# **Estimation of Cancer Incidence in Japan with an Age-Period-Cohort Model**

Mai Utada<sup>1\*</sup>, Yuko Ohno<sup>1</sup>, Midori Soda<sup>2</sup>, Ken-ichi Kamo<sup>3</sup>

## Abstract

Cancer has been the primary cause of death in Japan for many years and accurate cancer incidence data are necessary in order to make plans for cancer control. Although population-based cancer registries are the best answer, regrettably there are still many regions with low accuracy registries. In an alternative estimation, cancer incidences have been analyzed by age-period-cohort (APC) models, allowing future prediction of cancer incidences in 2004. Considering the unexpectedly rapid aging of the Japanese population after this figure was reported, it would be worthwhile to examine more recent data. In this study, we therefore projected major cancer incidences based on the earlier results leaving estimated values for the age and cohort effects. Relating to the period effect, the most adequate scenario was selected from 12 projection methods. Furthermore, incidences when registration rates varied between 70 and 100% were calculated. As a result, different trend from reported incidences were observed for liver cancer in males, and trends of registration rates differed by sites. Until stable accurate registration data become available, it is difficult to judge whether predicted increase is real or only looks so because the registration rate is not 100%. However, it is clearly necessary to continuously observe variation in cancer incidences.

Keywords: Cancer incidences - cancer registry - estimation - age-period-cohort models - Japan

Asian Pacific J Cancer Prev, 11, 1235-1240

## Introduction

In Japan, since 1981 cancer has been the primary cause of death in both males and females, and cancer incidences are consistently increasing (Foundation for Promotion of Cancer Research, 2008). In 1984, the Ministry of Health, Labor, and Welfare set into force the "Comprehensive Tenyear Strategy for Cancer Control" (from 1984 to 1993), followed in 1994 by the "2nd-Term Comprehensive Tenyear Strategy for Cancer Control" (from 1994 to 2003), and measures were taken that aimed at a marked decline in the incidence and death rate of cancer by the "3rd-term Comprehensive Ten-year Strategy for Cancer Control" in 2004. To achieve further advances in cancer control, the "Cancer Control Act" was passed in 2007 (Ministry of Health, Labour and Welfare, 2010). Furthermore with the "Basic Plan to Promote Cancer Control", which has been set into force for five years until 2011, two overall goals have been set. One is to reduce the number of deaths caused by cancer, and the other is relief of pain and to improve the quality of recuperation life for all cancer patients and their families. This plan aims at the comprehensive and systematic advancement of cancer control. Although implementation of this kind of cancer control has been successful, about 330,000 people died from cancer and cancer accounts for 30% of the causes of death in Japan in 2007 (National Cancer Center, 2009). It is useful to understand the trends in cancer incidence and mortality, in order to estimate future trends in cancer incidence and mortality as well as to make plans for cancer control. This requires getting a hold of the exact number of cancer incidences. It is possible to get a hold of the number of cancer incidences by population-based cancer registries (Matsuda et al., 2004). Regret to say, there exists no registration system for cancer incidences that is based on law in Japan, and the number of cancer incidences that has been reported till now is estimated incidence based on the numbers of cases reported in various reliable population-based cancer registries. Regarding populationbased cancer registries, through the Cancer Control Act in 2007, the number of regions that conduct cancer registry has increased, but there are still many regions with low accuracy of cancer registry and several prefectures has not been yet conducted (Kamo et al., 2007). Accordingly, there still exist problems when trying to know cancer incidence by totaling the number of incidences reported in all population-based cancer registries. We consider that in the meantime the number of cancer incidences need to be calculated by some kind of estimation (Kamo, 2007; National Cancer Center, 2009).

