

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 2015, the organization consisted of the following: the Epidemiology and Prevention Group (Division of Epidemiology and Division of Prevention), 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 Research), and the Division of Screening Practice, 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 cooperate to fulfill the group's mission. In 2015, 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 and biological samples. 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 by 5 Healthy Lifestyles," a series of diagnostic tools available online that determine cancer risks. The Division also has been coordinating the Japanese and Asian Cohort Consortium.

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 research like randomized controlled trials on cancer screening and investigations into the effectiveness of various cancer screenings, the Division also started the publication of updated cervical 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. The Division also updated its website contents for relevant government personnel.

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 survivorship). To establish a research infrastructure, the Division also conducts methodological research 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 (16 prefectures and 96 local governments), and develops and provides tools for further cancer screening and consultation awareness. Furthermore, in this fiscal year, the Division released its children's cancer education comics as e-books to promote their use, and conducted intervention trials to evaluate their effectiveness. In addition, the Division also registered 4,900 patients (cumulative total) in a breast cancer patient cohort study.

The Division of Screening Practice conducts cancer screenings with the primary goal of research based on the comprehensive consent of screening participants. In 2015, the total number of screening participants were 3,140 (40% were new and 75% were comprehensive screening participants). As part of its research, the Division has published several scientific papers in evaluating screening modalities such as CT screenings for lung cancer and PET for colorectal cancer screening.

Research results are returned to the public through paper publications, information on the Cancer Information Service by the Center for Cancer Control and Information Services, and other websites, leaflets and pamphlets, and so forth. 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

Prevention Research

Chief: Shoichiro Tsugane

Division of Epidemiology

Chief: Motoki Iwasaki

Division of Prevention

Chief: Shizuka Sasazuki

Screening Research

Chief: Hiroshi Saito

Division of Screening Assessment and Management

Chief: Hiroshi Saito

Division of Screening Technology and System Development

Chief: Hiroshi Saito

Common Research

Chief: Shoichiro Tsugane

Division of Public Health Policy Research

Chief: Seiichiro Yamamoto

Deputy Director

Chief: Yasuaki Arai

Division of Screening Practice

Chief: Takahisa Matsuda

Activities of the Divisions

DIVISION OF EPIDEMIOLOGY

Motoki Iwasaki, Norie Sawada, Taiki Yamaji, Izumi Mishiro, Akihisa Hidaka, Sanjeev Budhathoki, Masanori Goto, Kayo Ohashi, Jun Umesawa, Ari Nakamura, Tsuyuka Ohtsuki

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.

We investigated gene-environment interaction based on nested case-control studies within the JPHC study. In this study, we hypothesized that genetic polymorphisms related to alcohol and acetaldehyde dehydrogenase may modify association between alcohol consumption and the risk of gastric cancer. Alcohol consumption was significantly associated with an increased risk of gastric cancer among subjects with G allele of ADH1C gene, whose enzyme activity is lower than those with A allele or subjects with A allele of ALDH2 gene whose enzyme activity is lower than those with G allele only.

The JPHC study participates in several international consortium studies and one of them investigated the association between alcohol consumption and the risk of breast cancer subtypes defined by an estrogen receptor based on 20 cohort studies including about one million women. It

reported a significant positive association between alcohol consumption and the risk of breast cancer regardless of subtypes by estrogen receptor.

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 under way by obtaining questionnaire information from 95,671 participants, and by obtaining biological samples and information from 48,431 participants (see Table 1 below).

- 2) Molecular epidemiologic studies to investigate the cause of cancer through means such as omics data analysis

In order to develop a risk prediction model for cancer among Japanese using information on genetic factors and plasma biomarkers in addition to lifestyle factors, we conducted a case-cohort study of total cancer within the baseline survey of the JPHC study and have performed data analysis for identifying risk factors that contribute to personalized prevention.

Education

Supervised the research of three research resident fellowships and one senior resident in the hospital. Supervised the education of one medical student short-term trainee.

