

blood-borne infection (3). Information in this regard may be helpful to countries where HCV-related HCC is endemic, such as Mongolia, Myanmar and Taiwan.

Another example is lung cancer. Many Asian countries have high smoking rates in males. Male smoking rates in Japan have been decreasing, and the incidence of lung cancer has been decreasing since 1993, and also reduced incidence of squamous cell carcinoma because of a change from non-filter to filter cigarettes. The incidence rate of squamous cell carcinoma has been decreasing since 1994, whereas the incidence rate of adenocarcinoma increased until 1998, after which it plateaued. It took nearly 30 years for the decrease in non-filtered cigarettes to translate into a decrease in squamous cell carcinoma. Although it takes a long time, anti-smoking policies reduce the incidence of lung cancer. Evidence of this has been presented in Western countries, and it is important to advance such policies in Asia, as well, in order to reduce lung cancer.

A study group financially supported by a Grant-in-Aid for Comprehensive Cancer Control from Japanese Ministry of Health, Labor and Welfare conducted a collaborative study using a population-based cancer registry in East Asia (4). They have reported a 5-year relative survival rate of stomach cancer patients diagnosed between 1997 and 1999. The survival rates were higher in Japan, and even in Korea and Taiwan, than in Europe and the USA. The breast cancer 5-year survival rate was very high in Japan, Korea and Taiwan, and almost the same as in the EU and USA, whereas the survival rate of breast cancer was low in the Philippines, and hence improvement is needed there. The highest cervical cancer 5-year survival rate was seen in Korea, whereas several regions in Japan were not so high. Elucidation of the reasons for the lower rates in Japan is needed. Again, the Philippines had the lowest 5-year survival rate for cervical cancer, as well.

The next stage for cooperative studies is to collect individualized, anonymous data, which would make it possible to elucidate the factors that cause differences between populations, such as age, clinical stage at diagnosis, treatment procedures, etc. Individualized, anonymous data would also improve the comparability of survival data among the participating regions.

In conclusion, designing cooperative studies using cancer registry data involves a first stage in which information is exchanged among the participating countries to facilitate cancer control planning, a second stage consisting of a comparative study using non-individualized data and a third stage using individualized data (Fig. 2). Good human relationships among researchers are also very important, and the APCC represents a good platform for nurturing such good relationships.

### COLLABORATIVE EPIDEMIOLOGICAL STUDIES FOR CANCER PREVENTION

With regard to collaborative epidemiological studies to collect evidence concerning cancer risk and protective

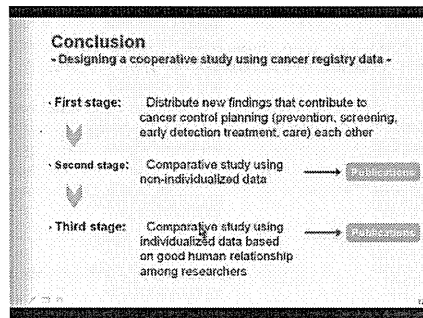


Figure 2. Designing a cooperative study using cancer registry data.

factors in the Asian region, recent trends show that the number of studies has been increasing, meta-analysis/pooled analysis of multiple studies has become very popular, and the importance of estimating the population-attributable fraction in each country/region/world has been recognized.

Collaboration between two countries is fairly simple, consisting of securing a research grant/funding, data collection by investigators and co-investigators in each country, and data analysis and manuscript preparation. The data center, data analysis and manuscript preparation are usually in the country of the principal investigator, while the grant is usually executed in the currency of the funding host.

In the case of collaboration between multiple countries, things get more complicated. The principal investigator is in one country, with a network including co-investigators collecting data in each of the participating countries, and the data analysis and manuscript preparation are performed at a data center, usually in the country of the principal investigator. However, the location of the data center and the manuscript writer are flexible.

An even more complicated example of collaboration is the Asia Cohort Consortium, which includes investigators from various countries and who change in accordance with the topic (Fig. 3). Interesting features are that the data center is outside Asia, in the USA, and the researchers include not only Asians but also Europeans and Americans, because they get funding, by topic, from their countries. Also, there is no firm funding base for network maintenance.

The funding agency in support of epidemiological research can be a domestic organization or an international organization. In the case of a domestic organization, the study is based in that country and is usually research topic-oriented. In the case of an international organization, the study base can be anywhere, and it is a potential research platform.

For good epidemiological research collaboration in Asian countries, the following points are important: each researcher must have an understanding of the significance of

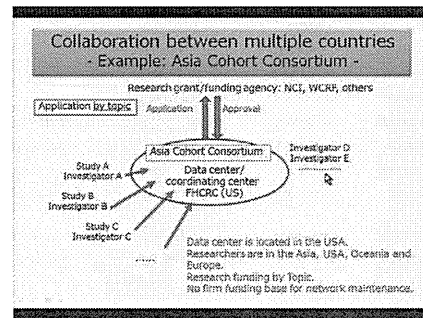


Figure 3. Collaboration between multiple countries: Example: Asia Cohort Consortium.

multinational collaborative studies; the leader must be a good coordinator; funding must be available for network maintenance and a multinational consortium; and the collaboration must be balanced and provide equal opportunity.

### CONCLUSIONS

The problems that are faced in relation to cancer registry in Asia are various (Fig. 4). They include insufficient quality of most registries, weak infrastructure, inadequate coverage in some countries, difficulty in sustainability due to insufficient financial support and turnover of trained personnel, few opportunities for education and training, and low response rates to IACR questionnaire surveys. Similarly, problems in relation to epidemiological studies include wide variation in expertise and resources among Asian countries, and limited understanding of epidemiology in some nations, which constrains funding for epidemiological studies (Fig. 5). Other key problems are the lack of opportunity for contact between experts in Asia via collaborative activities and language barriers among Asian countries.

As solutions, from the perspective of researchers, the highest priority should be placed on information-sharing among researchers within the Asia-Pacific region. Newly developed and widely used techniques, such as those for record linkage, should be shared. In addition, there is a need to promote coordination meetings/workshops/symposia, provide training courses, establish international standards and promote collaborative studies, publication and a common database for pooled analysis, both for cancer registries and epidemiological studies. In order to do this, an organization for Asian cooperation on cancer registration should be established in the field of cancer registries. In addition, a common hub for collaborative research will be needed for epidemiological studies. More opportunities for collaborative research projects, activities and publications

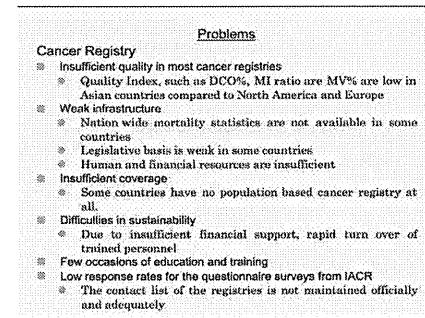


Figure 4. Problems: Cancer Registry.

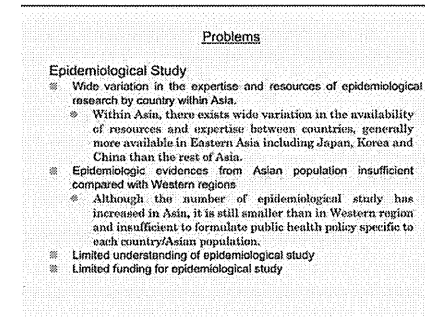


Figure 5. Problems: Epidemiological Study.

would improve the research skills and expertise in the region.

From the perspective of international organizations, such as the IARC and IACR, in a 2009 meeting the governing council of the IARC discussed how to provide greater support to cancer registries in developing countries. The IARC/IACR is planning to create a password-protected online system, so that questionnaires can be completed online and updated every year. The website would also allow registries to update their contact information. In October 2010, an Asian session will be held as a post-conference of the IACR annual meeting in Yokohama, Japan and Asian cooperation in cancer registration will be one of the main themes. To maintain a network of cancer registries, or an Asia Cohort Consortium, it will be necessary to maintain funding not only for topic-specific research proposals, but also for the research platform itself. To that end, funding should also be requested of other organizations.

In the future, the Asia-Pacific region must make full use of the platforms afforded by the WHO, IARC/IACR, UICC Headquarters, APFOCC and liaison societies in order to promote and achieve its goals of establishing cancer registries, accumulating cancer statistics, promoting and performing epidemiological studies and formulating regional and national cancer control programs.

With regard to concrete actions, from the perspective of researchers, there must be continued development of collaborative research projects and activities in subregions such as West Asia, Central Asia, Southeast Asia, East Asia and the Pacific. Publication of these activities should be encouraged to improve research skills and expertise in the study of Asia-Pacific populations. In that context, a steering committee for Asian cooperation for cancer registration will be assembled for the kick-off meeting in Yokohama 2010. At the same time, it will be proposed that the IARC supports the administrative work needed to maintain the network. Finally, collaborative and comparative epidemiological studies based on data from cancer registries should be promoted.

**Funding**

This working group meeting was financially supported by The Health and Labor Sciences Research Grant for Third Term Comprehensive Control Research for Cancer from Ministry of Health, Labor and Welfare, Japan, Grant-in-Aid for Cancer Research on Priority Areas from the Ministry of Education, Science, Sports Culture and Technology, Japan, 20th Asia Pacific Cancer Conference (President: Dr Hideyuki Akaza) and International Union Against Cancer (UICC) Asia Regional Office.

**Conflict of interest statement**

None declared.

**Appendix**

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Epidemiology Note

Cancer Incidence and Incidence Rates in Japan in 2004: Based on Data from 14 Population-based Cancer Registries in the Monitoring of Cancer Incidence in Japan (MCIJ) Project

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Received June 3, 2010; accepted June 11, 2010

The Japan Cancer Surveillance Research Group estimated the cancer incidence in 2004 as part of the Monitoring of Cancer Incidence in Japan (MCIJ) project, on the basis of data collected from 14 of 31 population-based cancer registries. The total number of incidences in Japan for 2004 was estimated as 623 275 (C00–C96). The leading cancer site according to the crude and age-standardized incidence rates was the stomach for men and breast for women. The apparent increase in age-standardized incidence rates in 2003 was calmed down in 2004.

Key words: cancer incidence – incidence estimates – cancer registry – Japan

The Japan Cancer Surveillance Research Group is involved in cancer monitoring in Japan since 2000 (1–4). This group estimated the cancer incidence in 2004 as part of the Monitoring of Cancer Incidence in Japan (MCIJ) project, on the basis of data collected from 14 of 31 population-based cancer registries: Miyagi, Yamagata, Chiba, Kanagawa, Niigata, Fukui, Shiga, Osaka, Tottori, Okayama, Hiroshima, Saga, Kumamoto and Nagasaki. If data from all 31 registries were used, this would have led to a large underestimation of national cancer incidence because of under-registration. The methods of registry selection, estimation of incidence and the limitations of these methods have been explained in previous studies (5–7). As is mentioned in the last article, there were two major methodological changes in the MCIJ2003, and we maintained these changes in the present study: (i) we invited all 31 population-based cancer registries in Japan to participate, and from these, we selected the 14 cancer registries with high-quality data in order to estimate the national incidence, and (ii) we used 2004 data alone for the national estimation. For this year, Kumamoto prefecture was newly selected as one of the registries with high-quality data for the national estimation, but the other registries remained since the previous estimations.

The number of incidences, crude rates, age-standardized rates and completeness of registration in 2004 are shown in Table 1, and the age-specific number of incidences and the rates according to sex and primary site are shown in Tables 2 and 3. The total number of incidences in Japan for 2004 was estimated as 623 275 (C00–C96). The time trends of age-standardized incidence rates for the five major sites and male- and female-specific sites in 1975–2004 are shown in Fig. 1 (standard population: the world population) and in Fig. 2 (standard population: the 1985 Japanese model population). The leading cancer site according to the crude and age-standardized incidence rates was the stomach for men and the breast for women, as shown in Figs 1 and 2. The apparent increase in age-standardized incidence rates in 2003 because of development of hospital-based cancer registry in designated cancer care hospitals was calmed down in 2004. The estimated cancer incidence data in Japan by sex, site, 5-year age group and calendar year during the period 1975–2004 are available as a booklet and as an electronic database on the website (only available in Japanese, <http://ganjoho.jp/professional/statistics/monita.html>).

Table 1. Incidence, completeness of reporting and accuracy of diagnosis in Japan according to sex and primary site, 2004

Primary sites	ICD-10h	Number of incidence	Crude rate	Age-standardized rate <sup>a</sup>		Completeness of reporting		Accuracy of diagnosis	
				World population	Japanese 1985 model population	DCOI (%)	EM	MV/I (%)	
Male									
All sites (incl. CIS)	C00–C96, D00–D09	372 914	598.6	282.3	400.4	17.1	1.93	73.8	
All sites	C00–C96	362 149	581.3	273.9	388.6	17.6	1.88	73.2	
Lip, oral cavity and pharynx	C00–C14	7136	11.5	6.0	8.1	14.1	1.77	79.7	
Esophagus	C15	15 215	24.4	11.8	16.4	15.4	1.62	78.8	
Stomach	C16	73 950	118.7	56.4	79.6	14.1	2.25	82.1	
Colon	C18	35 657	57.2	26.7	38.1	12.4	2.68	82.4	
Rectum	C19–C20	20 954	33.6	16.7	23.1	10.9	2.46	83.8	
Liver	C22	28 172	45.2	21.5	30.2	25.6	1.20	33.7	
Gallbladder etc.	C23–C24	9234	14.8	6.3	9.4	27.7	1.24	48.3	
Pancreas	C25	13 128	21.1	9.6	13.9	31.3	1.10	33.8	
Larynx	C32	3210	5.2	2.5	3.4	9.4	3.33	86.2	
Trachea, bronchus and lung	C33–C34	55 984	89.9	38.9	58.1	24.3	1.27	70.2	
Melanoma of skin etc.	C43–C44	4298	6.9	3.2	4.6	6.2	7.61	92.7	
Prostate	C61	39 321	63.1	26.6	39.7	10.9	4.45	83.6	
Bladder	C67	12 012	19.3	8.6	12.6	10.9	3.15	83.5	
Kidney, renal pelvis, ureter etc.	C64–C66, C68	9358	15.0	7.5	10.5	15.4	2.43	76.1	
Brain and nervous system	C70–C72	352	3.8	2.6	3.1	29.4	2.58	63.4	
Thyroid	C73	1933	3.1	1.8	2.4	8.3	4.53	86.9	
Malignant lymphoma	C81–C85, C96	9456	15.1	8.0	10.8	17.4	1.96	82.0	
Multiple myeloma	C88, C90	2723	4.4	1.9	2.8	29.4	1.37	64.9	
All leukemias	C91–C95	5282	8.5	5.3	6.5	25.3	1.28	85.6	
Female									
All sites (incl. CIS)	C00–C96, D00–D09	275 578	421.4	198.7	266.2	17.1	2.17	73.6	
All site	C00–C96	261 126	399.3	183.5	247.2	18.0	2.05	72.4	
Lip, oral cavity and pharynx	C00–C14	2980	4.6	2.1	2.8	14.7	1.94	78.1	
Esophagus	C15	2600	4.0	1.6	2.2	22.4	1.47	70.2	

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Table 1. Continued

Primary sites	ICD-10th	Number of incidence	Crude rate <sup>a</sup>	Age-standardized rate <sup>b</sup>		Completeness of reporting		Accuracy of diagnosis MV/I (%)
				World population	Japanese 1985 model population	DCO/I (%)	I/M	
Stomach	C16	35 822	54.8	21.5	30.2	17.8	2.02	78.2
Colon	C18	29 070	44.5	16.9	23.8	16.6	2.21	76.5
Rectum	C19–C20	11 585	17.7	7.7	10.5	14.4	2.30	80.6
Liver	C22	13 343	20.4	7.1	10.3	30.4	1.20	29.7
Gallbladder etc.	C23–C24	10 457	16.0	4.7	7.0	33.3	1.18	40.2
Pancreas	C25	11 314	17.3	5.7	8.4	33.8	1.10	30.3
Larynx	C32	224	0.3	0.1	0.2	13.4	2.87	71.6
Trachea, bronchus and lung	C33–C34	24 122	36.9	13.7	19.5	25.3	1.51	67.3
Melanoma of skin etc.	C43–C44	4326	6.6	2.2	3.2	8.5	7.55	90.7
Breast (incl. CIS)	C50, D05	50 549	77.3	48.1	62.0	5.4	4.80	91.1
Uterus (incl. CIS)	C53–C55, D06	24 422	37.3	26.0	32.6	7.2	4.42	89.7
Uterus (only invasive)	C53–C55	17 603	26.9	16.6	21.4	9.5	3.19	86.9
Cervix uteri	C53	9252	14.1	9.5	12.2	6.8	3.71	89.6
Corpus uteri	C54	7253	11.1	6.5	8.4	5.2	5.05	91.8
Ovary	C56	8655	13.2	8.1	10.3	13.5	1.96	79.3
Bladder	C67	4039	6.2	2.0	2.9	16.9	2.32	74.7
Kidney, renal pelvis, ureter etc.	C64–C66, C68	4374	6.7	2.8	3.8	19.5	2.11	70.2
Brain and nervous system	C70–C72	2220	3.4	2.1	2.4	29.5	3.23	56.5
Thyroid	C73	7062	10.8	6.8	8.5	6.6	7.03	87.7
Malignant lymphoma	C81–C85, C96	8063	12.3	5.8	7.6	17.2	2.22	80.4
Multiple myeloma	C88, C90	2247	3.4	1.2	1.7	31.8	1.17	62.5
All leukemias	C91–C95	3726	5.7	3.3	3.9	25.7	1.28	85.0

ICD-10th, International Classification of Disease, 10th Revision; DCO/I, proportion of cases with the death certificate only to incident cases; I/M, number of incidence/number of deaths; MV/I, proportion of microscopically verified cases to incident cases; CIS, carcinoma *in situ*.  
<sup>a</sup>Per 100 000 population.

