References

Abe T (1907). Clinical and statistical study on carcinoma. *Gann*, **1**, 576-600 (in Japanese).

Aoki K, Kurihara M (1994).The history of Cancer Registration in Japan: Contribution of Dr Mitsuo Segi. *Cancer Surveys*, **19**, 563-70.

Aoki K (2000). Contributions to cancer prevention of Non-Governmental Organizations. 1. The dawn of cancer control activities: Establishment of the UICC and its activities. *Asian Pac J Cancer Prev*, **1**, 181-93.

Aoki K (2001). Contributions to cancer prevention of Non-Governmental Organizations. 2. The dawn of cancer control activities: comparison of Japan and the USA. *Asian Pac J Cancer Prev*, **2**, 15-26.

Aoki K (2006). Early history of cancer epidemiology and prevention in Japan. *Asian Pac J Cancer Prev*, **7**, 170-6.

Assunta M, Chapman S (2006). Health treaty dilution: a case of Japn's influence on the language of teh WHO Framework Convention on Tobacco Control. *J Epidemiol Community Health*, **60**, 751-6.

Chikamatsu T (1918). Study on experimental carcinogenesis induced by tobacco tar. *Bulletin of Pathology and Haematology*, **1**, 1-61, (in Japanese).

Fujinami A (1913). Disposition of disease, especially on the tumors. *Nissin Igaku*, **2**, 999-1038 (in Japanese).

Fujinami A (1929). Contribution to the geographical pathology of malignant tumors in Japan. *Trans Jpn Pathol Soc*, **19**, 759-62 (in Japanese).

Fujinami A, Nakarai S (1908). Geographic and statistical investigations on malignant tumors in Kyoto city and its vicinity. *Gann*, 2, 452-455 (in Japanese).

Hanai A, Fujimoto I, Tsukuma H and Oshima A (1999) Cancer Registration and Cancer Trends in Japan. Proceeding of the International Symposium "Cancer Epidemiology and Control in the Asia-Pacific Region" (Dr Sato S, Miller MW et al. eds), International Center for Medical Research, Kobe, pp80-88

Hayashi N (1935). Geographic statistics of malignant neoplasms (Summing up reports of the studies in eight prefectures of Chubu district). *Trans Jpn Path Soc*, 25, 742-43 (in Japanese).

Hirohata T (1996). Epidemiological studies in Japan. *J Epidemiol*, 6, S13-7.

Kajikawa T (1930). Geographical and statistical study on malignant tumors in Nara prefecture(the 1st and 2nd parts). *Kyoto Med J*, **26**, 442-470 and 614-696 (in Japanese).

Katada T (1926). Geographical and statistical study on malignant tumors in Yamanashi prefecture *Arch Pathol*, **3**, 777-935 (in Japanese).

Kato T, Kato S (1936). Geographical and statistical study on malignant tumors in Ishikawa prefecture. *Arch Pathol*, **11**, 391-575 (in Japanese).

Monzen T and Wakabayashi T (1986) Tumor and tissue registries in Hiroshima and Nagasaki. *Gann Monogr Cancer Res*, 32, 29-40.

Nagayo M (1935). Statistical Studies on Malignant Tumors in Japan. Gann, **29** (Supplement) (in Japanese).

Nakarai S (1913). Statistical and geographic study on malignant tumors (2nd report). *Gann*, **7**, 183-4 (in Japanese).

Nomura H (1924). Geographical and statistical study on malignant tumors in Aichi prefecture. *Arch Pathol*, **1**, 495-782 (in Japanese).

Nomura H, Yoshida M (1925). Geographical and statistical study on malignant tumors in Gifu prefecture. *Arch Pathol*, **2**, 584-845 (in Japanese)

Ogata T (1955). Epidemiological study on cancer – Statistical study on risk factors of cancer. *Nippon Ishikai Zasshi*, **34**, 685-94 (in Japanese).

Okamoto N (2008). A history of the cancer registration system in Japan. *Int J Clin Oncol*, **13**, 90-96.

Sato K (1907). Statistical study on localization of cancer. *Gann*, **1**, 1-15 (in Japanese).

Sasaki T, Yoshida T (1935). Experimentelle Erzeugung des Leberkarzinoma durch Fuetterung mit o-amidoazotoluol Virchow Arch. Path. *Anat*, **295**, 175-200.

Segi M, et al (1960). Cancer in Japan and the World, Epidemiology, Statistics and Geopathology. Shinndan-to-Chiryou Co. Ltd. Tokyo (in Japanese).

Segi M, Fukushima I, Fujisaki S, et al (1957). Cancer morbidity in Miyagi prefecture, Japan and a comparison with morbidity in the United States. *J Natl Cancer Inst*, 18, 373-83.

Segi M, Fukushima I, Mikami Y, Fujisaki S, Kurihara M (1954) Cancer Illness; among Residents of Miyagi Prefecture, Japan, 1951. *Tohoku J Exp Med*, **59**, 213-24.

Sobue T (2008). Current activities and future directions of the cancer registration system in Japan. *Int J Clin Oncol*, **13**, 97-101.

Sugimura T, Wakabayashi K, Nakagama H, nagao M (2004). Heterocyclic amines: Mutagens/carcinogens produced during cooking of meat and fish. *Cancer Sci*, **95**, 290-9.

Suzuki N (1918). Statistical study on malignant tumors (the 1st part). *J Kyoto Med Assoc*, **15**, 849- 985 (in Japanese).

Suzuki N (1921). Statistical study on malignant tumors (the 2nd and 3rd parts). *J Kyoto Med Assoc*, **18**, 306-335, and 337-363 (in Japanese).

Wakai K, Matsuo K (2007). The JICA training course, Community-based Cancer Prevention for the Asian and Pan-Pacific Countries, fiscal year 2006 (epidemiological approach). *Asian Pac J Cancer Prev*, **8**, 150-4.

Yamagiwa K, Ichikawa K (1915). Experimentelle Studie über die Pathogenese der Epithelial Geschwülste. *Mitteilungen Med. Fakultät Kaiserl. Univer. Tokyo*, **15**, 295-344.