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 questionnaires	Total number of questionnaires and biospecimens	Status of data collection
Akita, Yokote	26,769	14,831	Ongoing
Nagano, Saku	31,395	13,333	Completed
Ibaraki, Chikusei	13,130	9,309	Ongoing
Kochi, Konan	3,872	1,594	Completed
Kochi, Aki	5,017	2,049	Completed
Nagasaki (2014 ~)	6,225	1,743	Ongoing
Ehime, Ohzu (2014 ~)	3,131	2,831	Ongoing
Iwate, Ninohe (2015 ~)	2,959	2,741	Ongoing
Total	95,671	48,431	

List of papers published in 2015

Journal

- Wang H, Iwasaki M, Haiman CA, Kono S, Wilkens LR, Keku TO, Berndt SI, Tsugane S, Le Marchand L. Interaction between Red Meat Intake and NAT2 Genotype in Increasing the Risk of Colorectal Cancer in Japanese and African Americans. *PLoS One*, 10:e0144955, 2015
- Kikuchi H, Inoue S, Odagiri Y, Inoue M, Sawada N, Tsugane S, Japan Public Health Centre (JPHC) study group. Occupational sitting time and risk of all-cause mortality among Japanese workers. *Scand J Work Environ Health*, 41:519-528, 2015
- Hidaka A, Shimazu T, Sawada N, Yamaji T, Iwasaki M, Sasazuki S, Inoue M, Tsugane S, Japan Public Health Center-based Prospective Study Group. Fish, n-3 PUFA consumption, and pancreatic cancer risk in Japanese: a large, population-based, prospective cohort study. *Am J Clin Nutr*, 102:1490-1497, 2015
- Schumacher FR, Schmit SL, Jiao S, Edlund CK, Wang H, Zhang B, Hsu L, Huang SC, Fischer CP, Harju JF, Idos GE, Lejbkowitz F, Manion FJ, McDonnell K, McNeil CE, Melas M, Rennert HS, Shi W, Thomas DC, Van Den Berg DJ, Hutter CM, Aragaki AK, Butterbach K, Caan BJ, Carlson CS, Chanock SJ, Curtis KR, Fuchs CS, Gala M, Giovannucci EL, Gogarten SM, Hayes RB, Henderson B, Hunter DJ, Jackson RD, Kolonel LN, Kooperberg C, Küry S, LaCroix A, Laurie CC, Laurie CA, Lemire M, Levine D, Ma J, Makar KW, Qu C, Taverna D, Ulrich CM, Wu K, Kono S, West DW, Berndt SI, Bezieau S, Brenner H, Campbell PT, Chan AT, Chang-Claude J, Coetzee GA, Conti DV, Duggan D, Figueiredo JC, Fortini BK, Gallinger SJ, Gauderman WJ, Giles G, Green R, Haile R, Harrison TA, Hoffmeister M, Hopper JL, Hudson TJ, Jacobs E, Iwasaki M, Jee SH, Jenkins M, Jia WH, Joshi A, Li L, Lindor NM, Matsuo K, Moreno V, Mukherjee B, Newcomb PA, Potter JD, Raskin L, Rennert G, Rosse S, Severi G, Schoen RE, Seminara D, Shu XO, Slattery ML, Tsugane S, White E, Xiang YB, Zanke BW, Zheng W, Le Marchand L, Casey G, Gruber SB, Peters U. Corrigendum: genome-wide association study of colorectal cancer identifies six new susceptibility loci. *Nat Commun*, 6:8739, 2015
- Kawabata-Shoda E, Charvat H, Ikeda A, Inoue M, Sawada N, Iwasaki M, Sasazuki S, Shimazu T, Yamaji T, Kimura H, Masuda S, Tsugane S. Trends in cancer prognosis in a population-based cohort survey: can recent advances in cancer therapy affect the prognosis? *Cancer Epidemiol*, 39:97-103, 2015
- Fowke JH, McLerran DF, Gupta PC, He J, Shu XO, Ramadas K, Tsugane S, Inoue M, Tamakoshi A, Koh WP, Nishino Y, Tsuji I, Ozasa K, Yuan JM, Tanaka H, Ahn YO, Chen CJ, Sugawara Y, Yoo KY, Ahsan H, Pan WH, Pednekar M, Gu D, Xiang YB, Sauvaget C, Sawada N, Wang R, Kakizaki M, Tomata Y, Ohishi W, Butler LM, Oze I, Kim DH, You SL, Park SK, Parvez F, Chuang SY, Chen Y, Lee JE, Grant E, Rolland B, Thornquist M, Feng Z, Zheng W, Boffetta P, Sinha R, Kang D, Potter JD. Associations of body mass index, smoking, and alcohol consumption with prostate cancer mortality in the Asia Cohort Consortium. *Am J Epidemiol*, 182:381-389, 2015
- Ueno M, Ohara S, Sawada N, Inoue M, Tsugane S, Kawaguchi Y. The association of active and secondhand smoking with oral health in adults: Japan public health center-based study. *Tob Induc Dis*, 13:19, 2015
- Schumacher FR, Schmit SL, Jiao S, Edlund CK, Wang H, Zhang B, Hsu L, Huang SC, Fischer CP, Harju JF, Idos GE, Lejbkowitz F, Manion FJ, McDonnell K, McNeil CE, Melas M, Rennert HS, Shi W, Thomas DC, Van Den Berg DJ, Hutter CM, Aragaki AK, Butterbach K, Caan BJ, Carlson CS, Chanock SJ, Curtis KR, Fuchs CS, Gala M, Giovannucci EL, Giovannucci EL, Gogarten SM, Hayes RB, Henderson B, Hunter DJ, Jackson RD, Kolonel LN, Kooperberg C, Küry S, Kury S, LaCroix A, Laurie CC, Laurie CA, Lemire M, Levine D, Ma J, Makar KW, Qu C, Taverna D, Ulrich CM, Wu K, Kono S, West DW, Berndt SI, Bezieau S, Brenner H, Campbell PT, Chan AT, Chang-Claude J, Coetzee GA, Conti DV, Duggan D, Figueiredo JC, Fortini BK, Gallinger SJ, Gauderman WJ, Giles G, Green R, Haile R, Harrison TA, Hoffmeister M, Hopper JL, Hudson TJ, Jacobs E, Iwasaki M, Jee SH, Jenkins M, Jia WH, Joshi A, Li L, Lindor NM, Matsuo K, Moreno V, Mukherjee B, Newcomb PA, Potter JD, Raskin L, Rennert G, Rosse S, Severi G, Schoen RE, Seminara D, Shu XO, Slattery ML, Tsugane S, White E, Xiang YB, Zanke BW, Zheng W, Le Marchand L, Casey G, Gruber SB, Peters U. Genome-wide association study of colorectal cancer identifies six new susceptibility loci. *Nat Commun*, 6:7138, 2015
- Abe SK, Inoue M, Sawada N, Iwasaki M, Shimazu T, Yamaji T, Sasazuki S, Tanaka Y, Mizokami M, Tsugane S, JPHC Study Group. Hepatitis B and C virus infection and risk of lymphoid malignancies: A population-based cohort study (JPHC Study). *Cancer Epidemiol*, 39:562-566, 2015