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Table 2. Age-specific incidence in Japan according to sex and primary site, 2004

Primary sites	ICD-10	All ages	Age group (years)																	
			0–4	5–9	10–14	15–19	20–24	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+
<b>Male</b>																				
All sites (incl. CIS)	C00–C96, D00–D09	372 913	388	171	210	282	535	1073	1727	2567	3891	8273	18 354	31 956	44 998	57 595	70 712	64 723	36 908	28 550
All sites	C00–C96	362 149	388	171	210	271	527	1056	1674	2438	3752	7980	17 771	30 896	43 301	55 799	68 663	63 034	36 053	28 165
Lip, oral cavity and pharynx	C00–C14	7136	0	0	0	16	15	33	63	58	124	290	602	812	1174	1176	1211	745	460	357
Esophagus	C15	15 215	0	0	0	0	0	1	5	8	65	328	863	1789	2633	2856	2744	2123	1198	602
Stomach	C16	73 950	0	0	5	6	10	154	243	369	739	2004	4117	7271	9433	11 844	14 072	12 063	6418	5202
Colon	C18	35 657	0	0	11	5	25	66	90	260	444	643	1762	2987	4635	5565	6765	6133	3462	2804
Rectum	C19–C20	20 954	0	0	0	0	1	31	61	235	305	558	1480	2740	3137	3508	3543	2808	1388	1159
Liver	C22	28 172	14	5	0	0	1	5	52	150	195	598	1450	2843	3811	5205	6061	4464	1952	1366
Gallbladder etc.	C23–C24	9234	0	0	4	0	0	3	28	39	32	122	292	446	733	1279	1668	1736	1447	1405
Pancreas	C25	13 128	0	1	0	0	0	9	16	31	133	274	765	1129	1555	1845	2340	2276	1535	1219
Larynx	C32	3210	0	0	0	0	0	0	8	8	11	80	166	348	548	555	630	474	228	162
Trachea, bronchus and lung	C33–C34	55 984	0	0	0	6	29	22	77	139	383	857	1952	3779	5646	7304	11 128	12 366	7287	5009
Melanoma of skin etc.	C43–C44	4298	10	0	0	7	20	35	33	51	77	108	179	270	336	520	739	820	522	571
Prostate	C61	39 321	0	0	0	0	0	0	0	21	19	96	549	1533	3952	7200	9284	8525	4534	3608
Bladder	C67	12 012	0	0	1	3	2	20	25	48	97	255	628	884	1171	1341	2224	2293	1668	1352
Kidney, renal pelvis, ureter etc.	C64–C66, C68	9358	20	2	0	0	22	21	53	82	151	442	715	1044	1039	1298	1736	1400	794	539
Brain and nervous system	C70–C72	2352	64	45	44	30	45	67	46	137	144	79	168	186	181	262	320	264	132	138
Thyroid	C73	1933	0	1	4	10	23	36	92	59	102	110	199	233	172	320	189	232	97	54
Malignant lymphoma	C81–C85, C96	9436	22	32	56	49	114	135	96	139	206	335	660	887	902	1296	1361	1392	1010	744
Multiple myeloma	C88, C90	2723	0	0	0	1	0	0	2	17	30	20	119	190	305	348	531	547	324	289
All leukemias	C91–C95	5282	127	71	41	53	67	131	119	165	187	140	334	504	562	611	611	775	462	322
<b>Female</b>																				
All sites (incl. CIS)	C00–C96, D00–D09	275 578	269	147	185	363	741	2395	4846	7321	10 069	13 866	20 044	24 791	27 244	29 778	34 370	34 462	29 140	35 547
All site	C00–C96	261 126	269	147	185	349	493	1514	3227	5874	8633	12 798	19 073	23 745	26 090	28 541	33 221	33 528	28 422	35 017

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Table 2. Continued

Primary sites	ICD-10	All ages	Age group (years)																	
			0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Lip, oral cavity and pharynx	C00-C14	2980	0	8	0	4	18	57	42	47	80	127	172	269	314	272	450	438	294	388
Esophagus	C15	2600	0	0	0	0	0	12	10	8	9	40	167	261	336	341	375	299	320	422
Stomach	C16	35 822	0	0	1	0	52	40	204	411	568	1161	1940	2747	3156	4000	5368	5409	4764	6001
Colon	C18	29 070	0	0	0	5	15	28	124	216	310	591	1507	2040	3161	3338	4365	4558	3966	4846
Rectum	C19-C20	11 585	0	0	0	0	4	10	75	206	194	483	813	1003	1363	1565	1602	1491	1273	1503
Liver	C22	13 343	14	1	0	3	0	4	30	10	45	80	353	624	1049	2066	2710	2558	1924	1872
Gallbladder etc.	C23-C24	10 457	0	0	0	0	0	0	6	15	31	87	247	380	625	967	1286	1796	2070	2947
Pancreas	C25	11 314	0	0	0	0	0	1	12	30	83	131	310	617	804	1350	1725	1936	1990	2325
Larynx	C32	224	0	0	0	0	0	0	0	0	1	0	5	22	21	17	53	55	28	22
Trachea, bronchus and lung	C33-C34	24 122	0	0	1	1	6	27	50	92	300	499	1080	1779	2288	2912	3811	3902	3156	4218
Melanoma of skin etc.	C43-C44	4326	0	2	2	4	7	31	55	55	30	61	126	215	307	340	535	673	659	1224
Breast (incl. CIS)	C50, D05	50 549	1	0	1	0	19	253	1039	2397	4204	6181	6635	6965	6556	5073	4060	3338	2104	1723
Uterus (incl. CIS)	C53-C55, D06	24 422	0	0	2	23	251	1168	2430	2605	2465	1909	2752	2636	1973	1737	1355	1256	788	1072
Uterus (only invasive)	C53-C55	17 603	0	0	2	12	32	334	900	1334	1433	1269	2397	2319	1738	1531	1267	1196	773	1066
Cervix uteri	C53	9252	0	0	0	8	27	297	759	1139	1094	673	994	878	753	645	528	592	385	480
Corpus uteri	C54	7253	0	0	2	4	5	37	134	172	321	560	1323	1371	927	827	657	478	209	226
Ovary	C56	8655	1	1	28	53	91	199	150	404	519	792	1202	1202	917	773	734	697	446	446
Bladder	C67	4039	0	0	0	1	4	0	0	30	22	72	101	248	298	366	628	579	683	1007
Kidney, renal pelvis, ureter etc.	C64-C66, C68	4374	25	6	3	4	2	5	35	29	71	141	244	303	445	508	676	701	560	616
Brain and nervous system	C70-C72	2220	43	22	58	58	11	57	48	68	67	76	180	177	122	265	231	307	197	233
Thyroid	C73	7062	0	0	8	43	130	191	297	327	402	562	761	1155	762	815	602	459	277	271
Malignant lymphoma	C81-C85, C96	8063	8	30	21	40	29	117	101	107	247	292	540	720	889	930	1042	1020	929	1001
Multiple myeloma	C88, C90	2247	0	0	0	0	0	0	3	6	10	19	60	183	163	235	375	522	346	325
All leukemias	C91-C95	3726	91	34	36	74	35	83	60	113	104	162	163	251	364	456	367	515	385	433

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Table 3. Age-specific incidence rate per 100 000 population in Japan according to sex and primary site, 2004

Primary sites	ICD-10	All ages	Age group (years)																		
			0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+	
Male																					
All sites (incl. CIS)	C00-C96, D00-D09	598.6	13.2	5.6	6.8	8.1	13.5	24.1	34.8	58.9	97.9	210.2	396.2	671.1	1073.2	1653.1	2396.2	2985.4	3266.2	3693.4	
All sites	C00-C96	581.3	13.2	5.6	6.8	7.8	13.3	23.7	33.8	55.9	94.4	202.7	383.6	648.8	1032.7	1601.6	2326.8	2907.5	3190.5	3643.6	
Lip, oral cavity and pharynx	C00-C14	11.5	0.0	0.0	0.0	0.5	0.4	0.7	1.3	1.3	3.1	7.4	13.0	17.1	28.0	33.8	41.0	34.4	40.7	46.2	
Esophagus	C15	24.4	0.0	0.0	0.0	0.0	0.0	0.1	0.2	1.6	8.3	18.6	37.6	62.8	82.0	93.0	97.9	106.0	77.9		
Stomach	C16	118.7	0.0	0.0	0.2	0.2	0.3	3.5	4.9	8.5	18.6	50.9	88.9	152.7	225.0	340.0	476.9	556.4	568.0	673.0	
Colon	C18	57.2	0.0	0.0	0.4	0.1	0.6	1.5	1.8	6.0	11.2	16.3	38.0	62.7	110.5	159.7	229.2	282.9	306.4	362.7	
Rectum	C19-C20	33.6	0.0	0.0	0.0	0.0	0.0	0.7	1.2	5.4	7.7	14.2	31.9	57.5	74.8	100.7	120.1	129.5	122.8	149.9	
Liver	C22	45.2	0.5	0.2	0.0	0.0	0.0	0.1	1.0	3.4	4.9	15.2	31.3	59.7	90.9	149.4	205.4	205.9	172.7	176.7	
Gallbladder etc.	C23-C24	14.8	0.0	0.0	0.1	0.0	0.0	0.1	0.6	0.9	0.8	3.1	6.3	9.4	17.5	36.7	56.5	80.1	128.1	181.8	
Pancreas	C25	21.1	0.0	0.0	0.0	0.0	0.0	0.2	0.3	0.7	3.3	7.0	16.5	23.7	37.1	53.0	79.3	105.0	135.8	157.7	
Larynx	C32	5.2	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.3	2.0	3.6	7.3	13.1	15.9	21.3	21.9	20.2	21.0		
Trachea, bronchus and lung	C33-C34	89.9	0.0	0.0	0.0	0.2	0.7	0.5	1.6	3.2	9.6	21.8	42.1	79.4	134.7	209.6	377.1	570.4	644.9	648.0	
Melanoma of skin etc.	C43-C44	6.9	0.3	0.0	0.0	0.2	0.5	0.8	0.7	1.2	1.9	2.7	3.9	5.7	8.0	14.9	25.0	37.8	46.2	73.9	
Prostate	C61	63.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5	0.5	2.4	11.8	32.2	94.3	206.7	314.6	393.2	401.2	466.8	
Bladder	C67	19.3	0.0	0.0	0.0	0.1	0.1	0.4	0.5	1.1	2.4	6.5	13.6	18.6	27.9	38.5	75.4	105.8	147.6	174.9	
Kidney, renal pelvis, ureter etc.	C64-C66, C68	15.0	0.7	0.1	0.0	0.0	0.6	0.5	1.1	1.9	3.8	11.2	15.4	21.9	24.8	37.3	58.8	64.6	70.3	69.7	
Brain and nervous system	C70-C72	3.8	2.2	1.5	1.4	0.9	1.1	1.5	0.9	3.1	3.6	2.0	3.6	3.9	4.3	7.5	10.8	12.2	11.7	17.9	
Thyroid	C73	3.1	0.0	0.0	0.1	0.3	0.6	0.8	1.9	1.4	2.6	2.8	4.3	4.9	4.1	9.2	6.4	10.7	8.6	7.0	
Malignant lymphoma	C81-C85, C96	15.1	0.7	1.1	1.8	1.4	2.9	3.0	1.9	3.2	5.2	8.5	14.2	18.6	21.5	37.2	46.1	64.2	89.4	96.2	
Multiple myeloma	C88, C90	4.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.4	0.8	0.5	2.6	4.0	7.3	10.0	18.0	25.2	28.7	37.4	
All leukemias	C91-C95	8.5	4.3	2.3	1.3	1.5	1.7	2.9	2.4	3.8	4.7	3.6	7.2	10.6	13.4	17.5	20.7	35.7	40.9	41.7	
Female																					
All sites (incl. CIS)	C00-C96, D00-D09	421.4	9.6	5.1	6.3	11.0	19.7	55.8	99.7	170.1	256.0	353.9	429.5	508.2	611.0	771.7	977.8	1176.2	1384.3	1811.8	
All sites	C00-C96	399.3	9.6	5.1	6.3	10.6	13.1	35.3	66.4	136.5	219.5	326.6	408.7	486.8	585.1	739.6	945.1	1144.3	1350.2	1784.8	

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Table 3. Continued

Primary sites	ICD-10	All ages																	
		Age group (years)																	
		0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	85+
Lip, oral cavity and pharynx	C00-C14	4.6	0.0	0.0	0.1	0.5	1.3	0.9	1.1	2.0	3.2	3.7	5.5	7.0	7.0	12.8	14.9	14.0	19.8
Esophagus	C15	4.0	0.0	0.0	0.0	0.0	0.3	0.2	0.2	0.2	1.0	3.6	5.4	7.5	8.8	10.7	10.2	15.2	21.5
Stomach	C16	54.8	0.0	0.0	0.0	1.4	0.9	4.2	9.6	14.4	29.6	41.6	56.3	70.8	103.7	152.7	184.6	226.3	305.9
Colon	C18	44.5	0.0	0.0	0.2	0.4	0.7	2.6	5.0	7.9	15.1	32.3	41.8	70.9	86.5	124.2	155.6	188.4	247.0
Rectum	C19-C20	17.7	0.0	0.0	0.0	0.1	0.2	1.5	4.8	4.9	12.3	17.4	20.6	30.6	40.6	45.6	50.9	60.5	76.6
Liver	C22	20.4	0.5	0.0	0.0	0.1	0.0	0.1	0.6	0.2	1.1	2.0	7.6	12.8	23.5	53.5	77.1	87.3	91.4
Gallbladder etc.	C23-C24	16.0	0.0	0.0	0.0	0.0	0.0	0.1	0.3	0.8	2.2	5.3	7.8	14.0	23.1	36.6	61.3	98.3	150.2
Pancreas	C25	17.3	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.7	2.1	3.3	6.6	12.6	18.0	35.0	49.1	66.1	94.5
Larynx	C32	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.5	0.5	0.4	1.5	1.9	1.3	1.1
Trachea, bronchus and lung	C33-C34	36.9	0.0	0.0	0.0	0.0	0.2	0.6	1.0	2.1	7.6	12.7	23.1	36.5	51.3	75.5	108.4	133.2	149.9
Melanoma of skin etc.	C43-C44	6.6	0.0	0.1	0.1	0.1	0.2	0.7	1.1	1.3	0.8	1.6	2.7	4.4	6.9	8.8	15.2	23.0	31.3
Breast (incl. CIS)	C50, D05	77.3	0.0	0.0	0.0	0.0	0.5	5.9	21.4	55.7	106.9	157.8	142.2	142.8	147.0	131.5	115.5	113.9	100.0
Uterus (incl. CIS)	C53-C55, D06	37.3	0.0	0.0	0.1	0.7	6.7	27.2	50.0	60.5	62.7	48.7	59.0	54.0	44.2	38.5	42.9	37.4	54.6
Uterus (only invasive)	C53-C55	26.9	0.0	0.0	0.1	0.4	0.8	7.8	18.5	31.0	36.4	32.4	51.4	47.5	39.0	39.7	36.0	40.8	36.7
Cervix uteri	C53	14.1	0.0	0.0	0.0	0.2	0.7	6.9	15.6	26.5	27.8	17.2	21.3	18.0	16.9	16.7	15.0	20.2	18.3
Corpus uteri	C54	11.1	0.0	0.0	0.1	0.1	0.1	0.9	2.8	4.0	8.2	14.3	28.3	28.1	20.8	21.4	18.7	16.3	9.9
Ovary	C56	13.2	0.0	0.0	0.9	1.6	2.4	4.6	3.1	9.4	13.2	20.2	23.8	24.6	20.0	20.9	23.8	21.2	22.7
Bladder	C67	6.2	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.7	0.6	1.8	2.2	5.1	6.7	9.5	17.9	19.8	32.4
Kidney, renal pelvis, ureter etc.	C64-C66, C68	6.7	0.9	0.2	0.1	0.1	0.1	0.1	0.7	0.7	1.8	3.6	5.2	6.2	10.0	13.2	19.2	23.9	26.6
Brain and nervous system	C70-C72	3.4	1.5	0.8	2.0	1.8	0.3	1.3	1.0	1.6	1.7	1.9	3.9	3.6	2.7	6.9	6.6	10.5	9.4
Thyroid	C73	10.8	0.0	0.0	0.3	1.3	3.4	4.4	6.1	7.6	10.2	14.3	16.3	23.7	17.1	21.1	17.1	15.7	13.2
Malignant lymphoma	C81-C85, C96	12.3	0.3	1.0	0.7	1.2	0.8	2.7	2.1	2.5	6.3	7.5	11.6	14.8	19.9	24.1	29.6	34.8	44.1
Multiple myeloma	C88 C90	3.4	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.3	0.5	1.3	3.8	3.7	6.1	10.7	17.8	16.4	16.6
All leukemias	C91-C95	5.7	3.3	1.2	1.2	2.2	0.9	1.9	1.2	2.6	2.6	4.1	3.5	5.1	8.2	11.8	10.4	17.6	18.3

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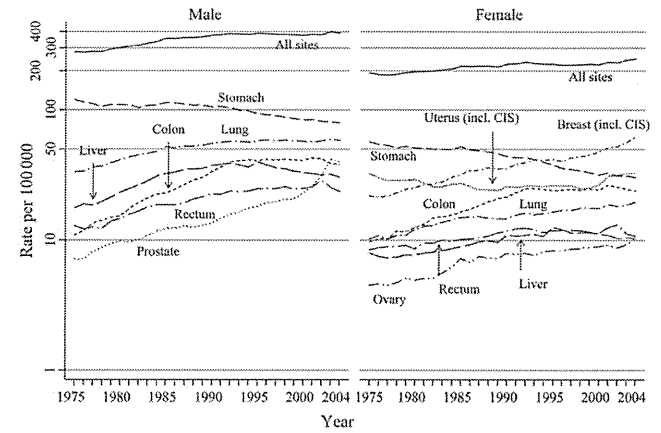


Figure 1. Trends of age-standardized cancer incidence rates for five major sites and specific sites for each sex (standard population: world population). CIS, carcinoma *in situ*.