Yoshida M (1926). Geographical and statistical study on malignant tumors in Shizuoka Prefecture *Arch Pathol*, **3**, 163-415 (in Japanese).

Jpn J Clin Oncol 2009;39(12)850–858
doi:10.1093/jjco/hyp106

Epidemiology Note

Cancer Incidence and Incidence Rates in Japan in 2003: Based on Data from 13 Population-based Cancer Registries in the Monitoring of Cancer Incidence in Japan (MCIJ) Project

Tomohiro Matsuda[1], Tomomi Marugame[1], Ken-ichi Kamo[2], Kota Katanoda[1], Wakiko Ajiki[1], Tomotaka Sobue[1] and The Japan Cancer Surveillance Research Group

[1]Cancer Information Services and Surveillance Division, Center for Cancer Control and Information Services, National Cancer Center, Tokyo and [2]Division of Mathematics, School of Medicine, Liberal Arts and Sciences, Sapporo Medical University, Hokkaido, Japan

Received July 14, 2009; accepted July 28, 2009; published online October 1, 2009

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

The Japan Cancer Surveillance Research Group is involved in cancer monitoring in Japan (1–3). This group estimated the cancer incidence in 2003 as part of the Monitoring of Cancer Incidence in Japan (MCIJ) project, on the basis of data collected from 13 of 31 population-based cancer registries: Miyagi, Yamagata, Chiba, Kanagawa, Niigata, Fukui, Shiga, Osaka, Tottori, Okayama, Hiroshima, Saga 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 (4–6). There were two major methodologic changes in the present study: (i) this was the first time we invited all 31 population-based cancer registries in Japan to participate, and from these we selected the 13 cancer registries with high-quality data in order to estimate the national incidence, and (ii) in consideration of timeliness, we did not apply the moving average which calculates the annual mean incidence rates of a year by using preceding and following years, and we used 2003 data alone for the national estimation. Because of the enlargement of the coverage area, Hiroshima 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. In 2007, we estimated incidences with and without the moving average based on the same registry data to compare the two methods. In conclusion, the estimated incidence without the moving average was comparatively unstable from year to year, but the gaps of the incidence numbers between the two estimations were subtle. These new methods therefore do not bring about changes in the estimated incidence numbers.

The number of incidences, crude rates, age-standardized rates and completeness of registration in 2003 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 2003 was estimated as 620 011 (C00–C96). The time trends of age-standardized incidence rates for the five major sites and male- and female-specific sites in 1975–2003 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 breast for women, as shown in Figs 1 and 2. The apparent increase in age-standardized incidence rates in 2003 is considered to be caused primarily by the development of hospital-based cancer registry in designated cancer care hospitals. The estimated cancer incidence data in Japan by sex, site, 5-year age group and calendar year during the period 1975–2003 are available as a booklet (7) and as an electronic database on the website (http://ganjoho.ncc.go.jp/professional/statistics/statistics.html).

For reprints and all correspondence: Tomohiro Matsuda, Cancer Information Services and Surveillance Division, Center for Cancer Control and Information Services, National Cancer Center, 5-1-1 Tsukiji, Chuo-ku, Tokyo 104-0045, Japan. E-mail: tomatsud@ncc.go.jp

Acknowledgements

The survey on cancer incidence in Japan was conducted with contributions from the 31 registries: Hokkaido, Aomori, Iwate, Miyagi, Yamagata, Ibaraki, Tochigi, Gunma, Chiba, Kanagawa, Niigata, Toyama, Ishikawa, Fukui, Gifu, Aichi, Shiga, Kyoto, Osaka, Tottori, Okayama, Hiroshima, Tokushima, Kagawa, Ehime, Kochi, Saga, Nagasaki, Kumamoto, Kagoshima and Okinawa.

© The Author (2009). Published by Oxford University Press. All rights reserved.

Table 1. Incidence, completeness of reporting and accuracy of diagnosis in Japan according to sex and primary site, 2003

Primary sites	ICD-10th	Number of incidence	Crude rate[a]	Age-standardized rate[a]		Completeness of reporting		Accuracy of diagnosis
				World population	Japanese 1985 model population	DCO/I (%)	I/M	MV/I (%)
Male								
All sites (incl. CIS)	C00–C96, D00–D09	372 374	597.7	288.0	409.8	16.5	1.99	74.8
All sites	C00–C96	364 072	584.3	281.4	400.5	16.8	1.95	74.4
Lip, oral cavity and pharynx	C00–C14	7835	12.6	6.7	9.1	11.7	1.94	81.0
Esophagus	C15	13 658	21.9	10.8	15.1	15.5	1.45	78.3
Stomach	C16	73 798	118.4	57.1	81.1	13.8	2.30	82.4
Colon	C18	35 262	56.6	27.0	38.5	11.9	2.74	82.6
Rectum and anus	C19, C20	21 892	35.1	18.0	24.8	11.1	2.68	84.2
Liver	C22	29 126	46.7	22.7	31.9	25.2	1.25	38.4
Gallbladder etc.	C23, C24	8755	14.1	6.1	9.2	27.2	1.20	46.0
Pancreas	C25	12 511	20.1	9.5	13.7	28.7	1.11	37.0
Larynx	C32	3921	6.3	3.1	4.3	7.3	4.24	88.5
Trachea, bronchus and lung	C33, C34	55 928	89.8	39.6	59.5	24.2	1.34	69.8
Skin	C43, C44	3325	5.3	2.6	3.6	7.1	6.08	90.6
Prostate	C61	40 062	64.3	27.3	41.4	9.5	4.76	85.7
Bladder	C67	12 646	20.3	9.3	13.6	11.1	3.40	84.7
Kidney, renal pelvis, ureter etc.	C64–C66, C68	8217	13.2	6.7	9.3	16.0	2.27	74.3
Brain and nervous system	C70–C72	2571	4.1	3.1	3.5	27.5	2.95	65.3
Thyroid	C73	2023	3.2	2.0	2.6	5.9	4.53	90.2
Malignant lymphoma	C81–C85, C96	12 881	20.7	11.6	15.5	17.0	2.65	79.9
Multiple myeloma	C88–C90	2251	3.6	1.6	2.4	30.6	1.20	65.8
All leukaemias	C91–C95	5606	9.0	5.8	7.0	25.3	1.37	82.9
Female								
All sites (incl. CIS)	C00–C96, D00–D09	269 220	412.2	193.9	260.8	17.1	2.20	73.6
All site	C00–C96	255 939	391.9	179.3	242.5	17.9	2.09	72.4

