RESEARCH COMMUNICATION

Comparison of Trends in Cancer Incidence and Mortality in Osaka, Japan, Using an Age-Period-Cohort Model

Yuri Ito[1]*, Akiko Ioka[1], Tomio Nakayama[1], Hideaki Tsukuma[1], Takashi Nakamura[2]

Abstract

Background. We aimed to estimate the effects of age, period and birth cohort on trends in cancer incidence and death for all sites and selected sites of cancer in Osaka using an age-period-cohort model. Methods. Cancer incidence data during 1968-2003 were obtained from the Osaka Cancer Registry, and cancer mortality with population data in Osaka during 1968-2007 were obtained from vital statistics departments. We estimated age, period and birth cohort effects for incidence and mortality using Nakamura's Bayesian Poisson age-period-cohort model. Results. For most sites of cancer, linear ageing effects were observed, the exceptions being breast and cervix which levelled-off at around 40 years old, while period effects were small. Decreasing cohort effects were observed in stomach and liver cancer. Cohort effects peaked at the generation born in the early 1950s for colorectal, lung, breast cancers. For most sites of cancer, incidence and mortality showed similar trends, but in the late cohorts for cervical cancer, cohort effects decreased in mortality, while increasing in incidence. Conclusion. Period effects reflecting immediate effects to cancer incidence and mortality, such as development of the effective treatment and screening programme were stable in most sites of cancer. Cohort effects influenced by long-term risk factors were prominently observed for every site, decrease in stomach and liver cancer cases being related to reduction in risk factor prevalence. Cancer control activities could be evaluated through the results, indicating utility for future cancer control planning.

Keywords: Cancer incidence and mortality - time trends - age-period cohort model - joinpoint analysis - Japan

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Introduction

Monitoring trends in cancer incidence and mortality is important to plan and evaluate cancer control policy. Cancer mortality data was monitored in all prefectures from vital statistics and was used in cancer control planning. Cancer incidence data, however, are available in some prefectures where population-based cancer registries have been conducted, and then the availability for cancer control planning was limited in some local governments. The Osaka Cancer Registry has a long history since 1962 and has exploited the registry data for the local cancer control activities. We used to evaluate the trends of age-standardised incidence and mortality. Trend analysis using only age-standardised rate cannot examine how the change of the distribution of age and birth cohort and period at diagnosis or death affected the whole trends. We aimed to estimate the effects of age, period and birth cohort on trends in cancer incidence and death for all sites and selected sites of cancer in Osaka, using an age-period-cohort model. Age-period-cohort model has been used to evaluate trends in cancer incidence and mortality for a long time. Most of the previous studies evaluate only incidence or mortality. In this study, we examined the both incidence and mortality trends and evaluated the cancer control activities in Osaka, Japan.

Materials and Methods

Data sources

Cancer incidence data during 1968-2003 were obtained from the Osaka Cancer Registry, and cancer mortality data with population data in Osaka during1968-2007 were obtained from vital statistics.

Statistical analysis

Joinpoint regression model. First, we applied annual age-standardised incidence and mortality rates in 1968-2007 to joinpoint regression model to show trends using a conventional approach for all ages. This is a piecewise log linear regression model, which is able to identify the years when the trends in incidence or mortality rate statistically changed, using the established Joinpoint 3.3 package (Kim et al., 2000; US National Cancer Institute, 2008).

*[1]Department of Cancer Control and Statistics, Osaka Medical Centre for Cancer and Cardiovascular Diseases, Osaka, [2]Department of Data Science, Institute of Statistical and Mathematics, Tokyo, Japan *For correspondence : itou-yu2@mc.pref.osaka.jp*

Age-period-cohort model. The 5-year age specific incidence and mortality rate were applied to the age-period-cohort model. We estimated age, period and birth cohort effects using Nakamura's Bayesian Poisson age-period-cohort model (BAPC model)(Nakamura, 1986) as follows:

$$y_{ij} \sim Poisson(\lambda_{ij}), i = 1,...,I,\ j = 1,...,J$$

$$\log \lambda_{ij} = \log P_{ij} + \beta^G + \beta_i^A + \beta_j^P + \sum_{k=1}^{K} w_{ij,k}\beta_k^C$$

$$\sum_{i=1}^{I} \beta_i^A = \sum_{j=1}^{J} \beta_j^P = \sum_{i=1}^{I}\sum_{j=1}^{J} w_{ij,k}\beta_k^C = 0, \quad \sum_{k=1}^{K} w_{ij,k} = 1$$

where y_{ij} is the number of observed deaths or incidence in the ith age group of jth period and are assumed to have a Poisson distribution with a mean λ_{ij} and an offset P_{ij}, the size of the population at risk. The parameters β^G, β_i^A, β_j^P and β_k^C are the grand mean, age, period and cohort effect, respectively. The weight $w_{ij,k}$ (≥0) is introduced to analyse a set of data arranged in general cohort table whose range of age group is not equal to the interval between periods and determined by the extent of overlap between the cohort ranges of data cell (i,j) and the kth cohort effect parameter.

As birth cohorts are determined from period and age, the relation among age, period and cohort causes an identification problem in that the linear components of age, period and cohort effects cannot be uniquely separated. Among many researchers to entangle this problem, Nakamura's BAPC model overcomes the problem by using an assumption that the effects change gradually or minimizing the weighted sum of squares of first-order differences of the effects parameters:

$$\frac{1}{\sigma_A^2}\sum_{i=1}^{I-1}\left(\beta_i^A - \beta_{i+1}^A\right)^2 + \frac{1}{\sigma_P^2}\sum_{j=1}^{J-1}\left(\beta_j^P - \beta_{j+1}^P\right)^2 + \frac{1}{\sigma_C^2}\sum_{k=1}^{K-1}\left(\beta_k^C - \beta_{k+1}^C\right)^2$$

The hyperparameters are introduced to control the smoothness of the parameters by minimizing Akaike's Bayesian Information Criterion (ABIC, (Akaike, 1980)). This assumption enables us to estimate not only the non-linear components but also the linear component of the effects.

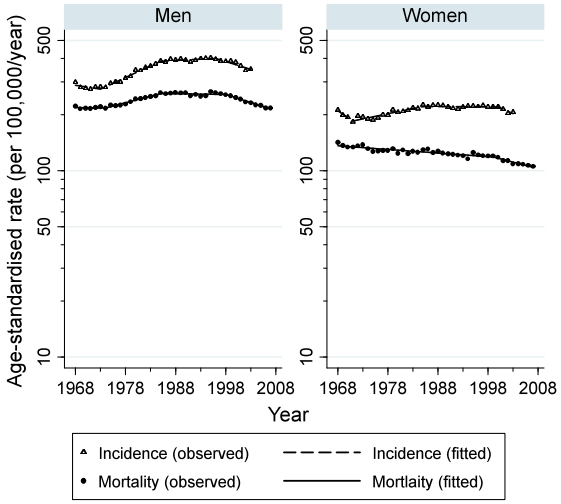

Figure 1. Trends in Age-standardised Incidence and Mortality Rates for All Sites of Cancer

Results

Joinpoint regression model

The results of joinpoint regression analysis are shown in Table 1 for trends of mortality and in Table 2 for trends of incidence. The trends in the overall cancer incidence and mortality by sex are shown in Figure 1. The trends in incidence and mortality by sex and cancer sites are shown in Figure 2.