For predicting the number of cancer incidences, Ohno et al. (2004) analyzed cancer incidence from 1975 to 1994 by age-period-cohort models (APC models), which take into account the age, period and cohort effects (Nakamura, 1982; 2002). Furthermore, based on these results, they reported future prediction of the cancer incidence made

<sup>1</sup>Osaka University, <sup>2</sup>Radiation Effects Research Foundation, <sup>3</sup>Sapporo Medical University, Center for Medical Education, Department of Liberal Arts and Sciences. \*For correspondence : m-utada@sahs.med.osaka-u.ac.jp

#### Mai Utada et al

by setting up various scenarios for the period effect from 1995 to 2020 for all cancers and sites. The results are displayed in the homepage of National Cancer Center as the latest figure on long-term future national projection of the cancer incidence having the limitation that the based data were up to 1994.

Considering the unexpectedly rapid aging of the Japanese population after this figure was reported, it would be worthwhile to examine these data at the present point. In this study, we compared the number of cancer incidences reported in the above report with the reported figures by National Cancer Center until 2003. Furthermore, using currently reported figures of the Japanese population and future prediction, we investigated the most adequate projection method by exploring various scenarios for the future period effects. Based on these results, we projected the number of incidences of stomach, lung, liver, rectum, colon, breast, and prostate cancer using the most adequate method until 2020. For this examination, we also calculated the number of cancer incidences based on studies regarding the accuracy of registry by Kamo (2007) as reference and considered future trends of cancer incidence in Japan.

### **Materials and Methods**

Projection Method for the Cancer Statistics Report 2004 In the projection of cancer incidence by Ohno et al. (2004) (Cancer Statistics Report 2004: CSR2004) the age, period and cohort effects were estimated by applying the Nakamura's Bayesian Poisson cohort model (Nakamura 1982; 2002), which is based on (1) cancer incidence data by age group and site from 1975 to 1994, which at that time were the latest definitely estimated incidence as analysis data, and used suitable scenarios for making future estimations until 2020 (Ohno et al., 2004). As the basic projection scenario, the estimated value was left unchanged for the age effect and the cohort effect, the same value as the most recent cohort effect estimated for the birth date cohort group, which newly entered the age of cancer onset, was used. Relating to the period effect, constant, linear and quadratic functions were applied for the variations of the period effects from 1985 to 1994, and the most adequate model was selected based on Baysian Akaike's Information Criterion (BAIC). Using the model, the period effects were projected up to 2020 under the conditions which were 1) the period effects would take the maximum or minimum value of a quadratic function at 2020, and 2) the differential coefficients of the model at the connecting point of time were the same as that of quadratic functions denoted above. Furthermore, similar APC analysis was performed using (2) cancer incidence data by age group and site from 1975 to 1998 also including provisional estimated figures (since registration was delayed in cancer registry, the number of incidences for a certain period of time is reported as provisional estimated figures, from 1995 to 1998) as reference.

For the period effect, we compared these three cancer incidences: the estimated cancer incidence until 2020 which used the period effect from 1994 as fixed

values; (1); and (2) for each cancer site, and as a general rule applied results of analysis obtained through basic scenarios based on the data of (1). The estimated incidence was compared with provisional estimated figures for 1998, and in case that it differed by 10% and more, the three cancer incidences were compared, and the method that calculated the cancer incidence most close to the provisional estimated figures for 1998 was adopted.

By this means, we projected the number of cancer incidences by age group until 2020 by using the age, period and cohort effects.

#### The projection methods in this study

In this study, the age and cohort effects were fixed in the same way as in the case of CSR2004 and the following scenarios were examined for the period effect. The scenarios were labeled by the combination of the abbreviation depending on the order of the fitting function (Constant: C, linear: L, quadratic: Q), the period for fitting examination (only the latest year: I, latest previous five years: V, and latest previous 10 years: X) and the year assumed to be stable, that is the slope became zero (2020: 20, 2030: 30).

(CI20) The period effect was fixed for the latest year. (CV20) The period effect was fixed for the mean value for the latest previous five years.

(CX20) The period effect was fixed for the mean value for the latest previous 10 years.

(LV20) Linear functions were applied for the period effect of the previous five years, and quadratic functions that were tangent to the linear function at the newest year and showed the turning point in 2020 were determined.

(LX20) Linear functions were applied for the period effect of the previous 10 years, and the rest were calculated the same way as LV20.

