

Research Center for Cancer
Prevention and Screening

Preface

The Research Center for Cancer Prevention and Screening (RCCPS) was established in February 2004 to research effective cancer prevention and screening methods, and create a scientific basis for the efficient dissemination of these methods to the public. As of 2013, the organization consisted of the following: the Epidemiology and Prevention Group (Division of Prevention and Division of Epidemiology), the Screening Research Group (Division of Screening Assessment and Management and Division of Screening Technology and System Development), the Common Research Group (Division of Public Health Policy), and the Division of Cancer Screening which is responsible for carrying out cancer screenings. Our mission is to advance cancer prevention and screening research in order to provide correct information and the most appropriate methods for preventing cancer cases and fatalities to the greatest degree possible.

The Epidemiology and Prevention Group consists of the Division of Epidemiology which mainly conducts evidence-building that contributes to the investigation of cancer causes and the clarification of pathologic conditions and the Division of Prevention which conducts the development of evidence-based prevention methods; both Divisions mutually cooperates to fulfill the group's mission. In 2014, the Division of Epidemiology pursued continuous, long-term epidemiological studies of various sizes such as the Japan Public Health Center-based Prospective Study (JPHC Study) and the JPHC Study for the Next Generation (JPHC-NEXT), and published analyses of the accumulated data sets. In addition, utilizing the know-how gained from managing large-scale, long-term cohort studies, the Division completed the drafting of standardized protocols for new molecular epidemiology cohort studies as well as a highly-acclaimed project that will form the basis for unifying the existing cohort data. On the other hand, the Division of Prevention played a central role in systematically collecting research results especially at the national level and evaluating anti-cancer effects and carcinogens, ultimately recommending (updating) prevention guidelines for the Japanese public. In addition, based on the results of the cohort studies, the Division developed and released the "Cancer Risk Check," a series of diagnostic tools available online that determine cancer risks. The Group also participated in international projects that contribute to cancer prevention worldwide.

With the aim of reducing cancer mortality rates, the Screening Research Group (Division of Screening Assessment and Management) promotes cancer screening assessments, cancer screening implementation management, and screening as a countermeasure to cancer. While the Division has been conducting continuous researches like randomized controlled trials on cancer screening and investigations into the effectiveness of various cancer screenings, in this fiscal year, the Division also achieved the publication of updated gastric cancer screening guidelines. Using checklists, the Division conducted investigations into municipal public screenings, evaluations and training workshops for the standardization of cancer screening accuracy control, and the standardization of improvements to Quality Assurance (QA) and Quality Assurance (QA) accuracy control. The Division also updated its website contents for relevant government personnel. Moreover, as a measure for increasing cancer screening consultation rates and as an investigation into cancer screening provision systems, the Division conducted a comparative study of cancer screening provision systems in Asia and Oceania.

The Common Research Group (Division of Public Health Policy Research) conducts research for the dissemination of scientific evidence concerning the public health field (cancer prevention, screening, and survival). To establish a research infrastructure, the Division also conducts methodological researches on behavioral science, epidemiology, and statistics, supports and accumulates know-how from large-scale interventional studies, and teaches medical research methodologies. The Division supports municipalities, and develops and provides tools for further cancer screening and consultation awareness. Starting in this fiscal year, it implemented model programs in five prefectures that achieved definite results.

Furthermore, in this fiscal year, the Division released its children's cancer education comics as e-books to promote their use, and conducted two evaluation studies.

In addition, the Division also registered 4,100 patients (cumulative total) in a breast cancer cohort study. Regarding human resources development, it created 45 units of new content for distribution on an e-learning site for clinical research education and developed an iPhone application.

The Division of Screening Practice conducts cancer screenings with the primary goal of research based on the comprehensive consent of screening participants. In the fiscal year 2013, malignant tumors were detected in 37 people out of 489 new participants and 1,467 repeat participants (8 people among new participants and 29 people among repeat participants) who underwent RCCPS screenings. Detection rates were 1.64% and 1.98%, respectively. As part of its research, the Division is continuously conducting evaluations of pulmonary nodules in lung cancer CT screenings. In addition, it has introduced tomosynthesis mammography cameras and ultrasound automated breast volume scanners in breast cancer screenings and begun evaluating their clinical utility.

Research results are returned to the public through paper publications, conference presentations, lectures, information on Cancer Information Service by the Center for Cancer Control and Information Services, and other websites, leaflets and pamphlets, etc. To achieve our mission, all members of the RCCPS share a strong will to keep moving forward steadily and diligently.

