for radiographic and endoscopic screenings. NNS refers to the necessary number needed to avoid one gastric cancer death, which suggests the magnitude of mortality reduction as benefits of gastric cancer screening (15). Risk difference was the calculated margin of risk reduction of gastric cancer death in 10 years by gastric cancer screening. The 10 years risk of gastric cancer screening was referred from the cancer statistics of the National Cancer Center in Japan (16), and the magnitude of mortality reduction was referred from the results of a case–control study by Hamashima et al. (17). The magnitude of mortality reduction of radiographic screening was referred from other studies (18,19). Although there are various harms, false positive results are one of the serious harms which increase unnecessary diagnostic examinations and complications. The recall rate for diagnostic examination is a surrogate outcome of a false positive result. Thus, NNR indicates the necessary number needed to avoid one gastric cancer death, which suggests the magnitude of harms (15). Recall rate was referred from annual reports: academic society reports for radiographic screening (20) and annual reports of the Niigata Medical Association (21). The results were compared between radiographic and endoscopic screenings. Translation into recommendations Considering the balance of benefits and harms of each screening method, five grades of recommendations were determined for population-based and opportunistic screenings (13). As these grades are supported by sufficient evidence and the benefits outweigh the harms, both Grades A and B recommendations could be conducted as population-based and opportunistic screening programs. However, a screening method with a Grade D recommendation should not be used for either a population-based screening program or an opportunistic screening program because the harms outweigh the benefits. A technique which has no evidence of reducing mortality from the targeted cancer is also included in a Grade D recommendation. A Grade C recommendation implies that the screening method should not be used for population-based screening. Even if there are benefits, a Grade C recommendation is given when the benefits and harms are nearly equal. However, a Grade C recommendation implies that the screening method could be used in clinical settings if both adequate risk management and informed consent with respect to the harms are assured. Screening methods that have insufficient evidence related to mortality reduction from gastric cancer are graded as I. Such methods are not recommended for population-based screening or as routine screening methods in clinical settings. However, the decision to undergo screening could be made at the individual level based on proper information provided by health professionals in clinical settings. Formulating the screening guidelines A draft of the screening guidelines has been written and uploaded on the 'Promoting Evidence-based Cancer Screening' website (. To improve and confirm the guidelines, comments from the public were collected. In addition, major issues identified during the review of the draft were discussed at a guidelines forum open to the public (13). Taking into account the comments received from external reviewers and the guidelines forum, the appropriateness of the recommendation and its language were re-discussed, and the guidelines were refined. After completing the consultations, the guidelines were approved by the National Cancer Center and published on the 'Promoting Evidence-based Cancer Screening' website ((6). Findings Evidence of the effectiveness of gastric cancer screening methods From the literature search using PubMed and Igaku-cyuo-zasshi, 1170 articles for CQ1 and CQ2, and 425 articles for CQ3 were identified (Fig. 2). After a two-stage review, 154 articles were selected and then narrowed to 60 articles. By searching the Web of Science and Cochrane Central database, 10 articles were selected. The final number of articles assessed for each screening method were as follows: 14 articles for radiographic screening, 21 articles for endoscopic screening and five articles for the serum pepsinogen test. Evidence of reduction of mortality from gastric cancer could not be found for the H. pylori antibody test and the combination method of the H. pylori antibody and serum pepsinogen tests. Body of evidence of gastric cancer screening (CQ1 and CQ2) Radiographic screening (level of evidence: 2+) In the previous