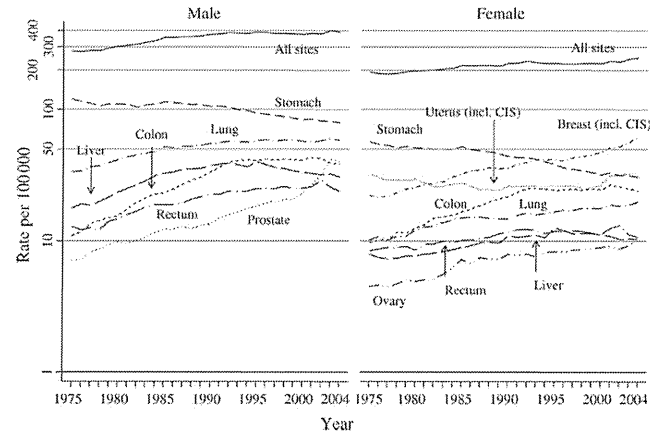


Figure 2. Trends of age-standardized cancer incidence rates for five major sites and specific sites for each sex (standard population: 1985 Japanese model population).

**Acknowledgement**

The survey on cancer incidence in Japan was conducted with contributions from the 31 registries: Aomori, Iwate, Miyagi, Yamagata, Ibaraki, Tochigi, Gunma, Chiba, Kanagawa, Niigata, Toyama, Ishikawa, Fukui, Gifu, Aichi, Shiga, Kyoto, Osaka, Tottori, Okayama, Hiroshima, Yamaguchi,

Tokushima, Kagawa, Ehime, Kochi, Saga, Nagasaki, Kumamoto, Kagoshima and Okinawa.

**Funding**

The study was supported by the 3rd-term Comprehensive 10-year Strategy for Cancer Control.

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**Conflict of interest statement**

None declared.

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**Do the Japanese feel more suspicious about cancer registration than the British?**

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**ARTICLE INFO****Article history:**

Accepted 2 February 2010

**Keywords:**Cancer registry  
Public's views  
Confidentiality  
Japan  
National survey**ABSTRACT**

**Background:** Cancer registration is indispensable, providing useful statistical measures for the appropriate evaluation of cancer control programs and medical treatment or screening. **Methods:** Following the British national survey on attitudes toward cancer registration, we conducted an investigation to correctly evaluate the general opinion of the Japanese population in this regard. We randomly recruited 3000 men and women aged 20–69 years from a research database. **Results:** Only 4% of all respondents had heard about the cancer registry system before the investigation. However, 77% of respondents thought that cancer registration was useful. Forty-three percent of respondents answered, regardless of the strictness of the data protection, that privacy had been violated if the registration occurred without an individual explanation. Compared with the British survey results, Japanese people seemed to be more suspicious about the largely unknown system of cancer registry. Nonetheless, it is noteworthy that Japanese respondents did not show active opposition to cancer registration; they tended to choose “I don't know” instead of “no” to questions asking if they supported the registry system. Multivariate analysis showed that male sex, older age, and living in the southern region were the factors significantly associated with support for cancer registration. **Conclusions:** We can seek society's understanding toward cancer registration by actively utilizing information from cancer registries, by using examples of how data are actually used that have wide appeal, and by educating the public on how the data are treated under the complete privacy policy.

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**1. Introduction****1.1. Cancer registration in Japan**

Registration of cancer cases is indispensable. It provides useful statistical measures for the appropriate evaluation of cancer control programs and medical treatment or screening. The Japanese cancer registration system has been running for more than 50 years, with the first population-based cancer registry having been started in Miyagi prefecture in 1951 [1]. Although cancer registries were in place in 35 of the 47 prefectures as of June 2008 [2], Japan lags behind Europe and the USA in completeness and timeliness of the registry system. In the Cancer Incidence in Five Continents vol. IX, for example, only seven Japanese registries published data [3]. The following reasons for this delay have been postulated: (1) cancer is not a reportable disease in Japan, and therefore the government is not actively engaged in the registration system; (2) hospital medical information systems are still being developed, and treating doctors are excessively burdened with cancer-recording tasks; and (3) medical institutions and the

public do not sufficiently understand the cancer registry system. Moreover, collection of cancer incidence data from medical institutions is sometimes considered a violation of privacy, although submission of patient data to the cancer registry is exempt from the Private Information Protection Law [4].

**1.2. Results of prior surveys on cancer registries in other countries and in Japan**

The British national survey on cancer registration, organized by the research group of Dr. Coleman of the London School of Hygiene and Tropical Medicine, was published in 2006 [5]. The survey examined the public's perception of the use of personal medical data by the national cancer registry. It concluded that the British people were supportive of cancer registration and were generous in supplying personal information used for the public interest, but only if this information was manipulated under strict conditions.

In Japan, the Cancer Control Act was approved in 2006 and the Basic Plan to Promote Cancer Control Program was implemented in 2007, and these policies recognize cancer registration as a central and important component for cancer control. Several surveys on attitude toward cancer registration have since been conducted in Japan. In the “Public opinion survey on cancer controls” organized by the Cabinet Office, 85.6% of the respondents “did not know about

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cancer registration" [6]. One question gave a simple explanation of the cancer registration system in Japan and in foreign countries, and asked how the respondents felt about a nationwide cancer registry. Only half of the respondents (54.6%) thought that such a system was necessary. In the "Public opinion poll on health and the aged society" conducted by the Mainichi Newspaper [7], the questionnaire asked: "A cancer registry system that registers the patient's name, date of birth, and medical information is enshrined in law in Europe and the United States. The data provide information about the extent and patterns of cancer and are used to evaluate treatment. What do you think of the cancer registry system?" Of those who responded, 18% answered, "it is necessary to enshrine the system in law because it is in our interests," and 62% answered, "cases should be registered only when patients give consent". Moreover, 15% answered "cancers should not have to be registered".

These survey results might suggest that Japanese people generally consider cancer registries to be unnecessary, and that this attitude is an obstacle to the development of cancer registration in Japan. However, the response rate of about 50% for these surveys indicates probable recruitment bias in that only people who are interested in cancer or in politics are likely to have answered. In addition since most people are unfamiliar with the topic of cancer registration, they are therefore obliged to answer the questions without sufficient information. The negative presentation of the question, such as "cancer registration is not included in the Cancer Control Act" and the answer choice that "priority should be put on protection of personal information, and cancer should be registered only if patients themselves agree" easily evoke anxiety, and could lead to the results lacking validity.

We therefore need to re-investigate opinion regarding cancer registration, to resolve the above-mentioned problem and to correctly evaluate the general opinion of the Japanese population. Moreover, a different investigative perspective from that of journalists or administrative officers is needed. The present study aimed to: (1) increase the response rate to avoid recruitment bias, (2) add objective and sufficient explanation about "cancer registration" to the questions, and (3) use a validated, internationally comparable questionnaire in order to assess the Japanese situation objectively.

## 2. Methods

### 2.1. Recruitment and questionnaire

For participant recruitment we used the database of Nikkei Research Ltd., in which about 140,000 people are registered as research monitors. These monitors are paid to be engaged in various types of research according to the study objectives. Mindful of the importance of a high response rate, we decided to use this service. We stratified individuals by sex, age, and address according to the proportions of the most recent National Census. Finally 3000 men and women aged from 20 to 69 were recruited at random from the database according to these proportions.

We carefully translated the questionnaire that was used for the British survey so as not to change the intention of the original questions [5], and added two questions which were regarded as important in Japan (Q7 and Q8). Back translation of the Japanese version into English was performed by a professional translator. The research team verified that the two English versions maintained the same meaning for each question. The questionnaire was composed of 17 questions and was mailed to participants in December 2007.

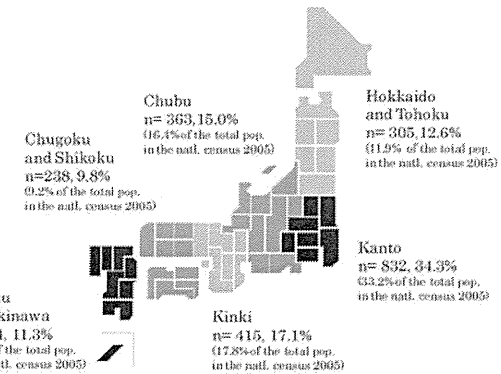
### 2.2. Statistical methods

A confidence interval of 95% was calculated for each answer. Correlations between the answers and socio-demographic vari-

**Table 1**  
Background of the respondents.

	n	%
<b>Sex</b>		
Male	1164	47.9
Female	1265	52.1
Total	2429	100.0
<b>Age (years)</b>		
20–29	384	15.9
30–39	495	20.4
40–49	465	19.2
50–59	588	24.3
60–69	490	20.2
Total	2422	100.0
<b>Marital status</b>		
Spouse	1807	74.4
No spouse	621	25.6
Total	2428	100.0
<b>Children</b>		
Yes	1741	76.0
No	649	28.3
Total	2290	100.0
<b>Region</b>		
Hokkaido, Tohoku	305	12.6
Kanto	832	34.3
Chubu	363	15.0
Kinki	415	17.1
Chugoku, Shikoku	238	9.8
Kyushu, Okinawa	274	11.3
Total	2427	100.0
<b>Occupation</b>		
Company employee/executive	900	37.3
Public officer	143	5.9
House husband/ wife	452	18.7
Self-employed	153	6.3
Freelance professional (MD, lawyer, etc.)	45	1.9
Part-time worker	347	14.4
Retired/unemployed	250	10.4
Others	122	5.1
Total	2412	100.0
<b>Educational background</b>		
Junior high school	92	3.8
High school	783	32.3
College	520	21.4
University/graduate school	1031	42.5
Total	2426	100.0
<b>Household income</b>		
≤4 million yen	567	23.8
4–8 million yen	993	41.6
>8 million yen	826	34.6
Total	2386	100.0

ables were examined by chi-square test. Attitude towards cancer registration and privacy protection were enquired about in Q8, and respondents answered this question by means of a Likert-type scale (1–5). For this discrete variable, an ordered logit model was employed to test for a significant effect of respondents' background factors, while controlling for each variable. The ordered logit model predicts the probability of an event occurring, allowing for more than two ordered response categories in a dependent variable. The model makes the proportional odds assumption for being in a chosen category or higher compared to being in a lower category. In addition we obtained modeled cut-off points between ordered categories allowing us to interpret the respondents' preference for each answer.



**Fig. 1.** Geographical distribution of the respondents.

## 3. Results

### 3.1. Respondents

A valid response was obtained from 2430 people, giving a response rate of 81.0%. Table 1 shows the socio-demographic background of respondents. When we analyzed attributes of those who responded to questions, male to female proportion was 47.9:52.1; 16% were in their 20s, 20% were in their 30s, 19% were in their 40s, 24% were in their 50s, and 20% were in their 60s. Geographical distribution of the respondents is shown in Fig. 1. The distribution of the respondents was close to the population distribution according to the 2005 national census. No significant difference was found in participation in the study according to these socio-demographic variables.

### 3.2. British and Japanese results

Table 2 shows the results for each question for the present Japanese respondents and the original British respondents. A few of the Japanese respondents (9%) felt that their privacy was violated when they received invitations to cancer screening (Q1). Four percent of all respondents in Japan had heard about cancer registries before reading the questionnaire, whereas this proportion in the UK was 17% (Q2). However, among Japanese respondents, 77% thought the cancer registry system was useful, while 3% answered that it was not (Q3). On the other hand, 95% of British respondents considered the cancer registry system useful. Regarding support for a new law that required medical information of cancer patients to be registered (Q4), more than 30% of Japanese respondents answered "I don't know," although nearly 60% supported such a law. In contrast, 81% of British respondents supported such a law.

In Japan, 43% answered that, regardless of the strictness of data protection, privacy had been violated if the registration occurred without an individual explanation (Q5), while over 80% of the British respondents replied that privacy had not been violated in this situation. The largest difference in response between the two countries was seen for this question. The proportion of Japanese respondents who believed privacy had been violated when individuals were contacted for research participation based on the cancer registry list decreased to 24% (Q6).

In Q7, an original question in the present study, 57% of respondents stated that residents of prefectures that had a registry system would be at an unfair advantage if this system was not available elsewhere (Table 3). For Q8, which asked about the balance between the violation of privacy and the usefulness of cancer registration, the mode of responses was 4. Answers were slightly skewed toward recognition of the system's usefulness.

### 3.3. Relationship between responses and socio-economic background

An overview of the relationship between responses and socio-economic background of the subjects is presented in Table 4. Because we conducted univariate analysis, all variables on socio-economic background were related to the question answers.

When compared with women, male respondents were more likely to believe that cancer registration provides useful information. Men were also more likely to support a new law to enforce cancer registration, and they were less likely to report invasion of privacy in Q5 and 6. Moreover, the number of respondents who felt that provision of information to a cancer registry constituted a violation of privacy decreased with age in both sexes (Fig. 2).

In Q5, a geographical difference was seen when respondents were divided into six regions. In the Kanto region, which includes the capital, Tokyo, 37.9% of respondents did not feel that their privacy was violated by provision of information to a cancer registry. The variation according to geographical region was remarkable; this proportion was 49.6% in the Kyushu and Okinawa area, in the south of Japan.

As for profession of the respondents, 85.3% of public officers answered "yes" in Q3, and this proportion was the highest. In contrast, home makers and part-time workers were less likely to answer "yes" (73.9% and 70.0%, respectively). Self-employed people and the unemployed/retired were most supportive of the cancer registration: 67.3% and 64.4%, respectively, answered "yes" to Q4. These groups were also less likely to report violation of privacy in response to Q5 (36.0% and 28.8%, respectively). Freelance professionals (doctors, lawyers, etc.) were significantly more aware of the cancer registry system; 15.6% answered that they had heard of it. At the same time, 51.1% of this group thought that registration without individual explanation violated their privacy (Q5). Respondents with higher levels of education (university/graduate school) tended to have positive opinions about cancer registration in Q5 and 6.