(QV20) Quadratic functions were applied for the period effect of the previous five years, and quadratic functions that were tangent to the function at the newest year and showed the turning point in 2020 were determined.

(QX20) Quadratic functions were applied for the period effect of the previous 10 years, and the rest were calculated the same way as QV20.

(LV30) Linear functions were applied for the period effect of the previous five years, and quadratic functions that were tangent to the function at the newest year and showed the turning point in 2030 were determined.

(LX30) Linear functions were applied for the previous 10 years, and the rest were calculated the same way as LV30.

(QV30) Quadratic functions were applied for the period effect of the previous five years, and quadratic functions that were tangent to the function at the newest year and showed the turning point in 2030 were determined.

(QX30) Quadratic functions were applied for the previous 10 years and the rest were calculated the same way as QV30.

In addition, the period effects up to 2020 calculated by APC analysis of cancer incidence data including provisional estimated figures up to 1998 used in CRS 2004 (1998 provisional estimated values: P-CSR2004)

#### **Table 1. Selected Projection Method**

	Male	Female
Stomach	QV30	CSR2004
Lung	LX30	P-CSR2004
Liver	P-CSR2004	P-CSR2004
Rectum	CSR2004	CV20
Colon	CSR2004	CI20
Breast	-	QV30
Breast	QX20	-

was used.

The numbers of major cancer incidences were calculated by these 13 methods, namely 12 projection methods and CRS 2004. Stomach, lung, liver, rectum, and colon cancer were examined according to gender, and breast and prostate cancer were only examined for females and males, respectively.

For the evaluation of the projection method, the sum of squares of errors of figures on the cancer incidences by site reported by National Cancer Center for a period of five years from 1995 to 1999 was calculated and the method showed the smallest differences were selected as adequate projection methods. The reason why figures from 1995 to 1999 were used was because we thought that from 2000 cancer incidence was affected by variations in the registration accuracy of population-based cancer registries.

Furthermore, estimated incidences calculated by the most adequate projection method among CRS 2004 and 12 projection methods as a result of the method described above were set as 100% registration rate of cancer registry, and incidences when registration rates varied between 70 and 100% were calculated. We also calculated the number of cancer incidences used as references for the registration rate reported by Kamo (2007). Regarding the Japanese population used for projection, we linearly applied interpolated values reported for every five years in the World Population Prospects by the UN, The 2007 Revision (United Nation Population Division, 2008).

# Results

#### Time trends in incidence by cancer site

For major cancers, the number of incidences reported in CRS 2004 is shown in Figure 1, and the time trends of incidences by the projection method judged to be the most adequate among 12 projection methods (Table 1) are shown in Figure 2. In Figures 1 and 2, the interval set as original data of the Bayesian cohort models in principle was from 1975 to 1994. 1994 is shown as broken line. Furthermore, the interval used for checking the projection method is from 1995 to 1999 and shown as gray diagonal line.

For incidences reported for males by National Cancer Center in 2003, the order of descending incidence was stomach, lung, prostate, colon, liver, and rectum cancer. In CRS 2004 for 2003, the order of descending incidence was stomach, lung, colon, prostate, liver, and rectum cancer. Hereafter, lung and prostate cancer incidences greatly increased, but there was almost no increase in the incidence of stomach cancer. In 2020, the incidences of



Figure 1. Time Trends in Incident Cases Reported in CSR2004



Figure 2. Time Trends in Incident Cases by the Projection Method

lung and prostate cancer largely surpassed that of stomach cancer. The order of descending incidence was therefore lung, prostate, stomach, colon, liver, and rectum cancer.

On the other hand, in terms of the incidences in dependence to the selected projection method, the order of descending cancer incidence was stomach, lung, colon, liver, rectum, and prostate cancer in 2003. Hereafter, a large increase in the incidences of lung and prostate cancer, and almost no increase in that of liver and colon cancer were observed. As a result, the incidence of lung cancer slightly surpassed that of stomach cancer, and the order of descending incidence was lung, stomach, prostate, colon, rectum, and liver cancer in 2020.

