

# Research Center for Cancer Prevention and Screening

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## Preface

The Japanese Government initiated the Third-Term Comprehensive 10-Year Strategy for Cancer Control in 2004, aimed at a dramatic decrease in the incidence and mortality rates of cancer in Japan. In order to achieve these aims, development of efficacious methods for cancer screening and cancer prevention and dissemination of information about cancer at the national level are particularly important. Consequently, the Research Center for Cancer Prevention and Screening (RCCPS) was established in the campus of the National Cancer Center, Tokyo, in February 2004. Research on cancer prevention and screening is directly in line with the aim of the Third-Term Comprehensive Cancer Control Project. Initially, this center was composed of four divisions, the cancer screening division, cancer screening technology division, epidemiology and prevention division, and statistics and cancer control division. After the establishment of the Center for Cancer Control and Information Service in October 2006, the last of the above mentioned divisions was transferred from the RCCPS to this new center.

In April 2008, a change in the organization was made to clarify the function of each division in the RCCPS. As a result, in two out of three divisions, names were changed: the cancer screening division became the Screening and Development division, and the cancer screening technology division became the Screening Assessment and Management Division. All clinicians moved to the former division.

The Screening and Development Division is responsible for multiphasic cancer screening using a variety of imaging modalities, such as helical-CT, positron emission tomography (PET) and total colonoscopy, to identify cancer patients among the participants in the study at the RCCPS. The performance characteristics of the screening modalities are measured in collaboration with other Divisions. In addition, clinical evaluation aimed at the application to cancer screening of not only new imaging modalities such as CT-colonography, MRI (3.0 Tesla), and mammography with a tomosynthesis system, but also of PET-pharmaceuticals (except FDG), is under way in collaboration with several divisions of the National Cancer Center Hospital. Among the 9,485 subjects who underwent the general courses for first time, 495 some type of cancers have been detected (5.2%). The Center is planning to provide general screening courses, including vision examinations, fundus examination, tonometry, ECG, and optimal brain checkups in addition to cancer screening.

The Screening Assessment and Management Division is responsible for data collection, integrated management, analysis and dissemination of information on cancer screening at the national level. Studies to evaluate the efficacy of cancer screening programs and development and updating of screening guidelines are undertaken at this division. Guidelines for colorectal, stomach and lung cancer screening have already been published. In addition, construction of a quality assurance system is under way. Studies on developing new technologies for early detection of cancer are performed, as well as measurements of the sensitivities and specificities of such modalities. These studies are intensively promoted to establish screening systems that would allow a reduction in the mortality and incidence rates of cancer in the country.

The Epidemiology and Prevention Division plans and conducts independent and collaborative studies on cancer etiology and prevention, with special focus on dietary factors, gene-environmental interactions and effective measures for cancer prevention. In this respect, several epidemiological projects are currently in progress, including ecological, case-control, cohort and intervention studies, while the methodological backgrounds of dietary assessment (nutritional epidemiology) and molecular biomarkers (molecular epidemiology) are intensively investigated.

I would like to express my sincere appreciation for the support that we have received from the Ministry of Health, Labour and Welfare, other governmental organizations, private organizations, individuals, and also the Foundation for the Promotion of Cancer Research. Moreover, I am grateful for the diligent efforts of my colleagues who have devoted their time and talent to developing the RCCPS.

Noriyuki Moriyama, M.D.  
Director, Research Center for Cancer Prevention and Screening