guidelines, four case–control studies and two cohort studies were cited for mortality reduction from gastric cancer by radiographic screening (5). After the publication the previous guidelines, three cohort studies (Table 1) and two case–control studies (Table 2) were reported (17,22–26). Although case–control studies mainly evaluated the effectiveness of endoscopic screening, the effectiveness of radiographic screening was found to be limited (17,25,26). These results were inconsistent with the results showing a big impact of radiographic screening from the previous studies. Table 1.Results of cohort studies for radiographic screening Authors Lee KJ Miyamoto A Rosero-Bixby L Publication year 2006 2006 2007 Country Japan Japan Costa Rica Number of screening group 26 961 24 014 6206 Age of screening group 49.2 ± 5.9 (mean) Men 52.33 women 53.2 (mean) 64.3 (mean) Number of no screening group 15 189 17 380 Control 1 20 030 Control 2 11 190 Control 3 11 915 Control 4 11 318 Age of no screening group 50.2 ± 5.8 (mean) Men 50.33 women 50.4 (mean) Control 1 57.9 Control 2 64.3 Control 3 58 Control 4 64.6 Follow-up periods 13.1 years (average) 11 years 2–7 years Relative risk (screened vs not screened)/95% CI Gastric cancer incidence 1.06 (0.90–1.25)a 0.94 (0.79–1.13)b – Gastric cancer mortality 0.52 (0.36–0.74)a 0.54 (0.38–0.77)b 0.42–0.52 All-causes mortalityc 0.71 (0.65–0.78)a 0.83 (0.77–0.90)b – Table 2.Results of case–control studies for radiographic screening and endoscopic screening Authors Hamashima C Matsumoto S Jun JK Publication year 2013 2014 2017 Country Japan Japan South Korea Number of case subjects 410 13 44 095 Age of case subjects 40–79 (range) 72 ± 10 (median) ≥40 Number of control subjects 2292 130 176 380 Age of control subjects 40–79 (range) 69 ± 10 (median) ≥40 Reference Never screened Never screened Never screened Odds ratio (95% CI) Radiographic screening 0.865 (0.631–1.185)a – 0.98 (0.95–1.01)b Endoscopic screening 0.695 (0.489–0.986)a 0.206 (0.044–0.965)b 0.53 (0.51–0.56)b The results of cohort studies suggested mortality reduction by radiographic screening, which was consistent with the evidence of radiographic screening in the previous version. Although a 40% mortality reduction from gastric cancer was suggested in these studies (22–24), careful interpretation is needed. The Japanese studies were analyzed based on large cohort studies which mainly focused on the association of risk factors for non-communicable diseases including cancers (22,23). However, these were not an incidence-mortality cohort studies and there were no screening opportunities that confirmed the absence of gastric cancer in the study participants during the recruitments. Participation in gastric cancer screening was identified by conducting a questionnaire survey and then dividing the participants into the radiographic screening group and the no screening group. As UGI was a standard method for diagnosing gastric diseases during the first survey in these cohort studies, there was a huge possibility of including symptomatic people in the screening group. In addition, participation in gastric cancer screening was not considered during the follow-up period and depended on individual decision. As positive results were obtained from Japanese studies, mortality reduction might be overestimated.The sensitivity and specificity of radiographic and endoscopic screenings have been reported in Korea and Japan (27,28). In a study conducted in Korea, the sensitivity of radiographic screening was found to be 38.2% (95% CI: 35.9–40.5) for the first round of screening and 27.3% (95% CI: 22.6–32.0) for the subsequent round (27). In a study conducted in Japan, the sensitivity of endoscopic screening was reported to be 0.893 (95% CI: 0.718–0.977) for prevalence screening (first round) and 0.885 (95% CI: 0.664–0.972) for incidence screening (subsequent round) (Table 3) (28). Table 3.Sensitivity of endoscopic and radiographic screenings for gastric cancer Screening round . Method . Sensitivity by detection method . Specificity by detection method . Sensitivity by incidence method . Prevalence screening Endoscopic screening 0.955 0.851 0.886 (0.875–0.991) (0.843–0.859) (0.698–0.976) Radiographic screening 0.893 0.856 0.831 (0.718–0.977) (0.846–0.865) (0.586–0.964) Incidence screening Endoscopic screening 0.977 0.888 0.954 (0.919–0.997) (0.883–0.892) (0.842–0.994) Radiographic screening 0.885 0.891 0.855 (0.664–0.972) (0.885–0.896) (0.637–0.970) Endoscopic screening (level of evidence: 2+) Although