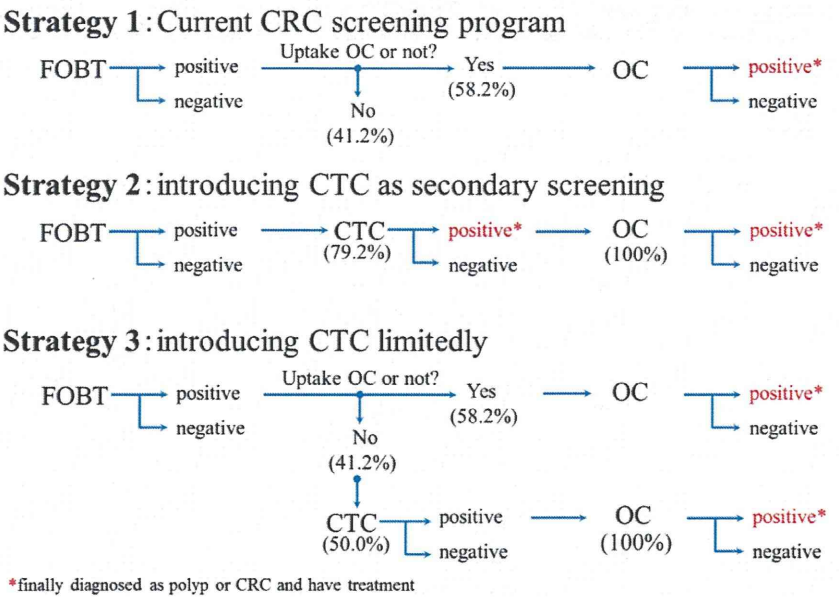

Fig. 1 – Flowchart of three CRC screening strategies. CRC, colorectal cancer; CTC, computed tomography colonography; FOBT, fecal occult blood test; OC, optical colonoscopy. *Finally diagnosed as polyp or CRC and have treatment.

them would undergo CTC. Therefore, CTC was performed in 20.9% [0.5 × (100 − 58.2%)] of all FOBT-positive people and OC was performed in all CTC-positive people (100%).

Analysis

Perspective

Analyses were carried out from a health care payer's perspective and included the costs of screening, polypectomy, and cancer treatment. FOBT costs were excluded from this study because they would be almost the same among all the three strategies.

Target population

We analyzed a hypothetical cohort consisting of all those who were 40 years old on April 1, 2011. They were composed of 1,968,500 persons, which was estimated from the number of people aged 39 and 40 years in the public report about the population on October 1, 2010 [18].

Model

We constructed a Markov model (Fig. 2) for colorectal cancer, with reference to previous studies [10–12], and adjusted it using the available epidemiological data from Japan [1–3,9,10] to estimate the effectiveness of CTC for colorectal cancer screening of working age population. One cycle of our Markov-model was set to 1 year, reflecting the shortest time period for data collected in our analysis [15,16,19].

Transition probability

We adjusted the transition probabilities (Table 1) among each stage on the basis of epidemiological data from Japan [1–3,9,10] and a previous study [16]. Non–colorectal cancer mortality was calculated on the basis of colorectal cancer mortality [1] and mortality table [2].

We set the sensitivity and specificity of each test to the values presented in Table 1 on the basis of previous Japanese and foreign studies [20–27] and discussions with clinical experts.

Previous studies on the sensitivity and specificity of FOBT [20–26] have various limitations such as an insufficient sample size, a biased population, or an insufficient description of the method. After discussion with clinical experts, we used the Japanese data [20] as provisional values in the base-case analysis and assumed distributions in the probabilistic sensitivity analysis.

Although the sensitivity and specificity of CTC depend largely on the skills of the physicians, we used the results of a clinical study [27] after assuming that interphysician variation had been equalized. Moreover, because there were few physicians in Japan

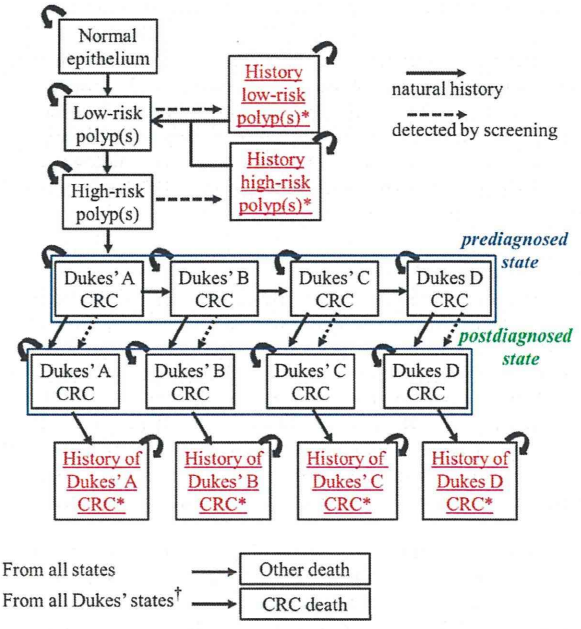

Fig. 2 – Markov model for CRC [–]. CRC, colorectal cancer. *Underline means already treated state. †Does not include the prediagnosed state.

Table 1 – Valuables in the Markov model (transition probability, cost, and screening characteristics).