## Organization

### President:

Tomomitsu Hotta

### Director:

Noriyuki Moriyama

Screening Technology and Development Division

Chief: Yukio Muramatsu

Screening Assessment and Management Division

Chief: Hiroshi Saito

Epidemiology and Prevention Division

Chief: Shoichiro Tsugane

# Activities of the Divisions

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## SCREENING TECHNOLOGY AND DEVELOPMENT DIVISION

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### Introduction

In April 2008, a change in the Research Center for Cancer Prevention and Screening (RCCPS) organization was made to clarify the function of each of its divisions. As a result, what was originally the Cancer Screening Division became the Screening and Development Division. Cancer screening is performed by medical staff from the new division. There are 7 radiologists, 3 gastroenterologists, 1 pharmacist, 7 radiologic technologists, 2 ultrasonographic technologists, 2 medical laboratory technologists, and 6 nurses. A gynecologist at the National Cancer Center Hospital (NCCH) supports gynecological examinations. 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. Our division now has one multi-detector computed tomography (MD-CT) system, two magnetic resonance imaging (MRI) systems (1.5 T and 3.0 T), two positron emission tomography/computed tomography (PET/CT) systems, one cyclotron system, one digital radiography (DR) system with a newly developed flat panel detector, two mammography (MMG) systems, three ultrasonography (US) systems, and three endoscopy systems. 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, for both men and women who undergo a complete set of screening, whole body scanning using 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 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.

#### 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, MRI for cancer of the uterus and ovary, gynecological examinations with Pap-smear, 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.

#### 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 2012 patients. We have therefore presented confirmed data from the previous year. Two thousand seven hundred and sixty four participants underwent multi-phasic programs (new, 1210; repeater, 1554). Malignant tumors were

detected in 43 out of 1210 new participants and in 32 out of 1554 repeaters who underwent multi-phasic clinical programs in 2011 (Tables 1 and 2). Detection rates were 3.55% and 2.06%, respectively.

#### 5. Imaging system

All medical images in our center are digitized. Original or compressed computed radiography (CR), DR, CT, MRI, PET, US, and endoscopy images can be easily and rapidly referenced on the medical information system for research, administration, and clinical expertise (MIRACLE). A reporting system has been established. MIRACLE for cancer screening is used for all routine work.

#### Research activity

(1) The first breast tomosynthesis system in Japan was installed at 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. The sensitivity and specificity of tomosynthesis in comparison with conventional MMG, US, other modalities, and pathological findings are in the process of evaluation. The usefulness of the adjunction of digital breast tomosynthesis to full-field digital mammography in evaluation

of the pathological response after neoadjuvant chemotherapy for breast cancer detected at the NCCCH has been assessed.

- (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) A computer-aided system for detection of pulmonary nodules on low-dose CT images is being developed and a super high-resolution CT scanner is also being developed.
- (5) The clinical usefulness of C11-methionine-PET in several kinds of brain tumors detected at the NCCCH has been assessed.
- (6) The clinical usefulness of MRI (3.0 T) in the cancer screening of the uterus and /or ovaries has been assessed.

#### Clinical trials

Cancer re-screening for those subjects who have finished a follow-up of five years began in February, 2009 in our center. As a result, a new study based on the follow-up data has been started.

**Table 1. Cancerous detection rate in new participants (2011)**

	No. of cancerous cases	No. of new participants	Detection rate (%)
colo-rectum	14	1210	1.16
stomach	10	1210	0.83
breast	3	420	0.71
prostate	4	790	0.51
lung	4	1210	0.33
uterus	1	420	0.24
thyroid	2	1210	0.17
esophagus	1	1210	0.08
pancreas	1	1210	0.08
kidney	1	1210	0.08
others	2	1210	0.17
total	43	1210	3.55

**Table 2. Cancerous detection rate in repeat participants (2011)**

	No. of cancerous cases	No. of repeat participants	Detection rate(%)
colo-rectum	7	1526	0.46
stomach	8	1526	0.52
breast	4	524	0.76
prostate	5	1030	0.49
lung	1	1554	0.06
uterus	1	524	0.19
thyroid	1	1554	0.06
esophagus	2	1526	0.13
pancreas	3	1554	0.19
total	32	1554	2.06