one cohort study was cited as evidence of endoscopic screening in the previous version, six observational studies were published from 2007 to 2012 (29–34). Five articles were cohort studies and the comparators were participants in radiographic screening or no participants in gastric cancer screening. The results of a study conducted in Niigata study were analyzed using an incorrect method, thus the results were subsequently reassessed (34,35). Although these studies attempted to evaluate mortality reduction from gastric cancer, they have serious flaws for adaptation as evidence for endoscopic screening as follows: (1) the sample size and follow-up periods were insufficient; (2) the subjects were not clearly limited to asymptomatic patients, and symptomatic people may have been included; (3) there is a possibility that the comparator included symptomatic patients and (4) the radiographic screening history before the start of observation was not considered.Since 2012, three case–control studies have been published in Korea and Japan (17,25,26,36). Although selection bias was a serious problem, the results were more reliable than the previously reported results. Although one case–control study conducted in Nagasaki prefecture had a small sample size (36), the studies conducted in Niigata and Tottori prefectures had a sufficient sample size for evaluating mortality reduction from gastric cancer by endoscopic screening. Individuals who had at least one history of endoscopic screening within 36 months had the possibility of reducing mortality from gastric cancer by 30% (OR ratio = 0.695, 95%CI: 0.489–0.986) (17). However, a significant reduction in mortality from gastric cancer could not be achieved by individuals who had a radiographic screening history.When we developed the updated Japanese version of gastric cancer screening, the Korean study we referred to was only described in a Korean report and was not a peer-reviewed article (25). Therefore, additional information was collected from the authors and used in the discussion when the Japanese version was developed. Similar results were obtained in an article published in 2017 and then confirmed as evidence of reduction in mortality from gastric cancer by endoscopic screening. Based on the national database, a nested case–control study from Korea reported a 47% mortality reduction from gastric cancer by endoscopic screening (26). In particular, mortality reduction from gastric cancer by endoscopic screening was observed in the 40- to 74-year age group when participating in endoscopic screening within 1–4 years and over before the date of gastric cancer diagnosis (26).Although five studies were found to calculate the test accuracy of endoscopic screening (27,28,37–39), the follow-up after obtaining negative results was insufficient in most of the studies. In a study conducted in Korea, the sensitivity of endoscopic screening using the detection method was 69.4% (95% CI: 66.4–72.4) for the first round of screening and 66.9% (95% CI: 59.8–74.0) for the subsequent round (27). In a study performed in Japan, the sensitivity was 0.955 (95% CI: 0.875–0.991) for prevalence screening (first round) and 0.977 (95% CI: 0.919–0.997) for incidence screening (subsequent round) (Table 3) (28). Serum pepsinogen test (level of evidence: 2−) In the previous guidelines of gastric cancer screening, one cohort study was cited for reduction in mortality from gastric cancer using the serum pepsinogen test (5). After the publication of the previous guidelines, two case series studies and one case–control study were reported in Japan (40–42). Although these studies suggested positive results, they had serious flaws as follows. First, the sample size and follow-up periods were insufficient. Second, the subjects were not clearly limited to asymptomatic patients. In a previous case–control study, individuals aged 80 years and older were included in the subjects (42). There was a possibility of including symptomatic patients. Third, there was a possibility of including prevalence cases because the diagnosis dates of gastric cancer were unclear in the case-series studies. Finally, radiographic screening history before the start of observation was not considered. Although the results were consistent overall, there is high potential for overestimating the magnitude of mortality reduction from gastric cancer.Two studies have reported the sensitivity of the serum pepsinogen test referred to the results of UGI at the same time (43,44). Yanaoka