**Table 2**  
Results of the surveys in Japan and the UK.

	Yes			No			Don't know		
	n	%	95% CI	n	%	95% CI	n	%	95% CI
<b>Q1. Many people get letters from their primary care trust (previously called the health authority) about screening tests for cancer, such as cervical smear tests or bowel cancer screening. If your primary care trust sent you a letter inviting you to a screening test, do you think this would be an invasion of your privacy? (corresponding to Q3 in the UK study)</b>									
Japan	209	9	7–10	2037	84	82–85	179	7	6–8
UK	93	3	2–4	2740	95	94–97	39	1	1–2
JP-UK		6			11			6	
<b>Q2. In Japan we have regional cancer registries, which are confidential databases of people who have cancer. Information is held under strict security. Have you ever heard of a cancer registry before? (corresponding to Q4 in the UK study)</b>									
Japan	103	4	3–5	2254	93	92–94	72	3	2–4
UK	479	17	15–18	2362	82	81–84	32	1	1–2
JP-UK		–13			11			2	
<b>Q3. The cancer registry is the only reliable source of information for monitoring trends in the risk of getting cancer and trends in cancer survival. The information is used to compare the effectiveness of cancer treatment around the country, and to evaluate the success of cancer screening programs. Do you think this is useful information for us to have in this country? (corresponding to Q5 in the UK study)</b>									
Japan	1863	77	75–78	75	3	2–4	491	20	19–22
UK	2737	95	94–96	68	2	2–3	69	2	2–3
JP-UK		–18			1			18	
<b>Q4. In the USA, Denmark, Sweden, South Korea, and many other countries, all cases of cancer have to be notified to the cancer registry by law. In the future, there may need to be a similar law in Japan, to ensure that the cancer registries continue to have the information needed for monitoring cancer in Japan. Would you support a new law that meant all cases of cancer have to be notified to the cancer registries? (corresponding to Q6 in the UK study)</b>									
Japan	1423	59	57–61	258	11	9–12	748	31	29–33
UK	2335	81	79–83	343	12	10–13	194	7	6–8
JP-UK		–22			–1			24	
<b>Q5. Currently, survival rates from cancer can only be compared between regions of the country by knowing cancer patients' names and addresses. If you had cancer and your name and address was included automatically in the cancer registries, to be held confidentially and under strict security, do you think this would be an invasion of your privacy? (corresponding to Q8 in the UK study)</b>									
Japan	1033	43	41–44	1029	42	40–44	366	15	14–17
UK	446	16	14–17	2326	81	79–83	101	4	3–4
JP-UK		27			–39			11	
<b>Q6. Finally, suppose that a research group from a university medical school wanted to do research with people who had a particular type of cancer. If you had cancer and the cancer registries sent you a letter, via your doctor, asking if you wanted to take part in the research, do you think this would be an invasion of your privacy? (corresponding to Q9 in the UK study)</b>									
Japan	594	24	23–26	1486	61	59–63	348	14	13–16
UK	261	9	8–10	2508	87	86–89	104	4	3–5
JP-UK		15			–26			10	
<b>Q16. Have any members of your immediate family (for instance, parents, children, husband/wife/partner, brothers, sisters) ever had cancer? (corresponding to Q2 in the UK study)</b>									
Japan	1056	44	42–45	1340	55	53–57	24	1	1–1
UK	1298	45	43–47	1528	53	51–56	50	2	1–2
JP-UK		–1			2			–1	
<b>Q17. Could I please start by asking if you have, or you have ever had, cancer? (corresponding to Q1 in the UK study)</b>									
Japan	96	4	3–5	2274	94	93–95	49	2	1–3
UK	174	6	5–7	2701	94	93–95	–	–	–
JP-UK		–2			0			–	

Cancer experience, either of the individual or their family, was related to awareness of the cancer registry system (6.0% for "without experience" and 8.3% for "with an experience", respectively). Cancer experience also seemed to be related to a positive

opinion of cancer registration in Q5 and 6; however, this correlation disappeared when age was adjusted for.

In Q8, we performed ordered logit modeling in order to calculate the adjusted odds ratio (OR) of the respondents'

**Table 3**  
Results for Q7 and Q8 (original questions in the Japanese questionnaire).

	Yes			No			Don't know			
	n	%	95% CI	n	%	95% CI	n	%	95% CI	
<b>Q7. Suppose that there is no cancer registry in your region which is monitoring trends in the risk of getting cancer and trends in cancer survival. Do you feel that other regions have an unfair advantage by using their cancer registry information for evaluation of regional cancer screening and treatment, or for cancer control?</b>										
1393	57	55–59		631	26	24–28	401	17	16–18	
<b>I think this is an invasion of our privacy</b>										
	1	2	3	4	5					
	n	%	n	%	n	%	n	%	n	
<b>Q8. Cancer registries are reliable information sources for cancer control, as they allow us to compare the outcomes of treatment and to evaluate anti-cancer programs by providing cancer patients' names and addresses. What would you think if this were done without the individual consent of the patients? Please circle the number that best represents your opinion.</b>										
	314	13	542	22	545	22	658	27	362	15

**Table 4**  
Overview of relationship between responses and socio-economic background (%).

	Q2			Q3			Q4			Q5			Q6			Q7			
	Yes	No	I don't know	Yes	No	I don't know	Yes	No	I don't know	Yes	No	I don't know	Yes	No	I don't know	Yes	No	I don't know	
Sex	4.3	93.0	2.8	80.3	3.3	16.4	62.1	12.7	25.2	40.2	25.4	62.4	25.4	62.4	12.2	25.4	62.4	12.2	
Male	4.2	92.6	3.2	73.4	2.9	23.7	55.4	8.7	35.9	44.8	23.6	60.1	23.6	60.1	16.3	23.6	60.1	16.3	
Female																			
Age	2.9	93.8	3.4	76.3	3.7	20.1	57.6	10.2	32.3	48.4	27.3	55.7	27.3	55.7	16.9	54.4	26.3	19.3	
20–29	3.6	93.1	3.2	77.4	2.8	19.8	57.2	9.7	33.1	46.7	25.8	55.8	25.8	55.8	14.1	50.1	23.5	16.2	
30–39	2.4	96.6	1.1	75.9	2.4	21.7	57.0	10.1	32.9	43.7	40.4	40.4	23.9	60.4	15.7	60.0	23.9	16.1	
40–49	4.3	92.8	2.9	75.1	3.6	21.3	57.4	11.9	31.7	41.7	43.8	44.5	22.8	63.4	13.8	55.0	27.6	17.4	
50–59	7.6	88.2	4.3	79.0	3.1	18.0	63.7	10.8	24.5	33.5	53.2	13.3	18.8	69.1	12.1	57.3	28.6	14.1	
60–69	16.7	83.3	0.0	100.0	0.0	0.0	83.3	16.7	0.0	50.0	33.3	33.3	33.3	66.7	0.0	83.3	66.7	0.0	
Others																			
Marital status	3.8	93.6	2.6	76.5	3.3	20.2	58.8	10.6	30.6	41.4	23.2	62.3	23.2	62.3	14.6	58.3	25.8	16.0	
Spouse	5.5	90.5	4.0	77.3	2.6	20.1	58.1	10.6	31.2	45.9	28.1	58.2	28.1	58.2	13.7	55.1	26.7	18.3	
No spouse																			
Unmarried	4.2	91.6	4.2	76.9	4.2	18.9	56.6	11.9	31.5	45.5	44.1	40.5	23.8	63.6	12.6	56.6	25.2	18.2	
Divorced	7.7	87.2	5.1	89.7	0.0	10.3	71.8	5.1	23.1	30.8	18.0	61.5	18.0	61.5	20.5	50.0	29.0	21.1	
Widowed	25.0	63.9	11.1	66.7	2.8	30.6	55.6	8.3	36.1	33.3	41.7	25.0	11.4	68.6	20.0	44.4	36.1	19.4	
Children	4.1	93.1	2.8	77.0	2.9	20.1	59.4	10.1	30.6	40.5	44.0	15.5	22.9	62.8	14.3	58.1	25.6	16.3	
Yes	4.3	92.5	3.2	77.0	3.4	19.6	57.8	11.1	31.1	47.8	38.7	13.6	28.2	57.6	14.2	55.8	27.1	17.2	
No																			
Profession	3.0	94.8	2.2	77.0	2.8	20.2	59.3	12.4	28.4	45.3	41.2	13.5	27.4	59.8	12.8	57.2	26.5	16.3	
Company worker/ executive	0.3	91.9	2.8	65.3	1.9	11.9	56.6	10.9	34.5	42.7	36.3	15.1	25.9	62.9	11.2	58.8	23.6	17.6	
Public officer	3.3	94.1	2.6	79.7	3.0	16.3	67.3	11.1	31.6	46.2	38.7	19.2	26.7	69.4	19.9	54.9	28.1	17.0	
Self-employed	15.6	84.4	0.0	77.8	4.4	17.8	51.1	11.1	37.8	51.1	31.1	17.8	28.9	57.8	13.3	62.2	33.3	4.4	
Freelance professional																			
MD, lawyer, etc.																			
Part-time worker	2.6	93.4	4.0	70.0	3.5	26.5	52.2	7.8	40.1	44.1	37.5	18.4	25.4	59.1	15.6	56.4	23.1	18.5	
Pensioner, unemployed	7.6	88.0	4.4	80.8	1.2	18.0	64.4	11.6	24.1	28.8	57.6	13.6	17.2	68.8	14.0	55.2	28.0	16.8	
Others	4.1	94.3	1.6	82.8	3.3	13.9	67.2	7.4	25.4	40.2	47.5	12.3	26.2	59.8	13.0	54.5	27.9	17.2	
Region	5.6	89.8	4.6	78.7	3.9	17.4	59.7	10.8	29.5	41.3	45.9	12.8	24.6	63.3	12.1	57.1	26.2	16.7	
Hokkaido/Tohoku	4.0	93.4	2.6	77.0	2.6	20.3	57.9	11.8	30.3	45.9	37.9	16.2	27.8	27.8	14.4	56.3	26.2	17.0	
Kanto	3.3	93.9	2.8	73.3	3.6	23.1	58.4	11.0	30.6	44.2	41.4	14.4	25.3	62.3	12.4	56.8	26.2	17.1	
Chubu	4.6	93.7	2.7	74.5	3.4	22.2	56.9	10.4	32.8	42.7	41.2	16.1	21.7	63.0	15.2	58.1	23.4	18.6	
Kinki	3.6	92.4	3.0	76.8	4.2	19.0	60.3	10.1	29.5	39.7	49.0	11.4	20.2	62.2	17.7	59.7	28.2	12.2	
Chugoku/Shikoku	5.5	91.6	2.9	81.4	1.5	17.2	61.0	7.3	31.8	33.9	49.6	16.4	21.2	63.9	15.0	57.9	27.1	15.0	
Kyushu/Okinawa																			
Educational background	5.4	89.1	5.4	76.1	3.3	20.7	56.5	17.4	26.1	31.5	48.9	19.6	27.2	55.4	17.4	43.5	35.9	20.7	
High school	4.6	91.2	4.2	73.0	4.2	22.8	58.5	13.0	30.6	38.5	45.8	15.6	22.6	63.4	14.1	56.4	27.2	16.4	
College	4.0	92.1	3.9	74.8	2.3	22.9	55.0	7.7	37.3	45.0	38.7	16.4	23.3	58.8	17.9	58.9	22.7	18.5	
University, Graduate school	4.0	94.7	1.4	80.6	2.6	16.8	62.3	9.7	28.0	45.5	40.9	13.6	26.3	61.2	12.5	58.7	26.0	15.4	

Table 4 (Continued)

	Q2			Q3			Q4			Q5			Q6			Q7		
	Yes	No	I don't know	Yes	No	I don't know	Yes	No	I don't know	Yes	No	I don't know	Yes	No	I don't know	Yes	No	I don't know
Family ever had cancer?																		
Yes	6.0	91.0	3.0	77.3	3.4	19.3	59.0	9.9	31.2	40.1	45.2	14.7	21.7	65.5	12.8	58.0	26.8	15.2
No	3.0	94.2	2.8	76.9	2.8	20.3	58.6	11.1	30.3	44.1	40.6	15.3	26.3	58.5	15.2	57.1	25.8	17.2
I don't know	0.0	91.7	8.3	54.2	0.0	45.8	45.8	20.8	33.3	62.5	25.0	12.5	37.5	37.5	25.0	58.3	16.7	25.0
		Pr=0.003		Pr=0.024			Pr=0.387			Pr=0.052			Pr=0.001			Pr=0.431		
Ever had cancer?																		
Yes	8.3	90.6	1.0	80.2	2.1	17.7	57.3	13.5	29.2	37.9	42.1	20.0	20.8	69.8	9.4	57.3	30.2	12.5
No	4.0	93.1	2.9	76.8	3.1	20.1	59.0	10.1	30.9	42.6	42.6	14.8	24.4	61.2	14.4	57.6	25.7	16.7
I don't know	8.2	81.6	10.2	71.4	4.1	24.5	49.9	20.2	26.5	44.5	37.7	16.4	32.7	35.1	14.3	54.2	33.3	12.5
		Pr=0.003		Pr=0.819			Pr=0.023			Pr=0.586			Pr=0.268			Pr=0.517		
Income																		
≤4 million yen	6.0	88.2	5.8	75.1	4.6	20.3	55.6	12.7	31.8	39.7	43.6	16.8	22.2	62.4	15.3	53.9	29.0	17.1
4–8 million yen	3.3	94.2	2.5	77.0	2.5	20.5	61.4	9.7	28.9	42.2	43.2	14.6	24.3	60.7	15.0	58.5	25.6	15.8
8–16 million yen	4.1	94.3	1.6	78.1	2.9	19.0	58.3	10.4	31.1	44.5	41.3	14.2	25.8	61.6	12.6	59.2	24.7	16.1
Others	0.0	95.0	4.5	61.9	0.0	38.1	38.1	9.5	52.4	57.1	19.1	23.8	42.9	38.1	19.1	38.1	14.3	47.6
		Pr<0.001		Pr=0.095			Pr=0.078			Pr=0.183			Pr=0.147			Pr=0.003		

N.B. Pr values are calculated according to chi<sup>2</sup> test.

background for the answer. The answer on the five-grade Likert scale was employed as the dependent variable. Sex, age, region of residence, family experience of cancer, personal experience of cancer, and awareness of cancer registration, which were all significantly correlated with response to Q8, were used as independent variables. The results are shown in Table 5. Male sex (OR 1.25), older age (OR 1.33), and living in the southern region (OR 1.31) were factors significantly associated with support for cancer registration. Cut-off points were arranged almost linearly, and no clear affinity between the answer categories was observed.

4. Discussion

4.1. Study results

This study clarified the current general opinion on cancer registration in Japan. The questionnaire alone could not fully inform respondents about cancer registration. However, the present results should be more reliable than those of previous surveys because the explanation was given in neutral terms rather than being phrased in a way that creates unrest about privacy.

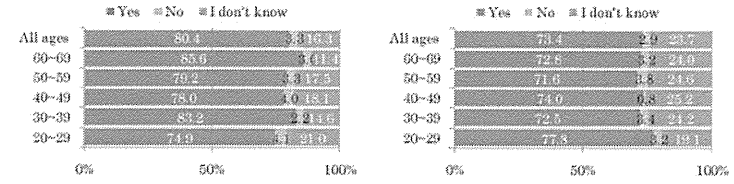
Awareness of the cancer registry system was remarkably low; most Japanese people were unaware of the system, despite increasing media coverage. In the UK study, the awareness was a little higher than in Japan. This is probably because British cancer registries or GPs provide more information on cancer registration to the public. The difference may also be related to frequency to see epidemiological study results based on cancer registration. Nonetheless, nearly 80% of the Japanese respondents answered "cancer registry is useful" when a short explanation on the system was provided.

Compared with the British, Japanese people seemed to be more suspicious about cancer registration according to their responses to Q4 and 5. We speculate that these two questions are correlated in terms of the trade-off that we see in Q8. Japanese respondents appear to believe that they should be informed which contents are transmitted to cancer registries and how this is done. Only when these requirements are satisfied would they agree with legislation of cancer registration. In a general survey on national character in Japan, 41% of the 1001 respondents answered "I am very worried about abuse of my own personal information by someone" [8]. In another international comparative study on information, 55.4% of UK respondents felt assured about the confidentiality of their information, while Japan was positioned at the bottom of the 7 countries surveyed, with only 34.3% of Japanese stating that they felt assured in this regard [9].

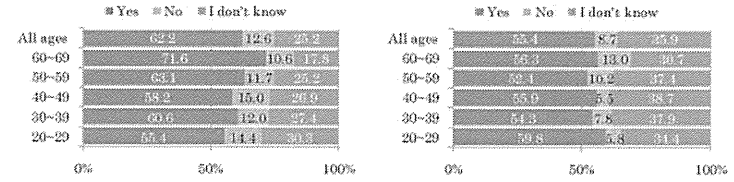
However, it should be noted that Japanese respondents did not show active opposition to cancer registration, as they tended to choose "I don't know" instead of "no". This probably stems from insufficient knowledge of cancer registration in Japan, or to the Japanese tendency to avoid a definitive "yes" or "no" answer. The information in the questionnaire allowed the respondents to consider cancer registration in detail, and to understand its utility. We believe, however, that the general population should receive more education in the long term, in order to form their opinion according to their social position or circumstances.

The tendency to think that cancer registration is an invasion of privacy in Japan may be related to the mass media coverage of the Act for Protection of Computer Processed Personal Data in 2003. Another possibility is the recent prevalence of crime that misuses or leaks personal information. Moreover, differences between the two countries in their attitudes to and understanding of public health and epidemiology and public interest might be another contributing factor.

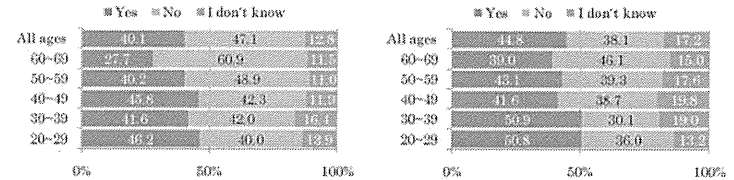
It is interesting that a large difference was seen in the responses to Q1, 5, and 6, although these three questions all covered privacy.