Shoichiro Tsugane, M.D., D.M.Sc.
Director, Research Center for Cancer Prevention and Screening

Organization

President:

Tomomitsu Hotta

Director:

Shoichiro Tsugane

Epidemiology and Prevention Research Group

Chief: Shoichiro Tsugane

Division of Epidemiology

Chief: Motoki Iwasaki

Division of Prevention

Chief: Shizuka Sasazuki

Screening Assessment and Management Group

Chief: Hiroshi Saito

Division of Screening Assessment and Management

Chief: Hiroshi Saito

Division of Screening Technology and System Development

Chief: Hiroshi Saito

Research Infrastructure Group

Chief: Shoichiro Tsugane

Division of Public Health Policy Research

Chief: Seichiro Yamamoto

Deputy Director:

Yasuaki Arai

Division of Screening Practice

Chief: Yukio Muramatsu

Activities of the Divisions

DIVISION OF EPIDEMIOLOGY

Motoki Iwasaki, Norie Sawada, Taiki Yamaji, Izumi Mishiro, Sanjeev Budhathoki, Thomas Svensson, Kayo Ohashi, Yuri Ishii, Tomomi Mukai, Jun Umesawa, Hiroko Ogata, Yurie Shinozawa, Izumi Matsumoto

Introduction

Research is conducted aimed at constructing evidence connected to the development of cancer prevention by clarifying the causes of cancer in humans by using a study base of large-scale cohort study and others of local residents.

Research activities

1. Japan Public Health Center-based Prospective Study (JPHC study) / JPHC Study for the NEXT Generation (JPHC-NEXT)

Follow-up surveys and data analysis of the Japan Public Health Center-based Prospective Study (JPHC study) with 140,000 local residents as subjects have been conducted continuously since 1990. This year, we reported results such that we observed no evidence of a protective association between soy food or isoflavone intake and endometrial cancer risk; and that dietary fiber is inversely associated with advanced prostate cancer.

Structuring of the cohort for the JPHC Study for the NEXT Generation (JPHC-NEXT) is proceeding according to schedule with the recruitment of participants currently underway by obtaining questionnaire information from about 76,000 participants, and by obtaining biological samples and information from about 38,000 participants (Table).

2. The Program to Improve Preventive Medicine by Analysis of Cohort Data Linked to Medical Records

We clarified issues and problems for the purpose of promoting a large-scale molecular epidemiologic cohort study in Japan, and at the same time, we proposed an implementation system necessary for the realization and implementation of a consortium formation based on large scale molecular epidemiologic cohort studies. We also obtained a comprehensive evaluation of "S" in

post-project evaluation.

3. Molecular epidemiologic studies to investigate the cause of cancer through means such as omics data analysis

We identified new susceptibility loci in Asians through genome-wide association studies of breast cancer and colon cancer conducted through international collaborative research.

4. Research by the Research Center for Cancer Prevention and Screening (RCCPS) on examinees who have undergone cancer screening

Through a case-control study of colorectal adenoma in colonoscopy examinees, we reported an association between coffee consumption and reduced risk of adenoma and an association between the intake of processed meats and heterocyclic amine and an increased risk of adenoma in women.

5. Epidemiologic studies of immigrants of Japanese descent

Comparison of plasma levels of nutrient-related biomarkers among Japanese populations in Tokyo, Japan, São Paulo, Brazil, and Hawaii, USA, was conducted and we reported that the highest level of blood carotenoid concentration was found in the Japanese population in Sao Paulo.

Education

- Supervised the research of two research resident fellowships and one graduate student. Supervised the education of one medical student of short-term trainee.
- Dispatched Dr. Norie Sawada, Section Head, to Imperial College London in England to carry out The European Prospective Investigation into Cancer and Nutrition (EPIC) from September 2, 2014 to March 6, 2015.

Future Prospects

While focusing on the cohort structure of the JPHC Study for the Next Generation (JPHC-NEXT) that becomes the study base, we hope to contribute to the development of cancer prevention

through the analysis of information and samples of existing epidemiologic studies by identifying new risk factors and the continued evaluation of risks in Japanese people.

Table 1. Progress of the JPHC for the NEXT generation (JPHC-NEXT)

Area	Total number of questionnaire	Total number of questionnaire and biospecimen	Status of data collection
Akita, Yokote	26,752	11,077	Ongoing
Nagano, Saku	31,395	13,333	Completed
Ibaraki, Chikusei	9,172	7,124	Ongoing
Kochi, Konan	3,840	1,594	Completed
Kochi, Aki	1,799	1,799	Ongoing
Nagasaki (2014~)	1,031	1,031	Ongoing
Ehime, Ohzu (2014~)	2,382	2,382	Ongoing
Total	76,317	38,340	