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11. Kato M, Noda M, Mizoue T, Goto A, Takahashi Y, Matsushita Y, Nanri A, Iso H, Inoue M, Sawada N, Tsugane S, JPHC Study Group. Diagnosed diabetes and premature death among middle-aged Japanese: results from a large-scale population-based cohort study in Japan (JPHC study). *BMJ Open*, 5:e007736, 2015
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13. Saito E, Inoue M, Sawada N, Shimazu T, Yamaji T, Iwasaki M, Sasazuki S, Noda M, Iso H, Tsugane S, JPHC Study Group. Association of green tea consumption with mortality due to all causes and major causes of death in a Japanese population: the Japan Public Health Center-based Prospective Study (JPHC Study). *Ann Epidemiol*, 25:512-518.e3, 2015
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16. Shimizu K, Nakaya N, Saito-Nakaya K, Akechi T, Ogawa A, Fujisawa D, Sone T, Yoshiuchi K, Goto K, Iwasaki M, Tsugane S, Uchitomi Y. Personality traits and coping styles explain anxiety in lung cancer patients to a greater extent than other factors. *Jpn J Clin Oncol*, 45:456-463, 2015
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24. Svensson T, Inoue M, Sawada N, Iwasaki M, Sasazuki S, Shimazu T, Yamaji T, Ikeda A, Kawamura N, Mimura M, Tsugane S, Japan Public Health Centre-based prospective Study Group. The association between complete and partial non-response to psychosocial questions and suicide: the JPHC Study. *Eur J Public Health*, 25:424-430, 2015
25. Budhathoki S, Iwasaki M, Yamaji T, Sasazuki S, Tsugane S. Coffee intake and the risk of colorectal adenoma: The colorectal adenoma study in Tokyo. *Int J Cancer*, 137:463-470, 2015
26. Hanibuchi T, Nakaya T, Honjo K, Ikeda A, Iso H, Inoue M, Sawada N, Tsugane S, Japan Public Health Center-based Prospective Study Group. Neighborhood contextual factors for smoking among middle-aged Japanese: a multilevel analysis. *Health Place*, 31:17-23, 2015
27. Budhathoki S, Iwasaki M, Sawada N, Yamaji T, Shimazu T, Sasazuki S, Inoue M, Tsugane S, JPHC Study Group. Soy food and isoflavone intake and endometrial cancer risk: the Japan Public Health Center-based prospective study. *BJOG*, 122:304-311, 2015
28. 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, 2015