Q3. The cancer registry is the only reliable source of information for monitoring trends in the risk of getting cancer and trends in cancer survival. The information is used to compare the effectiveness of cancer treatment around the country, and to evaluate the success of cancer screening programs. Do you think this is useful information for us to have in this country?



Q4. In the USA, Denmark, Sweden, South Korea and many other countries, all cases of cancer have to be notified to the cancer registry by law. In future, there may need to be a similar law in Japan, to ensure that the cancer registries continue to have the information needed for monitoring cancer in Japan. Would you support a new law that meant all cases of cancer have to be notified to the cancer registries?



Q5. Currently, survival rates from cancer can only be compared between regions of the country by knowing cancer patients' names and addresses. If you had cancer and your name and address was included automatically in the cancer registries, to be held confidentially and under strict security, do you think this would be an invasion of your privacy?

Fig. 2. Sex and age differences in the answers to Q3, 4, and 5.

It is already well known that personal information is manipulated by the local administration in the course of civil registration; hence, people may not care about this issue. In both countries, for example, breast and cervical cancer screening are managed by the government, and the population has already received announce-

ments about their health from city halls or health authorities. Even Japanese people are used to receiving such information with a nominative cover letter. On the other hand, cancer registration is an unknown system and people may still be suspicious about it, compared with medical research participation requested through

Table 5 Results of the ordered logit model for the association between response to Q8 and respondents' background factors.

Variables	Odds ratio	S.E.	Pr
n = 2406 log likelihood = -3762.2065 LR chi <sup>2</sup> (6) = 47.26			
Male	1.245467	0.090686	0.003
Age >49	1.333289	0.104200	0.000
Resident of southern regions	1.313561	0.118063	0.002
Own experience of cancer (Q17)	1.155135	0.090001	0.064
Experience of cancer in the family (Q16)	1.137620	0.220123	0.505
Aware of cancer registry (Q2)	1.346390	0.245652	0.103
Cut-off point 1	-1.566630	0.080296	
Cut-off point 2	-0.257750	0.069048	
Cut-off point 3	0.678866	0.070283	
Cut-off point 4	2.124766	0.083575	

their treating doctors. Cancer registration requires information about sensitive medical records in addition to personal identifiers. This may increase feelings of resistance. Moreover, cancer screening brings people a direct advantage; however, cancer registration seems not to provide any immediate merit.

The logit modeling showed us that only general background factors (age, sex, and residence region) affected opinions on the cancer registration. Cancer experience slightly increased respondents' knowledge of the cancer registry system, but it had no significant effect on their opinion of it. Such differences of opinion concerning privacy probably result from age and sex differences, rather than from the tendency for young women to be more concerned about conditions such as breast, ovarian or cervical cancer. For example, the "Public opinion poll concerning protection of individual information" in September 2006 showed more uneasiness regarding information leakage among female respondents [10]. In that poll, young respondents and city residents felt uneasiness regarding the misuse of personally identifiable information. We consider that the results of our study do not reflect a specific tendency about "cancer" or "cancer registration".

#### 4.2. Research limitations

The research subjects were recruited from those designated "research monitors" by Nikkei Research Ltd. Strictly speaking, this may introduce bias if we consider them to represent the general population, since the monitors are willing to be registered in Nikkei Research Ltd., and this motivation might lead to such people having similar characteristics. However, nowadays in Japan, it is not at all feasible to achieve a high response rate in social science research by selecting subjects from the telephone directory or electoral roll, although such methods were satisfactory a few decades ago. Research with low response rates, for example 30%, is much less reliable than the present survey. We believe strongly that using a database of a research and marketing company was the most efficient way to obtain answers as close as possible to the "real" opinion of the general population.

The difference in methodology between the two studies, i.e., telephone interview in the British study versus mailed questionnaires in the present study, might impede comparability. However, it is extremely difficult to maintain a high response rate with the telephone investigation method in Japan. We considered it more important to have a high response rate than to achieve methodological commonality between the two studies.

#### 4.3. The future of cancer registration in Japan

A decade ago, researchers were encouraged to achieve social recognition for cancer registration throughout the world. At that time, there remained criticism against the epidemiological research based on cancer registration without individual consent of the patients, based on the principles of the Helsinki Declaration [11,12]. Times have changed, in particular after the enactment of the European Commission directive in 1995, and we now have consensus that cancer registration is exempt from the basis of individual informed consent because it can only benefit society. The alternative of making the data anonymous by replacing all the identifiers with codes would impede cancer surveillance [13] and is not realistic. The unfortunate example in Estonia warns against the overzealous implementation of data protection, even under a favorable situation [14]. What we need is to achieve a proper balance between protection of patient privacy and public health interests by setting appropriate policies, regulations, and use of technology [15], while avoiding overly restrictive policies and an exaggerated reaction [16].

As for the anxiety regarding the treatment of personal information in Japan, we think that feelings will soften if transparency in data processing is improved, specifically regarding what information is accumulated by which route, and what it is used for. The public are then more likely to feel, "we are taking advantage of our predecessors' contributions now, and are proud to do the same for the following generation's health", which seems to be the prevailing sentiment in the UK. We also have to enhance the opinion of cancer registration in the general population by describing the rigor of the registries' safety management measures, which treat personal information according to strict international standards [17].

It is worth noting that the Japanese public thought that they would be disadvantaged if their region had no cancer registry system (Q7). Unlike countries with a national registry (e.g., Nordic countries) or those where the cancer registries have no plan to cover the whole country (e.g., England, France, Italy), the Japanese cancer registry system aims to create independent regional cancer registries to cover the whole country. Considering the National Cancer Control Act in 2006, pertaining to the standardization and the equalization of cancer information based on cancer registration, the results of the present study support the continuation of our project [16].

In the "Administrative divisions cancer measures" questionnaire which the Nikkei Newspaper sent to the cancer registries, the registries answered that legislation and financial support were of course important, and "understanding of society" was one of the most important factor considered to enhance the position of cancer registration. We need a long-term strategy to ensure that the public is well informed on cancer registration [18]. In the USA, 64.3% of registries had educational materials to explain the system and to describe the possibility that researchers may contact patients about participating in a study [16]. Japanese cancer registries should emulate the American example, and promote passive educational approaches (web sites, pamphlets, brochures, etc.).

After 50 years of cancer registration in Japan, we are at a crossroads. Compared with other developed countries, we have not yet completed a system that can provide sufficient cancer registry data for means of cancer control or to evaluate cancer screening. Nor have we been able to use cancer registry data in a large-scale cohort study. To obtain the "understanding of society," we need to actively utilize information from the cancer registry and to educate the public about examples of actual use that have wide appeal. The future of cancer control therefore depends on our efforts and on public cooperation.

#### Conflict of interest statement

There is no conflict of interest concerning this study.

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## Recent trends and patterns in breast cancer incidence among Eastern and Southeastern Asian women

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Received: 16 December 2009 / Accepted: 4 June 2010 / Published online: 18 June 2010  
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### Abstract

**Background** Incidence of breast cancer is rising in Asian countries, and breast cancer is the most common cancer among Asian women. However, there are few recent descriptive reports on the epidemiology of breast cancer among Eastern and Southeastern Asian populations.

**Methods** We examined incidence trends for invasive breast cancer in women aged  $\geq 20$  years from 15 registries in Eastern (China, Japan, the Republic of Korea, Taiwan) and Southeastern Asia (the Philippines, Singapore, Thailand) for the period 1993–2002 mainly using data from *Cancer Incidence in Five Continents*, Volumes VIII and

IX. We compared trends in annual incidence rates and age-specific incidence curves over a 10-year period. We also compared the incidence rates of Asian-Americans with the rates of their Asian counterparts.

**Results** Breast cancer incidence rates increased gradually over time in all study populations. Rates were relatively high in Southeastern Asia and became progressively lower along a south-to-north gradient, with a fourfold geographic variation within the study populations. Age-specific incidence curves showed patterns that gradually changed according to incidence rates. Breast cancer incidence among Asian women living in the

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United States was 1.5–4 times higher than the corresponding incidence rate in the women's respective countries of origin.

**Conclusion** Breast cancer incidence is expected to continue to increase for the next 10 years in Asia and may approach rates reported among Asian-Americans. The number and mean age of breast cancer cases is expected to increase as the female Asian population ages, the prevalence of certain risk factors changes (early menarche, late menopause, low parity, late age at first live birth, and low prevalence of breastfeeding), and as Asian countries introduce mass screening programs.

**Keywords** Breast cancer · Epidemiology · Incidence · Asian women

### Introduction

Breast cancer is the most common cancer among women in most Asian countries [1], and incidence rates are expected to increase rapidly in populations where they have been lowest [2–5]. Birth-cohort effects, changes in reproductive factors, and the introduction of screening programs have contributed to the increase in breast cancer incidence among Asian women living in Hong Kong [6, 7], urban Shanghai [8], Taiwan [9], Japan [10], Korea [11], the Philippines [12], Singapore [13, 14], and Thailand [15]. Much of the global variation in breast cancer rates may be attributable to country-specific differences in the prevalence of risk factors.

However, there have been no comparative studies of the epidemiology of breast cancer conducted among Eastern and Southeastern Asian women using current incidence data. Due to the paucity of Asian data available in the past, most global comparisons of breast cancer incidence [2–5] have included only a few Japanese and Chinese datasets as representative of the entire Asian region, thus providing a picture that is far from complete.

In this study, we examined the most current data from 15 cancer registries with information available on cases and population by year to provide comprehensive breast cancer incidence statistics for the period 1993–2002 for Eastern and Southeastern Asian populations that have experienced very rapid increases in breast cancer risk. In addition, to gain insight into the contributions of the westernization of traditional lifestyles to breast cancer risk in Asian women, we compared incidence rates in our study populations with incidence rates for Asian-Americans during the period 1998–2002 as reported in *Cancer Incidence in Five Continents* (CI5), volume IX.

### Methods

#### Incidence data

We extracted incidence datasets (encompassing at least 10 years) from CI5, volumes VIII (1993–1997) [16] and IX (1998–2002) [1] and compiled them with additional data from the following sources: (1) Qidong Registry, China [17]; (2) Taiwan Registry, which has almost 30 years of data and high-quality indices; (3) Korea Central Cancer Registry, 1993–2002 data [18]; (4) DOH Rizal Cancer Registry, the Philippines, unpublished data submitted to CI5 Volume IX. Data from all registries met the CI5 IX inclusion criteria in terms of quality of indices; with more than 85% of cases having been morphologically verified (an exception was Rizal for the period 1998–2002) (“Appendix A”).

We also used the CI5 IX website to obtain pooled estimates of breast cancer incidence rates by age group for Chinese-, Japanese-, and Filipino-Americans from Los Angeles, San Francisco, and Hawaii and for Korean-Americans from Los Angeles.

#### Incidence rates and age-specific curves

To estimate the incidence rates, we extracted from the collected databases the annual number of female breast cancer cases (International Classification of Disease-10, code C50, invasive breast cancer) and the corresponding population numbers according to 11 age groups (20–24, 25–29, 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, and  $\geq 70$ ).

There were few cases of breast cancer among women aged less than 20 years. Therefore, we included only breast cancer cases who were female adults aged 20 years or older, in order to avoid the influence of rates from the high proportion of young women aged less than 20 years in some study populations. We then calculated the population and annual number of cases by 5-year age groups. We computed the age-standardized incidence rates per 100,000 person-years for women aged  $\geq 20$  years on the basis of the truncated world standard population.

To compare changes in incidence over time, we calculated the estimated annual percentage changes for all women and by 4 age groups (20–34, 35–49, 50–69, and 70+) by fitting a log-linear regression of the logarithm of the standardized rates using the calendar year as an explanatory variable (proc genmod, SAS, version 9.1, SAS Institute Inc.). We applied joinpoint regression to detect significant changes in breast cancer incidence using software from the Surveillance Research Program of the US

National Cancer Institute (Joinpoint Regression Program, version 3.3. <http://srab.cancer.gov/joinpoint/>) [19]. The joinpoint regression starts with no joinpoint and tests whether one or more joinpoints are statistically significant and need to be entered into the model (a maximum of two joinpoints by default) to best fit the data over the study period.

**Results**

Breast cancer incidence rates and age-specific patterns

Table 1 presents the number of women in the year 2000 in the target population, number of breast cancer cases, crude incidence rates (age  $\geq 20$  years), and age-standardized

**Table 1** Study area population (women aged  $\geq 20$  years) and breast cancer incidence during the periods 1993–1997 and 1998–2002 by registry/country

Registry (coverage %)*	Population (thousands) in the year 2000**	1993–1997			1998–2002			% Change of ASR****
		No. of cases***	CR <sub>t</sub>	ASR <sub>t</sub>	No. of cases***	CR <sub>t</sub>	ASR <sub>t</sub>	
<i>Eastern Asia</i>								
Rural China (2.5%)	611	483	16.5	17.8	694	22.7	20.4	14.6
Jiashan	147	108	15.1	15.2	199	27.1	24.7	62.2
Qidong	464	375	17.0	19.0	495	21.3	19.1	0.7
Shanghai (100%)	2,491	6,638	52.1	45.4	8,506	68.7	58.7	29.3
Hong Kong (100%)	2,622	6,893	59.5	60.3	9,406	71.8	69.1	14.6
Taiwan (100%)	7,721	14,377	41.3	44.0	22,758	59.0	59.7	35.7
Japan (11.0%)	5,751	15,512	55.6	48.2	19,409	67.5	57.6	19.7
Miyagi	956	2,842	62.7	54.9	3,966	83.0	70.8	29.0
Nagasaki	639	1,890	60.1	49.4	2,481	77.7	63.2	28.0
Osaka	3,640	9,301	52.7	46.5	11,080	60.9	53.1	14.3
Yamagata	517	1,479	58.3	47.0	1,882	72.9	58.7	24.9
Republic of Korea (100%)	17,108	18,720	23.8	25.7	31,269	36.5	37.2	44.9
<i>Southeastern Asia</i>								
Philippines (16.8%)	3,313	7,896	52.4	80.2	9,801	59.2	84.4	5.2
Manila	1,586	4,383	58.6	89.2	5,063	63.8	90.5	1.4
Rizal	1,727	3,513	46.2	71.1	4,738	54.9	78.6	10.6
Singapore (100%)	1,174	3,529	67.6	72.6	5,332	90.7	90.1	24.2
Thailand (6.8%)	1,244	1,246	23.4	25.2	2,089	33.6	34.3	36.0
Chiang Mai	539	617	25.1	26.8	958	35.6	35.9	33.8
Lampang	282	376	26.7	28.4	538	38.1	36.6	29.1
Songkhla	422	253	17.3	19.4	593	28.1	30.3	56.4

CR<sub>t</sub>: Truncated crude rate per 100,000 woman-years

ASR<sub>t</sub>: Age-standardized rate per 100,000 woman-years, calculated using the truncated world standard population of Segi for women aged  $\geq 20$  years

Rural China: Pooled estimates with Jiashan (1993–2002) and Qidong (1993–2002)

Japan: Pooled estimates with Miyagi Prefecture (1993–2002), Nagasaki Prefecture (1993–2002)

Osaka Prefecture (1993–2002), and Yamagata Prefecture (1993–2002)

Philippines: Pooled estimates with Manila (1993–2002) and Rizal (1993–2002)

Thailand: Pooled estimates with Chiang Mai (1993–2002), Lampang (1993–2002), and Songkhla (1993–1996, 1998–2002)

\* Coverage: the registries from Shanghai, Hong Kong, Taiwan, Korea, and Singapore covered the entire population of their region. Coverage for rural China, Japan, the Philippines, and Thailand was estimated using the population covered by each registry and the total population of each country in 2000

\*\* Number of women aged  $\geq 20$

\*\*\* Number of incident breast cancer cases

\*\*\*\* Percent change of ASR 1993–1997 to ASR 1998–2002

incidence rates (truncated at age  $\geq 20$  years) of the 15 cancer registries included in this study.

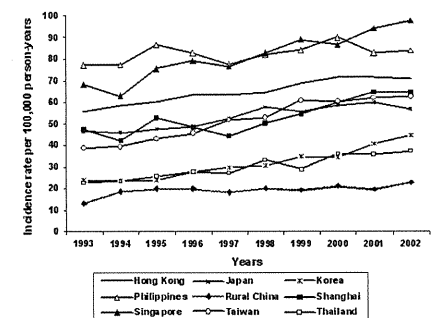
Coverage rates for registries from Shanghai, Hong Kong, Taiwan, Korea, and Singapore were 100%; however, those for rural China (2.5% coverage from two registries) and Thailand (6.8% from three registries) were very low and three registries in Japan (11.0%) and two registries in Philippines (16.8%) covered more than 10% of population, respectively.