Transition probability		Cost (JPY)		Other variables	
Progression (prediagnosed)		Test and treatment		Uptake rate of test	
Normal epithelium to low-risk polyp(s)	0.012	CTC*	31,500	FOBT†	0.248
Low-risk polyp(s) to high-risk polyp(s)	0.024	OC*	25,000	OC†	0.583
High-risk polyp(s) to Dukes' A	0.034	Polypectomy (≤2 cm in diameter)	78,000	CTC	0.500
Dukes' A to Dukes' B	0.583	Polypectomy (≥2 cm in diameter)	98,000	Sensitivity of FOBT	
Dukes' B to Dukes' C	0.656	Malignant tumor resection (colon)	840,400	Low-risk polyp	0.070
Dukes' C to Dukes' D	0.865	Malignant tumor resection (rectum)	1,130,900	High-risk polyp	0.200
Death from colorectal cancer		Postoperative chemotherapy	1,016,000	Dukes' A	0.538
Dukes' A‡	0.00545	Chemotherapy (Dukes' D, annual)	4,259,600	Dukes' B	0.700
Dukes' B‡	0.0282	Follow-up (Dukes' A and B)	35,600	Dukes' C and D	0.783
Dukes' C‡	0.0532	Follow-up (Dukes' C and D)	45,000	Sensitivity of CTC	
Dukes' D‡	0.310	Annual cost by stage		Low-risk polyp	0.650
Prediagnosed to postdiagnosed		Low-risk and high-risk polyps	78,000	Others	0.900
Dukes' A presentation	0.065	Dukes' A (1 y)	98,000	Sensitivity of OC	1.000
Dukes' B presentation	0.26	Dukes' A (2–5 y)	35,600	Specificity	
Dukes' C presentation	0.46	Dukes' B (1 y)	941,400	FOBT	0.948
Dukes' D presentation	0.92	Dukes' B (2–5 y)	35,600	CTC	0.860
Polyp recurrence after polypectomy		Dukes' C (1 y)	1,957,400	OC	1.000
History of low-risk polyp(s) (first year)	0.18	Dukes' C (2–5 y)	45,000		
History of low-risk polyp(s) (2 y)	0.05	Dukes' D (1–5 y)	4,304,600		
History of high-risk polyp(s) (first year)	0.25				
History of high-risk polyp(s) (2 y)	0.06				

CRC, colorectal cancer; CTC, computed tomography colonography; FOBT, fecal occult blood test; JPY, Japanese yen; OC, optical colonoscopy.

* Derived from the fee for the cancer screening program at the National Cancer Center in Japan and others were calculated from the guideline for CRC treatment [30] and health insurance fee schedule [28,29].

† Average values among people aged 40 to 60 y appear in this table. In the actual model, they were varied according to their age [9,10].

‡ Transition probabilities were adjusted by domestic epidemiological data [1–3,9,10] and the other probabilities were referred to a previous study [16].

who were experienced in CTC, the real-world sensitivity and specificity of CTC were likely to be lower than those published in this previous report [27]. We assumed distributions in the probabilistic sensitivity analysis to take account of this uncertainty.

Both the sensitivity and specificity of OC used in the final diagnosis were set to 1.00. If the specificity was below 1.00, some people would be false-positively diagnosed and unnecessarily treated for colorectal cancer. We did not, however, consider this issue in our model and did not perform any scenario analysis because there were insufficient Japanese epidemiological data about false-positive cases and the accuracy of OC itself was not in the scope of our analysis.

Uptake of each test

As mentioned earlier, we set the uptake of FOBT from the Comprehensive Survey of Living Conditions 2010 [9] and set the uptake of OC from the Report on Regional Public Health Services and Health Promotion Services 2010 [10]. Average uptake of FOBT and OC among people aged 40 to 60 years is presented in Table 1. Furthermore, scenario analysis was carried out for the case that the uptake of FOBT reached the government's target figure (50%) and the case that the uptake of OC was the lowest value (34.1% in Tokyo) or the highest value (75.0% in Iwate) among 47 prefectures [10].

Because colorectal cancer screening with CTC was not common in Japan, there were no national data about the uptake of CTC; therefore, from discussion with clinical experts, we assumed that a half of FOBT-positive persons who were reluctant to undergo OC would agree to CTC screening and that all CTC-positive people would agree to OC. The uptake of CTC is also presented in Table 1.

Cost

Costs are presented in Table 1 [28–30], all of which are direct costs. The costs of CTC and OC were based on those for cancer screening charged at the Japanese National Cancer Center. Treatment costs of colorectal cancer stratified by Dukes' classification were calculated from the newest guideline for colorectal cancer treatment [30]. Under the Japanese health insurance system, inpatient treatments for colorectal cancer in large hospitals were charged on the basis of the diagnosis-related group system. Thus, we used them instead of separately calculating unit price and resource use [28,29].

Outcome measures

We set QALY as the primary outcome and colorectal cancer death and expected life-years as secondary ones. Because there were insufficient Japanese data, we referred the utility scores in a previous UK study [15,16]. The Basic Plan to Promote Cancer Control Program aimed to decrease the number of cancer deaths and to prolong life-years with good health [7]. Thus, we set colorectal cancer death as well as expected life-year as secondary outcomes.