## List of papers published in 2012 Journal

1. Goshima S, Kanematsu M, Kobayashi T, Furukawa T, Zhang X, Fujita H, Watanabe H, Kondo H, Moriyama N, Bae KT. Staging hepatic fibrosis: computer-aided analysis of hepatic contours on gadolinium ethoxybenzyl diethylenetriaminepentaacetic acid-enhanced hepatocyte-phase magnetic resonance imaging. *Hepatology*, 55:328-329, 2012
2. Watanabe H, Kanematsu M, Goshima S, Kondo H, Kajita K, Kawada H, Noda Y, Moriyama N. Detection of focal hepatic lesions with 3-T MRI: comparison of two-dimensional and three-dimensional T2-weighted sequences. *Jpn J Radiol*, 30:721-728, 2012
3. Watanabe H, Kanematsu M, Kato H, Kojima T, Miyoshi T, Goshima S, Kondo H, Kawada H, Noda Y, Moriyama N. Enhancement of anatomical structures and detection of metastatic cervical lymph nodes: comparison of two different contrast material doses. *Jpn J Radiol*, 30:846-851, 2012
4. Kanematsu M, Goshima S, Watanabe H, Kondo H, Kawada H, Noda Y, Moriyama N. Diffusion/perfusion MR imaging of the liver: practice, challenges, and future. *Magn Reson Med Sci*, 11:151-161, 2012
5. Inoue K, Kurosawa H, Tanaka T, Fukushi M, Moriyama N, Fujii H. Optimization of injection dose based on noise-equivalent count rate with use of an anthropomorphic pelvis phantom in three-dimensional 18F-FDG PET/CT. *Radiol Phys Technol*, 5:115-122, 2012
6. Kakinuma R, Ashizawa K, Kobayashi T, Fukushima A, Hayashi H, Kondo T, Machida M, Matsusako M, Minami K, Oikado K, Okuda M, Takamatsu S, Sugawara M, Gomi S, Muramatsu Y, Hanai K, Kaneko M, Tsuchiya R, Moriyama N. Comparison of sensitivity of lung nodule detection between radiologists and technologists on low-dose CT lung cancer screening images. *Br J Radiol*, 85:e603-608, 2012
7. Umeda I, Tani K, Tsuda K, Kobayashi M, Ogata M, Kimura S, Yoshimoto M, Kojima S, Moribe K, Yamamoto K, Moriyama N, Fujii H. High resolution SPECT imaging for visualization of intratumoral heterogeneity using a SPECT/CT scanner dedicated for small animal imaging. *Ann Nucl Med*, 26:67-76, 2012
8. Kanematsu M, Kondo H, Goshima S, Tsuge Y, Watanabe H, Moriyama N. Giant high-flow type pulmonary arteriovenous malformation: coil embolization with flow control by balloon occlusion and an anchored detachable coil. *Korean J Radiol*, 13:111-114, 2012
9. Watanabe H, Kanematsu M, Goshima S, Yoshida M, Kawada H, Kondo H, Moriyama N. Is gadoxetate disodium-enhanced MRI useful for detecting local recurrence of hepatocellular carcinoma after radiofrequency ablation therapy? *AJR Am J Roentgenol*, 198:589-595, 2012
10. Kakinuma R, Ashizawa K, Kuriyama K, Fukushima A, Ishikawa H, Kamiya H, Koizumi N, Maruyama Y, Minami K, Nitta N, Oda S, Oshiro Y, Kusumoto M, Murayama S, Murata K, Muramatsu Y, Moriyama N. Measurement of focal ground-glass opacity diameters on CT images: interobserver agreement in regard to identifying increases in the size of ground-glass opacities. *Acad Radiol*, 19:389-394, 2012
11. Tateishi U, Terauchi T, Akashi-Tanaka S, Kinoshita T, Kano D, Daisaki H, Murano T, Tsuda H, Macapinlac HA. Comparative study of the value of dual tracer PET/CT in evaluating breast cancer. *Cancer Sci*, 103:1701-1707, 2012