Continued

Table 1. *Continued*

Primary sites	ICD-10th	Number of incidence	Crude rate[a]	Age-standardized rate[a]		Completeness of reporting		Accuracy of diagnosis
				World population	Japanese 1985 model population	DCO/I (%)	I/M	MV/I (%)
Lip, oral cavity and pharynx	C00–C14	3180	4.9	2.2	2.9	15.0	2.01	76.6
Esophagus	C15	2742	4.2	1.7	2.3	20.0	1.66	69.3
Stomach	C16	36 525	55.9	22.1	31.2	17.9	2.10	78.3
Colon	C18	29 859	45.7	17.4	24.7	15.8	2.30	77.1
Rectum and anus	C19, C20	11 902	18.2	7.9	10.9	13.1	2.43	81.5
Liver	C22	13 535	20.7	7.0	10.4	29.3	1.26	32.8
Gallbladder etc.	C23, C24	10 200	15.6	4.7	7.1	32.3	1.18	40.5
Pancreas	C25	10 371	15.9	5.5	7.9	34.0	1.05	30.1
Larynx	C32	448	0.7	0.3	0.4	3.8	7.34	91.4
Trachea, bronchus and lung	C33, C34	22 817	34.9	12.8	18.4	25.1	1.51	66.5
Skin	C43, C44	4497	6.9	2.5	3.4	9.6	8.52	89.2
Breast (incl. CIS)	C50, D05	45 716	70.0	43.4	56.1	5.6	4.66	90.5
Uterus (incl. CIS)	C53–C55, D06	24 240	37.1	25.5	32.3	7.4	4.57	88.9
Uterus (only invasive)	C53–C55	17 285	26.5	16.1	20.8	10.0	3.26	85.7
Cervix uteri	C53	8674	13.3	8.8	11.3	7.1	3.65	89.4
Corpus uteri	C54	7430	11.4	6.5	8.5	5.6	5.41	89.6
Ovary	C56	7946	12.2	7.2	9.2	17.2	1.88	77.0
Bladder	C67	3713	5.7	1.8	2.7	18.8	2.19	74.5
Kidney, renal pelvis, ureter etc.	C64–C66, C68	4689	7.2	3.0	4.1	18.3	2.38	71.7
Brain and nervous system	C70–C72	2034	3.1	1.8	2.1	24.6	3.10	60.2
Thyroid	C73	6046	9.3	5.6	7.2	7.6	6.17	87.4
Malignant lymphoma	C81–C85, C96	8592	13.2	6.1	8.2	16.8	2.36	80.8
Multiple myeloma	C88–C90	2234	3.4	1.2	1.7	34.4	1.23	62.3
All leukaemias	C91–C95	3951	6.0	3.8	4.3	25.2	1.35	81.0

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*.
[a]Per 100 000 population.

Table 2. Age-specific incidence in Japan according to sex and primary site, 2003

Primary sites	ICD-10th	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	372 374	401	290	190	416	656	1021	1510	2353	4422	7922	18 940	29 913	44 332	57 691	72 125	63 779	36 791	29 622
All sites	C00–C96	364 072	401	290	190	405	650	1020	1497	2310	4213	7732	18 421	29 054	43 110	56 281	70 601	62 386	36 217	29 294
Lip, oral cavity and pharynx	C00–C14	7835	2	0	2	8	34	39	99	127	117	316	626	924	1180	1342	1220	910	543	346
Esophagus	C15	13 658	0	0	0	0	0	0	0	14	93	317	850	1629	2351	2281	2621	1945	981	576
Stomach	C16	73 798	0	0	0	17	47	70	154	281	878	1741	4439	6714	9286	12 022	14 013	12 042	6472	5622
Colon	C18	35 262	0	3	0	8	18	54	120	204	339	713	1698	2905	4591	5634	7014	5589	3432	2940
Rectum and anus	C19, C20	21 892	0	0	1	8	5	15	83	158	420	709	1582	2564	3380	3828	3652	2925	1445	1117
Liver	C22	29 126	11	2	3	0	19	12	33	82	266	573	1792	2714	4018	5290	6146	4455	2127	1583
Gallbladder etc.	C23, C24	8755	0	0	0	0	0	1	4	23	57	79	294	410	820	1137	1483	1697	1438	1312
Pancreas	C25	12 511	0	0	0	0	14	4	1	41	157	194	727	1081	1666	1880	2247	2119	1365	1015
Larynx	C32	3921	0	0	0	0	19	0	0	6	31	72	229	434	604	713	746	616	304	147
Trachea, bronchus and lung	C33, C34	55 928	0	0	0	1	5	3	68	175	296	820	1944	3549	5091	7296	11 701	11 923	7446	5610
Skin	C43, C44	3325	0	0	3	0	13	42	68	50	46	77	107	148	349	358	572	590	364	538
Prostate	C61	40 062	0	0	0	0	0	0	0	0	9	58	430	1251	3704	6719	9914	9291	4852	3834
Bladder	C67	12 646	7	0	0	10	4	23	32	101	92	229	645	862	1196	1544	2623	2287	1520	1471
Kidney, renal pelvis, ureter etc.	C64–C66, C68	8217	14	5	0	0	26	50	35	70	164	280	648	834	932	1226	1487	1223	760	463
Brain and nervous system	C70–C72	2571	67	111	18	45	85	72	88	84	139	146	230	149	319	313	290	202	105	108
Thyroid	C73	2023	0	3	0	1	34	49	44	126	88	137	245	215	224	188	270	193	117	89
Malignant lymphoma	C81–C85, C96	12 881	12	38	76	96	113	123	175	307	528	680	791	1184	1415	2002	1705	1680	1107	849
Multiple myeloma	C88–C90	2251	0	0	0	0	0	0	4	8	10	33	88	184	240	344	349	450	304	237
All leukaemias	C91–C95	5606	138	94	50	77	73	162	142	81	200	211	319	459	518	795	844	699	390	354
Female																				
All sites (incl. CIS)	C00–C96, D00–D09	269 220	397	219	202	332	821	1909	4996	6722	9210	13 421	19 959	22 867	25 392	28 998	34 319	34 339	29 314	35 803
All site	C00–C96	255 939	397	219	202	315	612	1301	3433	5118	7788	12 156	18 900	21 931	24 287	28 108	33 190	33 601	28 888	35 493

