



Screening for Gastric Cancer

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Mass screening for gastric cancer in Japan has been conducted nationwide since 1960. The total number of examinees in 1985 amounted to 5,161,876 and 6,240 cases (0.12%) of gastric cancer were detected. Approximately half of these cases were early stage cancers. According to the studies of mass gastric screening in the Miyagi Prefecture, Japan, the sensitivity of the screening test by the indirect x-ray method was 82.4%, and the specificity was 77.2%. The positive predictive value was 1.78%. Recently, mortality from gastric cancer has been decreasing in Japan. Many studies have been carried out to investigate the relationship between the decreasing trend of mortality from cancer of the stomach and the effectiveness of mass gastric screening. From these studies and from time trend analyses of incidence and death rates, case-control studies, nonexperimental cohort studies, etc., it is believed that mass screening for gastric cancer is effective in reducing the death rate from cancer at this site.

Gastric cancer is relatively common worldwide, but there are considerable variations in the mortality rate from this disease among different regions and countries. Japan has had the highest age-adjusted mortality rate for gastric cancer in the world for both sexes since around 1960 [1, 2]. The age-adjusted death rate for cancer of the stomach in Japan during the period of 1978–1979 was 49.66 per 100,000 population for males and 25.15 for females. The next highest figures were found in Chile, followed by Costa Rica, Hungary, Poland, and so on. Caucasian males and females in the United States had the lowest death rate in the world.

In Japan, death from gastric cancer accounted for 51.6% of all cancer deaths in males and for 38.4% in females around 1960, ranking as the highest cause. At that time, therefore, in Japan, the control of gastric cancer was the most important part of the strategy against cancer. The main purpose of mass gastric screening was early detection at the preclinical stage and prompt treatment of gastric cancer, and finally the reduction of mortality from cancer at this site in a target population (Figs. 1, 2).

Recently, the mortality from gastric cancer has been decreasing in Japan. In 1986, however, the first in rank among all cancer deaths were deaths from cancer of the stomach, in both sexes, or 26.5% in males and 23.2% in females.

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This article concerns the history, results, and evaluation of gastric mass screening in Japan.

History of a Mass Survey for Gastric Cancer in Japan

In 1960, a mass survey for gastric cancer by mobile x-ray equipment was started actively and systematically in the Miyagi Prefecture, Japan. Fecal occult blood tests, gastric juice tests (measurement of gastric acid), palpation, and photofluorography were jointly used for some time after the start of this survey. The 3 former methods were, however, found to be ineffective in the detection of early gastric cancer.

At the beginning of the mass survey, none of the available diagnostic methods except double contrast x-ray examination of the stomach was thought to have any practical diagnostic ability. A car was therefore designed with a built-in photofluorographic apparatus. With the help of official and private groups, an “antigastric cancer” campaign was carried out and the mass screening technique using the double contrast method was applied as the main method of cancer detection.

In 1984, the Japanese Society of Gastroenterological Mass Survey recommended a standardized method of taking a series of 7 films (Table 1) and also annual or biennial screening [3]. This standard method has been widely used in mass gastric screening in Japan. The compliance or coverage rate of this screening in the target population was approximately 10% in the whole country at that time.

In conformity with the Law of Health and Medical Services for the Elderly, which came into effect in February, 1983, the mass survey is now conducted nationwide as Japanese government policy. The Japanese government set up a goal of an annual examination rate of 30% among the population at risk aged 40 years and older.