List of papers published in 2014

Journal

- Kuchiba A, Iwasaki M, Ono H, Kasuga Y, Yokoyama S, Onuma H, Nishimura H, Kusama R, Tsugane S, Yoshida T. Global methylation levels in peripheral blood leukocyte DNA by LUMA and breast cancer: a case-control study in Japanese women. *Br J Cancer*, 110:2765-2771, 2014
- Itoh H, Iwasaki M, Kasuga Y, Yokoyama S, Onuma H, Nishimura H, Kusama R, Yoshida T, Yokoyama K, Tsugane S. Association between serum organochlorines and global methylation level of leukocyte DNA among Japanese women: a cross-sectional study. *Sci Total Environ*, 490:603-609, 2014
- Kurotani K, Nanri A, Goto A, Mizoue T, Noda M, Oba S, Sawada N, Tsugane S. Cholesterol and egg intakes and the risk of type 2 diabetes: the Japan Public Health Center-based Prospective Study. *Br J Nutr*, 112:1636-1643, 2014
- Miki Y, Inoue M, Ikeda A, Sawada N, Nakaya T, Shimazu T, Iwasaki M, Yamaji T, Sasazuki S, Shibuya K, Tsugane S. Neighborhood deprivation and risk of cancer incidence, mortality and survival: results from a population-based cohort study in Japan. *PLoS One*, 9:e106729, 2014
- Wang H, Burnett T, Kono S, Haiman CA, Iwasaki M, Wilkens LR, Loo LWM, Van Den Berg D, Kolonel LN, Henderson BE, Keku TO, Sandler RS, Signorello LB, Blot WJ, Newcomb PA, Pande M, Amos CI, West DW, Bezieau S, Berndt SI, Zanke BW, Hsu L, Lindor NM, Haile RW, Hopper JL, Jenkins MA, Gallinger S, Casey G, Stenzel SL, Schumacher FR, Peters U, Gruber SB, Tsugane S, Stram DO, Le Marchand L. Trans-ethnic genome-wide association study of colorectal cancer identifies a new susceptibility locus in VT11A. *Nat Commun*, 5:4613, 2014
- Tsugane S, Sawada N. The JPHC study: design and some findings on the typical Japanese diet. *Jpn J Clin Oncol*, 44:777-782, 2014
- Cai Q, Zhang B, Sung H, Low S-K, Kweon S-S, Lu W, Shi J, Long J, Wen W, Choi J-Y, Noh D-Y, Shen C-Y, Matsuo K, Teo S-H, Kim MK, Khoo US, Iwasaki M, Hartman M, Takahashi A, Ashikawa K, Matsuda K, Shin M-H, Park MH, Zheng Y, Xiang Y-B, Ji B-T, Park SK, Wu P-E, Hsiung C-N, Ito H, Kasuga Y, Kang P, Mariapun S, Ahn SH, Kang HS, Chan KYK, Man EPS, Iwata H, Tsugane S, Miao H, Liao J, Nakamura Y, Kubo M, Delahanty RJ, Zhang Y, Li B, Li C, Gao Y-T, Shu X-O, Kang D, Zheng W. Genome-wide association analysis in East Asians identifies breast cancer susceptibility loci at 1q32.1, 5q14.3 and 15q26.1. *Nat Genet*, 46:886-890, 2014
- Honjo K, Iso H, Inoue M, Sawada N, Tsugane S. Socioeconomic status inconsistency and risk of stroke among Japanese middle-aged women. *Stroke*, 45:2592-2598, 2014
- Yamauchi T, Inagaki M, Yonemoto N, Iwasaki M, Inoue M, Akechi T, Iso H, Tsugane S. Death by suicide and other externally caused injuries after stroke in Japan (1990-2010): the Japan Public Health Center-based prospective study. *Psychosom Med*, 76:452-459, 2014
- Nakamura K, Kitamura K, Inoue M, Sawada N, Tsugane S. Physical activity and 10-year incidence of self-reported vertebral fractures in Japanese women: the Japan Public Health Center-based Prospective Study. *Osteoporos Int*, 25:2565-2571, 2014
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13. Pandey JP, Kistner-Griffin E, Namboodiri AM, Iwasaki M, Kasuga Y, Hamada GS, Tsugane S. Higher levels of antibodies to the tumour-associated antigen cyclin B1 in cancer-free individuals than in patients with breast cancer. *Clin Exp Immunol*, 178:75-78, 2014
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19. Wada K, Nagata C, Tamakoshi A, Matsuo K, Oze I, Wakai K, Tsuji I, Sugawara Y, Mizoue T, Tanaka K, Iwasaki M, Inoue M, Tsugane S, Sasazuki S. Body mass index and breast cancer risk in Japan: a pooled analysis of eight population-based cohort studies. *Ann Oncol*, 25:519-524, 2014
20. Abe SK, Inoue M, Sawada N, Iwasaki M, Ishihara J, Sasazuki S, Shimazu T, Yamaji T, Shibuya K, Tsugane S. Rice, bread, noodle and cereal intake and colorectal cancer in Japanese men and women: the Japan Public Health Center-based prospective Study (JPHC Study). *Br J Cancer*, 110:1316-1321, 2014
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26. Hidaka A, Sasazuki S, Goto A, Sawada N, Shimazu T, Yamaji T, Iwasaki M, Inoue M, Noda M, Tajiri H, Tsugane S; JPHC Study Group. Plasma insulin, C-peptide and blood glucose and the risk of gastric cancer: The Japan Public Health Center-based prospective study. *Int J Cancer*, 136:1402-1410, 2014