Time horizon (duration of analyses)

In the base-case analysis, the time horizon was set to 20 years. Governmental policy aimed at increasing the uptake of colorectal cancer screening, especially among those who were of working age [11]. Therefore, we think that 20 years was sufficient for capturing whole costs and outcomes accrued during the working age, or 40 years old to 60 years old. So far, some workers were still working even after they crossed 60 years, or until they become 65

years or 70 years old. Then, in scenario analyses, we varied the time horizon to 10 years, 30 years, and lifetime.

Discount rate

The annual discount rate was set at 3% for both cost and effectiveness. Scenario analysis was carried out for 0% and 7% in Shiroiwa et al. [31].

Sensitivity analyses

Scenario analyses were carried out for the following variables for which we could found the grounds of setting a lower or higher value: uptake of FOBT (50%) [7], uptake of CTC (25%–75%), uptake of OC (34.1% and 75.0%) [10], time horizon (10 years, 30 years, and lifetime), discount rate (0% and 7%) [31], and the cohort aged 50 years with a 10-year time horizon.

Probabilistic sensitivity analyses were also conducted by adopting distributions for variables incorporated into our model, as shown in Table 1. We adopted beta distributions for the parameters for which we could acquire raw data (denominator and numerator of parameters) and normal distributions for the parameters for which we could not acquire raw data. Also, we made estimations of the chemotherapy costs for Dukes' C and Dukes' D patients on the basis of chemotherapy strategies in the 2010 guideline [30] but there were various treatment modalities and it depends largely on the condition of the patient; therefore, we assumed the log-normal distribution for the chemotherapy cost on the basis of estimated costs distribution of each chemotherapy strategy, and considered uncertainties related to chemotherapy cost.

Results

Validity of the Model

We constructed a Markov model with reference to previous studies [15,16,19] and adjusted it for transition probability according to Japanese epidemiological data such as the 5-year observed survival rate, cumulative incidence rate, and cumulative mortality categorized by Dukes' classification [1–3,9,10]. For example, we calculated the annual mortality for each Dukes' classification from Japanese 5-year observed survival rate data. We adjusted the age-specific incidence of colorectal cancer using Japanese data for cumulative incidence rate and mortality. Because there were no data for transition probabilities among the four Dukes' stages, we referred previous studies [15,16,19] and calibrated those using current data for the cumulative incidence rate.

Result of the Base-Case Analysis

We calculated the total costs (screening cost + treatment costs), the QALYs, the number of colorectal cancer deaths, and the expected life-years for the hypothetical cohort consisting of all those who were 40 years old (N = 1,968,500 as of April 1, 2011); the data are summarized in Table 2.

For the base-case analysis (time horizon 20 years), differences against strategy 1 were as follows.

Strategy 2 required an additional cost of JPY 3,790,548,000 (from 69,405,291,000 to 65,614,743,000), increased QALYs by 2,303 (from 28,158,349 to 28,156,046), decreased the number of cancer deaths by 324 people (from 4,693 to 4,369), and increased the expected life-years by 1,752 person-years (from 28,713,132 to 28,711,380). The incremental cost-effectiveness ratios (ICERs) were JPY 1,646,000 per QALY gained, JPY 11,683,000 per colorectal cancer death averted, and JPY 2,164,000 per life-year gained.

Strategy 3 decreased cost by JPY 1,736,198,000 (from 65,614,743,000 to 63,878,545,000), increased QALYs by 3,012 (from 28,159,058 to 28,156,046), decreased the number of cancer deaths by 434 people (from 4,693 to 4,260), and increased the expected life-years by 2,323 person-years (from 28,713,702 to 28,711,380). Strategy 3 was dominant against strategy 1.

Result of scenario analyses

The scenario analyses were carried out for the following four variables: uptake of FOBT (50%), uptake of CTC (25%–75%), uptake of OC (34.1% and 75.0%), time horizon (10 years, 30 years, and lifetime), discount rate (0% and 7%), and the cohort aged 50 years with a 10-year time horizon.

When the uptake of FOBT reached the government's target figure (50%), the ICERs were JPY 2,795,000 per QALY gained for strategy 2 and JPY 154,000 per QALY gained for strategy 3, respectively, which was well below the Japanese threshold (JPY 5–6 million per QALY gained) [31].

When the uptake of CTC decreased from 50% to 25%, the ICER was JPY 6,175,000 per QALY gained for strategy 2 and strategy 3 was dominant against strategy 1. When the uptake of CTC improved from 50% to 75%, the ICER was JPY 850,000 per QALY gained for strategy 2 and strategy 3 was dominant against

Table 2 – Result of base-case analysis (unit: 1,968,500 persons aged 40 y on April 1, 2011).

Unit 1	Unit 2	Strategy 1*	Strategy 2	Strategy 3	Strategy 2 vs. strategy1	Strategy 3 vs. strategy 1
Cost (JPY 1,000)	Cost	65,615,000	69,405,000	63,879,000		
	⊿Cost				+3,790,548	−1,736,198
Outcome	QALY	28,158,046	28,158,349	28,159,058		
	CRC death	4,693	4,369	4,260		
	ELY	28,711,380	28,713,132	28,713,702		
	⊿QALY				2,303	3,012
	⊿CRC death				324	434
	⊿ELY				1,752	2,323
ICER (JPY 1,000)	per QALY				1,646	Dominant
	per CRC death averted				11,683	Dominant
	per LYG				2,164	Dominant

CRC, colorectal cancer; ELY, expected life-year; ICER, incremental cost-effectiveness ratio; JPY, Japanese yen; LYG, life-year gained; QALY, quality-adjusted life-year.