Results of the Mass Survey for Gastric Cancer

Nationwide Statistics

According to the report from the Japanese Society of Gastroenterological Mass Survey [4], the number of examinees in Japan has been increasing year by year since 1968 and, in 1985, the total number examined was 5,161,876. The number of cases of cancer of the stomach detected by the mass survey was 6,240 (0.12%). Among these cancer cases, surgical operations were

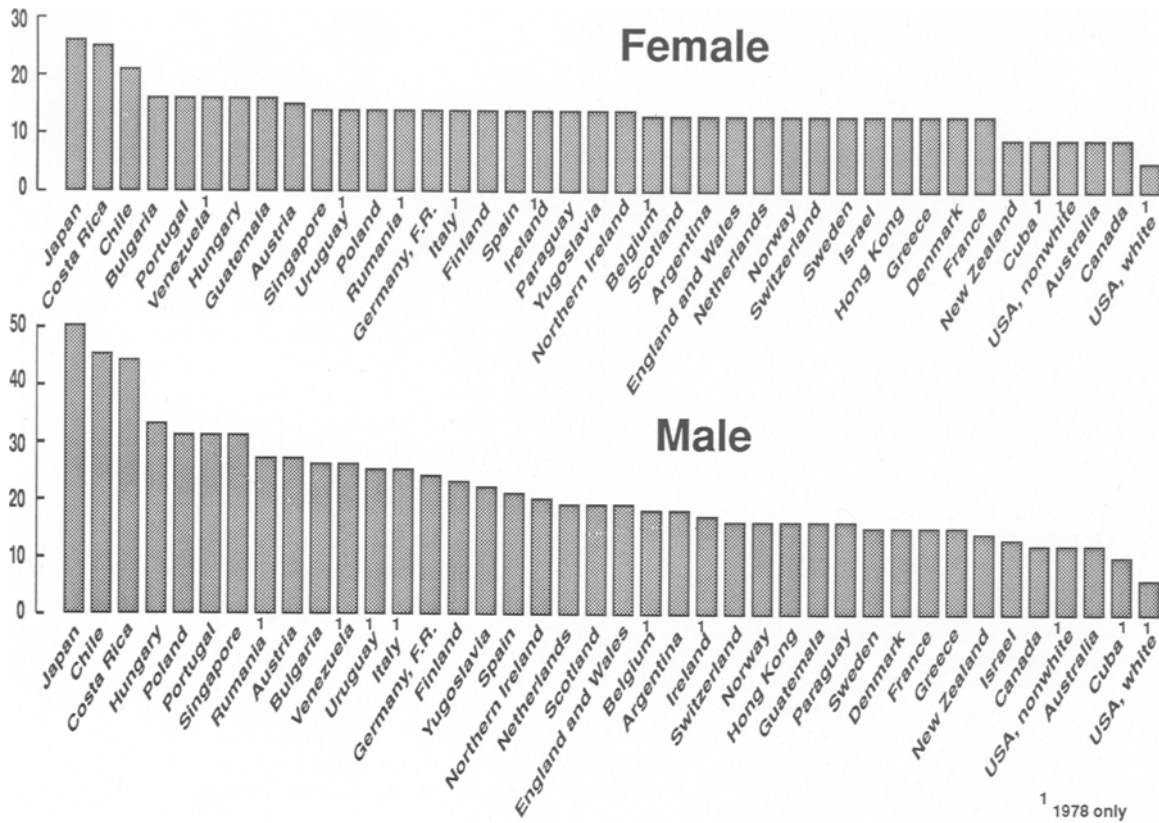


Fig. 1. Age-adjusted death rates for malignant neoplasm of the stomach in the period of 1978–1979 in 39 countries (rate per 100,000 population). Reprinted with permission of publisher [2].