DIVISION OF PREVENTION

Shizuka Sasazuki, Taichi Shimazu, Michihiro Mutoh, Charvat Hadrien, Akihisa Hidaka, Yoshitaka Tsubono, Masayuki Tatemichi, Junko Ishihara, Minatsu Kobayashi, Ribeka Takachi, Azusa Hara, Manami Inoue, Yingyan Gong, Eiko Saito, Issei Ezawa, Ruri Nakanishi, Rikako Ishigamori, Masami Sakano, Ayaka Miura, Ayako Toyama, Yasuko Iba, Michiko Okajima, Yuko Kato

Introduction

The Epidemiology and Prevention Division has conducted research activities as one division until May, 2013 and was then recognized as two divisions. Prevention Division focuses on prevention researches to investigate and develop prevention methods (lifestyle, chemoprevention, molecular marker etc.), risk prediction, risk stratification models, and evidence-based cancer prevention guideline.

Research activities

Evaluation of cancer prevention strategies in Japan and cancer prevention guideline

To develop an evidence-based cancer prevention strategy in Japan, a systematic review of epidemiological research was conducted. The strength of evidence was evaluated in a manner similar to that used in the WHO/FAO Expert Consultation Report, in which evidence was classified as 'convincing', 'probable', 'possible' and 'insufficient'. Through this method, diabetes was evaluated to have a "probable" effect on increasing the risk of liver cancer. Red meat was evaluated to have a "probable" effect on increasing the risk of colorectal cancer. A decrease in risk for breast cancer with consumption of soy products was "possible."

An evidence based, currently recommended cancer prevention guideline, 'Cancer prevention guideline for Japanese' was updated to meet the latest evaluation of evidence.

Pooled analysis of Japanese Cohort Studies and Asia Cohort Consortium

To obtain summary estimates of the relationship between factors and cancer, pooled analysis of Japanese cohort studies were conducted.

As of 2014 November, 10 cohort studies namely, the Japan Public Health Center-based Prospective Study, Cohort I (JPHC-I) and Cohort II (JPHC-II); the Japan Collaborative Cohort Study; the Miyagi Cohort Study; the Three-Prefecture Miyagi; the Ohsaki National Health Insurance Cohort Study; the Three-Prefecture Aichi; the Takayama Study; the Three-Prefecture Osaka; and the Life Span Study (being processed) were participated in this pooling project. Based on pooled analysis of eight cohort studies, an increased risk of postmenopausal breast cancer among women with higher BMIs was confirmed among Japanese. In addition, we reported a significant positive association between BMI and premenopausal breast cancer, suggesting that body mass in Asian women might have different effects on breast cancer compared with Western women. Based on another pooled analysis of four cohort studies, we reported that vegetable intake reduce gastric cancer risk, especially the risk of distal gastric cancer among men.

The Asia Cohort Consortium (ACC) is a collaborative effort seeking to understand the relationship between genetics, environmental exposures, and the etiology of disease through the establishment of a cohort of at least one million healthy people around the Asian countries. The ACC Coordinating Center has been established at the Fred Hutchinson Cancer Research Center and moved to the Prevention Division in 2014. The data analysis system on site and via remote access is now under construction. Burden of total and cause-specific mortality related to tobacco smoking among adults aged 45+ years in Asia was estimated. Among men, approximately 11.4%, 30.5%, and 19.8% of deaths due to cardiovascular diseases, cancer, and respiratory diseases, respectively, were shown to be attributable to tobacco smoking.

Development of prevention measures based on interventional research

We reported that aspirin suppresses the occurrence of new adenomas in patients with a history of multiple colorectal adenomas through a double-blind, randomized clinical trial. Now, we are trying to evaluate whether interval colonoscopy with polypectomy allows a safe strategy different from surgery to prevent development of colorectal cancer in familial adenomatous polyposis patients who decline surgery. Another clinical research aimed to develop colorectal cancer chemopreventive drugs is in progress.