DIVISION OF PREVENTION

Shizuka Sasazuki, Taichi Shimazu, Michihiro Mutoh, Charvat Hadrien, Shingo Miyamoto, Yoshitaka Tsubono, Masayuki Tatemichi, Junko Ishihara, Minatsu Kobayashi, Ribeka Takachi, Azusa Hara, Manami Inoue, Yingyan Gong, Eiko Saito, Issei Ezawa, Ruri Nakanishi, Masami Komiya

Introduction

The Division of Prevention focuses on prevention research to investigate and develop prevention methods (lifestyle, chemoprevention, molecular marker, etc.), risk prediction, risk stratification models, and evidence-based cancer prevention guidelines.

Research activities

- 1) Evaluation of cancer prevention strategies in Japan and cancer prevention guidelines

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, cigarette smoking was evaluated to have a 'convincing' effect on increasing the risk of head and neck cancer and bladder cancer. A web-based tool to predict the 10-year risk of developing cancer based on adherence to 5 healthy lifestyle factors was constructed and released to the press to be more widely used. A pooled analysis of Japanese cohort studies was conducted and we found that a moderate intake of fruit decreases the risk of lung cancer in men. The Asia Cohort Consortium (ACC) is a collaborative effort seeking to understand the relationship between genetics, environmental exposure, and the etiology of disease through the establishment of a cohort of at least one million healthy people throughout Asian countries. The ACC Coordinating Center was 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 established and several projects are ongoing.

- 2) Development of prevention measures based on interventional research

We started a double-blind, randomized clinical trial of aspirin and mesalazine to see if these drugs suppress the occurrence of new adenomas in patients with a history of multiple colorectal adenomas. Another clinical research project aiming to develop colorectal cancer chemopreventive drugs is in progress.

- 3) 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)

Based on a nested case-control study of the Japan Public Health Center-based prospective (JPHC) Study, the interaction of ADH1C, ALDH2 and alcohol consumption on the development of gastric cancer was shown. We also developed a risk prediction model for gastric cancer based on clinical and lifestyle-related characteristics in combination with biological variables (ABC method) that allows the estimation of the 10-year probability of gastric cancer occurrence. These results suggest the importance of risk stratification as a tool of gastric cancer prevention. In addition, we started research on collecting stomach cancer tissue in order to consider subtypes of tumors by molecular biomarkers.

Education

Supervised the research of one research resident fellowship and one senior resident in a hospital.

Future prospects

We 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 strategies by risk stratification.