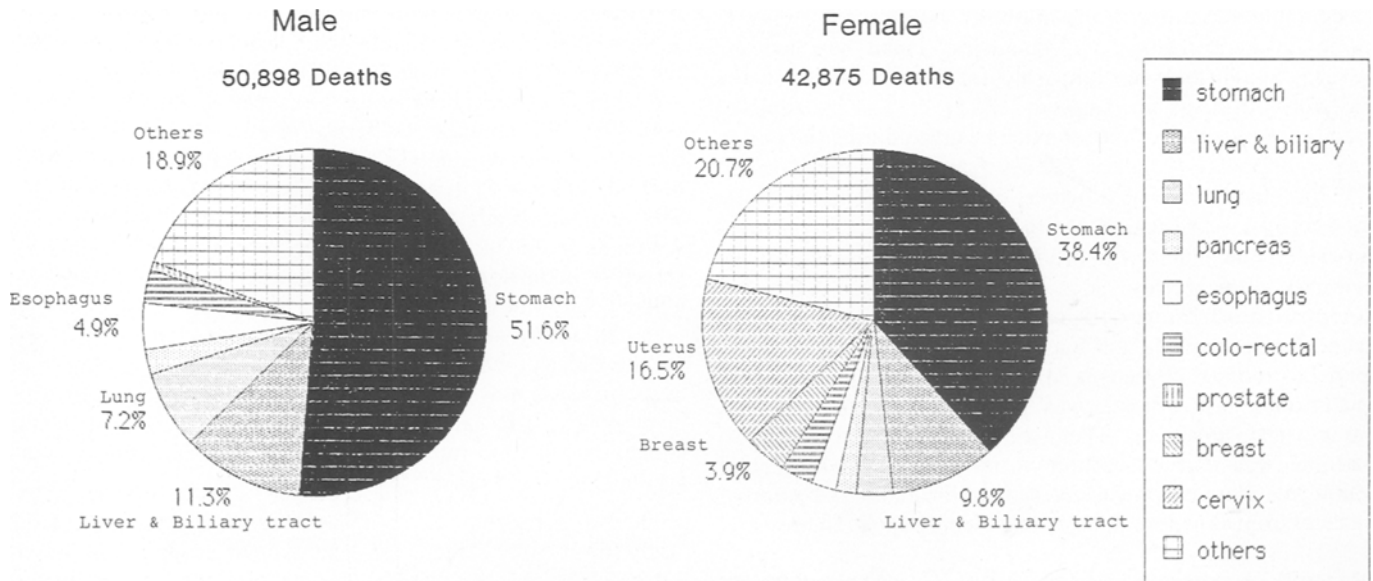


Fig. 2. Percentage numbers of deaths from gastric cancer compared with all cancer deaths in Japan, 1960.

performed in 98.1%. The proportion of cases of early gastric cancer, defined as the presence of cancer cells located within the mucosa or submucosa of the stomach, among detected cases was 47.1% (Table 2). Since persons over 40 years of age

were to be the subjects of the mass screening, the coverage rate was approximately 13% of the target population (3,200,000 persons) who were recommended or invited to attend the annual gastric screening by the Japanese government. Fig. 3

Table 1. Standard method of photofluorography in the gastric mass survey recommended by the Japanese Society of Gastroenterological Mass Survey (1984, [3]).

1. Examinee is asked to take effervescent granules before examination
2. Examiner is to make 7 exposures in the following positions, and to use a roll of film 70–100 mm in width, and 200–300 ml barium, 100 w/v%, as contrast medium.
3. Positions
 - A. Mucosal or double-contrast study in prone position
 - B. Filling method in prone position
 - C. Double-contrast radiograph in supine position
 - D. Double-contrast radiograph in supine and right anterior oblique position
 - E. Double-contrast radiograph in supine and left anterior oblique positions
 - F. Double-contrast radiograph in semiupright and left anterior oblique positions
 - G. Filling method in upright sagittal projection
 - H. Filling method in upright and right anterior oblique projections
4. Two types of combinations recommended:
 - A. A, B, C, D, E, G, H
 - B. A, B, C, D, E, F, G

Table 2. Results of mass screening for gastric cancer in Japan, 1985 (nationwide statistics).

Total screened	5,161,876
Gastric cancer cases detected	6,240; Gastric cancer cases ÷ total screened, 0.12%
% operated on	98.1
% with early cancer ^a	
In detected cases	47.1
In resected cases	59.6

^aEarly cancer is defined as the presence of cancer cells located within the mucosa or submucosa of the stomach.

shows the trend in the number of annual examinees. At present (in 1988), the goal of the Japanese government of a coverage rate of 30% has not yet been reached.