## Book

12. Uchiyama N, Kinoshita T, Hojo T, Asawa S, Suzuki J, Kawawa Y, Otsuka K. Optimization of digital breast tomosynthesis (DBT) for breast cancer diagnosis. *Mammography recent advances INTECH, Croatia*, pp 355-370, 2012
13. Uchiyama N. Breast CAD (computer aided detection) in FFDM (full field digital mammography). *Mammography recent advances INTECH, Croatia*, pp 281-292, 2012
14. Uchiyama N, Kinoshita T, Hojo T, Asawa S, Suzuki J, Kawawa Y, Otsuka K. Usefulness of adjunction of digital breast tomosynthesis (DBT) to full-field digital mammography (FFDM) in evaluation of pathological response after neoadjuvant chemotherapy (NAC) for breast cancer. *Breast imaging, 11<sup>th</sup> international workshop, IWDM 2012, Philadelphia, proceedings, Springer-Berlin Heidelberg*, pp 354-361, 2012
15. Uchiyama N, Kinoshita T, Hojo T, Asawa S, Suzuki J, Kawawa Y, Otsuka K. Diagnosis impact of adjunction of digital breast tomosynthesis (DBT) to full-field digital mammography (FFDM) and in comparison with full field digital mammography (FFDM). *Breast cancer. Breast imaging, 11<sup>th</sup> international workshop, IWDM 2012, Philadelphia, proceedings, Springer-Berlin Heidelberg*, pp 354-361, 2012

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## SCREENING ASSESSMENT AND MANAGEMENT DIVISION

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

### 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, our 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 breast cancer have been developed and will be published in 2013.
- Quality Assurance (QA) in cancer screening at municipalities  
The Division collected the information related to implementation of cancer screening and the situation regarding its management using Checklists (CLs) as a structure indicator in quality assurance 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 grade so that each city compares its indicator with those of other cities.
- Calculation of standardized screening rate  
The reported screening rate from the Ministry of Health, Labour and Welfare has not been standardized, because the method used to estimate

the target population differs by municipality. The Division calculated the standardized screening rate using the same method. This activity was performed in part as a project of the Center for Cancer Control and Information Services and will be continued on an annual basis. The calculated data were released on the website of the Center for Cancer Control and Information Services.

- Workshop on cancer screening management  
The Division held several educational workshops for the members of prefectural committees of cancer screening management, aiming at activating quality assurance activities in each of 47 prefectures. The themes this year were the stomach and colorectum. The main contents of the workshops were the methods of quality assurance of the screening programs within each prefectures. The committees were encouraged to release the evaluation results of the screening management status of each municipality in the prefectures. Other basic issues necessary for conducting organized cancer screening programs, such as issues concerning screening assessment, were also included in the workshop programs.  
There were 69 participants in the workshops from 43 prefectures, who consisted of administrative officers (one-third) and chairmen of each committee (two-thirds). This activity was performed as the project of the Center for Cancer Control and Information Services and will be continued on an annual basis.  
In the previous year, the Division held a workshop on lung cancer. According to the survey, 32 prefectures held meetings to discuss cancer screening management and 8 prefectures released the evaluation results. To evaluate the effect of the workshop on the activity of the prefectural committees, the Division will scrutinize the performance of each committee through surveillance in the municipalities.

## Research activities

- A randomized controlled trial of colonoscopic screening

A randomized controlled trial evaluating one-time colonoscopic screening (CS) 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 study fields were extended throughout the neighboring Daisen city which has a population of 43,000 as of this year. However, participation rate in the study was unexpectedly as low as one-third in the new field as compared to the previously-involved fields. Finally, the cumulative number of subjects who gave informed consent, and who were thus enrolled in the study, was 5001 during the 41 months after starting recruitment, corresponding to half of the planned number. Low participation in the new field was mainly due to the inadequate recruiting activity infrastructure, which is different from that in the previously involved fields and is now being redesigned to allow effective recruitment. In addition, low awareness of colon cancer and colonoscopy, such as fear of colonoscopy-related pain was confirmed as a major barrier. A campaign aimed at promoting knowledge of colorectal cancer screening, which was effective in the initially involved fields, was also put in place.