Continued

Table 2. *Continued*

Primary sites	ICD-10th	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	3180	0	0	2	18	42	23	33	56	74	100	219	248	332	370	363	468	385	447
Esophagus	C15	2742	0	0	0	0	0	0	1	14	13	123	140	243	250	378	392	335	323	530
Stomach	C16	36 525	0	0	0	2	17	70	234	418	783	1101	1851	2752	3010	4149	5208	5706	4850	6374
Colon	C18	29 859	0	0	0	2	11	36	121	214	346	634	1480	2021	2853	3709	4420	4681	4120	5211
Rectum and anus	C19, C20	11 902	0	0	0	0	0	12	62	120	239	414	852	1162	1444	1511	1695	1602	1264	1525
Liver	C22	13 535	1	0	11	0	0	12	13	10	36	68	246	575	946	1989	2754	2677	2228	1969
Gallbladder etc.	C23–C24	10 200	0	0	0	4	0	0	6	4	44	108	229	337	609	894	1274	1758	2086	2847
Pancreas	C25	10 371	0	0	0	0	0	6	6	33	69	197	394	551	860	1080	1583	1619	1637	2336
Larynx	C32	448	0	0	2	0	0	0	7	2	0	38	2	37	59	83	47	92	39	40
Trachea, bronchus and lung	C33, C34	22 817	5	0	0	5	0	36	35	126	190	417	955	1525	2005	2774	3558	3831	3272	4083
Skin	C43, C44	4497	10	0	10	7	15	13	24	98	56	90	137	168	250	512	441	561	734	1371
Breast (incl. CIS)	C50, D05	45 716	0	0	0	0	29	222	934	1986	3547	5722	6882	5832	5657	4570	3724	3098	2009	1504
Uterus (incl. CIS)	C53–C55, D06	24 240	0	0	0	8	268	835	2479	2529	2299	2167	2432	2876	2030	1557	1609	1360	899	892
Uterus (only invasive)	C53–C55	17 285	0	0	0	2	77	259	988	1114	1146	1408	1978	2557	1791	1377	1531	1291	879	887
Cervix uteri	C53	8674	0	0	0	2	74	223	791	889	870	832	753	879	701	613	600	552	443	452
Corpus uteri	C54	7430	0	0	0	0	3	29	193	203	245	520	1148	1577	997	661	817	606	248	183
Ovary	C56	7946	0	0	20	40	47	150	182	258	412	683	1183	1183	801	695	761	536	488	507
Bladder	C67	3713	0	0	0	0	0	0	2	14	10	42	78	136	197	403	608	659	684	880
Kidney, renal pelvis, ureter etc.	C64–C66, C68	4689	17	8	8	4	2	3	26	25	111	95	348	345	441	559	693	737	593	674
Brain and nervous system	C70–C72	2034	53	27	27	21	9	28	106	43	46	54	79	156	233	223	217	208	225	279
Thyroid	C73	6046	0	0	11	21	89	133	233	325	339	448	715	716	723	591	704	443	225	330
Malignant lymphoma	C81–C85, C96	8592	19	33	13	45	81	86	117	113	217	282	592	637	808	918	1471	1248	969	943
Multiple myeloma	C88–C90	2234	0	0	0	0	0	0	9	11	33	20	81	84	200	215	375	378	368	460
All leukaemias	C91–C95	3951	114	98	32	68	81	44	108	96	97	147	289	321	319	411	483	476	378	389

Table 3. Age-specific incidence rate per 100 000 population in Japan according to sex and primary site, 2003