Statistics of Miyagi Prefecture

The following discussion will be based mainly on the data of the mass survey in the Miyagi Prefecture. In this prefecture, the first mass screening for gastric cancer by mobile x-ray was started in 1960. This prefecture is located in the northeastern part of the Honshu Island in Japan and the 1985 census showed a population of 2,167,900 (Fig. 4). The population-based cancer registration system was started in 1952, and we were, therefore, able to use the data for both morbidity and mortality. Approximately 87% of the initial examinees were selected and 13% underwent closer examination, including a full-size film x-ray examination and gastrofiberscopic examination or biopsy (Fig. 5).

The results of mass screening in the Miyagi Prefecture are summarized in Table 3. During the 27-year period from 1960 to 1986, a total of 2,493,535 persons underwent examination. Gastric cancer was detected in 4,688 cases (0.19%). In 1986, the total number of persons examined in the Miyagi Prefecture was 166,956, and the coverage rate was 18% among the target population at risk (approximately 930,000 persons). The time trend of the number of gastric cancer cases detected by the

mass survey, the average annual detection rates of early and advanced cancer among examinees, and the proportion of early stage cancers among these detected cases are shown in Table 4. Since 1970, the proportion of early cancers (early cancers ÷ gastric cancers) has been increasing year by year and, in recent years, approximately 60% of the detected cases consist of early stage cancer. In the Miyagi Prefecture, the detection rate of gastric cancer by mass survey has been almost constant (0.18–0.20%) over a period of 26 years; however, the detection rate of early cancer of the stomach has increased from 1960 to 1985. In contrast, the detection rate of advanced cancer has decreased.

Iwai et al. [5] reported on the false-negative rate in the mass survey, which was estimated in order to examine the diagnostic capability of photofluorography as a primary screening method in the survey [5]. In this report, the “false-negative” diagnosis was defined as failure to detect a pathologic change at the mass survey in patients who received a diagnosis of gastric cancer within 1 year after the mass survey. Information on patients with gastric cancer was obtained from the Miyagi Prefectural population-based cancer registry or the local physicians’ network. According to the report, the sensitivity of the screening test by the indirect x-ray method (photofluorography) was 82.4%; the specificity, 77.2%; and the positive predictive value, 1.8%.

Evaluation of Mass Survey for Gastric Cancer

The most important target organ of cancer control in Japan has been the stomach. Recently, cancer of the lung, breast, liver, and colorectum, organs associated with increased mortalities in a decade, have also received increasing attention. It is, therefore, essential to determine whether the mass screening program is really effective and whether it is appropriate to continue the program for secondary prevention of gastric cancer.

Evaluation methods include assessment of the efficacy and effectiveness regarding decreasing mortality from gastric cancer by epidemiological methods, a technologic assessment with examination of the accuracy of the screening method in the mass survey, cost-effectiveness/cost-benefit analysis, and evaluation of the medical system for comprehensive cancer control. Of these methods, the most important and basic method is considered to be the effectiveness evaluation.

Evaluations by Randomized Controlled Trial and Nonrandomized Controlled Trial

The mass screening for gastric cancer in Japan has not been studied by a randomized controlled trial (RCT) as in the HIP study [6] on mass screening for breast cancer, or in the Mayo Lung Project [7] on mass screening for lung cancer in the United States. Japanese physicians and epidemiologists have made various trial studies to find the second best evaluation methods or several alternative methods, e.g., nonexperimental, nonrandomized studies. Recently, the RCT, by the method of group randomization, has been conducted in the Miyagi Prefecture by our joint research members. In this article, several reports of the effectiveness evaluation are described.