* Strategy 1 was set to control when calculating ICERs.

strategy 1.

When the uptake of OC decreased to the lowest value among 47 prefectures (34.1% in Tokyo), the ICER was JPY 21,000 per QALY gained for strategy 2 and strategy 3 was dominant against strategy 1. When the uptake of OC decreased to the highest value among 47 prefectures (75.0% in Iwate), the ICER was JPY 11,740,000 per QALY gained for strategy 2 and strategy 3 was dominant against strategy 1.

When the time horizon was 10 years, ICERs were JPY 19,085,000 per QALY gained for strategy 2 and JPY 5,288,000 per QALY gained for strategy 3, respectively. When the time horizon was 30 years, the ICER was JPY 416,000 per QALY gained for strategy 2 and strategy 3 was dominant against strategy 1. When the time horizon was lifetime, both strategy 2 and strategy 3 were dominant against strategy 1.

When the discount rate was 0%, the ICER was JPY 1,217,000 per QALY gained for strategy 2 and strategy 3 was dominant against strategy 1. When the discount rate was 7%, the ICER was JPY 2,401,000 per QALY gained for strategy 2 and strategy 3 was dominant against strategy 1.

When the target population was those who were aged 50 years on April 1, 2011, and the time horizon was 10 years, ICERs were JPY 2,685,000 per QALY gained for strategy 2 and JPY 5,468,000 per QALY gained for strategy 3 against strategy 1.

Result of the Probabilistic Sensitivity Analysis

The probabilistic sensitivity analyses showed that colorectal cancer screening programs with CTC were likely to be cost-effective compared with strategy 1 (current program without CTC).

Figure 3 illustrates that in 95.2% of the simulations, strategy 2 was found to be acceptable at a cost-effective threshold of JPY 5 to 6 million per QALY gained compared with strategy 1. Moreover, Figure 3 shows that strategy 2 was dominant against strategy 1 in 6.1% of the simulations.

Figure 4 illustrates that in all simulations, strategy 3 was found to be acceptable at the cost threshold of JPY 5 to 6 million per QALY gained compared with strategy 1; moreover, Fig. 4 shows that strategy 3 was dominant against strategy 1 in 74.7% of the simulations.

Discussion

Target Population

As mentioned earlier, since 2011, the Japanese government started to provide free colorectal cancer screening to those aged 40, 45, 50, 55, or 60 years, aiming to increase the colorectal cancer screening uptake to the target figure (50%) among the working age population [11]. Therefore, to reveal the effect of CTC for the colorectal cancer screening program among the working age population in Japan, we set a closed cohort comprising people aged 40 years on April 1, 2011, as our target population and set 20 years (from 40 to 60 years) as the time horizon in the base-case analysis.

The result of scenario analysis for time horizon showed the common trend between strategy 2 and strategy 3, that when the time horizon was longer, the cost-effectiveness of CTC for colorectal cancer screening would be improved more. Older persons, however, were more likely to be diagnosed with colorectal cancer when they took cancer screening, due to a higher prevalence rate than in younger people [3]. Therefore, to capture the entire effect of CTC implementation, we need to expand the time horizon to lifetime. If we expand the time horizon to lifetime, both strategy 2 and strategy 3 became dominant against strategy 1.

Recurrence of Colorectal Cancer

We did not adapt recurrence and metastasis to this model, which was due to the lack of data on the recurrence of colorectal cancer in Japan. Their effect on mortality, however, could implicitly be reflected in the 5-year observed survival rate, while their cost had

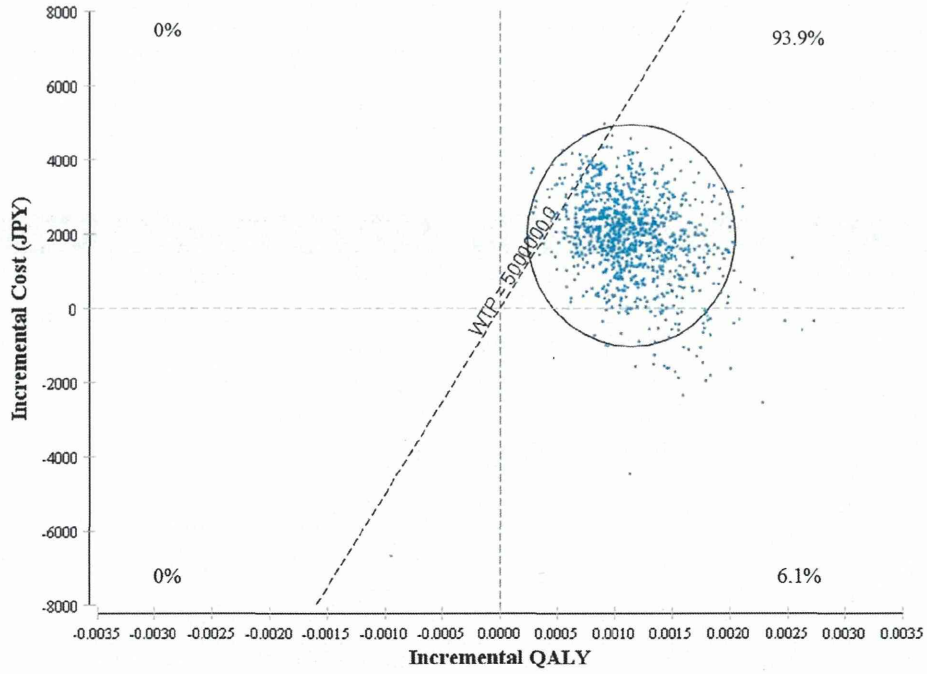

Fig. 3 – Scatter plot of probabilistic sensitivity analysis on the cost-effectiveness plane for strategy 2 compared with strategy 1. JPY, Japanese yen; QALY, quality-adjusted life-year; WTP, willingness to pay.