The overall cancer mortality for men increased until 1985, and levelled-off between 1985 and 1998, then decreased by -2.0% per year since 1998. Similar trends were observed for the overall incidence. For women, the

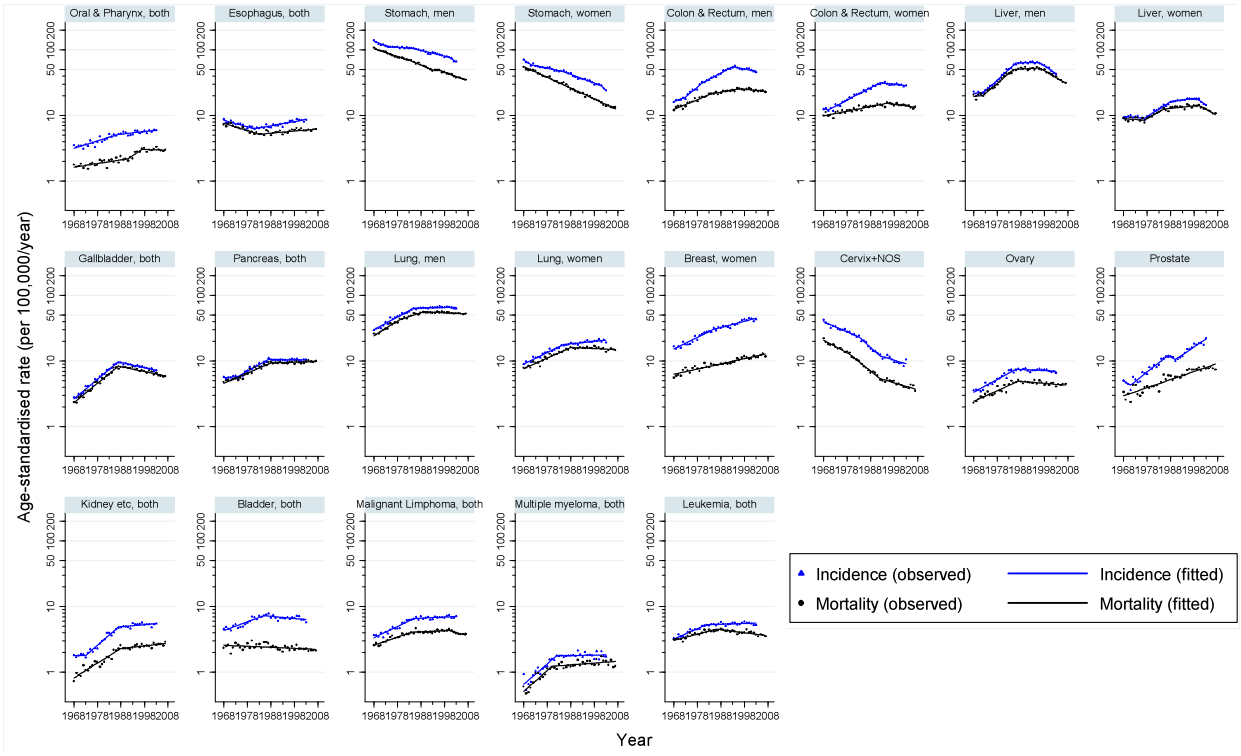

Figure 1. Trends in Age-standardised Incidence and Mortality Rates by Sex and Selected Cancer Site

trends of incidence increased by 1.3% per year between 1971 and 1985 ($P < 0.05$), then levelled-off from 1998. The overall mortality rates for women decreased gradually throughout. Both incidence and mortality for most sites of cancer decreased or levelled-off, while incidence for cancers of oral and pharynx, oesophagus, kidney renal pelvis, prostate, lung (women) and breast still increased.

Age-period-cohort model

All sites of cancer: For both incidence and mortality in both sexes, the age effect increased linearly with increasing age (Figure 3, left). The period effect was negligible (Figure 3, middle), while the cohort effect showed distinctive trends (Figure 3, right). The cohort effect in men increased for those who were born in 1900-1930s, and decreased for those born in mid-1930s to

Table 1 Trends in Age-standardised (Japanese Model Population in 1985) Mortality Rates with Joinpoint Analysis for 1975-2007 in Osaka, Japan, by Sex and Cancer Sites for All Ages