reported that the sensitivity of the serum pepsinogen test was 58.7% (95% CI: 45.6–70.8) and its specificity was 73.4% (95% CI: 72.1–74.6) when the cut-off value was defined as PG I ≤ 70 and PG I/II ≤3.0 (44). Helicobacter pylori antibody (level of evidence: 2−) There was no study that evaluated reduction in mortality from gastric cancer using the H. pylori antibody test. Combined method of H. pylori antibody and serum pepsinogen tests (level of evidence: 2−) There was no study that evaluated mortality reduction from gastric cancer using the combined method of H. pylori antibody and serum pepsinogen tests. Harms of gastric cancer screening (CQ 3) The major harms of radiographic and endoscopic screenings are complications, false-positive cases and overdiagnosis (5). The original harms of radiographic screening are radiation exposure and infection from endoscopic screening. Although overdiagnosis in radiographic screening is unclear, other harms have been reported in the previous guidelines. There were no studies related to harms for H. pylori antibody and serum pepsinogen tests. Thus, harms were compared between radiographic screening and endoscopic screening. False-positive and false-negative cases The false-positive rate is calculated as 1-specificity and the false-negative rate is calculated as 1-senstivity. Based on a Japanese study (Table 3) (28), the false-negative rate in the first round was 10.7% for radiographic screening and 4.5% for endoscopic screening. The false-negative rate in the subsequent round was lower in endoscopic screening than in radiographic screening (2.3% vs 11.5%). However, the false-positive rates were similar in endoscopic and radiographic screenings. The false-positive rate in the first round was 14.4% for radiographic screening and 14.9% for endoscopic screening. In the subsequent round, the false-positive rate was 10.9% for radiographic screening and 11.2% for endoscopic screening. Overdiagnosis When the observed number (O) detected by endoscopic screening was compared with the expected number (E), O/E was around twice in men and women (45). O included cases of overdiagnosis, but all excess number were not equivalent to overdiagnosis. The sensitivities of radiographic screening and endoscopic screenings were calculated using the detection and incidence methods (28). The sensitivities calculated using the detection method were always higher than those calculated using the incidence method in both screenings. The gap between the results calculated using both methods may indicate a proportion of overdiagnosis. The gaps of sensitivity calculated using different methods were small in both screening methods. Complications Several studies have reported the complication rates of radiographic screening (46–52). Recently, the incidence of barium meal aspiration has increased with the increase use of high-density barium meal for radiographic screening (46,50–52). Intestinal obstruction was reported as a severe complication of radiographic screening (47). Complications of endoscopic screening were reported in population-based screening and opportunistic screening (34,48,53–55). On the other hand, the main complication of endoscopic screening was nasal bleeding by nasal endoscopy.The Japanese Association of Gastroenterological Cancer Screening previously compared the complication rates between radiographic screening and endoscopic screening (Table 4) (48). The overall complication rates were 42.8/100 000 for radiographic screening and 87.4/100 000 for endoscopic screening. There was one case of death caused of these by a complication for radiographic screening. Although endoscopic screening was not yet commonly used during the survey period, complication rates were also reported for endoscopic examination. The Japanese Gastrointestinal Endoscopic Association conducts a survey of the complication rates of endoscopic examination every 5 years; however, their results are combined examinations of symptomatic and asymptomatic people (54). In their survey, the complication rate was low at 5.02/100 000, but death cases were reported. In a survey conducted by the Japanese Gastrointestinal Endoscopy Society, cases of death caused by sedation for endoscopic examination have been reported. The different results were based on the definitions of complication and the different subjects of the survey. Therefore, careful interpretation of these results is needed. Table 4.Complications of radiographic screening and endoscopic screening Academic association . Japanese Society of Gastrointestinal Cancer Screening . Japanese Gastrointestinal Endoscopy Society . Publication year of reports 2013 2010 Survey year 2010 2003–2007 Radiographic screening Total number 3 130 477 – Number of complications 1340 – Complication rate (/100 000) 42.8 – Number of death cases by complications 1 – Death rate by complications (/100 000) 0.03 – Endoscopic examination Total number 244 899 7 408 688 Number of complications 214 372 Complication rate (/100 000) 87.4 5.02 Number of death cases by complications 0 14 Death rate by complications (/100 000) 0 0.19 Balance of benefits and harms of radiographic and endoscopic screenings NNS and NNR were calculated for radiographic screening (Table 5) and endoscopic screening (Table 6). To avoid one gastric cancer death, a lower required number of screening participants is preferable. In both screenings, the NNS and NNR were decreased according to age. A huge gap was observed between individuals who were in their 40s and 50s. These results suggest that radiographic and endoscopic screenings could provide higher benefits for women aged 50 years and over. When the magnitudes of mortality reduction from other studies were adapted, similar trends were observed among the different age groups. Table 5.Benefits and harms of radiographic screening . Reference No . Target age (years) . . 40 . 45 . 50 . 55 . 60 . 65 . 70 . 75 . Radiographic screening (Men) Risk of gastric cancer death in 10 years (%) 16 0.052 0.111 0.248 0.477 0.770 1.137 1.604 2.124 Relative risk 17 0.865 0.865 0.865 0.865 0.865 0.865 0.865 0.865 Risk of gastric cancer death after introduction of endoscopic screening 0.045 0.096 0.214 0.412 0.666 0.984 1.387 1.837 Risk difference 0.007 0.015 0.033 0.064 0.104 0.154 0.216 0.287 Number needed to screen 14 113 6665 2990 1554 963 651 462 349 Recall rate (%) 20 4.75 6.03 7.94 9.84 11.25 11.91 12.24 12.24 Number needed to recall 670 402 237 153 108 78 57 43 Radiographic screening (Women) Risk of gastric cancer death in 10 years (%) 16 0.047 0.074 0.118 0.181 0.248 0.343 0.496 0.727 Relative risk 17 0.865 0.865 0.865 0.865 0.865 0.865 0.865 0.865 Risk of gastric cancer death after introduction of endoscopic screening 0.041 0.064 0.102 0.156 0.215 0.297 0.429 0.629 Risk difference 0.006 0.010 0.016 0.024 0.034 0.046 0.067 0.098 Number needed to screen 15 733 10 036 6303 4097 2981 2157 1494 1019 Recall rate (%) 20 4.14 4.72 5.69 6.54 7.26 7.92 8.46 8.46 Number needed to recall 651 474 359 268 216 171 126 86 Table 6.Benefits and harms of endoscopic screening . Reference No . Target age (years) . . 40 . 45 . 50 . 55 . 60 . 65 . 70 . 75 . Endoscopic screening (Men) Risk of gastric cancer death in 10 years (%) 16 0.052 0.111 0.248 0.477 0.770 1.137 1.604 2.124 Relative risk 17 0.695 0.695 0.695 0.695 0.695 0.695 0.695 0.695 Risk of gastric cancer death after introduction of endoscopic screening 0.036 0.077 0.172 0.331 0.535 0.790 1.115 1.476 Risk difference 0.016 0.034 0.076 0.145 0.235 0.347 0.489 0.648 Number needed to screen 6247 2950 1323 688 426 288 204 154 Recall rate (%) 21 2.86 8.89 11.56 9.71 11.46 10.99 11.21 11.21 Number needed to recall 179 262 153 67 49 32 23 17 Endoscopic screening (Women) Risk of gastric cancer death in 10 years (%) 16 0.047 0.074 0.118 0.181 0.248 0.343 0.496 0.727 Relative risk 17 0.695 0.695 0.695 0.695 0.695 0.695 0.695 0.695 Risk of gastric cancer death after introduction of endoscopic screening 0.033 0.051 0.082 0.126 0.173 0.239 0.345 0.505 Risk difference 0.014 0.023 0.036 0.055 0.076 0.105 0.151 0.222 Number needed to screen 6964 4442 2790 1813 1319 955 661 451 Recall rate (%) 21 5.79 5.38 6.40 6.68 7.46 7.30 7.28 7.28 Number needed to recall 403 239 179 121 98 70 48 33 Discussion In the Japanese guidelines of gastric cancer screening, the effectiveness of radiographic and endoscopic screenings was confirmed. Radiographic screening has been the main method for gastric cancer screening in Japan. Photofluorography was developed in Japan and has been used since the 1960s (6). However, the participation rate in gastric cancer screening has gradually decreased to about 10% (9). In the clinical setting, endoscopic examination has already been established as a standard method for examining gastric diseases. Therefore, endoscopic examination has already been introduced as opportunistic screening and population-based screening in several municipalities. However, to the best of our knowledge, there has been no studies evaluating mortality reduction by endoscopic