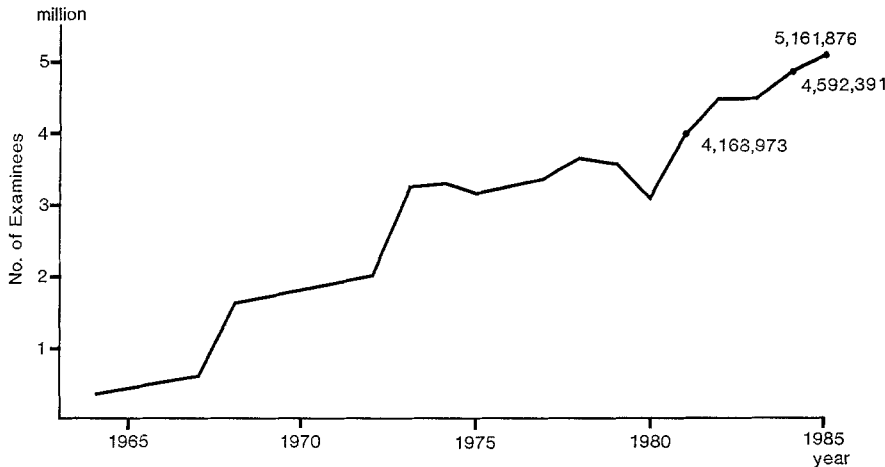


Fig. 3. Annual trend of the number of examinees in gastric mass screening (nationwide statistics, Japan [4]).

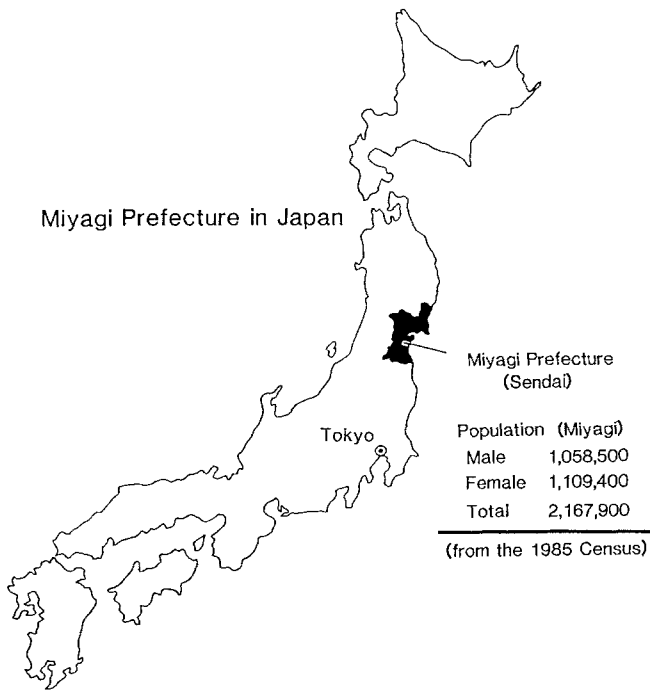


Fig. 4. Miyagi Prefecture in Japan (location and population, 1985).

Prognosis in Patients with Gastric Cancer Detected by the Mass Survey

According to a long-term follow-up study of patients with gastric cancer detected by mass survey by Sugawara et al. [8], the 5-year relative survival rate among the 352 patients who had undergone surgery during the period from 1960 to 1966 was 58.1%, and the 10-year relative survival rate was 52.1%. On the other hand, the 5-year relative survival rate among the 308 patients who had undergone surgery during the period from 1970 to 1972 was 71.8%, and the 10-year survival rate was 70.9%. The higher rates during the later period are considered to be due to the increasing proportion of cases of early cancer among gastric cancer cases detected by the mass screening during the later period (no. of early cancers ÷ no. of gastric cancers in Table 4).