	ICD-10 code	Segment 1		Segment 2		Segment 3		Segment 4		AAPC[b]	
		Years	APC[a]	Years	APC[a]	Years	APC[a]	Years	APC[a]	1st	2nd
Both Sexes											
All sites	C00-96	1968-1976	-0.4	1976-1985	0.9*	1985-1998	-0.2	1998-2007	-1.69*	-1.7*	-1.7*
Oral and Pharynx	C00-14	1968-1991	1.3*	1991-1997	5.6*	1997-2007	-0.3			-0.3	-0.3
Esophagus	C15	1968-1983	-2.5*	1983-2007	0.7*					0.7*	0.7*
Stomach	C16	1968-1993	-3.3*	1993-2007	-2.9*					-2.9*	-2.9*
Colon	C18	1968-1993	3.7*	1993-2007	-0.7*					-0.7*	-0.7*
Rectum	C19-20	1968-1981	1.4*	1981-2007	-0.3 *					-0.3*	-0.3*
Colon & Rectum	C18-20	1968-1991	2.4*	1991-2007	-0.2					-0.2	-0.2
Liver	C22	1968-1976	2.7*	1976-1985	7.0*	1985-1997	0.5	1997-2007	-4.50*	-4.5*	-4.5*
Gallbladder	C23-24	1968-1987	7.0*	1987-2007	-1.7*					-1.7*	-1.7*
Pancreas	C25	1968-1988	3.7*	1988-2007	0.3					0.3	0.3
Larynx	C32	1968-1986	-3.9*	1986-1992	-8.2*	1992-1995	12.4	1995-2007	-4.75*	-4.7*	-4.7*
Lung	C33-34	1968-1979	4.7*	1979-1989	2.7*	1989-2007	-0.2			-0.2*	-0.2*
Kidney Renal Pelvis	C64-66, 68	1968-1988	5.3*	1988-2007	0.9*					0.9*	0.9*
Urinary Bladder	C67	1968-2007	-0.4*							-0.4*	-0.4*
Malignant Lymphoma	C81-85, 96	1968-1984	2.9*	1984-2000	0.4	2000-2007	-2.3*			-1.7*	-2.3*
Multiple Myeloma	C88-90	1968-1980	7.6*	1980-2007	0.6*					0.6*	0.6*
Leukemia	C91-95	1968-1986	2.2*	1986-2007	-1.0*					-1.0*	-1.0*
Men											
All sites	C00-96	1968-1974	-0.1	1974-1985	1.6*	1985-1998	-0.1	1998-2007	-2.0*	-2.0*	-2.0*
Esophagus	C15	1968-1971	4.3	1971-1981	-2.9*	1981-2007	0.9*			0.9*	0.9*
Stomach	C16	1968-1984	-2.7*	1984-1993	-3.5*	1993-1996	-0.4	1996-2007	-3.1*	-3.1*	-3.1*
Colon	C18	1968-1993	4.4*	1993-2007	-1.1*					-1.1*	-1.1*
Rectum	C19-20	1968-1980	2.6*	1980-2007	0.0					0	0
Colon & Rectum	C18-20	1968-1984	3.5*	1984-1996	1.5*	1996-2007	-0.8			-0.8	-0.8
Liver	C22	1968-1972	1.0	1972-1985	7.2*	1985-1996	0.5	1996-2007	-4.7*	-4.7*	-4.7
Lung	C33-34	1968-1979	5.3*	1979-1989	2.8*	1989-2007	-0.4*			-0.4*	-0.4*
Prostate	C61	1968-2007	2.9*							2.9*	2.9*
Malignant Lymphoma	C81-85, 96	1968-1984	3.4*	1984-2007	-0.4					-0.4	-0.4
Multiple Myeloma	C88-90	1968-1973	21.5*	1973-2003	1.9*	2003-2007	-10.4			-3.8	-10.4
Leukemia	C91-95	1968-1984	3.3*	1984-2007	-0.7*					-0.7*	-0.7*
Women											
All sites	C00-C96	1968-1999	-0.4*	1999-2007	-1.6*					-1.4*	-1.6*
Esophagus	C15	1968-1991	-3.5*	1991-2007	0.1					0.1	0.1
Stomach	C16	1968-2007	-3.7*							-3.7*	-3.7*
Colon	C18	1968-1995	3.0*	1995-2007	-1.2*					-1.2*	-1.2*
Rectum	C19-20	1968-2007	-0.7*							-0.7*	-0.7*
Colon & Rectum	C18-20	1968-1995	1.7*	1995-2007	-1.1*					-1.1*	-1.1*
Liver	C22	1968-1977	-0.5	1977-1985	4.9*	1985-2000	0.9*	2000-2007	-4.6*	-3.4*	-4.6*
Lung	C33-34	1968-1988	3.8*	1988-2007	-0.4					-0.4	-0.4
Breast	C50	1968-2007	1.8*							1.8*	1.8*
Cervix Uteri	C53	1968-1981	1.5	1981-2007	-0.8*					-0.8*	-0.8*
Corpus Uteri	C54	1968-2007	5.7*							5.7*	5.7*
Uterus	C53-C55	1968-1993	-4.9*	1993-2007	-1.2*					-1.2*	-1.2*
Cervix + Uterus NOS	C53, 55	1968-1979	-4.3*	1979-1992	-6.4*	1992-2007	-2.4*			-2.4*	-2.4*
Ovary	C56	1968-1987	3.8*	1987-2007	-0.7*					0.7*	-0.7*
Malignant Lymphoma	C81-85, 96	1968-1988	2.6*	1988-2007	-0.2					-0.2	-0.2
Multiple Myeloma	C88-90	1968-1983	5.8*	1983-2007	0.5					0.5	0.5
Leukemia	C91-95	1968-1988	1.3*	1988-2007	-1.5*					-1.5*	-1.5*

*Statistically significant; [a]Annual percentage change in the segment; [b]Average annual percentage change; 1st, 1998-2007; 2nd, 2003-2007

Table 2. Trends in Age-standardised (Japanese Model Population in 1985) Incidence Rates with Joinpoint Analysis for 1975-2007 in Osaka, Japan, by Sex and Cancer Sites for all Ages