screening in Japan before the publication of the previous guidelines. There was one study from China in the previous guidelines, but the results of the study did not suggest mortality reduction from gastric cancer by endoscopic screening (5,7). In the updated version of the guidelines, endoscopic screening was recommended based on the results of case–control studies in Korea and Japan (17,25,26,36). Although one Korean study was not published in a peer-reviewed journal when the Japanese version of the guidelines was published, evidence was confirmed after its publication in 2017. An English version of the guidelines was subsequently published based on the peer-reviewed article. After the Japanese version was published, one Chinese case–control study (56) and one Japanese cohort study (57) were published. The results were consistent and evidence supported the inclusion of endoscopic screening. Based on the recommendation of the revised guidelines, the Japanese government decided to introduce endoscopic screening for gastric cancer in 2016 (6).Comparing the net benefit between radiographic screening and endoscopic screening, the impact of endoscopic screening was always higher than that of radiographic screening. Therefore, more benefits can be expected from endoscopic screening. On the other hand, endoscopic screening has also serious harms, namely complications and overdiagnosis. The complication rate of endoscopic screening is high and serious complications may lead to death. Infection control is also necessary by appropriate cleaning of the endoscope. To avoid these complications, appropriate quality assurance is required. To better understand endoscopic screening, an academic society has developed a quality assurance manual that can be referred to when endoscopic screening is introduced in communities (58). It has been reported that sensitivity of endoscopic screening is higher than that of radiographic screening, and that it can easily diagnose early cancer. However, this also suggests that the detected cancers by endoscopic screening may include more overdiagnosis cases than the detected cancers by radiographic screening (59). Although overdiagnosis by endoscopic screening cannot be ignored, studies reporting this harm remain insufficient.To avoid unnecessary examinations, appropriate screening frequency should be considered (59). Therefore, the target age and screening interval should be clearly defined at the introduction of population-based screening in communities. Since the introduction of gastric cancer screening, the incidence of gastric cancer has decreased. When gastric cancer screening was introduced in the national program in 1983, the incidence of gastric cancer adjusted for the world population was 77.0/100 000 for men and 35.8/100 000 for women (2). The incidence of gastric cancer in individuals who are in their 40s was about twice compared with that in 2015. Therefore, the detection rate of gastric cancer has become lower. In fact, a huge gap in the net benefit was found between individuals who are in their 40s and individuals who are in 50s. Based on these results, the starting age of screening could be defined as 50 years. However, the stopping age of screening could not be defined from the perspective of net benefit and change of incidence. For the definition of the stopping age, other theories are required, including a modeling approach. The impact of mortality reduction by endoscopic screening was maintained beyond 4 years in a Korean study (26). Mortality reduction achieved in individuals who had at least one screening within 3 years. Thus, the screening interval can be expanded to 2–3 years based on these results. Further research is needed to specifically define the target age group and screening interval.Helicobacter pylori infection is a major cause of gastric cancer development. IARC recommended H. pylori screening based on expert opinions (60), but evidence regarding its effectiveness has remained unclear. Although such evidence is not found in the revised guidelines, screening using H. pylori antibody test is still expected. In Japan, the combined method of H. pylori antibody and serum pepsinogen tests has become commonly used, and it has been actually adopted as an alternative method for gastric cancer screening. The risk of gastric cancer increases depending on the background condition, namely, H. pylori infection and gastric atrophy (61). Although the prediction sensitivity in gastric cancer development was reportedly high, the