## List of papers published in 2012

### Journal

1. Lambert R, Saito H, Lucas E, Sankaranarayanan R. Survival from digestive cancer in emerging countries in Asia and Africa. *Eur J Gastroenterol Hepatol*, 24:605-612, 2012
2. Ishikawa Y, Hirai K, Saito H, Fukuyoshi J, Yonekura A, Harada K, Seki A, Shibuya D, Nakamura Y. Cost-effectiveness of a tailored intervention designed to increase breast cancer screening among a non-adherent population: a randomized controlled trial. *BMC Public Health*, 12:760, 2012
3. Machii R, Saika K, Higashi T, Aoki A, Hamashima C, Saito H. Evaluation of feedback interventions for improving the quality assurance of cancer screening in Japan: study design and report of the baseline survey. *Jpn J Clin Oncol*, 42:96-104, 2012
4. Saika K, Matsuda T. Time trends in liver cancer mortality (1980-2008) in Japan, the USA and Europe. *Jpn J Clin Oncol*, 42:84, 2012
5. Matsuda T, Saika K. Trends in liver cancer mortality rates in Japan, USA, UK, France and Korea based on the WHO mortality database. *Jpn J Clin Oncol*, 42:360-361, 2012
6. Kumiko S, Tomotaka S, Masakazu N, Akira O, Keiji W, Nobuyuki H, Yumiko M, Rie Y, Kazuo T. Smoking prevalence and beliefs on smoking cessation among members of the Japanese Cancer Association in 2006 and 2010. *Cancer Sci*, 103:1595-1599, 2012
7. Kotani K, Hazama A, Hagimoto A, Saika K, Shigeta M, Katanoda K, Nakamura M. Adiponectin and smoking status: a systematic review. *J Atheroscler Thromb*, 19:787-794, 2012
8. Chihara D, Ito H, Matsuda T, Katanoda K, Shibata A, Saika K, Sobue T, Matsuo K. Decreasing trend in mortality of chronic myelogenous leukemia patients after introduction of imatinib in Japan and the u.s. *Oncologist*, 17:1547-1550, 2012
9. Saika K, Machii R. Cancer mortality attributable to tobacco in Asia based on the WHO Global Report. *Jpn J Clin Oncol*, 42:985, 2012
10. Matsuda T, Saika K. Worldwide burden of cancer incidence in 2002 extrapolated from cancer incidence in five continents Vol. IX. *Jpn J Clin Oncol*, 42:1111-1112, 2012
11. Mizota Y, Yamamoto S. Prevalence of breast cancer risk factors in Japan. *Jpn J Clin Oncol*, 42:1008-1012, 2012
12. Ishikawa Y, Nishiuchi H, Hayashi H, Viswanath K. Socioeconomic status and health communication inequalities in Japan: a nationwide cross-sectional survey. *PLoS One*, 7:e40664, 2012

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## EPIDEMIOLOGY AND PREVENTION DIVISION

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Shoichiro Tsugane, Shizuka Sasazuki, Motoki Iwasaki, Norie Sawada, Taichi Shimazu, Taiki Yamaji, Ai Noda, Izumi Suenaga, Hadrien Charvat, Azusa Hara, Yoshitaka Tsubono, Masayuki Tatemichi, Tsutomu Miura, Minatsu Kobayashi, Yuko Yamano, Junko Ishihara, Sana Yokoi, Ribeka Takachi, Takehiro Michikawa, Manami Inoue, Keiko Mori, Thomas Svensson, Kayo Ohashi, Yuri Ishii, Yingyan Gong, Jun Umesawa, Tomomi Mukai, Koichi Kawamura, Michiko Okajima, Ayako Toyama, Hideyo Ochi, Yurie Shinozawa, Izumi Matsumoto, Yasuko Iba

### Introduction

The Epidemiology and Prevention Division has planned and conducted independent and collaborative studies on cancer etiology and prevention, with a special focus on dietary, environmental and genetic factors. Several epidemiological projects are currently in progress.