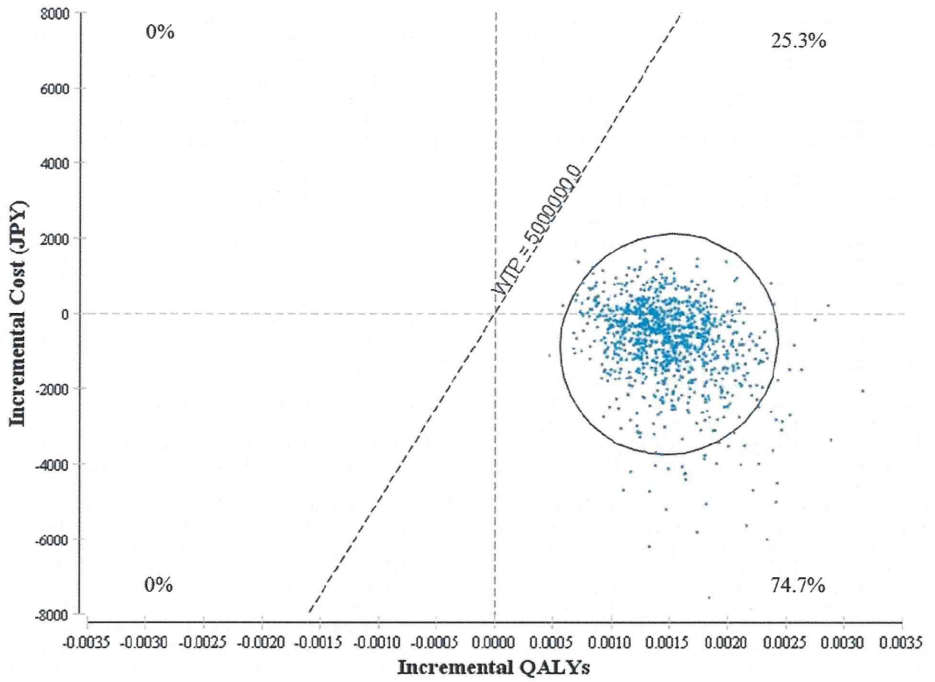

Fig. 4 – Scatter plot of probabilistic sensitivity analysis on the cost-effectiveness plane for strategy 3 compared with strategy 1. JPY, Japanese yen; QALY, quality-adjusted life-year; WTP, willingness to pay.

not been calculated. Therefore, we might underestimate the per-patient treatment cost and the amount of cost saving generated by CTC, especially for colorectal cancer with Dukes' C and Dukes' D. If we could include the costs of recurrence and metastasis, the ICER would improve more.

Limitations and Future Research

In this study, we constructed the model so that it worked adversely on introducing CTC where data were ambiguous, because colorectal cancer epidemiological data were not sufficient. It is desirable to perform a reanalysis with more data for the sensitivity and specificity of FOBT and a breakdown of the medical costs for each stage of the Dukes' classification.

However, we did not consider the adverse events that may occur with OC or CTC. Because OC was conducted by certified physicians who passed the training course in Japan, physicians in the National Cancer Center in Japan commented that adverse events such as perforation could be ignored in Japan. Also, radiologists commented that adverse events with CTC could be ignored because of small radiation exposure. Therefore, we ignored this issue in this model. But we had to take into account that the risk of adverse events with OC or CTC could not be zero. And, because this model ignores these risks, we should not forget this point when we use the result of this analysis. In any case, we would include these factors in future analyses to avoid this issue.

Policy Consideration

Overall results were largely affected by the uptake of OC. Larger OC uptake induced better ICER and vice versa because of the number of those who took OC, and the number of people with colorectal cancer detected would be increased with higher OC uptake. OC uptake varied much from one region to another, or 34.1% to 75.0% [10]. Thus, we need to take regional OC uptake into account when we consider implementing and/or promoting CTC to a specific region.

Conclusions

In our analysis, the cost-effectiveness of CTC for a colorectal cancer screening program in the working age population in Japan was as follows. The ICER was JPY 1,646,000 per QALY gained for strategy 2 and strategy 3 was dominant against strategy 1, both of which were well below the Japanese threshold (JPY 5–6 million per QALY gained) [31].

These ICER values will be further improved with a longer time horizon (i.e., 30 years) than used in the basic analysis. Therefore, adding CTC into the current colorectal cancer screening program for the working age population seems to be a cost-effective option.