All countries showed an increase in truncated age-standardized breast cancer incidence rates from the first 5-year period to the second, with the highest rates found in Korea (44.9%) and Thailand (36.0%) and the lowest rates in the Philippines (5.2%).

Over all age groups, the rates varied by a factor of approximately 4 during the period 1993–2002, from the lowest (19.2%) in rural China to the highest (82.5%) in the Philippines (Table 2).

Incidence rates increased gradually in all countries (no joinpoints were detected). We observed significant ( $P < 0.05$ ) mean annual percentage changes in Korea (7.9%), which had a low incidence rate (31.9%); in Taiwan (6.1%), which had an intermediate rate (52.5%); and in Singapore (4.4%), which had a high rate (82.2%) (Fig. 1; Table 2). Incidence rates increased significantly in Korea during the 10-year period in all age groups except the  $\geq 70$  group. The Philippines had the lowest annual percentage changes in most age groups. Women aged 50–69 years had significantly higher annual percentage changes in most countries and registries, but not in Japan, rural China, or the Philippines (Table 2).

Incidence rates and age-specific incidence curves exhibited four patterns (Fig. 2). The first pattern was low



**Fig. 1** Trends in invasive breast cancer incidence (truncated age-standardized incidence rate and estimated annual percentage change) during the period 1993–2002 by country/registry. The standard population used was the truncated population (aged  $\geq 20$ ). Rural China: Pooled estimates with Jiashan (1993–2002) and Qidong (1993–2002); Japan: Pooled estimates with Miyagi Prefecture (1993–2002), Nagasaki Prefecture (1993–2002), Osaka Prefecture (1993–2002), and Yamagata Prefecture (1993–2002); Philippines: Pooled estimates with Manila (1993–2002) and Rizal (1993–2002); Thailand: Pooled estimates with Chiang Mai (1993–2002), Lampang (1993–2002), and Songkhla (1993–1996, 1998–2002)

incidence with slow increases until age 50 years and then a gradual decrease (rural China, Korea, and Thailand). The second pattern was intermediate incidence with increases until age 50 years and then slow decreases in the elderly (Japan, Taiwan). The third pattern was intermediate incidence with rapid increases until age 50 years and then a plateau (Hong Kong, Shanghai). The fourth and final pat-

**Table 2** Breast cancer incidence rates and estimated annual percentage change (EAPC) 1993–2002 by age group

Country/registry	Age 20–34		Age 35–49		Age 50–69		Age 70+		Overall (age 20+)	
	ASR <sub>t</sub>	EAPC	ASR <sub>t</sub>	EAPC	ASR <sub>t</sub>	EAPC	ASR <sub>t</sub>	EAPC	ASR <sub>t</sub>	EAPC
Rural China	2.4	4.4	27.3	0.7	32.2	5.7	23.3	1.8	19.2	3.2
Shanghai	4.9	-1.4	64.7	3.4	92.2	5.6*	96.6	4.1*	52.2	4.4
Hong Kong	7.9	0.5	82.3	3.2	107.4	3.6*	133.9	0.2	65.2	2.8
Taiwan	9.0	3.5	73.1	6.0*	87.3	6.4*	59.6	7.3*	52.5	6.1*
Japan	5.8	3.3	73.0	2.6	88.5	3.6	79.5	3.6	52.9	3.2
Republic of Korea	6.9	6.0	51.0	7.7*	47.2	8.5*	22.1	7.0	31.9	7.9*
Philippines	7.3	1.4	84.0	-0.5	160.6	1.9	176.2	0.6	82.5	0.9
Singapore	7.5	5.6	98.9	2.8	152.4	5.7*	136.8	3.3*	82.2	4.4*
Thailand	5.5	2.5	43.3	5.0	47.6	6.9*	38.5	8.8*	30.3	5.9

ASR<sub>t</sub>: Truncated age-standardized rate per 100,000 women, calculated using the truncated world standard population as appropriate

\*  $P < 0.05$

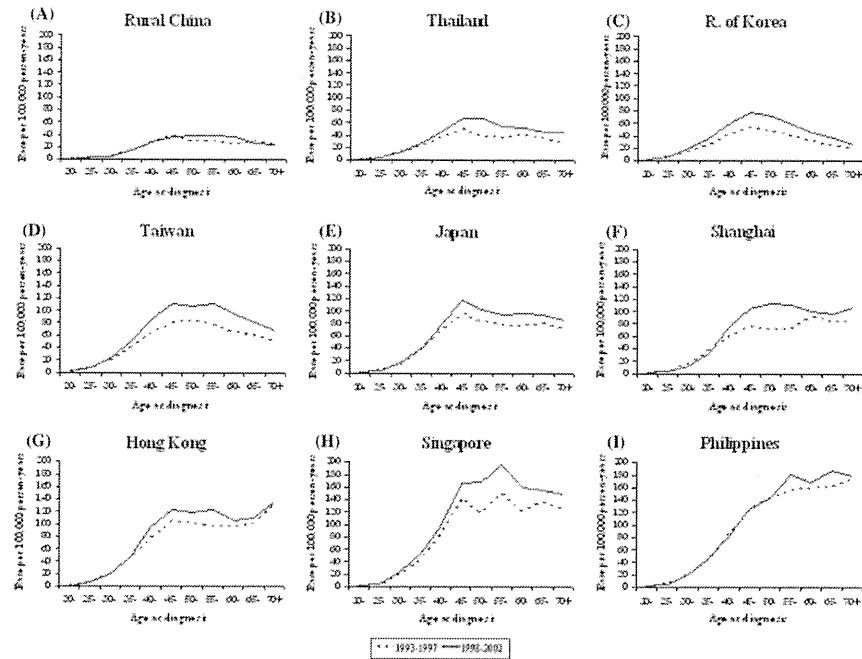


Fig. 2 Age-specific breast cancer incidence curves by registry/country. Dashed lines represent 1993–1997, continuous lines 1998–2002

tern was high incidence with rapid increases peaking after age 65 years (Singapore, the Philippines).

Comparison of breast cancer incidence between country of origin and immigrant country (United States)

Table 3 presents breast cancer incidence rates for the Asian populations and for their Asian-American counterparts for the period 1998–2002. For Asian women living in the United States, the highest incidence rate was for Japanese women and was approximately 4 times the incidence rate of Japanese women living in Japan. The incidence rate for Filipino women living in the United States, in contrast, was only 1.5 times the rate in the Philippines, the country with the highest incidence rate in Asia. For Korean women, the incidence rate for Korean women living in the United States was double the rate in Korea. The rate for Chinese women in the United States was equivalent to the rate for

Chinese women in Singapore, but it was almost five times higher than the rate in rural China.

Discussion

Rapid increases in the burden of breast cancer among Asian women have been described by other studies [4, 5, 20] and are in keeping with our finding of increases in breast cancer incidence rates among women aged 20 years or older during the period 1993–2002, with annual increases ranging widely from 0.9% in the Philippines to 7.8% in Korea. In countries that had high incidence rate changes, such as Korea and Taiwan, significant incidence rate changes were evident across most age groups. In countries with more moderate changes (Singapore and Shanghai), however, we observed significant rate changes in women aged  $\geq 50$  years, regardless of the incidence rate.

Table 3 Breast cancer incidence 1998–2002 in immigrant Asian populations of the United States and corresponding country of origin

Country of origin	ASR <sub>i</sub> (age $\geq 20$ years)	Incidence rates		Immigrants (in US)	ASR <sub>i</sub> (age $\geq 20$ years)	Incidence rates	
		Age 20–49 years	Age $\geq 50$ years			Age 20–49 years	Age $\geq 50$ years
Rural China	20.4	13.8	33.7	Chinese LA, SF, HI	94.7	50.4	183.2
Shanghai	58.7	34.5	107.2				
Hong Kong	69.1	44.1	118.3				
Taiwan	59.7	42.6	93.8				
Chinese in Singapore	93.9	54.3	173.2				
Korea	37.2	32.3	51.9	Korean LA	72.8	42.9	132.9
Japan	57.6	39.0	97.1	Japanese LA, SF, HI	160.5	63.6	355.6
Philippines	84.4	41.9	169.4	Filipino LA, SF, HI	123.7	60.2	251.4

ASR<sub>i</sub>: Truncated age-standardized incidence rate based on World Standard Population; LA: Los Angeles; SF: San Francisco; HI: Hawaii Data from C15 IX (1)

These results differ from the results of a study of 35 countries where the majority of the population was of European ancestry [21]. Incidence rates in European women were much higher and increases were observed mainly in women aged 50–69 [21]. We interpret this finding of increases in incidence in Asian populations as being mostly due to a birth-cohort effect. For example, women born in the 1930s may not have had the same exposures to breast cancer risk factors as those born after the 1960s [6, 8, 10, 12–14, 22, 23].

There was a fourfold variation in incidence rates and a marked pattern of an increasing breast cancer burden that progressed roughly from east to south; that is, from Eastern to Southeastern Asian populations. Breast cancer incidence rates in the Greater Manila area (the Philippines) were similar to those in the United States in the 1970s [24]. This high incidence rate could be explained, in part, by earlier exposure to a westernized lifestyle, because of the Spanish colonization of the Philippines four centuries ago [12]. In contrast, during nearly the same time period (1968–1982), breast cancer incidence in Singapore was about 50% lower than in most of Western Europe, North America, and Australia, but higher than in China (Shanghai) and Japan [25]. During the past three decades, urbanization, which has brought with it significant environmental changes, and the adoption of a “westernized” lifestyle, characterized by delayed age at first birth, decreased parity, a diet rich in saturated fats, and a sedentary lifestyle, may have contributed to the progressive rise of breast cancer incidence rates, which have shown an average annual increase of 3.7% between 1968 and 2002 in Singapore [26]. A similar impact is anticipated in other Asian countries that are experiencing economic progress. Given the association between a country’s economic level and the risk of breast cancer, Japan’s low breast cancer incidence rate is paradoxical and still unexplained [3, 27]. Unfortunately, a

comparison of breast cancer incidence rates in various Asian populations has not been possible in the past due to the paucity of incidence rate data for rural China, Korea, Thailand, and Taiwan.

Changes in lifestyle and reproductive factors, including early age at menarche, late age at menopause, delaying marriage, having fewer children later in life, and changes in infant feeding patterns are established risk factors of breast cancer—a hormonally regulated disease [28]. Findings among Asian women in terms of hormonal and reproductive risk factors [14, 15, 23, 29–33] are consistent with the findings of studies conducted in Western populations [28]. Hormone replacement therapy (HRT) increases the risk of breast cancer [34, 35], even though decreases in breast cancer incidence rates were observed shortly after the publication in 2002 of a report on the association of use of HRT and breast cancer [36]. HRT is not frequently used by Asian women [37, 38], and one case-control study showed no increase in breast cancer incidence in a population of Asian women who received HRT [39].

Increases in breast cancer incidence rates are due, in part, to the effect of mammography screening programs common in Western countries [35, 40–42]. In Asia, organized mammography screening programs started in the early 2000s in Japan, Korea, and Singapore [43–46], and a high-risk group approach was initiated in Taiwan [47]. Screening by breast self examination in China and by clinical examination of the breast in the Philippines was introduced as a suitable option for countries in economic transition and with limited resources [48, 49]. Considering this, screening programs are unlikely to have contributed substantially to the increases in breast cancer incidence rates during the period 1993–2002.

Asian immigrants have been shown to have an intermediate level of risk compared with their native country and current host country, and they are expected to reach

breast cancer incidence rates that progressively approach the pattern observed in the current host country [50, 51]. Our finding that breast cancer incidence rates among Asian women living in the United States were 1.5–4 times higher than incidence rates in women's respective countries of origin (Table 3) is in keeping with a report that exposure to a Western lifestyle has a substantial impact on breast cancer risk among Asian immigrants [50]. Moreover, the rate is rapidly rising [52]. Given continued exposure to risk factors correlated with decreasing fertility and high prevalence of a Western lifestyle, however, breast cancer incidence among Asian women may soon approach that of Asian-Americans. Breast cancer incidence rates in the United States declined between 1999 and 2003 and then reached a plateau. This recent trend in the United States suggests that the aggressive screening programs started in 1982 have ended decades of increasing incidence [53, 54]. If the same pattern occurs among Asian women following the initiation of mammography screening programs in Asian countries, increases in breast cancer incidence can be expected to approach levels similar to those seen in the United States, for at least another 10 years, because breast cancer incidence rates among Japanese-American and Filipino-American women in the mid-1980s are similar to rates among Korean-American and Chinese-American women in the mid-1990s [1, 16].

The strength of this study is its inclusion of a large amount of recent (the most current data analyzed by any study to date), high-quality incidence data from 15 cancer registries from Asia ("Appendix A"). Even this amount of data, however, cannot fully describe breast cancer patterns over such a large, populous, and diverse area.

The study has also some limitations. In terms of coverage, the registries used for pooled estimates for rural China, Thailand, and Japan are insufficiently representative to show country-level breast cancer incidence, although CI5 VIII and IX had breast cancer incidence information for the study period only for two registries in Rural China, three registries in Thailand, and four in Japan. In the Philippines, for example, we were able to include data only from urban areas, potentially limiting the applicability of our findings to other study populations.

Likewise, incidence rates from the three principal ethnic groups of Singapore (Chinese, Malay, and Indian) were presented together, but previous reports of breast cancer incidence in Singapore have shown that the most rapid increases have occurred in the Chinese population [55]. Thus, the overall breast cancer incidence rate in Singapore is driven by the rates in Chinese women, and there are likely to be ethnic differences in risk factors such as fertility, breastfeeding, and prevalence of obesity [14, 55]. Therefore, these differential changes require further analysis, even though the marked overall temporal

trend is unlikely to be entirely explained by ethnic differences.

Unfortunately, data covering only 10 years were insufficient to find joinpoints for changes in incidence trends or to partition the different temporal components. However, regional variations with different patterns of age-specific incidence curves provide some signposts that point to the underlying changes in lifestyle. Moreover, the number of breast cancer cases and their mean age are likely to increase in the near future, due to not only the changes in reproductive factors and obesity but also to the rapidly aging population [56–58].

With continuing changes in lifestyle and the prevalence of reproductive factors, breast cancer incidence rates are expected to reach the level found in Western countries in the coming decades and to be attributed mostly to the introduction of organized screening programs and the rapid aging of the female Asian population.

**Acknowledgments** We gratefully acknowledge the cancer registries that contributed data to Cancer Incidence in Five Continents, volumes VIII and IX, and those that permitted us to use their data. We thank Mr. Mathieu Mazuir for data extraction and Mr. John Daniel for manuscript editing.

**Competing interests** None declared.

**Appendix A**

See Table 4.