### Research activities

Population-based prospective study (the JPHC study and the JPHC-NEXT study)

Diet has been implicated in the etiology of cancer and in the unique patterns of cancer incidence in Japan. However, the epidemiological evidence for this contention has been limited. The division therefore initiated a cohort study, the Japan Public Health Center-based Prospective Study (JPHC Study), in 1990, in collaboration with 11 public health centers and other institutes, in which approximately 140,000 individuals from 11 areas were scheduled to be followed up for at least 30 years. A total of 22,911 deaths, 18,376 cases of cancers, 6,105 cases of strokes and 1,189 cases of myocardial infarctions, had been documented as of September, 2012.

In the cohort, lifestyle factors that were assessed in the baseline and/or 5 and/or 10 year follow up questionnaire, examination data from health checkups or stored blood samples were investigated in relation to the subsequent risk of total death, total or specific cancer and other lifestyle-related diseases.

Total Cancer: The association between five combined healthy lifestyle factors (not smoking, moderate drinking, eating minimum salt-preserved foods, being physically active, and having an appropriate body mass index) and cancer incidence was evaluated and the risk was reduced 14% and 9% by each one healthy lifestyle for men and women, respectively, suggesting that the combined lifestyle factors have a considerable impact on preventing cancer (1). The association between cadmium

exposure and incidence of cancer was examined but no association was observed (2). Stomach Cancer: The association between isoflavone intake and stomach cancer incidence was investigated but no association was seen. Colorectal Cancer: The association between zinc and heme iron intakes and colorectal cancer incidence was investigated but no association was observed (4). Liver Cancer: The association between fish and n-3 polyunsaturated fatty acids (PUFA) consumption and hepatocellular carcinoma (HCC) incidence was investigated and consumption of n-3 PUFA-rich fish and individual n-3 PUFAs was inversely associated with HCC irrespective of hepatitis B virus (HBV) or hepatitis C virus (HCV) status (5). A risk estimation model for the 10-year risk of hepatocellular carcinoma (HCC) was developed (6). Ovarian Cancer: The risk factors for invasive primary epithelial ovarian cancer were evaluated among the female subjects and inverse associations were seen for giving birth more than once and a usual sleep duration of more than 7 hours per day (7). Thyroid Cancer: The association between consumption of seaweed that is rich in iodine and the thyroid cancer incidence among the female subjects in which most of the cases were papillary carcinoma and an increased risk of papillary carcinoma was observed in postmenopausal women but not in premenopausal women (8). The others: Not only cancer but also other non-communicable diseases (NCDs) are designed to be endpoints of the cohort study. Associations between lifestyle factors and stroke (9, 10), coronary heart disease (11), cardiovascular disease (CVD) (12, 13), dentition status (14) and diabetes (15) were investigated. The reproducibility and validity of dietary patterns assessed with a food frequency questionnaire (FFQ) used in the 5-year follow-up survey were examined (16).

Recruitment for the JPHC-NEXT study and the collaborative studies set for 100,000 participants started in 2011 and is in progress in several areas in order to update evidence with the current generation. Men and women of 40-74 years old of age at the baseline survey are to be followed up for

20 years. Overall survival and NCDs such as cancer, CVD, diabetes and mental illness are listed as the main endpoints. The collected data and samples are to be analyzed with up-to-date technology including genomics. A standard protocol for a molecular epidemiology cohort study in Japan is projected to be developed based on the JPHC-NEXT protocol. To conduct verification of the feasibility and validation study to consolidate data together with the other cohort study and its original protocol, a new cohort study by Strategic Funds for the Promotion of Science and Technology was launched and about 1800 men and women were recruited in 2 areas in 2012. The eventual goal of the project is to promote the Japanese Consortium for Cohort Studies of Molecule and Lifestyle presenting a vision of all molecular epidemiology cohort studies united nationwide.