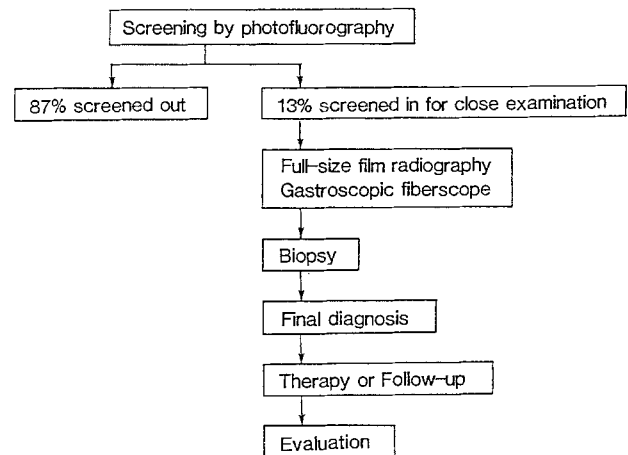


Fig. 5. Screening process in mass survey.

Table 3. Results of Mass Survey for gastric cancer (1960-1986, Miyagi Prefecture)

Diseases detected	No. of cases	% of total examinees
Stomach cancer	4,688	0.19
Benign polypoid tumor	7,514	0.30
Atypical epithelium	275	0.01
Submucosal tumor	740	0.03
Gastric ulcer and scar	45,853	1.84
Duodenal ulcer and scar	40,402	1.62
Coexisting ulcer	1,541	0.06
Total examinees	2,493,535	100.0%

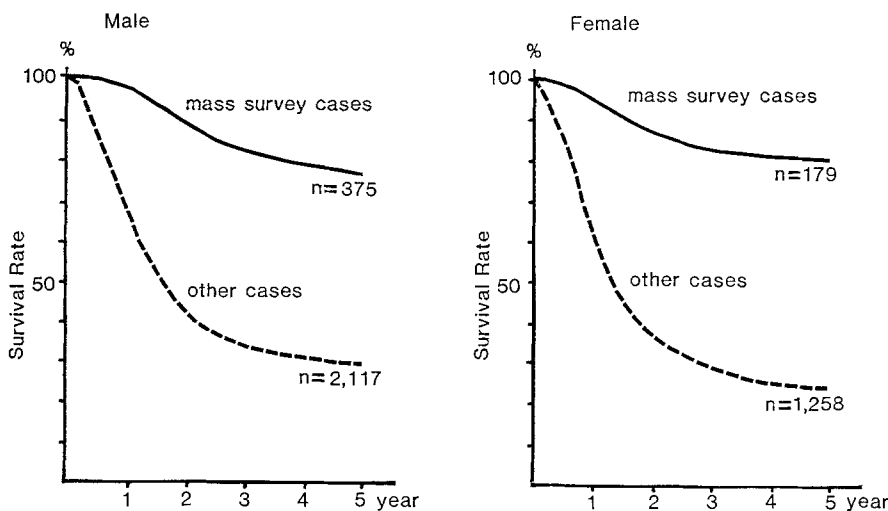
Furthermore, a comparison of the prognosis between patients with gastric cancer detected at mass screening and those detected at a general outpatient clinic in the same period showed that the mass survey was highly effective (Fig. 6) [9].

We should, however, consider various biases, especially length bias, self-selection bias, and lead time bias, when we compare the effectiveness of the mass screening with that of another project in a nonrandomized trial. According to the report by Masuda, one of our coinvestigators, the lead time bias was calculated to be approximately 9 months between the

Table 4. Detection rates of early and advanced cancer among examinees, and the proportion of early cancer cases among the cases of gastric cancer detected (1960–1986, Mass Survey Cases, Miyagi Prefecture).

Year	No. of examinees	No. of gastric cancers detected	No. of early cancers	No. of advanced cancers	Proportion (%) of early cancers ÷ gastric cancers
1960–1964	203,814	407 (0.19) ^a	56 (0.03)	351 (0.17)	13.8
1965–1969	370,274	663 (0.18)	235 (0.06)	428 (0.12)	35.4
1970–1974	396,907	717 (0.18)	364 (0.09)	353 (0.09)	50.8
1975–1979	528,615	1,016 (0.19)	561 (0.11)	455 (0.09)	55.2
1980–1984	671,031	1,213 (0.18)	745 (0.11)	468 (0.07)	61.4
1985–1986	322,894	672 (0.20)	417 (0.13)	255 (0.08)	62.1
Total	2,493,535	4,688	2,378	2,310	50.7

^aNumbers in parentheses signify average annual detection rate (%).