	ICD-10 code	Segment 1		Segment 2		Segment 3		Segment 4		AAPC[b]	
		Years	APC[a]	Years	APC[a]	Years	APC[a]	Years	APC[a]	1st	2nd
Both Sexes											
All sites (incl. *in situ*)	C00-96[2]	1968-1971	-3.5*	1971-1986	1.9*	1986-1999	0.1	1999-2003	-2.6*	-1.1*	-2.6*
All sites	C00-96	1968-1971	-3.8*	1971-1986	2.0*	1986-1999	0.0	1999-2003	-2.6*	-1.2*	-2.6*
Oral & Pharynx	C00-14	1968-1987	2.6*	1987-2003	0.9*					0.9*	0.9*
Esophagus	C15	1968-1981	-2.2*	1981-2003	1.5*					1.5*	1.5*
Stomach	C16	1968-1971	-5.8*	1971-1985	-1.2*	1985-2001	-2.3*	2001-2003	-6.9*	-3.4*	-4.7*
Colon	C18	1968-1992	6.4*	1992-2003	-1.0*					-1.0*	-1.0*
Rectum	C19-20	1968-1972	-0.5	1972-1981	4.7*	1981-1994	1.8*	1994-2003	-1.4*	-1.4*	-1.4*
Colon & Rectum	C18-20	1968-1972	1.5	1972-1980	6.2*	1980-1993	4.3*	1993-2003	-1.3*	-1.3*	-1.3*
Liver	C22	1968-1976	2.4*	1976-1985	8.2*	1985-1996	1.0*	1996-2003	-5.0*	-3.7*	-5.0*
Gallbladder	C23-24	1968-1987	7.1*	1987-2003	-1.9*					-1.9*	-1.9*
Pancreas	C25	1968-1974	0.8	1974-1987	4.7*	1987-2003	-0.1			-0.1	-0.1
Larynx	C32	1968-2003	-1.8*							-1.8*	-1.8*
Lung	C33-34	1968-1978	5.0*	1978-1987	2.9*	1987-2003	0.4*			0.4*	0.4*
Renal + Pelvis	C64-66, 68	1968-1973	0.0	1973-1987	7.5*	1987-2003	0.7*			0.7*	0.7*
Urinary Bladder	C67	1968-1985	3.1*	1985-2003	-0.8*					-0.8*	-0.8*
Malignant Lymphoma	C81-85, 96	1968-1985	4.1*	1985-2003	0.4					0.4	0.4
Multiple Myeloma	C88-90	1968-1982	7.4*	1982-2003	0.2					0.2	0.2
Leukemia	C91-95	1968-1982	3.7*	1982-2003	0.2					0.2	0.2
Colon[1]	C18[3]	1968-1994	6.3*	1994-2003	-1.4*					-1.4*	-1.4*
Rectum[1]	C19-20[4]	1968-1972	-0.6	1972-1980	4.9*	1980-1995	2.1*	1995-2003	-1.5*	-1.1*	-1.5*
Colon & Rectum[1]	C18-20[5]	1968-1972	1.5	1972-1980	6.2*	1980-1994	4.4*	1994-2003	-1.0*	-1.0*	-1.0*
Men											
All sites (incl. in situ)	C00-96[2]	1968-1973	-1.0	1973-1985	2.9*	1985-1998	0.3	1998-2003	-2.7*	-1.4*	-2.7*
All sites	C00-96	1968-1973	-1.0	1973-1985	2.9*	1985-1996	0.3	1996-2003	-1.9 *	-1.4*	-1.9*
Esophagus	C15	1968-1980	-1.9*	1980-2003	1.7*					1.7*	1.7*
Stomach	C16	1968-1974	-3.3*	1974-1984	-0.4	1984-2000	-2.0*	2000-2003	-5.4*	-3.1*	-4.6*
Colon	C18	1968-1992	7.1*	1992-2003	-1.6*					-1.6*	-1.6*
Rectum	C19-20	1968-1971	-0.7	1971-1981	5.2*	1981-1994	2.1*	1994-2003	-1.3*	-1.3*	-1.3*
Colon & Rectum	C18-20	1968-1973	3.2*	1973-1980	7.3*	1980-1993	4.5*	1993-2003	-1.6*	-1.6*	-1.6*
Liver	C22	1968-1972	0.2	1972-1986	7.8*	1986-1996	0.2	1996-2003	-5.5*	-4.3*	-5.5*
Lung	C33-34	1968-1985	4.6*	1985-2003	0.1					0.1	0.1
Prostate	C61	1968-1971	-4.7	1971-1987	6.8*	1987-1990	-5.0	1990-2003	5.7*	5.7*	5.7*
Malignant Lymphoma	C81-85, 96	1968-1972	-1.4	1972-1983	5.3*	1983-2003	0.1			0.1	0.1
Multiple Myeloma	C88-90	1968-1982	8.1*	1982-2003	0.0					0.0	0.0
Leukemia	C91-95	1968-1982	4.3*	1982-2003	0.3					0.3	0.3
Colon[1]	C18[3]	1968-1994	7.0*	1994-2003	-2.1*					-2.1*	-2.1*
Rectum[1]	C19-20[4]	1968-1971	-0.7	1971-1981	5.2*	1981-1996	2.2 *	1996-2003	-1.9*	-1.0	-1.9*
Colon & Rectum[1]	C18-20[5]	1968-1973	3.1*	1973-1980	7.3*	1980-1995	4.5*	1995-2003	-2.0*	-1.3*	-2*
Women											
All sites (incl. in situ)	C00-96[2]	1968-1971	-3.6*	1971-1985	1.3*	1985-2000	0.0	2000-2003	-2.5	-0.8	-1.8
All sites	C00-96	1968-1971	-4.1*	1971-1985	1.3*	1985-2000	0.0	2000-2003	-2.7	-0.9	-2.0
Esophagus	C15	1968-1992	-2.4*	1992-2003	1.3					1.3	1.3
Stomach	C16	1968-1971	-5.5*	1971-1985	-1.7*	1985-2001	-3.1*	2001-2003	-7.9	-4.2*	-5.5*
Colon	C18	1968-1992	5.7*	1992-2003	-0.5					-0.5	-0.5
Rectum	C19-20	1968-1991	2.3*	1991-2003	-1.6*					-1.6*	-1.6*
Colon & Rectum	C18-20	1968-1970	-2.5	1970-1992	4.4*	1992-2003	-0.9*			-0.9*	-0.9*
Liver	C22	1968-1977	-0.6	1977-1988	5.4*	1988-1999	1.1*	1999-2003	-6.0*	-2.1*	-6.0*
Lung	C33-34	1968-1985	4.1*	1985-2003	0.9*					0.9*	0.9*
Breast	C50	1968-1985	4.2*	1985-2003	2.2*					2.2*	2.2*
Cervix Uteri	C53	1968-1981	-1.3*	1981-2000	-5.7*	2000-2003	4.2			-2.5	1.7
Corpus Uteri	C54	1968-1970	-22.1*	1970-1980	11.7*	1980-2003	1.9*			1.9*	1.9*
Uterus	C53-55	1968-1983	-2.7*	1983-1992	-5.5*	1992-2003	-1.1			-1.1	-1.1
Ovary	C56	1968-1986	4.6*	1986-2003	-0.4					-0.4	-0.4
Malignant Lymphoma	C81-85, 96	1968-1986	4.4*	1986-2003	0.7*					0.7*	0.7*
Multiple Myeloma	C88-C90	1968-1983	6.7*	1983-2003	0.1					0.1	0.1
Leukemia	C91-C95	1968-1982	3.1*	1982-2003	0.1					0.1	0.1
Colon[1]	C18[3]	1968-1994	5.6*	1994-2003	-0.8					-0.8	-0.8
Rectum[1]	C19-20[4]	1968-1992	2.3*	1992-2003	-1.4*					-1.4*	-1.4*
Colon & Rectum[1]	C18-20[5]	1968-1970	-2.5	1970-1993	4.4*	1993-2003	-0.6			-0.6	-0.6
Breast[1]	C50[6]	1968-1985	4.2*	1985-2003	2.4*					2.4*	2.4*
Cervix Uteri[1]	C53[7]	1968-1979	0.7	1979-2001	-4.5*	2001-2003	9.5			-1.6	2.3
Uterus[1]	C53-C55[7]	1968-1980	-1.4*	1980-1993	-4.3*	1993-2003	-1.1			-1.1	-1.1
Cervix + Uterus NOS[1]	C53, C55[7]	1968-1981	-2.0*	1981-1989	-6.0*	1989-2001	-3.5*	2001-2003	7.0	-1.3	1.6
Cervix + Uterus NOS	C53, C55	1968-1983	-3.5*	1983-1992	-7.1*	1992-2003	-2.5*			-2.5*	-2.5*

*Statistically significant; [a]Annual percentage change in the segment; [b]Average annual percentage change; 1st, 1998-2007; 2nd, 2003-2007; [1]including in situ; [2]D00-09; [3]D010, [5]D011-12; [5]D011-13; [6]D05; [7]D06

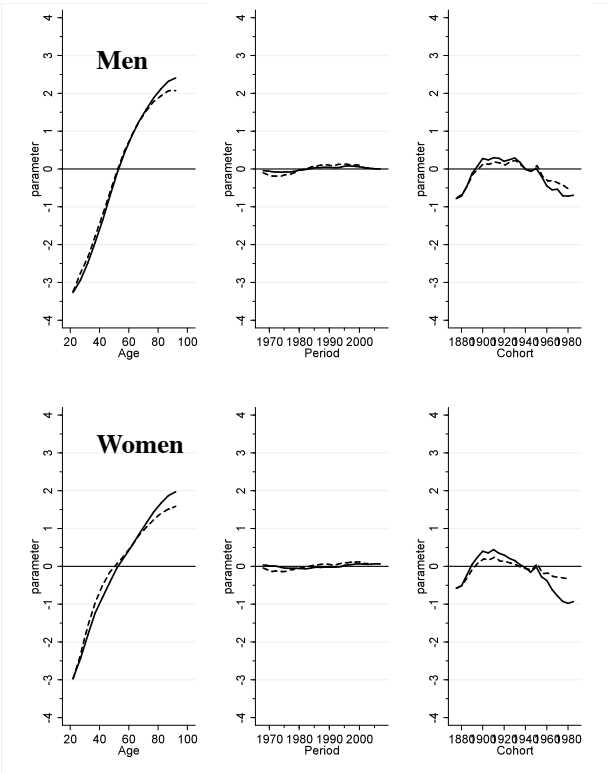

Figure 3. Age, Period and Birth Cohort Effects for all Sites of Cancer Dotted line, incidence, solid, mortality

mid-1940s. A small peak was observed at the cohort born in 1950s and then decreased. The cohort effect in women peaked at the cohort born in 1900-1910s and decreased with small re-ascending at the cohort of 1950s. The cohort effect of the latest born after 1960s has decreased; the trend was more remarkable in mortality than in incidence.

Stomach

Age effects increased as ageing. For incidence, the effects were levelled-off after age of 70. Period effects were stable. Cohort effects decreased dramatically after the 1900s birth cohort for both incidence and mortality (Figure 4).