For incidences reported for females by National Cancer Center for 2003, the order of descending incidence was breast, stomach, colon, lung, liver, and rectum cancer. In CRS 2004 for 2003, the order of descending incidence was breast, stomach, colon, lung, rectum, and liver cancer. Hereafter, a large increase in the incidence of breast, colon, and lung cancer, and almost no increase in that of



Figure 3. Time Trends in Incident Cases of Stomach Cancer



Figure 4. Time Trends in Incident Cases of Lung Cancer

stomach cancer were observed. In 2020, the incidence of breast and colon cancer reached comparable levels and surpassed that of stomach cancer. The order of descending incidence was therefore breast, colon, stomach, lung, rectum, and liver cancer.

On the other hand, in terms of the incidence in dependence to the selected projection method, the order of descending cancer incidence was breast, stomach, colon, lung, rectum, and liver cancer in 2003. Hereafter, a large

Table 2. Relative Changes in Incident Cases Between2000 and 2020

	CSR2004		12 projection methods	
	Male	Female	Male	Female
Stomach	1.04	1.07	1.12	1.14
Lung	1.79	1.67	1.62	1.71
Liver	1.19	1.48	0.82	1.23
Rectum	1.57	1.56	1.64	1.37
Colon	1.51	1.69	1.43	1.45
Breast	-	1.36	-	1.36
Breast	3.41	-	2.66	-

**1238** Asian Pacific Journal of Cancer Prevention, Vol 11, 2010



Figure 5. Time Trends in Incident Cases of Liver Cancer



Figure 6. Time Trends in Incident Cases of Rectum Cancer

increase in the incidence of breast and lung cancer, and almost no increase in that of cancer in other sites were observed. As a result, the order of descending cancer incidence was breast, stomach, colon, lung, rectum, and liver cancer in 2020.

In Table 2, the number of incidences for 2000 was compared with that for 2020 by site. In males, sites with a highly increased incidence ratio in CRS 2004 were prostate 3.41, and lung 1.79. On the other hand, by the selected projection methods, the increased incidence ratios of prostate, rectum and lung cancer were 2.66, 1.64, and 1.62.

In females, sites with a highly increased incidence ratio in CRS 2004 were colon 1.69, and lung 1.67. On the other hand, by selected projection methods, the increased incidence ratio of lung cancer was 1.71.

## Time trends in incidences in terms of registration rates

For major cancers, the number of incidences calculated by the most adequate projection method among CRS 2004 and 12 projection methods was set as a registration rate of



Figure 7. Time Trends in Incident Cases of Colon Cancer



Figure 8. Time Trends in Incident Cases of Breast Cancer in Females (Left) and Prostate Cancer in Males (Right)

100%, and that increased at 5% pitches from a registration rate of 70% are shown in Figures 3 to 8. In these Figures, solid lines represent the number of incidences reported by National Cancer Center for 1975 to 2003, broken lines represent projection incidence calculated by the most adequate projection method, dotted lines represent incidence trends deriving from differences in registration rates when the projection method is set as a registration rate of 100%, gray solid lines represent incidences in case that the registration rates derived from the incidences calculated by Kamo (2007), and black circles represent incidences reported by CRS 2004.

While in recent years a rapid upward trend in the incidence for males with stomach cancer was seen, which was coming close to 95%, and for females with stomach cancer, the incidence almost the same as 100%. Furthermore, for males with lung cancer in recent years, the incidence rose close to 95%, and in females with lung

cancer, the incidence was almost the same as 100%. For males with liver cancer, the incidence exceeded 90% and was close to 85%, while for females with liver cancer, the incidence was coming close to 85%. For males with rectum cancer, the incidence was almost 100%, but decreased in the newest year 2003 and came close to the incidence reported by CRS 2004.