**Fig. 6.** Comparison of relative survival rates between gastric cancer cases detected by mass survey and those detected by other means (1973–1975, Miyagi Prefecture [9]).

patients with gastric cancer detected at mass screening and those at outpatient clinics [10]. Tsukuma et al. conducted a prospective study of “early” gastric cancer in an attempt to elucidate its natural history, and calculated that the median duration of early gastric cancer was 37 months [11].

Comparison of the Mortality from Gastric Cancer between Screened and Unscreened Groups

In order to investigate the epidemiologic effects of the mass survey, 4 towns in the Miyagi Prefecture were chosen as model areas and we made a long-term follow-up study on 7,008 persons aged 40 to 69 years (4,325 in the screened group and 2,683 in the unscreened group). This retrospective cohort study of the 18-year follow-up period from 1960 to 1977 showed that the mortality rate (61.9 per 100,000 person-years) from gastric cancer in the screened group in males was approximately half that (137.2 per 100,000 person-years) of the unscreened group ($p < 0.005$). A similar result was obtained in females. On the other hand, there was no difference in the incidence rate of gastric cancer between the 2 groups in either sex [9].

Discrepancy between Decreasing Trends of Incidence Rate and Death Rate from Cancer of the Stomach

We compared the decreasing trends in the mortality from gastric cancer and the incidence rate in the Miyagi Prefecture

from 1960 to 1980 (Table 5). The percentage decrease in the age-adjusted mortality rate was larger than that of the incidence rate. This discrepancy between the 2 decreasing trends was especially shown in the target age population of the mass gastric screening [12]. A similar result in Osaka, Japan has been reported by Oshima et al. [13].

Evaluation by Case-Control Study

Fukao et al. carried out a case-control study (218 advanced cancer cases and 218 controls) for evaluation of mass gastric screening [14]. They found that the relative risk of diagnosing an advanced cancer was 0.4–0.7, and that the risk was dependent on the screening interval. The relative risk was lowest (0.4) in the group undergoing screening every year ($p < 0.01$), 0.60 for a 2-year interval ($p < 0.05$), 0.73 for a 3-year interval ($p < 0.05$), and 0.71 for a 4-year interval (not significant), when relative risk was 1.0 in the group undergoing screening at a 5-year interval and longer. It seemed as if there was a dose-response relationship. Oshima et al. conducted another case-control study and reported that the risk of dying from cancer of the stomach among screened cases was 50% of that of unscreened cases, or less [15].

Conclusions and Discussion

From these investigations undertaken to evaluate the effectiveness of mass gastric screening, in spite of the fact that second-

Table 5. Changes in the age-adjusted^a incidence rate of gastric cancer and the age-adjusted death rate from this cancer in the Miyagi Prefecture (from 1960 to 1980; for patients 40 years of age and older; per 100,000).

Year	Male		Female	
	Incidence rate	Death rate	Incidence rate	Death rate
1960	95.4	71.6	47.2	37.5
1965	91.2	74.6	43.9	35.2
1970	85.4	63.5	40.6	33.2
1975	90.3	56.1	42.2	29.0
1980	80.6	48.7	37.4	23.9
Change ^b (%)	-15.5	-31.9	-20.8	-36.3

^aStandard population: Segi and Doll's World Population (UICC World population).

$${}^b\text{Change} = \frac{(\text{Rate in 1980} - \text{rate in 1960})}{\text{Rate in 1960}} \times 100 (\%)$$

best methods were used and they were not randomized trials, it is believed that this screening is effective in Japan in reducing the death rate from gastric cancer in the screened population and also in the target age population of the survey. Furthermore, it is undisputed by most Japanese physicians, researchers, and administrative policy makers that mass gastric screening contributed to reducing the mortality rate from cancer of the stomach in Japan during the period from 1960 to 1985. No firm conclusion has been drawn, however, as to what percentage contribution has been made by the mass gastric survey to the decreasing trend in the death rate from cancer of the stomach in Japan. Tominaga [16] regards the remarkable decreasing trends in the mortality from gastric cancer in the United States and other Western countries as a "natural experiment" or "passive primary prevention," since nationwide mass gastric screening has not been conducted in these countries. He considers at the same time that the decrease in the mortality from gastric cancer in Japan is largely due to a decrease in the incidence of cancer at this site, reflecting a recent change of dietary habits among the Japanese [16].