Primary sites	ICD-10th	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	597.7	13.5	9.5	6.1	11.6	16.3	22.1	30.8	55.2	111.9	199.2	379.7	661.4	1100.6	1643.2	2488.8	3093.1	3541.0	3954.9
All sites	C00–C96	584.3	13.5	9.5	6.1	11.3	16.2	22.0	30.6	54.2	106.6	194.5	369.3	642.4	1070.3	1603.0	2436.2	3025.5	3485.8	3911.1
Lip, oral cavity and pharynx	C00–C14	12.6	0.1	0.0	0.1	0.2	0.8	0.8	2.0	3.0	3.0	7.9	12.6	20.4	29.3	38.2	42.1	44.1	52.3	46.2
Esophagus	C15	21.9	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	2.4	8.0	17.0	36.0	58.4	65.0	90.4	94.3	94.4	76.9
Stomach	C16	118.4	0.0	0.0	0.0	0.5	1.2	1.5	3.1	6.6	22.2	43.8	89.0	148.4	230.5	342.4	483.5	584.0	622.9	750.6
Colon	C18	56.6	0.0	0.1	0.0	0.2	0.4	1.2	2.5	4.8	8.6	17.9	34.0	64.2	114.0	160.5	242.0	271.0	330.3	392.5
Rectum and anus	C19, C20	35.1	0.0	0.0	0.0	0.2	0.1	0.3	1.7	3.7	10.6	17.8	31.7	56.7	83.9	109.0	126.0	141.9	139.1	149.1
Liver	C22	46.7	0.4	0.1	0.1	0.0	0.5	0.3	0.7	1.9	6.7	14.4	35.9	60.0	99.8	150.7	212.1	216.1	204.7	211.3
Gallbladder etc.	C23, C24	14.1	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.5	1.4	2.0	5.9	9.1	20.4	32.4	51.2	82.3	138.4	175.2
Pancreas	C25	20.1	0.0	0.0	0.0	0.0	0.3	0.1	0.0	1.0	4.0	4.9	14.6	23.9	41.4	53.5	77.5	102.8	131.4	135.5
Larynx	C32	6.3	0.0	0.0	0.0	0.0	0.5	0.0	0.0	0.1	0.8	1.8	4.6	9.6	15.0	20.3	25.7	29.9	29.3	19.6
Trachea, bronchus and lung	C33, C34	89.8	0.0	0.0	0.0	0.0	0.1	0.1	1.4	4.1	7.5	20.6	39.0	78.5	126.4	207.8	403.8	578.2	716.7	749.0
Skin	C43, C44	5.3	0.0	0.0	0.1	0.0	0.3	0.9	1.4	1.2	1.2	1.9	2.1	3.3	8.7	10.2	19.7	28.6	35.0	71.8
Prostate	C61	64.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	1.5	8.6	27.7	92.0	191.4	342.1	450.6	467.0	511.9
Bladder	C67	20.3	0.2	0.0	0.0	0.3	0.1	0.5	0.7	2.4	2.3	5.8	12.9	19.1	29.7	44.0	90.5	110.9	146.3	196.4
Kidney, renal pelvis, ureter etc.	C64–C66, C68	13.2	0.5	0.2	0.0	0.0	0.6	1.1	0.7	1.6	4.1	7.0	13.0	18.4	23.1	34.9	51.3	59.3	73.1	61.8
Brain and nervous system	C70–C72	4.1	2.3	3.6	0.6	1.3	2.1	1.6	1.8	2.0	3.5	3.7	4.6	3.3	7.9	8.9	10.0	9.8	10.1	14.4
Thyroid	C73	3.2	0.0	0.1	0.0	0.0	0.8	1.1	0.9	3.0	2.2	3.4	4.9	4.8	5.6	5.4	9.3	9.4	11.3	11.9
Malignant lymphoma	C81–C85, C96	20.7	0.4	1.2	2.4	2.7	2.8	2.7	3.6	7.2	13.4	17.1	15.9	26.2	35.1	57.0	58.8	81.5	106.5	113.4
Multiple myeloma	C88–C90	3.6	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.2	0.3	0.8	1.8	4.1	6.0	9.8	12.0	21.8	29.3	31.6
All leukaemias	C91–C95	9.0	4.6	3.1	1.6	2.1	1.8	3.5	2.9	1.9	5.1	5.3	6.4	10.1	12.9	22.6	29.1	33.9	37.5	47.3
Female																				
All sites (incl. CIS)	C00–C96, D00–D09	412.2	14.1	7.5	6.8	9.7	21.4	42.6	104.0	159.9	235.7	339.5	397.2	492.1	594.0	744.7	991.9	1211.3	1479.0	1904.4
All site	C00–C96	391.9	14.1	7.5	6.8	9.2	16.0	29.1	71.5	121.8	199.3	307.5	376.1	471.9	568.1	721.8	959.2	1185.2	1457.5	1887.9

Continued

Table 3. *Continued*

Primary sites	ICD-10th	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	4.9	0.0	0.0	0.1	0.5	1.1	0.5	0.7	1.3	1.9	2.5	4.4	5.3	7.8	9.5	10.5	16.5	19.4	23.8
Esophagus	C15	4.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.3	3.1	2.8	5.2	5.8	9.7	11.3	11.8	16.3	28.2
Stomach	C16	55.9	0.0	0.0	0.0	0.1	0.4	1.6	4.9	9.9	20.0	27.9	36.8	59.2	70.4	106.5	150.5	201.3	244.7	339.0
Colon	C18	45.7	0.0	0.0	0.0	0.1	0.3	0.8	2.5	5.1	8.9	16.0	29.5	43.5	66.7	95.2	127.7	165.1	207.9	277.2
Rectum and anus	C19, C20	18.2	0.0	0.0	0.0	0.0	0.0	0.3	1.3	2.9	6.1	10.5	17.0	25.0	33.8	38.8	49.0	56.5	63.8	81.1
Liver	C22	20.7	0.0	0.0	0.4	0.0	0.0	0.3	0.3	0.2	0.9	1.7	4.9	12.4	22.1	51.1	79.6	94.4	112.4	104.7
Gallbladder etc.	C23, C24	15.6	0.0	0.0	0.0	0.1	0.0	0.0	0.1	0.1	1.1	2.7	4.6	7.3	14.2	23.0	36.8	62.0	105.2	151.4
Pancreas	C25	15.9	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.8	1.8	5.0	7.8	11.9	20.1	27.7	45.8	57.1	82.6	124.3
Larynx	C32	0.7	0.0	0.0	0.1	0.0	0.0	0.0	0.1	0.0	0.0	1.0	0.0	0.8	1.4	2.1	1.4	3.2	2.0	2.1
Trachea, bronchus and lung	C33, C34	34.9	0.2	0.0	0.0	0.1	0.0	0.8	0.7	3.0	4.9	10.5	19.0	32.8	46.9	71.2	102.8	135.1	165.1	217.2
Skin	C43, C44	6.9	0.4	0.0	0.3	0.2	0.4	0.3	0.5	2.3	1.4	2.3	2.7	3.6	5.8	13.1	12.7	19.8	37.0	72.9
Breast (incl. CIS)	C50, D05	70.0	0.0	0.0	0.0	0.0	0.8	5.0	19.4	47.3	90.8	144.8	137.0	125.5	132.3	117.4	107.6	109.3	101.4	80.0
Uterus (incl. CIS)	C53–C55, D06	37.1	0.0	0.0	0.0	0.2	7.0	18.7	51.6	60.2	58.8	54.8	48.4	61.9	47.5	40.0	46.5	48.0	45.4	47.4
Uterus (only invasive)	C53–C55	26.5	0.0	0.0	0.0	0.1	2.0	5.8	20.6	26.5	29.3	35.6	39.4	55.0	41.9	35.4	44.2	45.5	44.3	47.2
Cervix uteri	C53	13.3	0.0	0.0	0.0	0.1	1.9	5.0	16.5	21.2	22.3	21.0	15.0	18.9	16.4	15.7	17.3	19.5	22.4	24.0
Corpus uteri	C54	11.4	0.0	0.0	0.0	0.0	0.1	0.6	4.0	4.8	6.3	13.2	22.8	33.9	23.3	17.0	23.6	21.4	12.5	9.7
Ovary	C56	12.2	0.0	0.0	0.7	1.2	1.2	3.4	3.8	6.1	10.5	17.3	23.5	25.5	18.7	17.8	22.0	18.9	24.6	27.0
Bladder	C67	5.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.3	1.1	1.6	2.9	4.6	10.3	17.6	23.2	34.5	46.8
Kidney, renal pelvis, ureter etc.	C64–C66, C68	7.2	0.6	0.3	0.3	0.1	0.1	0.1	0.5	0.6	2.8	2.4	6.9	7.4	10.3	14.4	20.0	26.0	29.9	35.9
Brain and nervous system	C70–C72	3.1	1.9	0.9	0.9	0.6	0.2	0.6	2.2	1.0	1.2	1.4	1.6	3.4	5.5	5.7	6.3	7.3	11.4	14.8
Thyroid	C73	9.3	0.0	0.0	0.4	0.6	2.3	3.0	4.9	7.7	8.7	11.3	14.2	15.4	16.9	15.2	20.3	15.6	11.4	17.6
Malignant lymphoma	C81–C85, C96	13.2	0.7	1.1	0.4	1.3	2.1	1.9	2.4	2.7	5.6	7.1	11.8	13.7	18.9	23.6	42.5	44.0	48.9	50.2
Multiple myeloma	C88–C90	3.4	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.3	0.8	0.5	1.6	1.8	4.7	5.5	10.8	13.3	18.6	24.5
All leukaemias	C91–C95	6.0	4.0	3.4	1.1	2.0	2.1	1.0	2.2	2.3	2.5	3.7	5.8	6.9	7.5	10.6	14.0	16.8	19.1	20.7