specificity of predication was low, which led to a high false-positive rate (62). Therefore, the H. pylori antibody and serum pepsinogen tests may lead to a mislabeling of gastric cancer risk for individuals and an increase the number of unnecessary endoscopic examinations. As sensitivity and specificity were imbalanced in these methods, it is difficult to adopt them in the primary screening and risk prediction model. However, a combination with endoscopic screening might be another possibility to extend the screening interval for individuals who have a low risk of gastric cancer.Gastric cancer remains a heavy burden in East Asian countries including Japan (1). Although screening has played a major role in preventing gastric cancer, evidence was weak for cancer screening programs because it was obtained from observational studies. Therefore, primary studies to evaluate reduction in mortality from gastric cancer should be encouraged and accumulated for evidence confirmation. On the other hand, H. pylori eradication has been covered by health insurance in Japan since 2015. Although H. pylori eradication has been anticipated to prevent gastric cancer development, the efficacy of this procedure remained unclear, and a systematic prevention program has not yet been developed worldwide. To identify and confirm the best available method for gastric cancer screening in Japan, assessment of new techniques is needed to achieve the goal of gastric cancer prevention. After 5 years, a schedule is launched will be set to revise the guidelines of gastric cancer screening based on the results of new studies. Recommendations Based on the balance of benefits and harms, recommendations were formulated for population-based and opportunistic screenings (Table 5). Benefits were defined as evidence that mortality from gastric cancer was reduced by cancer screening.Radiographic screening is recommended for population-based and opportunistic screenings as its benefits outweigh its harms (Recommendation Grade B). Endoscopic screening is also recommended for population-based and opportunistic screenings as its benefits outweigh its harms (Recommendation Grade B). Both screenings are recommended to individuals aged 50 years and older. As there remains insufficient evidence of mortality reduction from gastric cancer, the H. pylori antibody and serum pepsinogen tests used alone or in combination are not recommended for population-based screening (Recommendation Grade I). With respect to opportunistic screenings, if individuals request these screenings, they should be given appropriate information with the decision made at the individual level.

Acknowledgements We thank Dr Edward F. Barroga (, for reviewing and editing the manuscript. We also thank Ms. Kanoko Matsushima, Ms. Junko Asai, Ms. Ikuko Tominaga and Ms. Noriko Hida for research assistance. Funding This work was supported in part by the National Cancer Center Research and Development Fund (29-A-16). The funder had no role in the conceptualization of the study design, data collection and analysis, decision to publish, or preparation of the manuscript. Conflict of interest statement The author declares that she has no conflicts of interest associated with this study.

References 1International Agency for Research on Cancer [Internet] GLOBOCAN 2012. Estimated cancer incidence, mortality and prevalence worldwide in 2012. [cited 2018 Jan 4] Available from: , , , et al. . No impact of repeated endoscopic screens on gastric cancer mortality in a prospectively followed Chinese population at high risk. ;:-.10 , , , , . Current status and evaluation of endoscopic screening for gastric cancer. Jpn J Cancer Detect Diagn ;:-. In Japanese.12 . 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 ;:–.13 , , , , . The standardized development method of the Japanese guidelines for cancer screening. ;:–.17 , , , , , . A community-based, case-control study evaluating mortality reduction from gastric cancer by endoscopic screening in Japan. ;:.18 , , , , , . The evaluation of screening for gastric cancer in Miyagi Prefecture, Japan: a population-based case-control study. ;:–.19 , , , , . Epidemiological evaluation of the protective effect for dying of stomach cancer with applying a method of case-control study. A study of an efficient screening programme for stomach cancer. ;:–. In Japanese.22 , , , , , , . Gastric cancer screening and subsequent risk of gastric cancer: a large-scale population-based cohort study, with a 13-year follow-up in