Population-based Prospective Study (the JPHC study and the JPHC-NEXT Study) (primarily the development of preventive measures such as risk prediction; searching for chemoprevention candidates and the establishment of an integrated methodology for data harmonization)

Based on a nested case-control study of the JPHC Study, it was shown that plasma insulin is positively associated with two-fold increased risk of gastric cancer. In men, C-peptide and higher HOMA-IR were also positively associated with a significant risk, which suggested that Japanese population with higher insulin and C-peptide levels derived from insulin resistance have an elevated risk of gastric cancer. Based on another nested case-control study of the JPHC Study, considering gene-environmental interaction, ADH1C G allele carriers who drink ≥ 150 g/week of ethanol had a 2.5-fold increased risk of gastric cancer relative to AA genotype carriers who drink 0 to < 150 g/week (P for interaction = 0.02). ALDH2 A allele carriers who drink ≥ 150 g/week also had an increased risk relative to GG genotype carriers who drink 0 to < 150 g/week (P for interaction = 0.08).

In addition, we started research on collecting stomach cancer tissue in order to consider subtypes of tumors by molecular biomarkers which can be derived through mutational analysis of oncogenes or tumor suppressor genes in tumor tissues and the analysis of epigenetic abnormalities such as CpG island methylator phenotype (CIMP).

A standard protocol for a genomic epidemiological cohort study in Japan is projected to be developed based on the JPHC-NEXT protocol. The method for calibration of data derived from different questionnaires and the results of analysis were reported.

Education

Instructed data analysis, scientific paper-writing, and conference presentation for a research resident and led to submission of two scientific papers (results are mentioned in the earlier section: the JPHC Study). The presentation of one of his works was registered as 'Selected Paper Workshop' in the 25th Annual Scientific Meeting of the Japan Epidemiological Association. Provided data analysis guidance to a Central Hospital resident.

Future prospects

We will focus on research for the development of effective cancer prevention strategies. In addition to current established evidence, new perspectives such as biomarkers from blood and tumor tissues will be incorporated. This approach may lead to more accurate cancer prevention strategy by risk stratification. Also, we continuously expand human resource development in the relating field.

List of papers published in 2014

Journal

1. Hori M, Takahashi M, Hiraoka N, Yamaji T, Mutoh M, Ishigamori R, Furuta K, Okusaka T, Shimada K, Kosuge T, Kanai Y, Nakagama H. Association of pancreatic fatty infiltration with pancreatic ductal adenocarcinoma. *Clin Transl Gastroenterol*, 5:e53, 2014
2. Kondo S, Shimazu T, Morizane C, Hosoi H, Okusaka T, Ueno H. A retrospective analysis of factors associated with selection of end-of-life care and actual place of death for patients with cancer. *BMJ Open*, 4:e004352, 2014
3. Miki Y, Inoue M, Ikeda A, Sawada N, Nakaya T, Shimazu T, Iwasaki M, Yamaji T, Sasazuki S, Shibuya K, Tsugane S. Neighborhood deprivation and risk of cancer incidence, mortality and survival: results from a population-based cohort study in Japan. *PLoS One*, 9:e106729, 2014
4. Honjo K, Iso H, Inoue M, Sawada N, Tsugane S. Socioeconomic status inconsistency and risk of stroke among Japanese middle-aged women. *Stroke*, 45:2592-2598, 2014
5. Yamauchi T, Inagaki M, Yonemoto N, Iwasaki M, Inoue M, Akechi T, Iso H, Tsugane S. Death by suicide and other externally caused injuries after stroke in Japan (1990-2010): the Japan Public Health Center-based prospective study. *Psychosom Med*, 76:452-459, 2014
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8. Iwasaki M, Mukai T, Takachi R, Ishihara J, Totsuka Y, Tsugane S. Validity of a self-administered food frequency questionnaire in the estimation of heterocyclic aromatic amines. *Cancer Causes Control*, 25:1015-1028, 2014
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10. Eshak ES, Iso H, Yamagishi K, Kokubo Y, Saito I, Yatsuya H, Sawada N, Inoue M, Tsugane S. Rice consumption is not associated with risk of cardiovascular disease morbidity or mortality in Japanese men and women: a large population-based, prospective cohort study. *Am J Clin Nutr*, 100:199-207, 2014
11. Eshak ES, Iso H, Yamagishi K, Kokubo Y, Saito I, Yatsuya H, Sawada N, Inoue M, Tsugane S. Modification of the excess risk of coronary heart disease due to smoking by seafood/fish intake. *Am J Epidemiol*, 179:1173-1181, 2014
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16. Takachi R, Ishihara J, Iwasaki M, Ishii Y, Tsugane S. Self-reported taste preference can be a proxy for daily sodium intake in middle-aged Japanese adults. *J Acad Nutr Diet*, 114:781-787, 2014
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DIVISION OF SCREENING ASSESSMENT AND MANAGEMENT

Hiroshi Saito, Chisato Hamashima, Kumiko Saika, Chikako Yamaki, Ryoko Machii, Koichi Nagata, Ayako Aoki, Yoshiki Ishikawa, Sayuri Amanuma, Junko Asai, Kanoko Matsushima, Kazuko Matsuda, Noriaki Takahashi, Akiko Totake, Keiko Kawarabata

Introduction

The Screening Assessment and Management Division has conducted studies on the assessment and management of screening programs, particularly nationwide programs, and on other issues relevant to cancer screening.