5つの健康習慣によるがんリスクチェック

5つの習慣

がんを遠ざける5つの健康習慣とは

これまでの研究から、がんの原因は喫煙や飲酒、食事などの日常生活習慣に関わる場合も多く、以下のような健康的な生活習慣を送ることで、ある程度、がんは予防できることがわかっています。

5つの健康習慣

- 非喫煙
- 活発な身体活動
- 適正なBMI値
- 塩蔵品を控える
- 節酒

左図内の5つの円の上にマウスを置いたり、タッチしてみましょう。それぞれの項目についてのアドバイスが、この欄に表示されます。

上記「5つの習慣」は、ひとつよりもふたつ、3つと、多くをこなせるほどがんに罹るリスクが低くなりますが、リスクの度合いは、「ひとつ」の場合も「どのひとつか？」によって異なり、複数守る場合も「どれを組み合わせるのか？」によることが、わかってきました。このサイトの「リスク診断」では、いまのあなたが、5つの健康習慣をいくつ満たしているか判断し、今後10年の間に、がんに罹るリスクを計算します。また、その後の「シミュレーション」では、生活習慣を改善することで、どうリスク値が変化するかがわかります。

Figure 1. Web-based tool 'Five healthy lifestyle factors and cancer risk'.

List of papers published in 2015

Journal

1. Asada K, Nakajima T, Shimazu T, Yamamichi N, Maekita T, Yokoi C, Oda I, Ando T, Yoshida T, Nanjo S, Fujishiro M, Gotoda T, Ichinose M, Ushijima T. Demonstration of the usefulness of epigenetic cancer risk prediction by a multicentre prospective cohort study. *Gut*, 64:388-396, 2015
2. Yoneoka D, Henmi M, Sawada N, Inoue M. Synthesis of clinical prediction models under different sets of covariates with one individual patient data. *BMC Med Res Methodol*, 15:101, 2015
3. Kikuchi H, Inoue S, Odagiri Y, Inoue M, Sawada N, Tsugane S, Japan Public Health Centre (JPHC) study group. Occupational sitting time and risk of all-cause mortality among Japanese workers. *Scand J Work Environ Health*, 41:519-528, 2015
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10. Ueno M, Ohara S, Sawada N, Inoue M, Tsugane S, Kawaguchi Y. The association of active and secondhand smoking with oral health in adults: Japan public health center-based study. *Tob Induc Dis*, 13:19, 2015
11. Abe SK, Inoue M, Sawada N, Iwasaki M, Shimazu T, Yamaji T, Sasazuki S, Tanaka Y, Mizokami M, Tsugane S, JPHC Study Group. Hepatitis B and C virus infection and risk of lymphoid malignancies: A population-based cohort study (JPHC Study). *Cancer Epidemiol*, 39:562-566, 2015
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Book

1. Miyamoto S, Fujii G, Komiya M, Terasaki M, Mutoh M. Potential for sesame seed-derived factors to prevent colorectal cancer. In: Ullah MF, Ahmad A (eds), *Critical Dietary Factors in Cancer Chemoprevention*, Switzerland, Springer International Publishing, pp 183-197, 2015

DIVISION OF SCREENING ASSESSMENT AND MANAGEMENT

Hiroshi Saito, Chisato Hamashima, Koichi Nagata, Kumiko Saika, Ryoko Machii, Kanako Kono, Ayako Aoki, Yoshiki Ishikawa, Sayuri Amanuma, Junko Asai, Kanoko Matsushima, Kazuko Matsuda, Akiko Totake, Taeko Aiko, Asako Kowada, Ikuko Tominaga, Masae Omaru

Introduction

The 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 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 were published in 2015. Evidence report for cervical cancer will be published in 2016.

• Revision of Cancer Screening Checklists (CLs)

The screening programs performed as the Health Promotion Services by the Ministry of Health, Labour and Welfare consist of screening programs provided through large screening facilities and those via primary physicians. CLs were primarily developed targeting the former type of programs but could not cover the latter programs. The Division developed new structure indicators that cover all of the screening programs by revising the original CLs. The appropriateness of the new CLs was confirmed through preliminary use in six areas. The new CLs were proposed as

the substitute for the present CLs for use after 2016 and adoption as the new ones was decided by the council of the Ministry of Health, Labour and Welfare.