**Table 4** Quality of indices of breast cancer incidence data from 15 cancer registries for 1993–1997 and 1998–2002

Country/registry*	Morpho- logically verified cases (%)		Death certificate only (%)		Mortality/ incidence ratio (%)	
	93– 97	98– 02	93– 97	98– 02	93– 97	98– 02
<i>Eastern Asia*</i>						
Rural China						
Jiashan	98	99.5	0	–	45	45
Qidong	96	95.2	0	–	69	46.1
Shanghai	88	91.4	0	0.2	31	21.5
Hong Kong	93	97.3	1	0.2	25	21.1
Taiwan	94	98.2	4	–	30	25.6
Japan						
Miyagi Prefecture	93	93.0	4	2.7	25	21.4
Nagasaki Prefecture	95	96.6	2	1.3	24	22.8
Osaka Prefecture	90	90.1	3	2.5	30	30.5
Yamagata Prefecture	94	94.6	3	2.1	21	23.5
Republic of Korea	87.4	95.8	6.7	1.3	24.3	18.4

**Table 4** continued

Country/registry*	Morpho- logically verified cases (%)		Death certificate only (%)		Mortality/ incidence ratio (%)	
	93– 97	98– 02	93– 97	98– 02	93– 97	98– 02
<i>Southeastern Asia*</i>						
Philippines						
Manila	85	86.3	5	0.1	–	–
Rizal	90	81.7	7	1.8	–	–
Singapore	99	99.1	0	–	33	25.5
Thailand						
Chiang Mai	94	96.5	2	0.1	–	–
Lampang	86	89.6	2	1.9	–	–
Songkhla	95	94.6	0	3.0	–	–

\* Based on "Definition of major areas and regions" from the website of the United Nations Population Division ([http://esa.un.org/unpp/index.asp?panel=5#\\_ftn5](http://esa.un.org/unpp/index.asp?panel=5#_ftn5)). Among registries from mainland China, Jiashan and Qidong were categorized as rural China and Shanghai as urban China

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## Secular trends in breast cancer mortality in five East Asian populations: Hong Kong, Japan, Korea, Singapore and Taiwan

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(Received December 21, 2009/Revised January 22, 2010/Accepted January 25, 2010/Online publication March 2, 2010)

Breast cancer risk is increasing in most Asian female populations, but little is known about the long-term mortality trend of the disease among these populations. We extracted data for Hong Kong (1979–2005), Japan (1963–2006), Korea (1985–2006), and Singapore (1963–2006) from the World Health Organization (WHO) mortality database and for Taiwan (1964–2007) from the Taiwan cancer registry. The annual age-standardized, truncated (to  $\geq 20$  years) breast cancer death rates for 11 age groups were estimated and joinpoint regression was applied to detect significant changes in breast cancer mortality. We also compared age-specific mortality rates for three calendar periods (1975–1984, 1985–1994, and 1995–2006). After 1990, breast cancer mortality tended to decrease slightly in Hong Kong and Singapore except for women aged 70+. In Taiwan and Japan, in contrast, breast cancer death rates increased throughout the entire study period. Before the 1990s, breast cancer death rates were almost the same in Taiwan and Japan; thereafter, up to 1996, they rose more steeply in Taiwan and then they began rising more rapidly in Japan than in Taiwan after 1996. The most rapid increases in breast cancer mortality, and for all age groups, were in Korea. Breast cancer mortality trends are expected to maintain the secular trend for the next decade mainly as the prevalence of risk factors changes and population ages in Japan, Korea, and Taiwan. Early detection and treatment improvement will continue to reduce the mortality rates in Hong Kong and Singapore as observed in Western countries. (*Cancer Sci* 2010; 101: 1241–1246)

In Asian countries, the mortality rates from breast cancer are relatively lower than in Western, industrialized countries<sup>(1)</sup> and have been on the increase until recently in China,<sup>(2,3)</sup> Japan,<sup>(4)</sup> Korea,<sup>(5,6)</sup> and Taiwan.<sup>(7)</sup>

In contrast, breast cancer mortality has been declining in Western countries for decades.<sup>(8,9)</sup> The decline has been explained in part by the cohort effect in women born after 1920 (a group that had more children and began childbearing at a lower age) and in part to improved management and treatment of women with the disease.<sup>(9)</sup>

In the 1980s, after it was shown in Sweden that mammography screening could lead to reduced breast cancer mortality,<sup>(10–13)</sup> other European countries started to establish screening programs.<sup>(14)</sup>

Because of the low breast cancer incidence rates in Hong Kong, Singapore, and Taiwan, population-based screening programs were not recommended in those populations until the early 1990s.<sup>(15–17)</sup> Taiwan started mammography screening for high-risk groups in 1995,<sup>(18)</sup> and Japan,<sup>(19)</sup> Korea,<sup>(20)</sup> and Singapore<sup>(16,21)</sup> started organized mammography screening programs

in the early 2000s. In Hong Kong, screening is done by voluntary ('opportunistic') mammography.<sup>(22)</sup>

In this paper, we review the most available data on breast cancer mortality in Hong Kong, Japan, Korea, Singapore, and Taiwan, and we attempt to describe and compare their secular changing patterns.

### Materials and Methods

We extracted annual breast cancer mortality data for Hong Kong (1979–2005), Japan (1963–2006), Korea (1985–2006), and Singapore (1963–2006) from the World Health Organization (WHO) mortality database and also used the WHO population data. We obtained mortality data for Taiwan (1964–2007) from the Taiwan Cancer Registry.

To detect significant changes in breast cancer mortality, we applied joinpoint regression using Joinpoint software version 3.3 (Surveillance Research Program, US National Cancer Institute) based on the Poisson assumption.<sup>(23)</sup> We used the default settings and allowed a maximum of three joinpoints. To determine the change in breast cancer mortality by age group within a time period, we compared the estimated annual percentage change (EAPC). We also compared age-specific mortality rates for three calendar periods (1975–1984, 1985–1994, and 1995–2006).

### Results

Breast cancer mortality rates of the five study populations grew closer together over the past three decades in spite of the fact that the female populations in 2005 were about 2 to 7 times as large as they were in 1970 (Table 1). Breast cancer mortality in Singapore was the highest of the five, with relatively large yearly variations attributable to the relatively small female population. The mortality rate did not change significantly during 1963–2006 but increased slightly before 1990 (to 1.13% of the EAPC) and decreased slightly after 1990 (to –1.5% of the EAPC) (95% confidence interval [CI], –2.4 to –0.6). In Hong Kong, there was an overall decreasing tendency for breast cancer mortality during 1979–2005, with a –0.37% EAPC and a more rapid decline since 1991 (EAPC, –0.99%; 95% CI, –1.6 to –0.4). In Taiwan, Japan, and Korea, in contrast, breast cancer death rates increased throughout the entire study period.

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Table 1. Female breast cancer deaths, women aged  $\geq 20$  years and age-adjusted breast cancer mortality rates in different calendar years by population

Country/Region	Period	No. of breast cancer deaths	Population ( $\geq 20$ years) in 1000s		Age-adjusted breast cancer death rate ( $\geq 20$ years) per 100 000 women			
			1970	2005	1970	1980	1990	2005
Hong Kong	1979–2005	8595	579	3063	N/A	13.3	14.4	13.1
Japan	1963–2006	239 477	23 748	57 780	7.27	9.2	10.4	14.3
Korea	1985–2006	20 789	4543	18 563	N/A	N/A	4.7	8.2
Singapore	1963–2006	6902	240	1641	15.8	23.1	23.4	16.6
Taiwan	1964–2007	25 549	3202	8405	7.34	8.7	11.5	16.4

N/A, data not available.

Before the 1990s, breast cancer death rates were almost the same in Taiwan and Japan; thereafter, up to 1996, they rose more steeply in Taiwan (EAPC, 4.63; 95% CI, 3.30–6.10) and then they began rising more rapidly in Japan (EAPC, 1.34; 95% CI, 0.9–10.8) than in Taiwan (EAPC, 0.89; 95% CI, 0.2–1.4) after 1996. The most significant increases were in Korea (EAPC, 3.41%; 95% CI, 3.17–3.65), which had the lowest mortality rate among the study populations (Fig. 1, Table 2).

The patterns of age-specific mortality curves during the last 30 years in Hong Kong and Singapore, which showed gradual increases with age, are different from those in Japan, Korea, and Taiwan where they are rather flat or declining after age 50 (Fig. 2). Figure 3 shows changes of mortality rates by age group. For women aged 20–34 years, the breast cancer mortality rate was low in all five study populations and tended to decrease in recent years except in Korea and Taiwan. For women aged 35–49 and 50–69 years, the rate has been increasing significantly in recent years in Japan, Korea, and Taiwan but decreasing in Hong Kong and Singapore. For women aged  $\geq 70$  years, risk tended to increase, except in Hong Kong, where there was an estimated annual change of  $-3.0\%$  (data not shown). We observed no statistically significant EAPC for four age groups over three calendar periods (two calendar periods for Korea) (Fig. 3) (data not shown).

## Discussion

In this study, we compared and assessed the secular trends and patterns of age-specific breast cancer mortality among five East Asian female populations. The overall breast cancer mortality in Hong Kong (1979–2005) and Singapore (1963–2006) showed increases up to 1990 and a slight reduction after that, but were

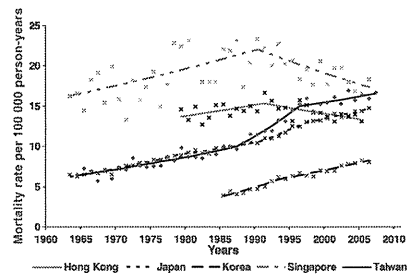


Fig. 1. Breast cancer mortality rate trend (truncated age-standardized mortality rates) obtained by jointpoint regression in five female Asian populations, 1963–2007. The standard population is the age-truncated population ( $\geq 20$  years) of world standard population.

Table 2. Estimated annual percent change (EAPC) of breast cancer death rates and 95% confidence intervals (CI)

Country/Region	EAPC	95% CI	
Hong Kong			
1979–1991	0.93	-0.1	1.9
1991–2005	-0.99	-1.6	-0.4
Japan			
1963–1978	2.40	2.0	2.8
1978–1990	1.47	1.1	1.9
1990–1997	3.11	2.2	4.0
1997–2006	1.34	0.9	1.8
Korea			
1985–1993	5.62	3.9	7.4
1993–2006	2.63	2.1	3.2
Singapore			
1963–1990	1.13	0.5	1.8
1990–2006	-1.50	-2.4	-0.6
Taiwan			
1964–1987	1.95	1.5	2.4
1987–1996	4.63	3.3	6.1
1996–2007	0.89	0.2	1.4

not significant. Breast cancer mortality rates, however, increased steadily until 2006, in Japan with a slightly high EAPC in the early 1990s, in Korea with a highest EAPC between 1985–1993, and in Taiwan with a rather great increment from the mid-1980s to the mid-1990s.

In most Western countries, in contrast, breast cancer mortality increased until at least the 1980s.<sup>(1,8,24)</sup> Mortality started to decline in the USA in 1989<sup>(24,25)</sup> and in Yorkshire in the United Kingdom, from 1983 to 1998<sup>(26)</sup> due in part to birth cohort effects for women born from the end of the 19th century to the mid-1920s<sup>(27)</sup>, and the decrease is expected to continue in the current decade as a long-term result of both mammography screening and improved medical intervention.<sup>(26)</sup>

In the present study, we observed a relatively high reduction in breast cancer mortality in Hong Kong and Singapore after 1995 except in women aged 70+ in Singapore. In contrast, increases of breast cancer mortality in women in all age groups, with a rather greater rising in women after age 50, were observed in Japan, Korea, and Taiwan.

Many Asian studies observed that age-specific incidence rates reached a peak at around age 50 and then declined with age and that it is mostly due to a birth-cohort effect in which risk increases progressively from one generation to the next.<sup>(6,28–33)</sup> Furthermore, increases of incidence rates are anticipated with the ageing of the population in the present study populations. The shapes of age-specific mortality curve in Japan, Korea, and Taiwan in women after age 50 are similar to those curves among estrogen-receptor (ER)-negative breast cancer in Western

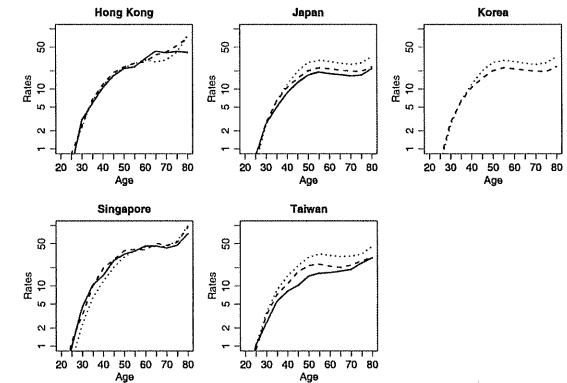


Fig. 2. Age-specific breast cancer mortality rates (per 100 000) in five study populations for calendar years 1975–1984 (continuous line), 1985–1994 (dashes), and 1995–2006 (dots).

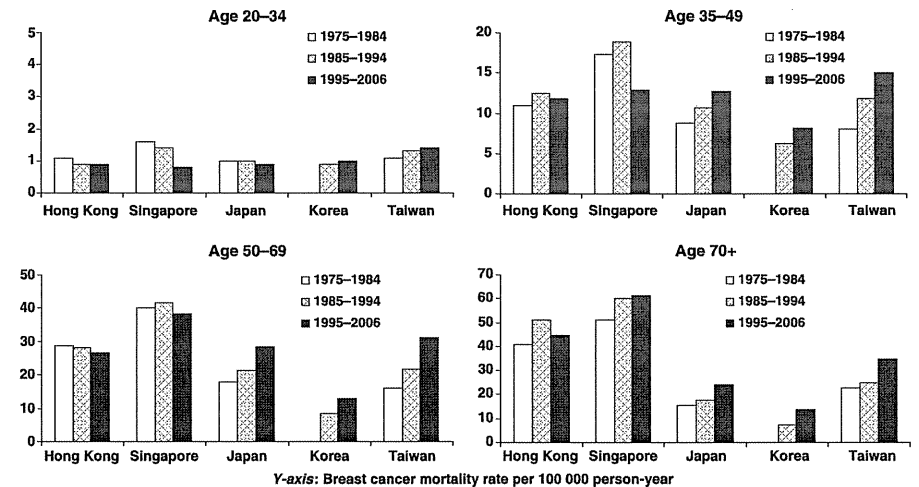


Fig. 3. Breast cancer mortality by age group, period, and country/region. Y-axis, breast cancer mortality rate per 100 000 person-year.

countries.<sup>(34,35)</sup> In the 1990s, reported ER positivity among breast cancer patients in Asia was lower than in Western women<sup>(36)</sup>; however, an increased proportion of ER-positive cases in Asian women in recent years was observed in a couple of studies.<sup>(37,38)</sup> This pattern of mortality curve will, therefore, change to be more similar to the curves in Western women from shapes of age-specific curve in Japan, Korea, and Taiwan to shapes in Hong Kong and Singapore.

Cancer risk discrepancies between various populations may reflect different levels of risk by birth cohort as well as differences in the detection and management of the disease.

In Hong Kong, more than 80% of breast cancer cases were detected in a symptomatic setting due to the lack of region-wide breast cancer screening programs.<sup>(39,40)</sup> However, the guidelines for surgeons in the management of symptomatic breast disease published in 1995 in the United Kingdom were widely used.<sup>(41)</sup> During the 1990s, there were significant improvements in the concepts of the diagnosis services as well as in the treatment policy for primary breast cancer and services for breast cancer patient management (services which, especially in the surgical aspects, have reached quality standards).<sup>(42,43)</sup> The overall utilization of breast conserving therapy (BCT) increased from 30%

to 50% since the mid-1990s.<sup>(39,40)</sup> In the beginning of the 1990s, the overall survival of breast cancer was 83%.<sup>(42)</sup>

The Japanese Breast Cancer Society published evidence-based clinical practice guidelines for the treatment of early stage breast cancer in Japanese women in 2000<sup>(43)</sup> and brought out treatment guidelines for systemic adjuvant therapy of breast cancer in 2006.<sup>(44)</sup> Since 2001, the adjusted proportion of breast conserving surgery in clinical practice has increased dramatically from 26.4% before the guidelines to 59.9% after their publication.<sup>(45)</sup>

In Korea, the Breast Cancer Society first published the practice recommendations of breast cancer in 2002 (2nd edition in 2006 and 3rd edition in 2008) (<http://www.kbcs.or.kr>). According to a nationwide survey to evaluate the chronological changes in Korean breast cancer characteristics from 1996 to 2004, there were continuous increases of the percentage of early stage breast cancer and asymptomatic cases incidentally detected at mammography screening. During the same period, a rise of BCT was observed from 18.7% to 41.9%.<sup>(46)</sup> The proportion of early breast cancer (carcinoma *in situ* and stage I) increased from 24.2% in 1993 to 36.6% in 2002 in the national breast cancer incidence database and showed gradual increases of the 5-year relative survival from 75.2% in 1993 to 83.5% in 1999 (overall survival by stage I, II, III, IV was 98.2%, 91.7%, 68.2%, 30.5%, respectively).<sup>(6)</sup>

In Singapore, a decline in breast cancer mortality was observed before the introduction of a national screening program.<sup>(21)</sup> In a study conducted in the 1990s prior to the advent of the screening program in Singapore, 73% of breast cancer patients received adjuvant radiation therapy and 88% received some form of systemic therapy (chemotherapy or tamoxifen).<sup>(47)</sup> In reflection of this intervention, the 5-year survival of each patient stage (for stages I–IV, survival rates are 97%, 78%, 51%, and 13%, respectively), was equivalent to those from Western countries.<sup>(48,49)</sup>

In Taiwan, the overall survival of 1378 breast cancer patients (71.6% with ER and 22% in early onset cases under age 40) who were treated from 1995 to 2001 and were followed up until June 2007 was 89% (95% CI, 87% to 9%). Two-thirds of the patients in this study showed 100% adherence to the quality indicators in the clinical protocols.<sup>(50)</sup> Rather low proportions of BCT, despite the increases of performance of BCT from 17.6% of all eligible patients for surgery between 1990 and 1997<sup>(51)</sup> to 28.6% in the mid-2000s,<sup>(52)</sup> were partially explained on the basis of more advanced disease at initial presentation and misperception of radiation therapy among Taiwanese compared to the practices for preserving breasts for women with breast cancer in the Western countries.<sup>(53)</sup>

Taken together, services for breast cancer patient management, especially in the surgical aspects, have reached the quality standards in the guidelines in Asian countries since the late 1990s<sup>(45,54)</sup>; however, non-conformity with both chemo- and hormone therapy guidelines was associated with higher risk of death.<sup>(55)</sup>

Although secular changes in risk factors should be considered along with the effects of screening and therapies when interpreting mortality trends, population-level changes in risk factors have not been well examined. Hormonal and reproductive risk factors such as early menarche, late menopause, low parity, late age of first live birth, low prevalence of breastfeeding, high fat intake, alcohol consumption, and little physical activity in Hong Kong,<sup>(15)</sup> Japan,<sup>(56)</sup> Korea,<sup>(57)</sup> Singapore,<sup>(58)</sup> and Taiwan<sup>(59–61)</sup> are consistent with those already observed in Western populations.