Colon and rectum

Age effects showed linear increase for incidence and mortality in both sexes (Figure 5, left). For incidence, distinctive period effects were observed. The period effects for incidence increased until the mid-1990s, and then decreased.

For mortality, similar period effects were observed, but more moderate (Figure 5, middle). Cohort effects increased rapidly until the generation born in the 1900s, and then levelled-off/moderately increased. After peaking vwith the generation born in the 1950s, cohort effects were decreased in the latest generation (Figure 5, right).

Liver

Almost all effects showed similar trends between incidence and mortality. Increasing age effects were observed. Period effects increased until the middle of the 1980s, and decreased from the end of the 1990s. The cohort effect peaked with the birth cohort in the early 1930s and decreased immediately. Both sexes

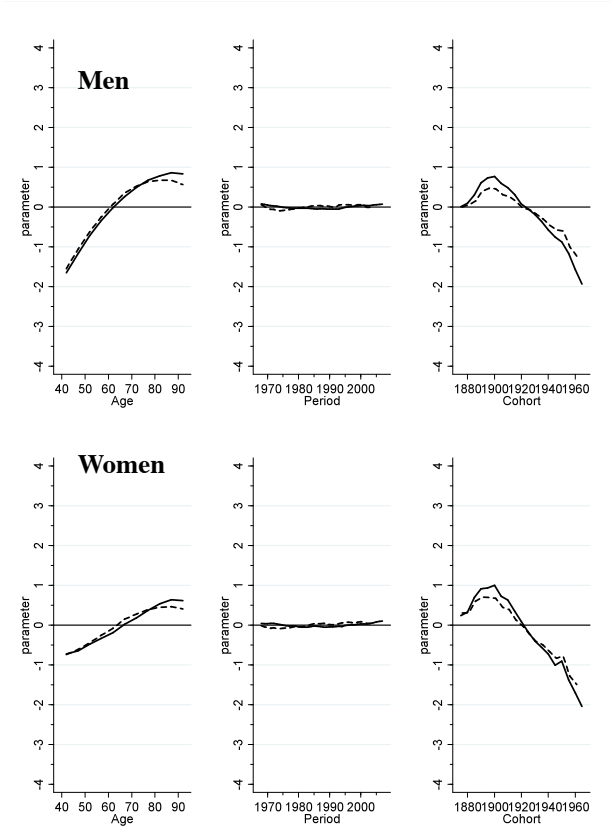

Figure 4. Age, Period and Birth Cohort Effects of Stomach Cancer in Osaka, Japan Dotted line, incidence, solid, mortality

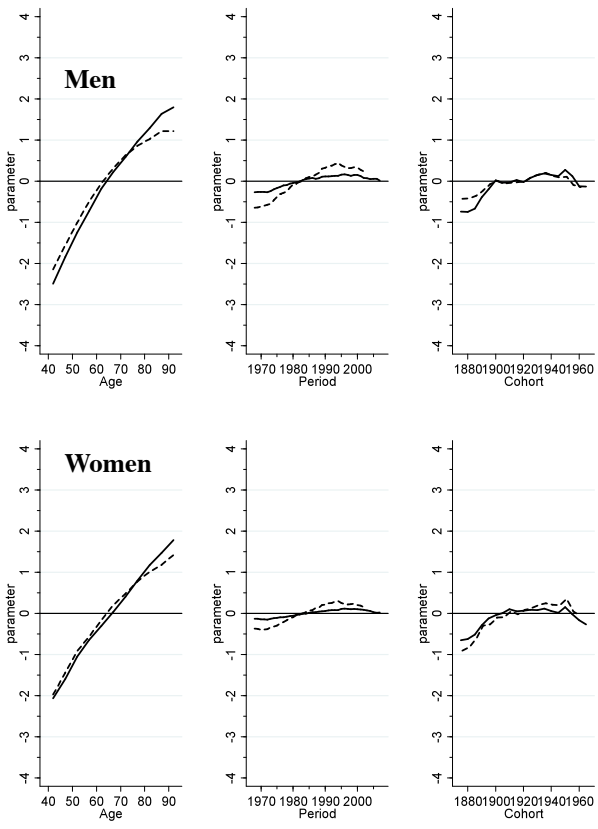

Figure 5. Age, Period and Birth Cohort Effects of Colorectal Cancer in Osaka, Japan Dotted line, incidence, solid, mortality

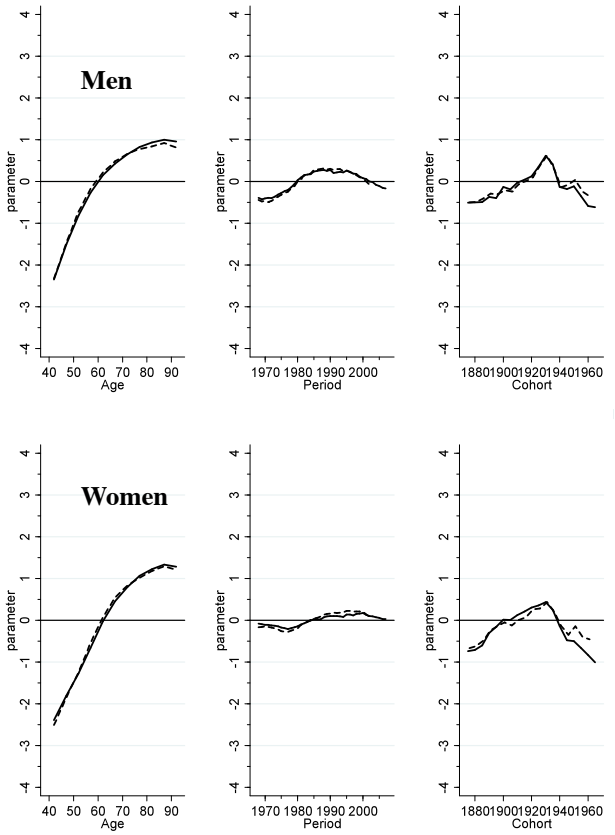

Figure 6. Age, Period and Birth Cohort Effects of Liver Cancer in Osaka, Japan

showed similar trends, but period effects in women were moderate (Figure 6).