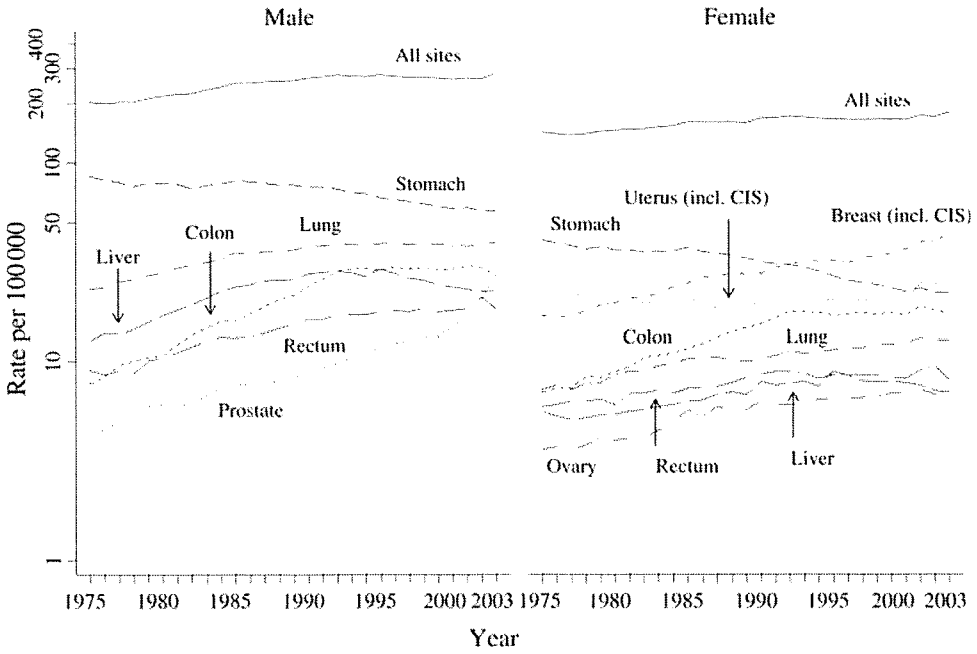

Figure 1. Trends of age-standardized cancer incidence rates for five major sites and specific sites for each sex (standard population: the world population). CIS, carcinoma *in situ*.

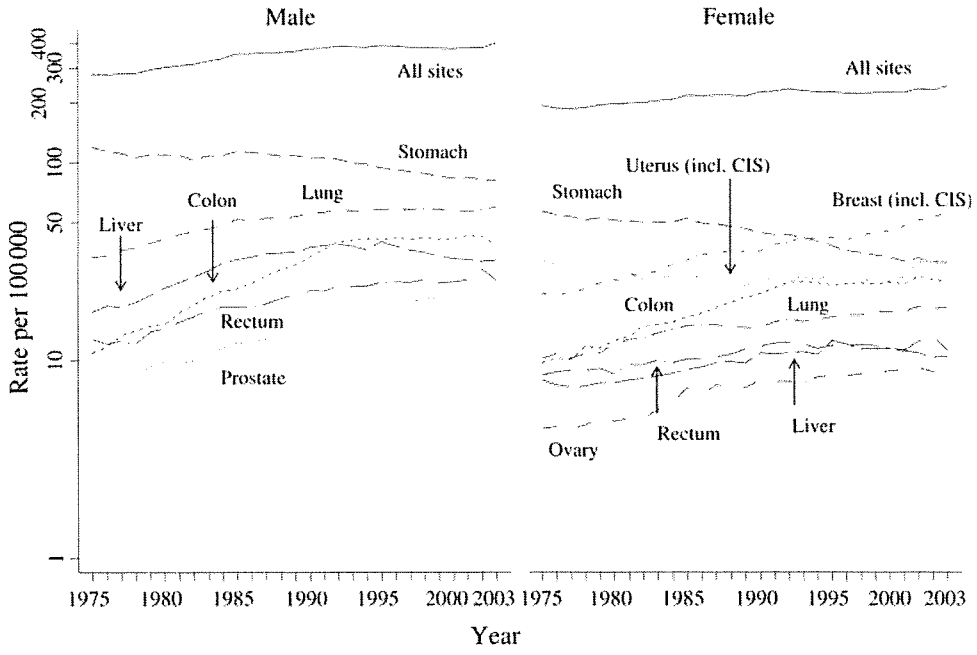

Figure 2. Trends of age-standardized cancer incidence rates for five major sites and specific sites for each sex (standard population: 1985 Japanese model population)