• Quality Assurance (QA) in cancer screening at municipalities and prefectures

The Division collected the information related to implementation of cancer screening and its management situation using the Cancer Screening Checklists (CLs) as a structure indicator in quality assurance at municipalities. The Division set up the website in 2013 that allows support for municipalities such as provision of their QA data archives and information relevant to cancer screening. CLs data were collected from municipalities and evaluation results were fed back on the website. In this year, 1,592 municipalities (91%) utilized the website by registering as members of the site. Analysis of the results in 2015 will be available early in 2016. The Division evaluated QA activity in each of the 47 prefectures and published the results. For those prefectures whose performance level was below the defined level, instructions were sent to ask them to improve the status.

The Division also investigated the method to calculate the participation rate in screening programs provided at worksites as well as the construction of the QA system of those programs.

• Workshop on cancer screening management

The Division held one-day educational workshops for the members of prefectural committees for cancer screening management, aiming at activating quality assurance activities in each of the 47 prefectures. The themes this year were the breast and cervix. 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 for screening assessment were also included in the contents. The Division also held a similar workshop targeting the new members of the 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 a project for 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, 37 to 39 prefectures held meetings to discuss cancer screening management and 20 to 22 (15 to 18 in the previous year) released the evaluation results of municipalities using CLs for each of the 5 cancers. These figures have been increasing after starting the workshop, suggesting there was an 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 8,576 at December 2015, corresponding to 86% 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 also participated in other RCTs (breast cancer and lung cancer screening) as a member of the headquarters of the research and supported those studies.

• A cohort study to evaluate the efficacy of cervical cancer screening using human papilloma virus in conjunction with pap smear cytology.

The Division has supported the management of the study as the head office. A total of 20,459 subjects have participated in the study as of the end of 2015 in 36 municipalities.

• 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 2015

Journal

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8. Lauby-Secretan B, Scoccianti C, Loomis D, Benbrahim-Tallaa L, Bouvard V, Bianchini F, Straif K, International Agency for Research on Cancer Handbook Working Group. Breast-cancer screening--viewpoint of the IARC Working Group. *N Engl J Med*, 372:2353-2358, 2015
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11. Machii R, Saika K. Morphological distribution of esophageal cancer from Cancer Incidence in Five Continents Vol. X. *Jpn J Clin Oncol*, 45:506-507, 2015
12. Saika K, Matsuda T. Morphological distribution of ovarian cancer from Cancer Incidence in Five Continents Vol. X. *Jpn J Clin Oncol*, 45:793, 2015
13. Matsuda T, Machii R. Morphological distribution of lung cancer from Cancer Incidence in Five Continents Vol. X. *Jpn J Clin Oncol*, 45:404, 2015
14. Nagata K, Fujiwara M, Shimamoto T, Iida N, Mogi T, Mitsuishi T. Colonic distention at CT colonography: randomized evaluation of both IV hyoscine butylbromide and automated carbon dioxide insufflation. *AJR Am J Roentgenol*, 204:76-82, 2015
15. Nagata K, Fujiwara M, Kanazawa H, Mogi T, Iida N, Mitsuishi T, Lefor AT, Sugimoto H. Evaluation of dose reduction and image quality in CT colonography: comparison of low-dose CT with iterative reconstruction and routine-dose CT with filtered back projection. *Eur Radiol*, 25:221-229, 2015

DIVISION OF PUBLIC HEALTH POLICY RESEARCH

Seiichiro Yamamoto, Yuri Mizota, Michiyo Tada, Hiromi Koitabashi, Yoko Takahashi, Kumiko Toyoshima, 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 the people for cancer prevention and screening by supporting local governments and directly approaching the public. In addition, because of the lack of evidence, we try to establish scientific evidence for cancer survivorship.

As for the activities to establish a research infrastructure, we conduct methodological research and education concerning behavioral science, epidemiology and biostatistics and support large-scale interventional studies.