On the other hand, we Japanese could not wait for the long-term effects, e.g., effects of a "natural experiment" or "passive primary prevention," as in the United States, and wanted to speed up the decreasing trend in the mortality. Fortunately, a discrepancy between the decreasing trend in the incidence rate and that in the mortality rate has been especially evident during the last 10 years.

From the viewpoint of the international situation, Chamberlain et al. [17] presented a summary of the UICC workshop of the Project on Evaluation of Screening Programs for gastrointestinal cancer and the recommendations of each screening program. According to their report, mass screening programs for gastric cancer have not been recommended as a public health policy, except in Japan, and more randomized, controlled trials and the development of inexpensive, specific, low-technology tests have been considered desirable [17]. It is important to consider these points of view and to discuss the issues and problems of technology transfer to the countries concerned in the mass gastric screening approach.

It is concluded that mass gastric screening plays an important role in a campaign to save human lives from the threatening shadow of gastric cancer, and the contribution of the survey to the reduction of the gastric mortality rate in Japan is not small. Finally, in comprehensive cancer control, the importance of combined cancer control activity, using both primary preven-

tion (elimination of risk factors by changing dietary habits, and reduction of the incidence) and secondary prevention (early detection and reduction of mortality), should be emphasized.

Résumé

Le dépistage national pour le cancer gastrique est établi au Japon depuis 1960. Le nombre de patients examinés en 1985 était 5,161,876; 6,240 (0.12%) cas de cancer gastrique ont été détectés. La moitié environ de ces cas étaient des cancers à un stade précoce. Selon les chiffres de la Préfecture de Miyagi, la sensibilité du dépistage par la radioscopie mobile était de 82.4%, la spécificité de 77.2%, et la valeur prédictive positive de 1.78%. Plus récemment, la mortalité due au cancer gastrique était en régression au Japon. Bien des études ont été consacrées à l'efficacité du dépistage de masse dans l'abaissement du taux de mortalité du cancer. De ces résultats et d'après les analyses actuarielles de l'incidence et de la mortalité, les études rétrospectives comparant les groupes atteints de cancer et ceux qui restent indemnes, les études non expérimentales de groupes et autres, on a conclu que le dépistage de masse est efficace pour réduire la mortalité du cancer gastrique.

Resumen

El tamizaje masivo para cáncer gástrico a nivel nacional ha sido realizado en el Japón desde 1960. El número total de personas examinadas en 1985 ascendió a 5,161,876 y se detectaron 6,240 (0.12%) cánceres gástricos. Aproximadamente la mitad de estos casos fueron cánceres en estadio temprano. Según los estudios de tamizaje gástrico masivo en la Prefectura Miyagi, Japón, la sensibilidad de la prueba de tamizaje mediante el método indirecto de rayos x es 82.4%, y la especificidad, 77.2%. El valor de predicción positiva es 1.78%. Recientemente, la tasa de mortalidad del cáncer gástrico ha venido disminuyendo. Muchos estudios han sido realizados para investigar la relación entre la decreciente tendencia de la mortalidad por cáncer del estómago y la efectividad del tamizaje gástrico masivo. Los resultados de tales estudios, así como los análisis de incidencia cronológica, los estudios sobre casos controlados, y sobre cohortes no experimentales, etc., permiten afirmar que el tamizaje masivo para cáncer gástrico es efectivo en cuanto a la reducción de tasa de mortalidad del cáncer de estómago.

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