Funding

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

Conflict of interest statement

None declared.

References

1. Marugame T, Kamo K, Katanoda K, Ajiki W, Sobue T. Cancer incidence and incidence rates in Japan in 2000: estimates based on data from 11 population-based cancer registries. *Jpn J Clin Oncol* 2006;36:668–75.
2. Marugame T, Matsuda T, Kamo K, Katanoda K, Ajiki W, Sobue T. Cancer incidence and incidence rates in Japan in 2001 based on the data from 10 population-based cancer registries. *Jpn J Clin Oncol* 2007;37:884–91.

3. Matsuda T, Marugame T, Kamo K, Katanoda K, Ajiki W, Sobue T. Cancer incidence and incidence rates in Japan in 2002: based on data from 11 population-based cancer registries. *Jpn J Clin Oncol* 2008;38:641–8.
4. The Research Group for Population-based Cancer Registration in Japan. Cancer incidence and incidence rates in Japan in 1988: estimates based on data from ten population-based cancer registries. *Jpn J Clin Oncol* 1994;24:299–304.
5. The Research Group for Population-based Cancer Registration in Japan. Cancer incidence in Japan, 1985–89: re-estimation based on data from eight population-based cancer registries. *Jpn J Clin Oncol* 1998;28:54–67.
6. The Research Group for Population-based Cancer Registration in Japan. Cancer incidence in Japan. In: Tajima K, Kuroishi T, Oshima A editors. *Cancer Mortality and Morbidity Statistics—Japan and the World.* Tokyo: Japanese Scientific Societies Press 2004;95–130.
7. National Cancer Center. Center for Cancer Control and Information Services. Monitoring of Cancer Incidence in Japan, MCIJ2003. Tokyo: National Cancer Center 2008 (in Japanese) (http://ganjoho.jp/professional/registration/monita.html).

J Epidemiol 2009;19(5):266-270
doi:10.2188/jea.JE20090037

Statistical Data

Secular Trends in Neuroblastoma Mortality Before and After the Cessation of National Mass Screening in Japan

Kota Katanoda[1], Kunihiko Hayashi[2], Keiko Yamamoto[2], and Tomotaka Sobue[1]

[1]Cancer Information Services and Surveillance Division, Center for Cancer Control and Information Services, National Cancer Center, Tokyo, Japan
[2]Department of Basic Allied Medicine, School of Health Sciences, Gunma University, Maebashi, Japan

Received March 1, 2009; accepted April 26, 2009; released online August 1, 2009

ABSTRACT

Background: In 2003, the Japanese government halted the national mass screening program for neuroblastoma (NB), which had been running since the mid-1980s. It is not known whether the NB mortality rate subsequently increased or decreased.

Methods: Utilizing vital statistics data from 1980 through 2006, we analyzed the secular trends in NB mortality by using cancer of the adrenal gland as a surrogate. We examined the validity of this substitution by comparing the results with data from death certificates. Using a joinpoint regression model, we examined the trends in age-specific mortality rates by calendar year and cumulative mortality rates by birth year. The cumulative mortality rate was analyzed for age under 1 or 2 years for infants born after the cessation of the mass screening program.

Results: The number of deaths from cancer of the adrenal gland was closely correlated with the number of deaths from NB. Significant decreases in the mortality rate were observed from 1980 through 2006 by calendar year for those aged under 1 year, 1 to 4 years, and 5 to 9 years. The cumulative mortality rates by birth year also significantly decreased from the 1980 birth cohort. Although the cumulative mortality rates under the age of 2 appear to have increased after the 2003 birth cohort, the change was not statistically significant.

Conclusions: No significant increase in the NB mortality rate was detected after the cessation of the mass screening program in Japan. However, continuous monitoring is still needed to fully evaluate this health policy decision.

Key words: mass screening; mortality; neuroblastoma

INTRODUCTION

Studies conducted in Germany and in the province of Quebec, Canada showed that screening infants for neuroblastoma (NB) did not result in lower NB mortality.[1,2] Although a large number of epidemiological studies have been conducted in Japan, the findings regarding the effectiveness of NB screening have been inconsistent.[3–8] Clinical studies have reported that a considerable fraction of NB patients whose disease was detected by mass screening had favorable outcomes, which suggests the possibility of over-diagnosis.[9–14] In 2003, the Japanese government halted the national mass screening program—which had been in place since the mid-1980s for infants aged 6 months—because of the potential for over-diagnosis and the lack of evidence for its effectiveness in reducing NB mortality.[15] Most local municipalities in Japan stopped the program during the following year. It is not known whether the NB mortality rate increased or decreased after this national change. Therefore, we analyzed secular trends in NB mortality in Japan before and after the cessation of the national mass screening program.