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

In order to increase participation rates for cancer screening, we developed several client reminders of cancer screening such as leaflets and supported local municipalities by conducting workshops and disseminating information through the website. As a result, a total of 96 municipalities in 16 prefectures used our materials. We evaluated the participation rates of cancer screening for the municipalities that used our materials last year and most of them obtained increased participation rates. To promote cancer education for kids, we developed “Gan no Himitsu (Secret of Cancer)” two years ago as comic-style education material. It is available from the website (<http://kids.gakken.co.jp/>) and also by downloading an application for smartphones free of charge. We conducted an evaluation study of the book this year. We are

also developing materials for the promotion of participation in HCV testing and smoking cessation using a social marketing approach.

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 2016, we had recruited more than 700 breast cancer patients this fiscal year and 4,945 patients in total. The cohort became one of the largest patient cohorts in the world. We also started a patient cohort with the same objectives for colon and rectal cancer in December. We have already recruited 80 patients in three months.

Education of staff involved in clinical research

We developed an e-learning website, ICRweb (<http://icrweb.jp/>), for the education of staff involved in clinical research such as researchers, data managers, clinical research coordinators, and members of institutional review boards. As of February 2016, more than 12,000 new users were registered this fiscal year and more than 49,900 users were registered in total. ICRweb provided 22 new content items this year and more than 160 content items are available in total. In order to improve convenience for the users, we developed an Android application in addition to the iPhone application, which provides off-line lectures, research ethics guidelines, and statistical tools such as a sample size calculator.

List of papers published in 2015

Journal

1. Taira N, Arai M, Ikeda M, Iwasaki M, Okamura H, Takamatsu K, Yamamoto S, Ohsumi S, Mukai H, Japanese Breast Cancer Society. The Japanese Breast Cancer Society clinical practice guideline for epidemiology and prevention of breast cancer. *Breast Cancer*, 22:16-27, 2015
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3. Taira N, Akiyama I, Ishihara S, Ishibe Y, Kawasaki K, Saito M, Shien T, Nomura T, Hara F, Mizoo T, Mizota Y, Yamamoto S, Ohsumi S, Doihara H, Executive Committee for the Setouchi Breast Cancer Cohort Study. Impact of modifiable lifestyle factors on outcomes after breast cancer diagnosis: the Setouchi Breast Cancer Cohort Study. *Jpn J Clin Oncol*, 45:600-602, 2015
4. Shimizu C, Kato T, Tamura N, Bando H, Asada Y, Mizota Y, Yamamoto S, Fujiwara Y. Perception and needs of reproductive specialists with regard to fertility preservation of young breast cancer patients. *Int J Clin Oncol*, 20:82-89, 2015

DIVISION OF SCREENING PRACTICE

Takahisa Matsuda*, Yukio Muramatsu, Gen Iinuma*, Miyuki Sone*, Nachiko Uchiyama, Hiroaki Kurihara*, Hirokazu Watanabe*, Ryutaro Kakinuma*, Takashi Terauchi*, Minoru Machida*, Mari Kikuchi*, Tomoko Manabe*, Mototaka Miyake*, Shunsuke Sugawara*, Hideaki Kobayashi*, Koji Tomita*, Seiko Kuroki*, Yasuo Kakugawa*, Minoru Matsumoto*, Yosuke Otake*, Masayoshi Yamada*, Masau Sekiguchi*, Takaaki Tsuchida*, Takehiro Izumo*, Tomoyasu Kato*, Shunichi Ikeda*, Mitsuya Ishikawa*, Takashi Uehara*, Hanako Shimizu*, Yasuaki Arai* (*NCCH)

Introduction

In the Division of Screening Practice, since 2004, we have provided a wide range of opportunistic cancer screenings by using newly developed modalities. Most of the staff doctors hold two posts concurrently in both NCCH and the Research Center for Cancer Prevention and Screening (RCCPS). Our screening practice division consists of 13 radiologists, six gastroenterologists, two bronchoscopists, five gynecologists, seven radiologic technologists, four ultrasonographic technologists, two medical laboratory technologists, and four nurses. Our Division is in charge of multiphasic cancer screening using several imaging modalities to develop new cancer screening systems and to assess 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

The basic plan for males consists of screening for cancer of the lung, esophagus, stomach, colorectum, 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 multiphasic programs, an independent cancer 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 (RCCPS) carried out 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. In contrast, there are no conditions set to receive cancer screening programs for 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. Furthermore, methionin PET-CT/MRI has been provided as an optional examination from this year.