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ORIGINAL ARTICLE

Observational Study

Impact of endoscopic screening on mortality reduction from gastric cancer

Chisato Hamashima, Kazuei Ogoshi, Rintarou Narisawa, Tomoki Kishi, Toshiyuki Kato, Kazutaka Fujita, Masatoshi Sano, Satoshi Tsukioka

Chisato Hamashima, Cancer Screening Assessment and Management Division, Research Center for Cancer Prevention and Screening, National Cancer Center, Tokyo 104-0045, Japan
Kazuei Ogoshi, Cancer Registry Section, Niigata Cancer Center Hospital, Niigata 951-8566, Japan
Rintarou Narisawa, Toshiyuki Kato, Division of Gastroenterology, Niigata Cancer Center Hospital, Niigata 951-8566, Japan
Tomoki Kishi, Graduate student, Department of Health Management, Keio University, Fujisawa 252-0882, Japan
Kazutaka Fujita, Masatoshi Sano, Committee of Gastrointestinal Cancer Screening, Niigata city Medical Association, Niigata 951-8131, Japan
Satoshi Tsukioka, Niigata city Public Health Center, Niigata city Government, Niigata 950-1197, Japan
Author contributions: Ogoshi K, Hamashima C, and Narisawa R designed the study; Kato T, Fujita K, Sano M, and Tsukioka S performed the follow-up survey and collected data; Hamashima C and Kishi T conducted the statistical analysis; Ogoshi K, Hamashima C, and Narisawa R wrote the initial draft of the article, which was revised and approved by the authors.
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Correspondence to: Chisato Hamashima, MD, Cancer Screening Assessment and Management Division, Research Center for Cancer Prevention and Screening, National Cancer Center, 5-1-1 Tsukiji Chuo-ku, Tokyo 104-0045, Japan. chamashi@ncc.go.jp
Telephone: +81-3-35475305
Fax: +81-3-35478587
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Abstract

AIM: To investigate mortality reduction from gastric cancer based on the results of endoscopic screening.

METHODS: The study population consisted of participants of gastric cancer screening by endoscopy, regular radiography, and photofluorography at Niigata city in 2005. The observed numbers of cumulative deaths from gastric cancers and other cancers were accumulated by linkage with the Niigata Prefectural Cancer Registry. The standardized mortality ratio (SMR) of gastric cancer and other cancer deaths in each screening group was calculated by applying the mortality rate of the reference population.

RESULTS: Based on the results calculated from the mortality rate of the population of Niigata city, the SMRs of gastric cancer death were 0.43 (95%CI: 0.30-0.57) for the endoscopic screening group, 0.68 (95%CI: 0.55-0.79) for the regular radiographic screening group, and 0.85 (95%CI: 0.71-0.94) for the photofluorography screening group. The mortality reduction from gastric cancer was higher in the endoscopic screening group than in the regular radiographic screening group despite the nearly equal mortality rates of all cancers except gastric cancer.

CONCLUSION: The 57% mortality reduction from gastric cancer might indicate the effectiveness of endoscopic screening for gastric cancer. Further studies and prudent interpretation of results are needed.

Key words: Gastric cancer screening; Mortality; Upper gastrointestinal endoscopy; Upper gastrointestinal radiography; Standardized mortality ratio

Core tip: We investigated mortality reduction from gastric cancer on the basis of results of endoscopic screening. The standardized mortality ratio (SMR) of gastric cancer and other cancer deaths in each screening group was calculated by applying the mortality rate of the reference population. Based on the results calculated from the mortality rate of the population of Niigata city, the SMRs of gastric cancer death were 0.43 (95%CI: 0.30-0.57) for the endoscopic screening group. The 57% mortality reduction from gastric cancer might indicate the effectiveness of endoscopic screening for gastric cancer.

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INTRODUCTION

Despite the recent decline in the incidence and mortality of gastric cancer worldwide, gastric cancer remains to be the third leading cause of cancer mortality worldwide[1]. Moreover, the burden of gastric cancer still remains in Asia and East European countries. In most countries, gastric cancer screening has not been commonly carried out. However, in some Asian countries, gastric cancer screening using endoscopy has been performed as opportunistic screening[2]. Endoscopy, which is commonly used in clinical practice, is anticipated to be a promising screening method for gastric cancer. Although gastric cancer screening has been actively performed in South Korea and Japan[2-4], endoscopic screening has been carried out as a national program only in Korea.

Gastric cancer screening using the upper gastrointestinal series (UGI) (*i.e.*, radiographic screening) is recommended in the Japanese guidelines for gastric cancer screening[5]. In particular, radiographic screening for gastric cancer was initiated in Japan in the 1960s[6]. The UGI with double-contrast study was originally adopted for radiographic screening. Photofluorography is one of the radiographic methods and it can be performed on board a vehicle because the equipment used is small compared with the regular radiographic equipment. In Japan, photofluorography was originally performed on a mobile car and has been used in communities. Regular radiographic screening has also been performed in clinical settings.

On the other hand, endoscopic examination has been widely used in clinical settings, but rarely for population-based screening programs. Since endoscopy can detect the early stage of gastric cancer, its introduction into communities for gastric cancer screening has been highly anticipated. To effectively introduce new techniques for population-based screening, mortality reduction should be evaluated. Except for radiographic screening, other methods have not been evaluated in terms of reduction of mortality from gastric cancer. Various screening methods for gastric cancer have been developed. In particular, the evaluation method used for radiographic screening was not randomized controlled studies but was limited to observational studies. Although several studies have reported the possibility of reducing mortality by endoscopic screening[7-10], definitive evidence remains to be established.