In addition, the most important mission of the Research Center for Cancer Prevention and Screening in terms of screening is the central activity of assessing and managing cancer screening at the national level, which is closely related to the pillars in the Individual Targets for Cancer Screening in the Basic Cancer Control Plan issued in 2007 and revised in 2012. Thus, the Screening Assessment and Management Division has developed and updated screening guidelines (Cancer Screening Assessment) and constructed quality assurance systems for the screening programs (Cancer Screening Management).

Routine activities

- Development of cancer screening guidelines
Guidelines on screening for gastric cancer have been developed and will be published in 2015.
- Quality Assurance (QA) in cancer screening at municipalities
The Division collected the information related to implementation of cancer screening and its management situation using Checklists (CLs) as a structure indicator in QA at municipalities. The Division also evaluated process indicators such as rate of work-up, and ranked those indicators in all cities by prefecture in order of goodness so that each city compares its indicator with those of other cities. CLs score in 2014 collected this year were improved by 5-8% for 5 cancer screening programs as compared to those in 2009. An additional survey

on prevalence of a call-recall system, which is essential for high screening participation rate, revealed only less than 5% of municipalities have been fully equipped with the system. The data is used for interim evaluation of progress status of the Basic Cancer Control Plan.

The Division set up the website which allows support toward municipalities such as provision of their QA data archives and information relevant to cancer screening. In this year, the manual of QA for staffs at each municipality was placed on the website. CLs data were collected from municipalities and evaluation results were fed back on the website. 1414 municipalities (81%) utilized the website by registering as members of the site.

- Workshop on cancer screening management

The Division held one-day educational workshops for the members of prefectural committees of cancer screening management, aiming at activating QA activities in each of 47 prefectures. The themes this year were stomach and colorectum. The main contents of the workshops were the methods of quality assurance of the screening programs within each prefecture. Other basic issues required to conduct organized cancer screening programs such as those issues of screening assessment were also included in the contents. As of this year, the Division added a similar workshop targeting the new members of cancer control section at each prefectural government.

There were 63 participants in the workshops from 34 prefectures, who consisted of administrative officers (51%) and members of the committee (49%). This activity was performed as the project of the Center for Cancer Control and Information Services and will be continued on an annual basis.

According to the survey on the activity of the prefectural committees, 36 to 38 prefectures

held the meeting to discuss on cancer screening management and 25 to 27 (9 to 22 in the previous year) released the evaluation results of municipalities using CLs for each of 5 cancers. These figures have been increasing after starting the workshop suggesting the effect of the previously held workshop on the activity of the committees.

Research activities

- A randomized controlled trial (RCT) of colonoscopic screening and other RCTs

A randomized controlled trial evaluating one-time colonoscopic screening for colorectal cancer was started in 2009. The division has been responsible for designing and managing the study as the head office of the study. The cumulative number of subjects who gave informed consent,

and who were thus enrolled in the study, was 7,680 at December 2014, corresponding to 77% of the planned number. Data monitoring results showed randomization has been performed successfully. No serious adverse effect was reported on screening colonoscopy. The Division has participated also in other RCTs (breast cancer and lung cancer screening) as a member of headquarters of the research and supported those studies.

- Evaluation and accuracy studies on gastric cancer screening

A community-based, cohort study was conducted to evaluate the effectiveness of endoscopic screening in Niigata city. The 57% mortality reduction from gastric cancer was suggested by endoscopic screening for gastric cancer.

List of papers published in 2014

Journal

1. Ishida T, Suzuki A, Kawai M, Narikawa Y, Saito H, Yamamoto S, Tohno E, Sobue T, Fukuda M, Ohuchi N. A randomized controlled trial to verify the efficacy of the use of ultrasonography in breast cancer screening aged 40-49 (J-START): 76 196 women registered. *Jpn J Clin Oncol*, 44:134-140, 2014
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DIVISION OF PUBLIC HEALTH POLICY RESEARCH

Seiichiro Yamamoto, Yuri Mizota, Michiyo Tada, Takako Osato, Hiromi Koitabashi, Yoko Takahashi, Kumiko Toshima, Rika Nakamura

Introduction

The Division of Public Health Policy Research was established in June 2013. The Division investigates the methods of distribution and dissemination of scientific evidence concerning cancer prevention, screening, and survivorship. The aim of the research is to fill the gap between the scientific evidence and the behavior of people for cancer prevention and screening by supporting local government and directly approaching to the public. In addition, because of the lack of evidence, we try to establish scientific evidence for cancer survivorship.