Japan. ;:–.23 , , , et al. . Lower risk of death from gastric cancer among participants of gastric cancer screening in Japan: a population-based cohort study. ;:–.29 , , , . Results of mass endoscopic examination for gastric cancer in Kamigoto Hospital, Nagasaki Prefecture. ;:–.30 , , , et al. . Decreased death from gastric cancer by endoscopic screening: association with a population-based cancer registry. ;:–.32 . Effectiveness of gastric endoscopic screening in reducing the mortality of gastric cancer, in comparison with barium X-ray examination and non-examination. J Gastroenterol Cancer Screen ;:–. In Japanese.33 , , , . Impact of opportunistic endoscopic screening on the decrease of mortality from gastric cancer. J Gastroenterol Cancer Screen ;:–. In Japanese.39 , , , et al. . Evaluation of false-negative patients with gastric cancer in gastroscopic screening. J Gastroenterol Cancer Screen ;:–. In Japanese.41 , , , . Evaluation of mortality reduction from gastric cancer by 2 stage strategy using serum pepsinogen test for gastric cancer screening in local community. J Jpn Assoc Cancer Detect Diagn ;:–. In Japanese.42 , , , et al. . Reduction in gastric cancer mortality by screening based on serum pepsinogen concentration: a case-control study. ;:–.43 , , , . Utility of serum pepsinogen test in combination with upper gastrointestinal series in screening for stomach cancer. J Gastroenterol Mass Survey ;:–. In Japanese.44 , , , 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 ;:–.45 , , , , , . Comparison of observed and expected numbers of detected cancers in the research center for cancer prevention and screening program. ;:–.48Committee of quality assurance for gastric cancer screening. The report of questionnaire survey of adverse effect for gastric cancer screening 2010. J Gastroenterol Cancer Screen ;:–. In Japanese.49 , . A study of an estimation method for the adverse effects of the upper gastrointestinal series using high-density barium meal. J Gastroenterol Cancer Screen ;:–. In Japanese.54 , , , et al. . 5th report of endoscopic complications: results of the Japan Gastroenterological Endoscopy Society survey from 2003 to 2007. ;:–. In Japanese.5561 , , , et al. . Prediction of gastric cancer development by serum pepsinogen test and s seropositivity in Eastern Asians: a systematic review and meta-analysis. ;:.62 , , , . Receiver operating characteristic analysis of prediction for gastric cancer development using serum pepsinogen and Helicobacter pylori antibody tests. ;:. Appendix Systematic review group of gastric cancer screening guidelinesChisato Hamashima (Chair, National Cancer Center), Katsuaki Kato (Miyagi Cancer Assciation), Isao Miyashiro (Osaka International Cancer Center), Hiroshi Nishida (AMS New Ohtani Clinic), Reo Takaku (Institute of Health Economics and Policy), Teruhiko Terasawa (Fujita Health University), Takaki Yoshikawa (Kanagawa Cancer Center).Guideline development group of gastric cancer screening guidelinesChisato Hamashima (National Cancer Center), Satoshi Honjo (National Hospital Organization Fukuoka National Hospital), Kazuhiko Inoue (Kawasaki Medical University), Takeo Nakayama (Kyoto University), Tomio Nakayama (Osaka International Cancer Center), Rintaro Narisawa (Nigiatta Prefecture Cancer Center Hospital), Motoyasu Sagawa (Tohoku Medical and Pharmaceutical University), Hiroshi Saito (National Cancer Center), Daisuke Shibuya (Miyagi Cancer Assciation), Tomotaka Sobue (Chair, Osaka University). Public Health Report

01/07/2018 · In the Japanese guidelines of gastric cancer screening, the effectiveness of radiographic and endoscopic screenings was confirmed. Radiographic screening has been the main method for gastric cancer screening in Japan. Photofluorography was developed in Japan and has been used since the 1960s (6). 26/07/2022 · Gastric cancer is the second leading cause of cancer incidence in Japan, although gastric cancer mortality has decreased over the past few decades. This decrease is attributed to a decline in the prevalence of H. pylori infection. Radiographic examination has long been performed as the only method of gastric screening with evidence of reduction in mortality in … 01/04/2008 · The guideline for gastric cancer screening guideline was developed based on the previously established method. Gastric cancer screening using photofluorography is recommended for population-based and opportunistic screening in Japan. gastric cancer, cancer screening, guideline, recommendation, photofluorography.