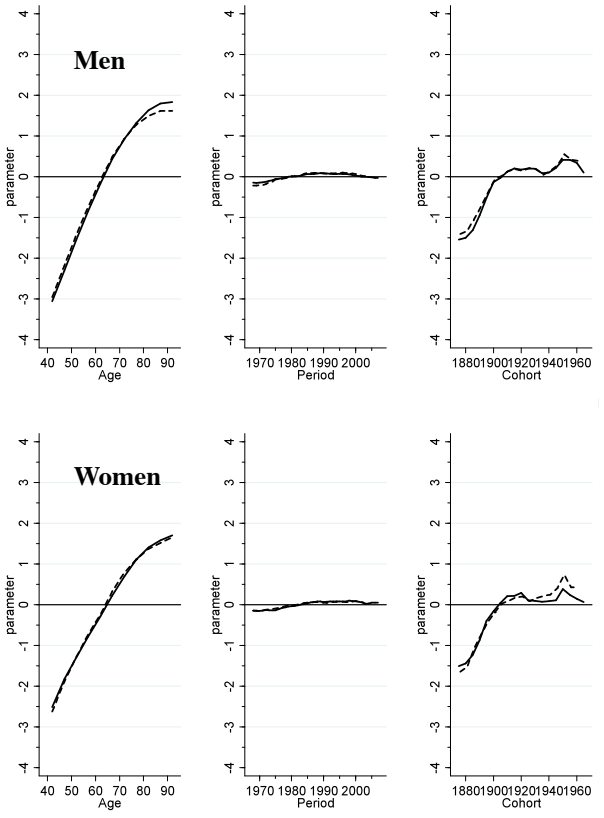

Figure 7. Age, Period and Birth Cohort Effects of Lung Cancer in Osaka, Japan

Lung

Almost all effects showed similar trends between incidence and mortality. Ageing effect was similar with other sites of cancer. Period effects were relatively small. For men, Cohort effect increased rapidly until the 1900s birth cohort and then levelled-off. Subsequently a dip in incidence in the late 1930s birth cohort was observed. The cohort effect then increased again and peaked with the 1950s cohort. The latest cohort effects (1950-60s) were still striking. For women, these effects showed similar trends in men. A small dip in the cohort born in the late 1920s was observed, and the cohort effects peaked with the1950s cohort (Figure 7).

Breast

Ageing effects showed different trends in incidence and mortality (Figure 8). For mortality, rapid increase of age effect until 50s and then moderate increase until 80s, subsequently increased rapidly again. On the other hand, age effects for incidence showed levelled-off after 40s. For mortality trends, age-cohort model was selected. This means that there was no period effect for breast cancer mortality. For incidence, small increase of period effects was observed. Cohort effects increased and peaked with the cohort born in the 1950s, and then slightly decreased.

Cervix (C53+C55)

Age and cohort effects showed different trends in incidence and mortality (see Figure 10). Ageing effect for mortality increased until the middle 50s and then levelled-off. While ageing effects for incidence peaked with the age of 40 and then decreased. Period effects were small for both incidence and mortality. Cohort effects peaked with the cohort born in the 1900s and subsequently decreased. Cohort effects for incidence

Figure 8. Age, Period and Birth Cohort Effects of Breast Cancer in Women in Osaka, Japan

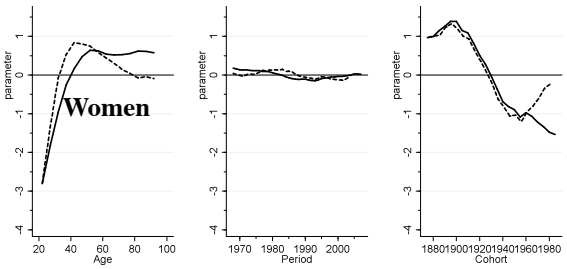

Figure 9. Age, Period and Birth Cohort Effects of Cervical Cancer (ICD 10: C53+C55) in Osaka, Japan

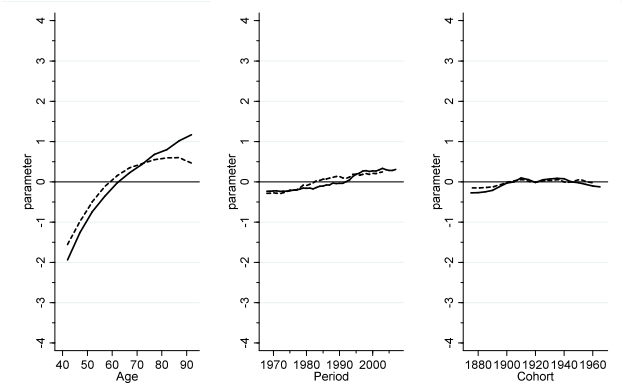

Figure 10. Age, Period and Birth Cohort Effects of Oral/ Pharynx Cancer in Both Sexes in Osaka, Japan

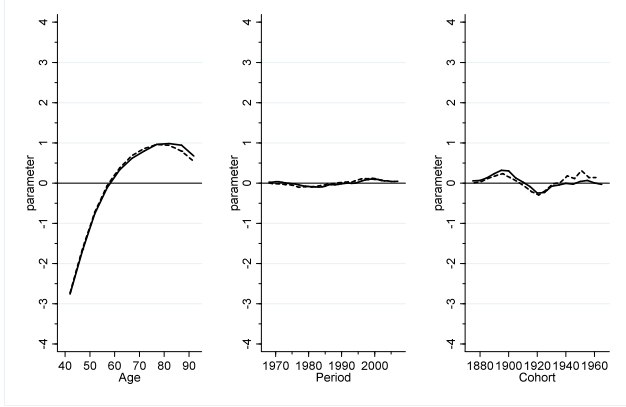

Figure 11. Age, Period and Birth Cohort Effects of Esophageal Cancer in Both Sexes in Osaka, Japan

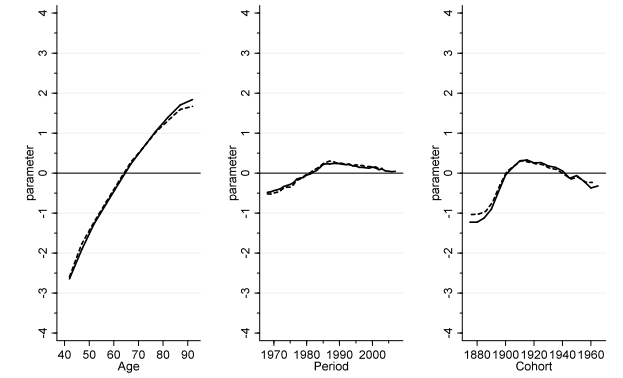

Figure 12. Age, Period and Birth Cohort Effects of Gallbladder Cancer in Both Sexes in Osaka, Japan

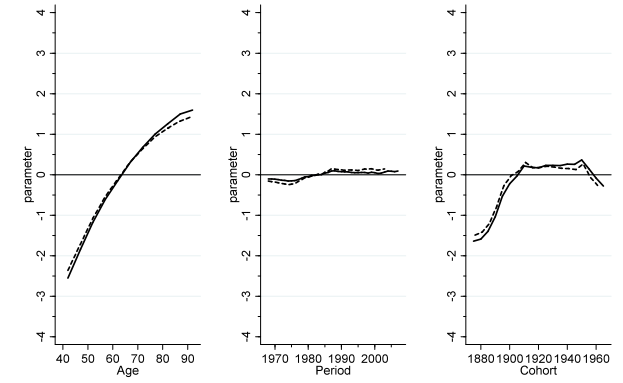

Figure 13. Age, Period and Birth Cohort Effects of Pancreas Cancer in Both Sexes in Osaka, Japan

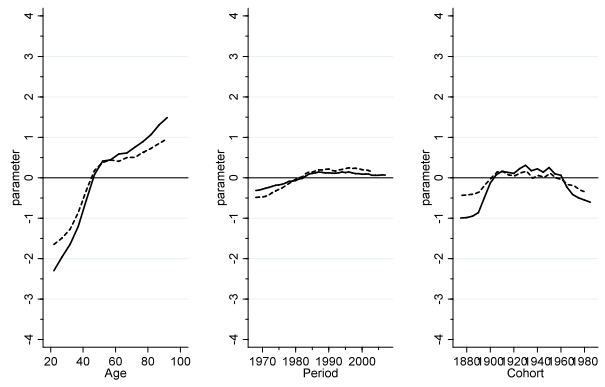

Figure 14. Age, Period and Birth Cohort Effects of Ovarian Cancer in Females in Osaka, Japan