As for the activity for establishing research infrastructure, we conduct methodological research and education concerning behavior science, epidemiology and biostatistics and support large scale interventional studies.

Research concerning promotion of cancer prevention and screening using social marketing method

The examples of the achievement of this year for promoting cancer screening participation are as follows: development of materials for client reminder such as the leaflets for stomach and lung cancer, the post cards for colorectal, breast, and cervical cancer, and the envelopes (Figure 1), support of the local municipalities by conducting workshops 9 times and disseminate information from the website. In addition, we evaluated the participation rates of cancer screening for 5 model municipalities which we supported in 2013 and obtained increased participation rates for almost all the cities and towns. To promote cancer education for kids, we developed an e-book version of “Gan no Himitsu (Secret of Cancer)” which we had developed last year as a comic style education material. It is available from the website (<http://kids.gakken.co.jp/index.html>) and also by

downloading its application for smartphone for free of charge. We promoted the book strategically using newspaper, radio, magazine, and website. We are also planning to conduct research for the promotion of participation for the HCV testing in collaboration with local municipalities in order to prevent liver cancer.

Research for cancer survivorship

A large cohort is being established for breast cancer patients, to investigate the effect of lifestyle and psychosocial factors on their QOL and prognosis. The cohort consists of several sub-cohorts including collaborative cohorts of clinical trials, a cohort in the National Cancer Center, and a collaborative cohort with Setouchi cancer registry. As of February 2015, we recruited more than 700 breast cancer patients this year and 4,100 patients in total. The cohort became one of the largest patient cohorts in the world. We are planning to extend the cohorts for other cancer such as colon and rectum.

Education of staffs involved in clinical research

We develop an e-learning website for the education of staffs involved in clinical research such as researchers, data managers, clinical research coordinators, and members in institutional review boards. ICRweb (<http://icrweb.jp>) provides more than 120 contents. As of February 2015, more than 8,000 new users were registered this year and more than 35,000 users were registered in total. We conducted 11 seminars and provided 45 new contents from the website. In order to improve convenience of the users, we developed iPhone applications as well.



Figure 1. Leaflets for client reminder for stomach and lung cancer screening



Figure 2. Postcards for client reminder for breast, colorectal, and cervical cancer screening



Figure 3. Envelopes for client reminder for lung cancer screening

List of papers published in 2014

Journal

1. Ishida T, Suzuki A, Kawai M, Narikawa Y, Saito H, Yamamoto S, Tohno E, Sobue T, Fukuda M, Ohuchi N. A randomized controlled trial to verify the efficacy of the use of ultrasonography in breast cancer screening aged 40-49 (J-START): 76 196 women registered. *Jpn J Clin Oncol*, 44:134-140, 2014

DIVISION OF SCREENING PRACTICE

Yukio Muramatsu, Ryutaro Kakinuma*, Takashi Terauchi*, Gen Iinuma*, Nachiko Uchiyama*, Yasuo Kakugawa*, Minoru Machida*, Seiko Kuroki*, Yosuke Otake*, Takehiro Izumo*, Minoru Matsumoto, Tomoyasu Kato*, Mitsuya Ishikawa*, Syunichi Ikeda*, Yasuaki Arai* (*NCCH)

Introduction

The Division of Screening Practice moved in the first floor of the Sinryoto in April, 2014. But, CT, PET, gynecological examination, barium enema and endoscopy were carried out at the National Cancer Center Hospital except for ultrasonography, mammography and blood and urinary sampling. The Division is in charge of multiphasic cancer screening using several imaging modalities to develop new cancer screening systems and to evaluate new screening tests. All medical images are digitalized and all imaging diagnosis can be made from CRT monitors.

Routine activities

1. Course of cancer screening

Basic plan for males consists of screening for cancer of the lung, esophagus, stomach, colon, liver, gall bladder, pancreas, kidney, and prostate. In the basic plan for females, the screening for cancer of the breast, uterus, and ovary are added to the plan for males, excluding the prostate. In addition, PET is provided as an option. Other than multi-phasic programs, a screening program has been prepared for lung and female genital cancers, including cancer of the uterus and ovary, breast cancer and gastrointestinal cancer. Blood samples are also obtained for biochemistry and tumor markers such as CA19-9, CEA, CA125, PSA, and genetic analysis.

2. Eligibility criteria for participants

The cancer screening program at the Research Center for Cancer Prevention and Screening before 2013 has been planned for applicants 40 years or older who give written informed consent for the screening, including blood samples for genetic analysis, and who take the questionnaire survey concerning lifestyles. These study protocols have been approved by the Institutional Review Board

(IRB). Applicants who have been diagnosed as having cancer, and/or have a history of cancer treatment, such as surgery or endoscopic mucosal resection or chemotherapy within the previous one year, are excluded. On the other hand, there is not condition setting to receive cancer screening programs about the new participants after May, 2014. But an inclusion agreement about the study is optionally demanded.