We must also take into account sources of bias, such as errors in death certification, incidence registration, and cure rates.<sup>(62)</sup>

(1) Errors in death certification are likely to have been reduced over the past decades with the establishment of national health-

care systems in Japan,<sup>(63)</sup> Hong Kong,<sup>(64)</sup> Singapore,<sup>(65)</sup> Korea,<sup>(66)</sup> and Taiwan.<sup>(67)</sup> The increased risk observed for women aged  $\geq 70$  years in all those areas except Hong Kong might not be due to such errors. (2) Errors of incidence registration have decreased due to improvements in cancer registration in Japan,<sup>(68)</sup> Korea,<sup>(69)</sup> and Taiwan,<sup>(70)</sup> as well as in Hong Kong and Singapore, which have been publishing incidence rates with high quality since 1983 and 1968, respectively.<sup>(71)</sup> The recent increases in incidence rates in Korea may be partly attributable to the expanded coverage provided by the improved registration system.<sup>(6)</sup> (3) Errors in estimation of cure rates have changed as breast cancer prognosis has improved, both by advances in management and by early detection through mammography screening. Improvements in breast cancer survival were reported in Japan,<sup>(72,73)</sup> Korea,<sup>(6,74)</sup> and Singapore.<sup>(75)</sup> In Taiwan, the attributable proportions for improved survival of breast cancer due to early detection and medical care were 77% and 23% respectively.<sup>(60)</sup> Predominance of early onset and aggressive ER-negative breast cancers may partially account for the high breast-cancer mortality in Asian countries.<sup>(76)</sup> With advances in medical care, women in populations we studied may receive similar medical care in spite of living under differing healthcare systems. (4) In terms of the validity of mortality data, the completeness of population coverage is estimated to be 100% in Japan, 93% in Korea, and  $< 80\%$  in Singapore<sup>(77)</sup> (data are unavailable for Hong Kong and Taiwan). Any biases that resulted from incomplete coverage may have decreased as the time periods covered in the present study progressed. Error can also be caused by inaccurate population estimates.

In the early 1990s, after many European countries established screening programs,<sup>(14)</sup> there was a sudden decline in breast-cancer mortality. The decline was not likely attributable to the programs, however, because randomized prospective trials indicate that the effects of screening generally take at least 10 years to be reflected in mortality statistics.<sup>(78)</sup> Mammography, which was introduced in the early 1980s, is recommended for breast cancer screening in all five study populations. Japan and Korea organized a breast cancer screening program in 2002 that combines mammography with clinical breast examination<sup>(19,20)</sup>; since that time, breast cancer mortality has increased. Taiwan implemented a stratified breast cancer screening program in 1995,<sup>(79)</sup> and the mortality rate stopped increasing in the mid-1990s. The mortality rate in Singapore decreased before the introduction of screening (mammography with clinical breast examination) in 2002.<sup>(21)</sup> In Hong Kong, where screening is voluntary with no recommendation due to low incidence,<sup>(22)</sup> breast cancer mortality tended to decrease slightly after 1990. The decline of mortality rates was more pronounced for women younger than 50 years and is likely to be attributed to improved treatments.<sup>(80)</sup>

It is difficult and too early to assess the impact of breast cancer screening among Asian populations with the current trends of breast cancer mortality. Breast cancer mortality trends are expected to maintain the secular trend for the next decade mainly as the prevalence of risk factors changes and population ages in Japan, Korea, and Taiwan. Early detection and treatment improvement will continue to reduce the mortality rates in Hong Kong and Singapore as observed in Western countries.

#### Acknowledgments

We thank Katuska Veselinovic for assisting in the preparation of the manuscript and John Daniel for manuscript editing.

#### Disclosure Statement

The authors have no conflict of interest.

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## Nonfilter and filter cigarette consumption and the incidence of lung cancer by histological type in Japan and the United States: analysis of 30-year data from population-based cancer registries

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Shifts in the histologic type of lung cancer accompanying changes in lung cancer incidence have been observed in Japan and the United States. We examined the association between the shift in tobacco design from nonfilter to filter cigarettes with changes in the incidence of adenocarcinoma (AD) and squamous cell carcinoma (SQ) of the lung. We compiled population-based incidence data from the Surveillance, Epidemiology and End Results in the United States (1973-2005) and from selected Japanese cancer registries (1975-2003). Trends in age-standardized rates of lung cancer incidence by histologic type were characterized using joinpoint analyses. A multiple regression framework was used to examine the relationship between tobacco use and incidence by histologic type. We observed that AD has replaced SQ as the most frequent histologic type in males and females in both Japan and the United States. Filter cigarette consumption was positively associated with the incidence of AD, with time lags of 25 and 15 years in Japan and the United States, respectively ( $\beta_{AD}^{AD}$ :  $1.946 \times 10^{-3}$ ,  $p < 0.001$  and  $3.142 \times 10^{-3}$ ,  $p < 0.001$ ). In contrast, nonfilter cigarette consumption was positively associated with the incidence of SQ, with time lags of 30 and 20 years in Japan and the United States, respectively ( $\beta_{SQ}^{SQ}$ :  $0.464 \times 10^{-3}$ ,  $p = 0.006$  and  $0.364 \times 10^{-3}$ ,  $p = 0.008$ ). In conclusion, the shift from nonfilter to filter cigarettes appears to have merely altered the most frequent type of lung cancer, from SQ to AD.

### Epidemiology

The association between cigarette smoking and lung cancer was firmly established in the 1950s.<sup>1</sup> The rapid increase in incidence rates in the 20th century has led to an epidemic of lung cancer, particularly among men in industrialized countries.<sup>2,3</sup> In the United States, where serious smoking control efforts were instituted almost 50 years ago, the incidence of

lung cancer among men peaked in 1982 and began to decline thereafter,<sup>4</sup> but it continues to rise in countries where smoking control efforts have been less aggressive. In Japan, despite a continuous decline in smoking rates over the last 50 years, lung cancer incidence continues to rise.<sup>4,5</sup>

Lung cancer incidence patterns and trends vary by histological type<sup>6</sup> and have been shown to be related to smoking patterns and exposures to other lung risk factors.<sup>3</sup> Shifts in histologic type have been reported to accompany changes in lung cancer incidence. Relative and absolute increases in adenocarcinoma (AD) of the lung were first recognized in the 1970s<sup>7</sup> and continued to be observed in the United States<sup>8,9</sup> and European countries.<sup>10</sup> Although this trend has now peaked in the United States,<sup>11,12</sup> incidence appears to be still increasing in certain areas of Japan.<sup>13-15</sup>

Trends in the incidence of lung cancer by histologic type are of interest in the evaluation of the impact of changes in cigarette manufacture. In particular, although low-tar, low-nicotine, filtered cigarettes appear to have contributed to the overall decline in lung cancer, and most notably in squamous

**Key words:** population-based cancer registration, lung adenocarcinoma, filter cigarettes

**Grant sponsor:** The study was supported in part by 2 grants from the Ministry of Health, Labour and Welfare of Japan. 1. The 3rd-term Comprehensive Ten-year Strategy for Cancer Control. 2. A Grant-in Aid for Cancer Research (20-2)

**DOI:** 10.1002/ijc.25531

**History:** Received 24 Nov 2009; Accepted 11 Jun 2010; Online 29 Jun 2010

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cell carcinoma (SQ),<sup>16</sup> they may have simultaneously increased the risk of certain peripheral tumors, such as AD.<sup>17-20</sup> and it has been hypothesized that the upward trend in the incidence of AD is mainly due to the dissemination of low-tar filtered cigarettes.<sup>18-20</sup> Smoke from low-yield filter-tipped cigarettes is inhaled more deeply than that from earlier unfiltered cigarettes.<sup>21,22</sup> Inhalation transports tobacco-specific carcinogens more distally toward the bronchioalveolar junction, where ADs often arise. The change in cigarette consumption from nonfiltered to filtered cigarettes also reduces the yield of carcinogenic polycyclic aromatic hydrocarbons, which are inducers of SQs, while simultaneously increasing that of carcinogenic tobacco-specific N-nitrosamines, which are inducers of ADs.<sup>19</sup>

Here, we investigated differences in the effects of nonfilter and filter cigarette consumption on changes in the incidence of SQ and AD in Japan and the United States.

### Material and Methods

Lung cancer incidence data in Japan were obtained from nine of the 36 regional registries used to estimate nationwide incidence, namely Yamagata, Niigata, Fukui, Shiga, Osaka, Okayama, Saga, Nagasaki and Hiroshima City, which together account for about 18% of the Japanese population. For the United States, lung cancer incidence data were obtained from the Surveillance and End Results (SEER) program of the US National Cancer Institute, which makes aggregate data available to the public. The data cover about 10% of the US population in nine geographical regions, namely the states of Connecticut, Hawaii, Iowa, New Mexico and Utah, as well as the metropolitan areas of Atlanta (GA), Detroit (MI), San Francisco-Oakland (CA) and Seattle-Puget Sound (WA). We selected cases diagnosed with lung or bronchus cancer from 1973 through 2005 for the US data and from 1975 through 2003 for the Japanese data. Morphology codes indicating lung cancer cell type were grouped into eight major categories according to the WHO scheme<sup>23</sup>: (i) SQ (International Classification of Disease for Oncology version 3 (ICD-O-3) codes 8050-8078, 8083-8084); (ii) AD (8140, 8211, 8230-8231, 8250-8260, 8323, 8480-8490, 8550-8551, 8570-8574, 8576); (iii) small cell carcinoma (8041-8045, 8246); (iv) large cell carcinoma (including giant cell, clear cell and large cell undifferentiated carcinoma 8010-8012, 8014-8031, 8035, 8310); (v) other specified carcinoma; (vi) sarcoma (8800-8811, 8830, 8840-8921, 8990-8991, 9040-9044, 9120-9133, 9150, 9540-9581); (vii) other specified malignant neoplasm and (viii) unspecified malignant neoplasm (8000-8005). The percentages of cases with unspecified morphology in the United States and Japan differed by an order of magnitude: only 3.9% of the US cases had morphology codes of 8000-8005, indicating "unspecified malignant neoplasm," whereas 33.6% of case reports in Japan were coded 8000-8005. In accordance with Devesa *et al.*,<sup>10</sup> we proportionally allocated the cases with unspecified morphology to the other seven categories on a registry-, year at diagnosis-, sex- and age-specific basis.

US age-standardized incidence rates (ASR) were calculated for the years 1973-2005 and Japanese ASR for the years

1975-2003, by major morphological type, namely SQ, AD and small cell carcinoma. Age standardization incorporated the Segi world standard.<sup>24</sup> All incidence rates were expressed as newly diagnosed cases of malignant neoplasm per 100,000 person-years.

The trends in ASR were also characterized by the widely used joinpoint regression analysis, as described in detail elsewhere.<sup>25</sup> Briefly, joinpoint regression is a statistical technique that describes changing trends over successive segments of time and the magnitude of an increase or decrease within each segment after identifying the best fitting model. Essentially, within each time segment, the log of the ASR is modeled as a linear function of time (calendar year), thereby yielding annual exponential rates of change in ASR. The technique identifies the timepoint(s), also referred to as joinpoint(s), at which there is a statistically significant change in the incidence trend. A maximum of three joinpoints in the model was allowed in the model fitting. The resulting trend segments, as delimited in time by joinpoints, were described by the annual percentage change (APC), that is, the slope of the line segment.<sup>25</sup> The calculation assumes that rates increase or decrease at a constant rate over time, although the validity of this assumption has not been tested. APC is calculated based on the following regression model:

$$\log(R_y) = b_0 + b_1 y$$

where  $\log(R_y)$  is the natural log of the rate in year  $y$

The APC from year  $y$  to  $y + 1$

$$\begin{aligned} &= \left( \frac{R_{y+1} - R_y}{R_y} \right) \times 100 \\ &= \left( \frac{e^{b_0 + b_1(y+1)} - e^{b_0 + b_1 y}}{e^{b_0 + b_1 y}} \right) \times 100 \\ &= (e^{b_1} - 1) \times 100 \end{aligned}$$

In describing the trends, the terms "increase" or "decrease" were used when the slope (APC) of the trend was statistically significant ( $p < 0.05$ ); otherwise, the terms "stable" or "level" were used.

Data on cigarette consumption were based on the market share of nonfilter and filter cigarettes sale in each year. These data were obtained from the US Federal Trade Commission,<sup>26</sup> the Ministry of Health, Labour and Welfare, Japan,<sup>27</sup> the Ministry of Finance, Policy Research Institute, Japan,<sup>28</sup> Japan Tobacco and Salt Co. and the Tobacco Institute of Japan.

To assess whether the incidence rates of SQ and AD of the lung were correlated to annual nonfilter and filter cigarette consumption per capita, we used a multiple regression framework.<sup>29</sup> For a specific subpopulation (*i.e.*, Japanese), we let  $Y^{AD}(t)$  represent the ASR (per 100,000 person-years) of AD at time  $t$ , and  $Y^{AD}(t^+)$  represent the ASR of AD at one time point ahead of time  $t$ . For example:

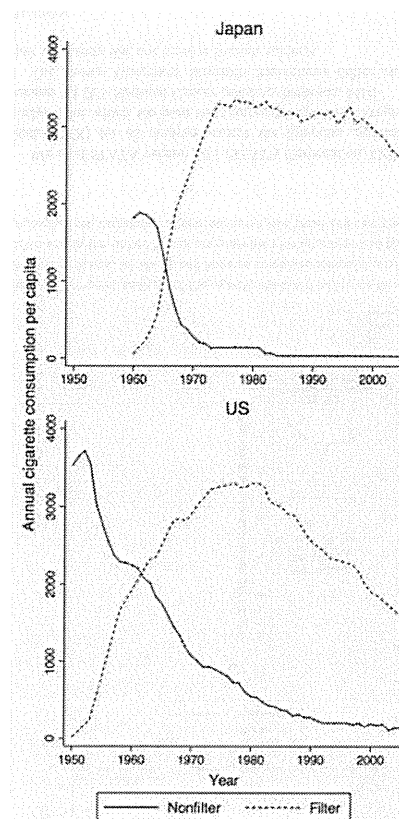


Figure 1. Japan and US nonfilter and filter cigarette consumption. Data for annual consumptions of nonfilter (solid line) and filter (dashed line) cigarettes per capita are presented. The shift from nonfilter to filter cigarettes occurred in the 1960s and the 1950s in Japan and the United States, respectively.

$$Y^{AD}(t) = [Y^{AD}(1), Y^{AD}(2), \dots, Y^{AD}(T-1)]$$

$$Y^{AD}(t^+) = [Y^{AD}(2), Y^{AD}(3), \dots, Y^{AD}(T)]$$

Likewise, we let  $Y^{SQ}(t)$  represent the ASR (per 100,000 person-years) of SQ at time  $t$  and  $Y^{SQ}(t^+)$  represent the ASR of SQ at one time point ahead of time  $t$ . Additionally, we let

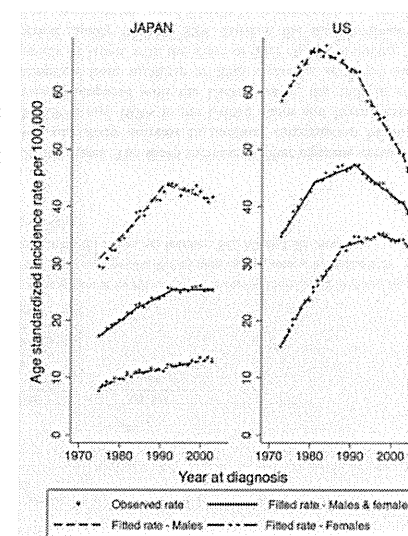


Figure 2. Joinpoint analysis of the overall age-standardized incidence rates (ASR) of lung cancer among individuals in Japan and the United States.

$X(t^+ - \tau)$  represent the nonfilter or filter cigarette consumption at time  $t^+ - \tau$ , where  $\tau$  is the appropriate time lag. Thus, for each subpopulation, we have the following models:

$$Y^{SQ}(t^+) = \beta_0^{SQ} + \beta_1^{SQ} Y^{SQ}(t) + \beta_2^{SQ} X(t^+ - \tau) + \epsilon^{SQ} \quad (1)$$

$$Y^{AD}(t^+) = \beta_0^{AD} + \beta_1^{AD} Y^{AD}(t) + \beta_2^{AD} X(t^+ - \tau) + \epsilon^{AD} \quad (2)$$

We set  $\tau$  from 5 to 30 years according to the epidemiological evidence: in this regard, because the incidence of lung cancer does not appear to be lower among ex-smokers who quit smoking within 5 years than current smokers,<sup>30,31</sup> the sum of the induction period and latent period of lung cancer caused by tobacco smoking is likely longer than 5 years.

We then examined the adjusted  $R^2$  in the model with different time lags  $\tau$  among subpopulations and cigarette designs to find the best fitting models (1) and (2) for nonfilter and filter cigarettes among Japanese and Americans.  $R^2$  value was interpreted to mean that for every unit increase in annual nonfilter or filter consumption per capita, we expect a  $\beta_2$  point increase in the ASR of AD or SQ, holding all other variables constant.