Serologic testing, including serum pepsinogen and *Helicobacter pylori* antibody testing, has also been used for targeting the high-risk group for gastric cancer; however, the effectiveness of these screening methods has not been fully clarified[2,4]. In this study, we investigated mortality reduction from gastric cancer on the basis of the results of gastric cancer screening by endoscopy and radiography in Niigata city, Japan.

MATERIALS AND METHODS

Ethics

This study was approved by the Institutional Review Board of National Cancer Center, Japan.

Screening program

Gastric cancer screening has been conducted and supported by the Health Service Law for the Aged since 1983 and it has been offered by local governments. Since 2003, endoscopic examination has been added to the screening programs for gastric cancer in Niigata city[10]. Both photofluorography and regular radiographic screening for the UGI have also been continued. Photofluorography has been performed as a mass screening program using mobile cars mainly in local areas. On the other hand, as endoscopic and regular radiographic screenings have been performed in clinical settings, individuals who visited regularly for any disease treatment were often recommended to undergo cancer screening by their own primary care physicians. The target populations of these screening programs vary as follows: individuals aged 40, 45, and 50 years or over can undergo endoscopic and regular radiographic screenings; individuals aged more than 40 years can undergo photofluorography. Individuals could choose any screening method based on their own preference. There is no upper age limit and the screening interval is every year for all screening methods. Although the participation rate in gastric cancer screening has increased since the introduction of endoscopic screening, the screening rate has remained at approximately 25%[10].

Physicians who perform endoscopic screening for

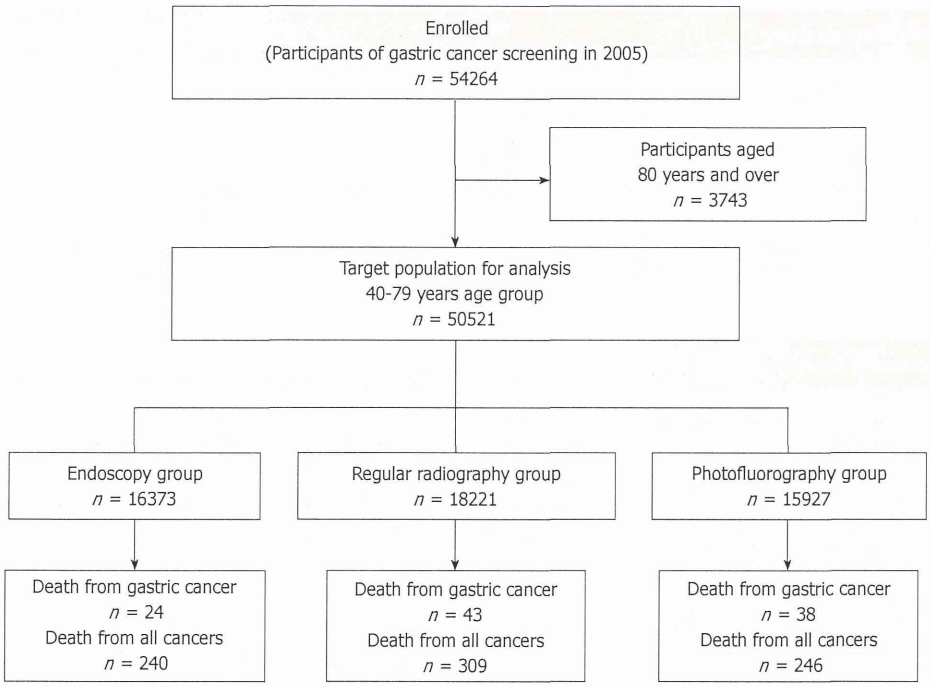

Figure 1 Flowchart for the selection of the target population. The target population consisted of participants of gastric cancer screening by endoscopy, regular radiography, and photofluorography at Niigata city, in 2005. The total number of participants of the gastric cancer screening in 2005 was 54264. The target population of this study was defined as individuals whose ages ranged from 40 years to 79 years; individuals belonging to the age group of 80 years and over were excluded from the study. The final numbers of subjects for the defined age group were 16373 for the endoscopic screening, 18221 for the regular radiographic screening, and 15927 for the photofluorography screening.

gastric cancer in Niigata city have been approved by the local committee for gastric cancer screening based on certain requirements[10]. Although these endoscopic screenings have been performed in clinical settings, the results have been evaluated on the basis of a monitor screen review by the local committee, including experienced endoscopists.

Study population

The study population consisted of 54264 participants of gastric cancer screening by endoscopy, regular radiography, and photofluorography at Niigata city in 2005. The target population of this study was defined as individuals whose age was from 40 years to 79 years at the screening date in 2005. Individuals belonging to the age group of 80 years and over were excluded from the study. A flowchart showing the selection process for the study populations is shown in Figure 1. After the selection process, the total numbers of subjects for each screening group were 16373 for the endoscopic screening, 18221 for the regular radiographic screening, and 15927 for the photofluorography screening.