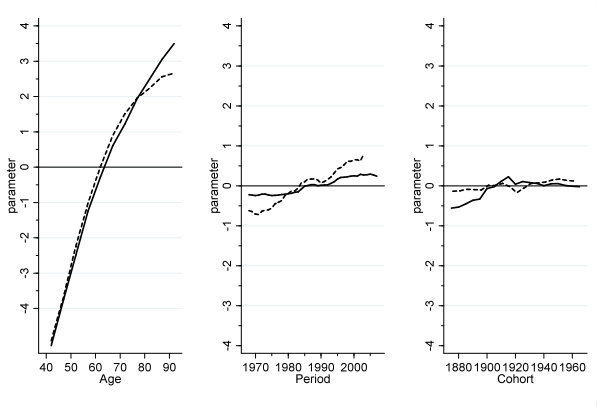

Figure 15. Age, Period and Birth Cohort Effects of Prostate Cancer in Males in Osaka, Japan

increased again after the 1950s birth cohort, while the effects for mortality still decreased. Parameters for age-cohort effects are illustrated in Figure 9.

Other sites of cancer

For oral and pharyngeal cancer in both sexes, increasing period effects were observed for both incidence and mortality (Figure 10). The cohort effects for oesophageal cancer were peaked at the cohort born in 1900s. Small dip was observed at the cohort born in the early 1920s, and then the cohort effects increased in the latest cohort (Figure 11). For gallbladder cancer, the period effects increased until the mid-1980s and then gradually decreased. The cohort effects were higher in the cohort born between 1900s and 1930s (Figure 12). For pancreas cancer, higher cohort effects were observed in the cohorts born in between 1910s and 1950s. (Figure 13)

The period effects were small for ovarian cancer. Decreased cohort effects were observed in the oldest and youngest cohorts. (Figure 14). For prostate cancer, largest aging effects were observed. Strongly increasing period effects were observed especially for incidence, while the cohort effects were small (Figure 15). Similar period effects were observed for trends in kidney cancer incidence with those in prostate cancer. The cohort effects increased until the cohort born in 1910s (Figure 16). For mortality of bladder cancer, the period effects were small. The cohort effects were peaked at the cohort

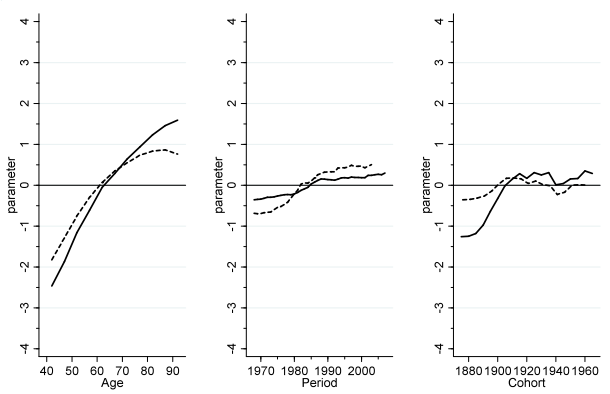

Figure 16. Age, Period and Birth Cohort Effects of Kidney Cancer in Both Sexes in Osaka, Japan

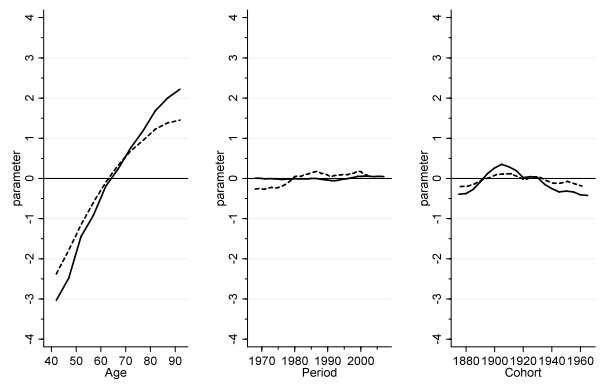

Figure 17. Age, Period and Birth Cohort Effects of Bladder Cancer in Both Sexes in Osaka, Japan

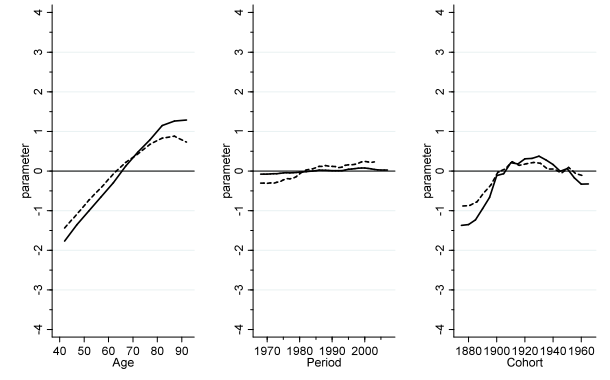

Figure 18. Age, Period and Birth Cohort Effects of Malignant Lymphoma in Both Sexes in Osaka, Japan

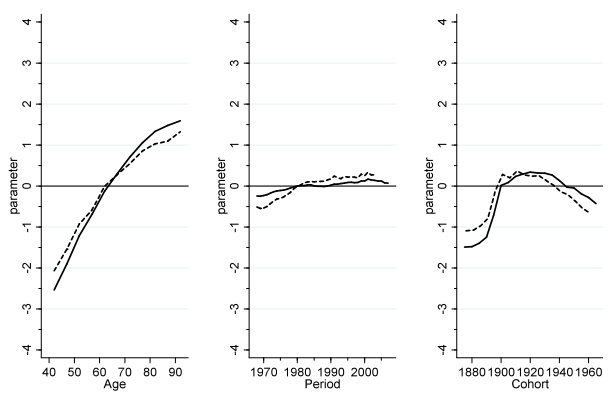

Figure 19. Age, Period and Birth Cohort Effects of Multiple Myeloma in Both Sexes in Osaka, Japan

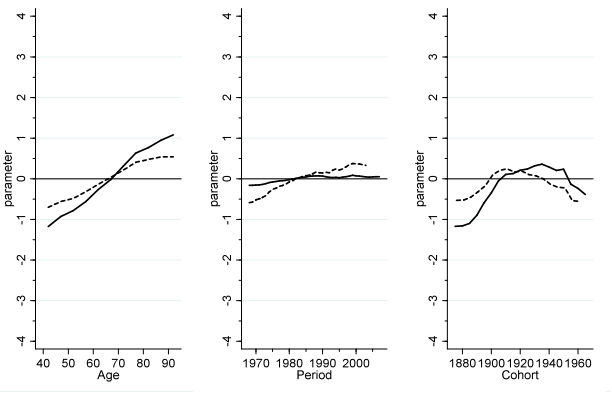

Figure 20. Age, Period and Birth Cohort Effects of Leukemia in Both Sexes in Osaka, Japan

born in 1900s, and then decreased (Figure 17).