On the other hand, also for females with rectum cancer in 2003 a decrease in the incidence was observed, and it showed less than 100%. Also for males with colon cancer, the incidence fell below CRS 2004 values. For females with colon cancer, the incidence was between 95 and 90%. In case of breast cancer, the incidence further increased from 95% and was coming more and more close to 80%. In case of prostate cancer, the incidence has been rapidly increasing since 2000 and has increased up to higher than 70%.

# Discussion

Since the Cancer Control Act was set into force in 2007, the number of hospitals that conduct hospital-based cancer registries has increased. When the population-based cancer registry reflects these reports, it will also become possible to get a hold of the real number of cancer incidences in the future. Regrettably, since the rules of the hospital-based cancer registry are even difficult for cancer registers who underwent professional training, the accuracy of hospital-based cancer registries is not the same all over Japan. Furthermore, only care hospitals are obliged to conduct hospital-based cancer registries, therefore we cannot say that the registered number of cancer incidences is 100%.

Under these circumstances, it is considered important to know the time trends in incidences in Japan in the future, at least the trend of the major cancers. In this study, after estimating future incidences based on the number of cancer incidences all over Japan, we assumed that these projections were for registration rates of 95% to 70%, and reported trends in incidences. The number of cancer incidences reported by the National Cancer Center, except for rectum cancer in males and females and colon cancer in males, showed an increase from 2002 to 2003, particularly a significant increase in prostate cancer.

Until the number of cancer incidences based on hospital-based cancer registries is reported with stable registration accuracy and at stable registration rates in the future, it is difficult to judge whether this increase is a real increase or it looks like an increase because the registration rate is not 100%. It is necessary to observe variations in the number of cancer incidences continuously.

### Acknowledgments

We thank very much Professor Takashi Nakamura, who provided detailed data onf APC analysis and commented much on the study. Professor Midori Soda at Radiation Effects Research Foundation in Nagasaki gave us the valuable comments. In addition, this study was supported by a Health and Labour Sciences Research Grant for Clinical Cancer Research (H19-009) and a *Mai Utada et al* Cooperative Research from the Institute of Statistical Mathematics (21-CR-2024).

# References

- Foundation for Promotion of Cancer Research (2008). Cancer Statistics.(http://www.fpcr.or.jp/publication/statistics.html), Feb, 1.
- Matsuda T, Marugame T, Kamo K, et al (2004). Cancer incidence and incidence rates in Japan in 2003: based on date from 13 population-based cancer registries in the monitoring of cancer incidence in Japan (MCIJ) Project. *Jpn J Clin Oncol*, **39**, 850-8.
- Kamo K, Kaneko S, Satoh K, et al (2007). A mathematical estimation of true cancer incidence using data from population-based cancer registries. *Jpn J Clin Oncol*, **37**, 150-5.
- Kamo K (2007). The completeness of cancer registry in Japan. WHERE?
- Kato H, Sobue T, Katanoda K, et al (2007). Cancer statistics in Japan 2007. Eds the editorial board of the cancer statistics in Japan. *Foundation Promotion Cancer Res (FRCR)*, Tokyo, 5-9.
- Ministry of Health, Labour and Welfare (2010). Population survey report. (http://www.mhlw.go.jp/toukei/saikin/hw/ jinkou/suii01/index.html), Feb, 1.
- National Cancer Center (2009). Center for cancer control and information service. (http://ganjoho.jp/professional/ statistics/statistics.html), Nov. 27.
- Ohno Y, Nakamura T, Murata K, et al (2004). Prediction of cancer incidence in Japan. In 'Cancer Statistics Report 2004', Eds Oshima A, Kuroishi T, Tajima K. Shinohara Shuppan, Tokyo, 201-17.
- Nakamura T (1982). Bayesian cohort models for general cohort table analyses. Ann Inst Statistical Mathematics, 29, 77-97.
- Nakamura T (2002). Cohort analysis of data obtained using a multiple choice question. In 'Measurement and Multivariate Analysis', Eds Nishisato S, Baba Y, Bozdogan H, et al. *Springer-Verlag*, Tokyo, 241-8.
- United Nation Population Division (2008). World population prospects (http://www.un.org/esa/population/unpop.htm) Dec. 1.