Since we could not obtain data regarding immigration rates and deceased cases except for cases of cancers, the number of all-cause mortality was estimated from the population data of Niigata city[11]. The immigration rates were calculated from the National Population Survey in 2010[12]. The all-causes mortality and immigration rates of the screening group were assumed to be equal to those of the whole population of Niigata city. Based on a 5-year immigration rate in the National Population Survey, our calculated annual immigration rates per 1000 individuals from Niigata city were as follows; for men: 19.2 (aged 40-44 years), 16.4 (45-49 years), 13.3 (50-54 years), 9.2 (55-59 years), 5.0 (60-64 years), 2.7 (65-69 years), 1.6 (70-74 years), and 1.5 (75-79 years); for women: 13.3 (aged 40-44 years), 6.8 (45-49 years), 4.5 (50-54 years), 3.2 (55-59 years), 2.6 (60-64 years), 2.0 (65-69 years), 1.4 (70-74 years), and 1.7 (75-79 years). The immigration rates and all-causes mortality were adopted for calculating the number of the study population of the 3 different screening groups within 5 years of follow-up (Table 1).

Statistical analysis

The follow-up period was defined as 5 years from the index date of the screening in 2005. The observed numbers of cumulative death cases from gastric cancers and other cancers in each screening group were ascertained by linkage with the Niigata Prefectural Cancer Registry.

The expected numbers of gastric cancer death for the 5-year follow-up were calculated on the basis of a 5-year age group interval from 40 years to 79 years in both men and women by applying the mortality rate of the population of Niigata city[11], Niigata prefecture[12],

Table 1 Target population of the follow-up study

Screening method	Sex	Participants in 2005 (*n*)	Follow-up				
			2006	2007	2008	2009	2010
Endoscopy	Men	6476	6314	6170	6029	5897	5771
	Women	9897	9797	9707	9615	9525	9442
Regular radiography	Men	7019	6841	6683	6548	6384	6246
	Women	11202	11087	10985	10879	10775	10682
Photofluorography	Men	5188	5056	4939	4824	4717	4614
	Women	10739	10638	10545	10450	10357	10270

Table 2 Characteristics of the screening groups *n* (%)

	Endoscopy	Regular radiography	Photofluorography
Age group			
40-49 yr	229 (1.40)	216 (1.19)	1836 (11.53)
50-59 yr	2033 (12.42)	2087 (11.45)	3521 (22.11)
60-69 yr	7880 (48.13)	8568 (47.02)	5830 (36.60)
70-79 yr	6231 (38.06)	7350 (40.34)	4740 (29.76)
Sex			
Men	6476 (39.55)	7019 (38.52)	5188 (32.57)
Women	9897 (60.45)	11202 (61.48)	10739 (67.43)

and Japan[13,14]. The standardized mortality ratios (SMRs) and 95%CIs were also determined. The SMRs of gastric cancer death were the ratios in which the numerator represented the number of observed cancer and the denominator indicated the number of expected cancer in a reference population. The SMRs of all cancer deaths except gastric cancer deaths were also calculated using the same methods. Statistical analyses were carried out using STATA 11.0 (STATA, College Station, TX, United States).

RESULTS

The study population was divided into 3 screening groups on the basis of their participation in the screening programs in 2005. The total number of the study population was 50521 individuals and the number for each program was as follows: 16373 for the endoscopic screening, 18221 for the regular radiographic screening and 15927 for the photofluorography screening. Table 2 shows the basic characteristics of the 3 different screening groups. The participants in the photofluorography screening were younger than those in the endoscopic screening and regular radiographic screening. The number of female participants was higher in all the 3 screening groups. The cancer detection rate was higher in the endoscopic screening group than in the regular radiographic and photofluorography screening groups (Table 3). The total numbers of death from gastric cancer for 5 years after the index date of the screening in 2005 were 24 for the endoscopic screening group, 43 for the regular radiography group, and 38 for the photofluorography screening group.

The SMRs were calculated on the basis of the death rates of the 3 different reference populations (Table 4). Based on the results calculated for the population of Niigata city, the SMRs of gastric cancer death were 0.43 (95%CI: 0.30-0.57) for the endoscopic screening group, 0.68 (95%CI: 0.55-0.79) for the regular radiographic screening group and 0.85 (95%CI: 0.71-0.94) for the photofluorography screening group. The SMRs of all cancer deaths except gastric cancer deaths were 0.62 (95%CI: 0.57-0.67) for the endoscopic screening group, 0.68 (95%CI: 0.63-0.73) for the regular radiographic screening group, and 0.74 (95%CI: 0.68-0.79) for the photofluorography screening group. The mortality reduction from gastric cancer was higher in the endoscopic screening group than in the regular radiographic screening group despite the nearly equal mortality rates of all cancers except gastric cancer. The same results were obtained even if the reference population were changed to the population of Niigata prefecture and Japan. The SMRs for the endoscopic screening was 0.41 (95%CI: 0.29-0.55) in reference to the population of Niigata prefecture and 0.45 (95%CI: 0.31-0.59) in reference to the population of Japan. The same results for each screening group were obtained in both men and women. These results suggested mortality reduction from gastric cancer by endoscopic screening.

DISCUSSION

We assessed the SMRs of gastric cancer deaths in endoscopic screening and 2 radiographic screening procedures at the community level. The risk of gastric cancer death for the participants in the endoscopic screening was reduced by 57% compared with the risk for the reference population of Niigata city, Niigata prefecture, and Japan. Even if the reference population was changed, the SMRs of the endoscopic screening group were similar. The SMRs of all cancer deaths except gastric cancer deaths were nearly equal among the endoscopic screening group and the regular radiographic screening group, suggesting that the participants in the screening groups had a similar risk for gastric cancer. Even if the participants were a healthy population, morality reduction from gastric cancer was consistently higher in the endoscopic