Malignant lymphoma, multiple myeloma and leukaemia showed similar trends. Small increase in the period effects were observed for incidence trends but not for mortality. Cohort effects in the latest cohort decreased (Figure 18-20).

Discussion

Ageing effects for incidence and mortality are well-known in biological reason. For most sites of cancer, people increase the risk of growing cancer by ageing. Period effects reflect immediate effects to cancer incidence/mortality such as development of the effective treatment and screening programme. For all sites of cancer, the small period effects were observed. On the other hand, cohort effects reflect distant effects of risk factors such as smoking, dietary habits, and infectious agents. The cohort effects for all sites of cancer showed small peak at the 1950s birth cohort and decreased in the younger generation. The declining cohort effect for incidence and mortality may be mainly related with the decrease of prevalence of cancer risk factors. But the risk factors of cancer varied according to site of cancer. We need precise monitor of the trends by site, comparing with trends in the prevalence of each risk factor.

Remarkable cohort effects strongly related with decrease of the prevalence of the risk factor for stomach cancer, due to improvement of hygiene, the decrease of salt intake (Ministry of Health Labour and Walfare 1975-2007) and the prevalence of *H. pylori* infection (Haruma et al. 1997; Kobayashi et al. 2004). As a result, both age-standardised incidence and mortality rates also showed constant decrease. Small period effects indicated that there was little improvement of treatment and early detection, which should have showed immediate effect for stomach cancer.

Increasing age-standardised incidence and mortality of colorectal cancer until the mid-1990s would be explained as a result of increasing period and cohort effects. Increases of meat intake, obesity and less physical activities were risk factors of colorectal cancer. The prevalence of these risk factors is increasing in Japan, because of the change to Western lifestyle. Smoking is also one of the risk factors of colorectal

cancer. We need further investigation whether the trends of the prevalence of these risk factors corresponded with the trends in incidence and mortality. Trends of period effect indicated possibility of the immediate effect of the risk factor (Westernised lifestyle) to colorectal cancer incidence. This was confirmed at the previous study that Japanese immigrants in the US had higher incidence of colon cancer than Japanese in Japan (Haenszel and Kurihara, 1968; Shimizu et al., 1987). Improvement of diagnostic tools and treatments would be also related with the period effects.

With the liver the earlier increase in period effect could be the influence of improved diagnosis of liver cancer due to the development of diagnostic tools such as ultrasound sonography. The recent decrease was possibly caused by the effect of treatment for viral hepatitis. The influence of the prevalence of risk factors on cohort effects is clearly shown. The birth cohort born in around 1935 was suggested to show highest prevalence of HCV antibodies. The prevalence decreased in the younger generation (Tsukuma et al., 2005). As previous descriptive studies have reported, the highest cohort effect of incidence and mortality of liver cancer was observed at the cohort with the highest prevalence of HCV. The prevalence of HCV has been decreasing, so the incidence of liver cancer will continue to decrease.

Regarding the lung, the observed small period effect suggested that there was no change from immediate effects, such as development of treatment and introduction of effective screening programmes. Cohort effects reflecting change of prevalence of risk factors showed distinctive trends. The observed small dip in the middle 1930s birth cohort was consistent with the generation who had limited access to tobacco after World War II (Marugame et al., 2006). The early 1950s birth cohort peaked at the highest risk of incidence of lung cancer; they will be common age for lung cancer in the near future. Therefore the incidence will start to increase again. In some countries in Europe where tobacco control has been successful, the cohort effect of lung cancer mortality in men decreased dramatically. We need further efforts for tobacco control to decrease lung cancer in Japan (Bray and Weiderpass, 2009).

The pattern of age effect for breast cancer incidence was distinctive, which was different from the pattern in the US and western countries (Holford et al., 2006; Matsuno et al., 2007) and similar with many Asian countries(Sim et al., 2006). The pattern of age effect in mortality showed similar pattern with some other countries (Cayuela et al., 2004; Choi et al., 2006). Increasing cohort effect may be related with the recent Westernised lifestyle in Japan, in addition to dietary factor(Ministry of Health Labour and Walfare 1975-2007), reproductive factor related with the tendency to marry later and decrease of birth rate(Iwasaki et al. 2007; Ministry of Health Labour and Walfare 2010). Period effect in incidence increased in succession, while there was no effect in mortality. In some countries, decreasing period effect for mortality was observed by the improvement of treatment and effective mammography screening.(Cayuela et al., 2004; Niclis et al., 2010; Oberaigner et al., 2010).

In the cervix, decreasing cohort effect for incidence and mortality was mainly due to the improvement of the public hygiene. Since 1983, cervical cancer screening started in Japan as a nationwide public health service. But the proportion of the screening participation has been very low (about 20%). The period effect of cervical cancer incidence and mortality did not show any trend, this is because the screening programme was not successful as some countries in Europe (Quinn et al., 1999; Sasieni and Adams, 1999; Bray et al., 2005). Increase of incidence in the latest cohort possibly explained by the earlier onset of sexual activities, as the results, the prevalence of HPV also increased. Opportunistic cervical cancer screening at the gynaecological checkups also may be related with the increasing cohort effects of the younger generation in incidence.

For prostate, kidney and renal pelvis cancer, the increased period effects in incidence may be explained by the wider spread use of diagnostic tools; PSA for prostate cancer and ultrasound diagnosis for kidney cancer. These earlier detections, however, have not shown the decrease of period effect in mortality yet. For oesophageal, pancreas, kidney cancer, higher cohort effects were observed in the cohort born after 1950s. These trends suggested the possibility of increase in the incidence or mortality for these sites of cancer in future.

Although we have long-term data for both incidence and mortality in Osaka, the timeliness of incidence data is not so well at the moment. These results might not generalise to whole Japanese population, because the cancer incidence and mortality have been a little different in Osaka from other prefectures. Incidence and mortality of some sites of cancer (lung and liver) were higher than those in whole Japan.

We need to keep in mind the change in the completeness of cancer registration in Osaka when we evaluate incidence data. The percentage of under-ascertainment cases was not estimated routinely, but as an alternative index, the percentage of cases registered by death certificate only (% of DCO) was approximately 10-15% and stable in Osaka Cancer Registry during most recently two decades.(Parkin et al. 2005; Curado et al., 2007)

Among many approaches to disentangle the identification problem in the age-period-cohort model, Holford's is the most popular one in the descriptive cancer epidemiology area (Holford, 1985) and some other approaches (Yang et al., 2004; Carstensen, 2007) are still developing. Although Nakamura's method has been scarcely used in articles concerning cancer data, we adopted the method because it tackles straight on and overcome the problem in that the linear components of the three effects cannot be identified. Controlling the weighted sum of squares of first-order differences of the parameters as small as possible is a key to overcome the identification problem and Nakamura's method realizes to separate the three effects by using the framework of Bayesian approach and the minimization of the information criterion ABIC. When we compare such results, we need to pay close attention to the difference between the methods. In near future, we will need to

evaluate the difference between those methods and Nakamura's one.

In conclusion, this is the first report to show the effects of age, period and birth cohort using both incidence and mortality for various sites of cancer in Japan. Age-period-cohort model is useful approach to show these effects separately. We could evaluate cancer control activities through the results and can exploit next cancer control planning.

Acknowledgements

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