3. Cancer screening methods

In the multiphasic cancer screening programs, CT for lung cancer, abdominal US for cancer of the liver, gall bladder, pancreas, and kidney, gynecological examinations with Pap-smear and HPV test for uterus cancer, and MMG and US for breast cancer are performed on the first day. On the following day, gastroscopy for cancer of the esophagus and stomach, and total colonoscopy for cancer of the colon and rectum are conducted. If a barium enema is chosen, the examination is carried out on the third day. Moreover, from the beginning of December 2010, CT-colonography (CTC) has been provided as an optional method for cancer screening. FDG-PET is offered on the first day as an option, if the participants wish to undergo the examination. In addition, the one day cancer screening programs with the combination of gastrointestinal endoscopic examinations and other methods except PET or the combination of PET and other methods except for total colonoscopy were newly started in May, 2014.

4. Results of cancer screening

Recent accurate data on cancers have not been obtained due to lack of adequately long follow-up data from our 2014 patients. We have therefore presented confirmed data from the previous year. 1,956 participants underwent multi-phasic programs (new, 489; repeater, 1467) in the research data. Malignant tumors were detected in 8 out of

489 new participants and in 29 out of 1467 repeaters who underwent multi-phasic clinical programs in 2013 (Tables 1 and 2). Detection rates were 1.64% and 1.98%, respectively.

Research activities

1. The first breast tomosynthesis system in Japan was installed at the RCCPS in September 2009. Since October 2010, a breast tomosynthesis study has started in cooperation with breast surgeons at the NCC hospital. Regarding the study, NCC IRB approval was granted in December 2008. From May, 2014 in breast cancer screening, the examination that combined tomosynthesis with automated breast volume scanner (ABVS) began. The sensitivity and specificity of tomosynthesis in comparison with ABVS and pathological findings are in the process of evaluation.

2. The clinical usefulness of CT-colonography has been assessed.
3. In order to establish guidelines for the management of pulmonary nodules detected with low-dose chest CT screening, patients with pulmonary nodules between 5 mm and 10 mm in size are being examined in the follow-up clinic.
4. The follow-up system of pulmonary solitary solid nodules for evaluation of growth is being developed with CANON.

Future prospects

Based on cancer screening data such as an examination result, medical institution findings, follow-up findings, the questionnaire survey concerning lifestyles for 10 years, the effective evaluation of chest CT, endoscope and PET-CT are enabled.

Table 1. Cancerous detection rate in new participants (2013.4.1-2014.3.31)

	No. of cancerous cases	No. of new participants	Detection rate (%)
prostate	2	313	0.64
colo-rectum	2	489	0.41
esophagus	1	489	0.20
stomach	1	489	0.20
lung	1	489	0.20
pharynx	1	489	0.20
Total	8	489	1.64

Table 2. Cancerous detection rate in repeat participants (2013.4.1-2014.3.31)

	No. of cancerous cases	No. of new participants	Detection rate (%)
breast	7	496	1.41
prostate	6	971	0.62
stomach	7	1467	0.48
colo-rectum	5	1467	0.34
liver	1	1467	0.07
kidney	1	1467	0.07
urinary bladder	1	1467	0.07
others	1	1467	0.07

List of papers published in 2014

Journal

1. Sakamoto T, Sato C, Makazu M, Sekiguchi M, Mori G, Yamada M, Kinjo Y, Turuki E, Abe S, Otake Y, Nakajima T, Matsuda T, Saito Y. Short-term outcomes of colorectal endoscopic submucosal dissection performed by trainees. *Digestion*, 89:37-42, 2014
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9. Yoneyama T, Tateishi U, Terauchi T, Inoue T. Correlation of metabolic tumor volume and ¹¹C-choline uptake with the pathology of prostate cancer: evaluation by use of simultaneously recorded MR and PET images. *Jpn J Radiol*, 32:155-163, 2014
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Book

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2. Uchiyama N, Machida M, Tani H, Kikuchi M, Arai Y, Otsuka K, Fieselmann A, Jerebko A, Mertelmeier T. Clinical Efficacy of Novel Image Processing Techniques in the Framework of Filtered Back Projection (FBP) with Digital Breast Tomosynthesis (DBT). In: Fujita H, Hara T, Muramatsu C (eds), *Breast Imaging: 12th International Workshop, IWDM 2014*, Gifu City, Japan, June 29 - July 2, 2014. Proceedings, Switzerland, Springer International Publishing, pp 320-326, 2014
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