4) Number of participants of cancer screening

Recent accurate data of cancers have not been obtained due to the lack of adequate follow-up data from this year's participants. Therefore, we present the number of participants of cancer screening between January and December 2015 in this report (Table 1). A total of 3,140 people including 1,261 initial cases received cancer screening at the RCCPS in 2015. Most of the participants (76%; n=2,390) chose the comprehensive cancer screening course. Regarding the cancer detection rate data in each modality, we will report them in the next number.

Research activities

- 1) The follow-up system of pulmonary solitary solid nodules for evaluation of growth is being developed and published.
- 2) A large-scale analysis of diagnostic sensitivity of PET-CT for colorectal advanced neoplasm has been published.
- 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.

Future prospects

Based on cancer screening data such as examination results, medical institution findings, follow-up findings, and the questionnaire survey concerning lifestyles for 10 years, we started to assess them supported by the National Cancer Center Research and Development Fund (27-A-5).

Table 1. Number of participants of cancer screening

Comprehensive Cancer Screening Course										
Jan-Dec 2015	Initial			5-year Follow-up			Repeater			Total
	M	F	Total	M	F	Total	M	F	Total	
Total	542	373	915	343	203	546	618	311	929	2,390
Independent Cancer Screening Course*										
Jan-Dec 2015	Initial			5-year Follow-up			Repeater			Total
	M	F	Total	M	F	Total	M	F	Total	
Total	140	206	346	20	19	39	107	143	250	635
Chest CT Follow-up Course										
Jan-Dec 2015	Initial			5-year Follow-up			Repeater			Total
	M	F	Total	M	F	Total	M	F	Total	
Total	0	0	0	0	0	0	81	34	115	115

Independent Cancer Screening Course*

Lung cancer screening course, Breast cancer screening course, Gastrointestinal (GI) cancer screening course, Colorectal cancer screening course using CT-colonography, Cervical cancer screening course, PET-CT course

List of papers published in 2015

Journal

1. Kamiyama Y, Kobayashi Y, Fukuhara S, Morikawa N, Munakata W, Miyagi Maeshima A, Maruyama D, Kim SW, Watanabe T, Terauchi T, Muramatsu Y, Tobinai K. Incidental detection of malignant lymphoma in subjects in a cancer surveillance programme. *Br J Haematol*, 169:138-142, 2015
2. Tateishi U, Tatsumi M, Terauchi T, Ando K, Niitsu N, Kim WS, Suh C, Ogura M, Tobinai K. Prognostic significance of metabolic tumor burden by positron emission tomography/computed tomography in patients with relapsed/refractory diffuse large B-cell lymphoma. *Cancer Sci*, 106:186-193, 2015

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4. Toyoshima N, Sakamoto T, Makazu M, Nakajima T, Matsuda T, Kushima R, Shimoda T, Fujii T, Inoue H, Kudo SE, Saito Y. Prevalence of serrated polyposis syndrome and its association with synchronous advanced adenoma and lifestyle. *Mol Clin Oncol*, 3:69-72, 2015
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11. Iacopini F, Saito Y, Yamada M, Grossi C, Rigato P, Costamagna G, Gotoda T, Matsuda T, Scozzarro A. Curative endoscopic submucosal dissection of large nonpolypoid superficial neoplasms in ulcerative colitis (with videos). *Gastrointest Endosc*, 82:734-738, 2015
12. Saito Y, Saito S, Oka S, Kakugawa Y, Matsumoto M, Aihara H, Watari I, Aoyama T, Nouda S, Kuramoto T, Watanabe K, Ohmiya N, Higuchi K, Goto H, Arakawa T, Tanaka S, Tajiri H. Evaluation of the clinical efficacy of colon capsule endoscopy in the detection of lesions of the colon: prospective, multicenter, open study. *Gastrointest Endosc*, 82:861-869, 2015
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