#### Epidemiological study of Japanese Brazilians (Sao Paulo-Japan cancer study)

The ethnic differences in the incidence of cancer suggest an interaction between environmental and genetic factors. Several epidemiologic studies in Brazil, a multi-ethnic nation with 1.2 million people of Japanese ancestry, are in progress. A case-control study was conducted with subjects in Nagano, Japan, and São Paulo, Brazil to clarify the association between particular genetic markers of immunoglobulin G (IgG) and susceptibility to breast cancer. The GM 3 allele was significantly associated with susceptibility to breast cancer in white subjects from Brazil (17). A colorectal adenoma case-control study in Japanese Brazilians in São Paulo is in progress. The validity of the FFQ used in the study was examined.

#### Studies in Nagano and Hiraka and other intramural projects

Based on a cross-sectional study of women in Nagano, a higher folate intake was significantly associated with a lower level of global methylation of leukocyte DNA (18), whereas postmenopausal endogenous sex hormones were not (19). Vitamin C supplementation in relation to inflammation in individuals with atrophic gastritis was assessed in a randomised controlled trial at Hiraka, in Akita Prefecture, an area of high stomach cancer incidence, suggesting that vitamin C supplementation may not have a strong effect on reducing infections in individuals with atrophic gastritis. Studies are being conducted to search for the cause of cancer and develop effective cancer prevention methods, using samples from subjects seen at the Research Center for Cancer Prevention and Screening (RCCPS). The association between plasma 25-hydroxyvitamin D and colorectal adenoma according to dietary calcium

intake and vitamin D receptor polymorphism was investigated. The results suggested that Vitamin D might protect against colorectal neoplasia, mainly through mechanisms other than the indirect mechanism via calcium metabolism (20). The association of biomarkers for insulin and the insulin-like growth factor (IGF) axis with colorectal adenoma was investigated and a significant gender difference was observed in the results (21). A comprehensive analysis using data from the Lung Cancer Database Project was conducted to search for clinical biopsychosocial risk factors for depression in lung cancer patients, suggesting that depression was most strongly linked with personality traits and coping style (22). The design of a Japanese multicenter prospective cohort study on endoscopic resection for early gastric cancer using a Web registry (J-WEB/EGC) was introduced to the public (23).

#### Cancer prevention study

To develop an evidence-based cancer prevention strategy in terms of lifestyle intervention suitable for the Japanese population, a systematic literature review project (24-28) and some pooled analyses (29-31) were conducted. Evidence on smoking, alcohol, anthropometry, fruit and vegetables, other foods and lifestyles and infectious diseases as risk factors of the main cancers in Japan was reviewed to make final or updated judgments, each of which has been made public on the WEB ([http://epi.ncc.go.jp/can\\_prev/](http://epi.ncc.go.jp/can_prev/)) and distribution of booklets. Based on the judgments, current evidence-based cancer prevention recommendations for Japanese provided by the study group were also updated. The evidence-based materials to develop the recommendations were handed in to develop measures and policies in national health promotions. A systematic assessment was performed to estimate the current burden of cancer attributable to known preventable risk factors in Japan (32). Prediction model applications that calculate changes in risk through lifestyle modification were put on the internet based on results from the JPHC study. Data on the probability of 10-year survival free from cancer and cardiovascular incidence, and, for men, of the 10-year risk of colorectal cancer development are now available (<http://epi.ncc.go.jp/riskcheck/>).

#### International collaborative projects

International collaborative projects to contribute on to the global scale with a focus on Asian cancer prevention strategies (Japan-China cooperative research work, Asia Cohort Consortium (ACC) (33), Asia Breast Cancer Consortium (34, 35), Pooling project of Prospective Studies of Diet and Cancer (36), Collaborative Group on Hormonal

Factors in Breast Cancer (37), etc.) are in progress.

#### Reviews and others

The effects of 16 risk factors on cause-specific deaths and life expectancy in Japan were estimated from data from the National Health and Nutrition

Survey, epidemiological studies and statistics (38). Two reviews on alcohol, smoking, and obesity epidemiology in Japan (39) and epidemiological evidence for insulin resistance and cancer (40) and a commentary on translational research for preventive medicine (41) were published.

### List of papers published in 2012

#### Journal

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