METHODS

As is the case in most countries, the Japanese government collects vital statistics data, in which the causes of death are classified according to the International Classification of Diseases (ICD). NB mortality cannot be directly identified in this classification because deaths attributable to NB are coded based on the organ affected, and are grouped together with deaths due to other cancers affecting the same organ.[16] Two different methods have been adopted to address this issue. The first approach (hereafter referred to as method-1) is to extract the data on deaths due to cancer of the candidate sites, inspect the relevant individual death certificates, and identify NB

Address for correspondence. Dr. Kota Katanoda, Center for Cancer Control and Information Services, National Cancer Center, 5-1-1 Tsukiji Chuo-ku, Tokyo 104-0045, Japan (e-mail: kkatanod@ncc.go.jp).
Copyright © 2009 by the Japan Epidemiological Association

deaths based on the description of the cause of death or the histological type.[16] The second approach (hereafter referred to as method-2) is to use deaths from cancer of the adrenal gland as a surrogate index.[17]

Method-2 is less accurate than method-1 because NB can occur at sites other than the adrenal gland, and because other histological types of cancer can occur in this organ. Method-1 requires official permission for the use of unpublished vital statistics data, whereas method-2 uses only published vital statistics data, at least for the years after the ICD version 10 was applied.

The present study used method-1 to analyze data from the year 2006. We obtained individual mortality data from the vital statistics, with official permission, according to the following criteria: year of death = 2006; age at death = 0 to 14 years; cause of death (ICD) = malignant neoplasms of mediastinum (ICD-9 164.2, 164.3, 164.9; ICD-10 C38.1, C38.2, C38.8), connective and soft tissue (ICD-9 171.0, 171.2, 171.3, 171.4, 171.5, 171.6, 171.7, 171.8, 171.9), peripheral nerves and autonomic nervous system (ICD-10 C47.0, C47.1, C47.2, C47.3, C47.4, C47.5, C47.6, C47.8, C47.9), retroperitoneum and peritoneum (ICD-9 158.0, 158.8, 158.9; ICD-10 C48.0, C48.1, C48.2, C48.8), adrenal gland (ICD-9 194.0; ICD-10 C74.0, C74.1, C74.9), or other/ill-defined sites (ICD-9 195.0, 195.1, 195.2, 195.3, 195.4, 195.5, 195.8; ICD-10 C76.0, C76.1, C76.2, C76.3, C76.4, C76.5, C76.7, C76.8). Then, we inspected individual death certificates for the extracted data, and identified NB deaths based on the recorded causes of death or histological types. This process was performed by one of the authors (K. K.) and was confirmed by another author (K. Y., a pediatrician). For the data from 1980 through 2001, we obtained data on NB deaths from previous reports[16,18] that had used a method identical to the present method-1 for extracting and identifying NB deaths. Thus, in the present study, data on the number of NB deaths based on method-1 were available for the years from 1980 through 2001, and for the year 2006. We could not apply method-1 to the time period from 2002 through 2005 because a previous application to use death certificates for research had been rejected,[19] and the document storage period had expired by the time of our application.

For method-2, we calculated the age-specific number of deaths from adrenal gland cancer, based on officially obtained individual mortality data from the vital statistics. The criteria for data collection were as follows: year of death = 1980 to 2006; age at death = 0 to 14 years; cause of death (ICD) = malignant neoplasms of the adrenal gland (ICD-9 194.0; ICD-10 C74.0, C74.1, C74.9).

To validate method-2, we calculated the Pearson correlation coefficient between the number of NB deaths and the number of adrenal gland cancer deaths, using data from 1980 through 2001, and from 2006.

We obtained population data from the published vital statistics and calculated the age-specific mortality rate by calendar year for cancer of the adrenal gland. For the age-specific mortality rate, age was stratified into the following 4 groups: 0 years, 1 to 4 years, 5 to 9 years, and 10 to 14 years. We also calculated the cumulative mortality rate by birth year, by summing the 1-year age-specific mortality rate according to each birth year.[20] The number of deaths according to each age and each birth year was used as the numerator for the 1-year age-specific mortality rate. The denominator was the number of births (for age younger than 1 year) or the population for each age (for 1 year or older). The most recent birth year that we analyzed was 2005 for the cumulative mortality rate under 1 year of age, 2004 for 2 years of age, 2003 for 3 years of age, and 2002 for 4 years of age.

For the statistical analysis, we used a joinpoint regression model,[21] implemented in the Joinpoint Regression Program (version 3.3.1) developed by the US National Cancer Institute. This method describes changes in data trends by connecting several different line segments on a log scale at joinpoints. The analysis starts with the minimum number of joinpoints (that is, 0, representing a straight line) and tests for the model fit with a maximum number of joinpoints. A Monte Carlo permutation method is used for tests of significance. In addition, the annual percent change (APC) for each line segment and the corresponding 95% confidence interval (CI) were estimated. In the statistical analysis, the number of deaths was assumed to follow a Poisson distribution. The maximum number of joinpoints was set at 3, the minimum number of observations from a joinpoint to either end of the data was set at 2 (including the end and joinpoint), and the minimum number of observations between 2 joinpoints was set at 4 (including the joinpoints).

RESULTS

Table 1 shows the secular trends in the age-specific number of deaths, according to the 2 methods. Although method-1 tended to yield slightly larger numbers than method-2, the secular trends were similar. The Pearson correlation coefficients between the annual numbers of deaths according to the 2 methods were close to 1 (1.00 for 0–14 years, 0.96 for <1 year, 0.98 for 1–4 years, 0.96 for 5–9 years, and 0.73 for 10–14 years; all 5 correlation coefficients were significantly different from 0 [number of data points = 23, $P < 0.001$]). In 2006, 45 deaths from cancer of the adrenal gland were observed, one of which was non-NB (malignant pheochromocytoma). In comparison, 45 NB deaths were identified by the inspection of death certificates from 2006, of which 1 case occurred at a site other than the adrenal gland (retroperitoneum).

Table 2 shows the results of the joinpoint analysis. Significant decreases in the age-specific mortality rate were observed from 1980 through 2006 by calendar year for those aged less than 1 year, 1 to 4 years, and 5 to 9 years. The cumulative mortality rates by birth year also significantly

Table 1. Numbers of deaths due to neuroblastoma (NB) and adrenal gland cancer from 1980 to 2006

Calendar year[a]	1) Number of deaths from NB identified by individual death certificates[b]					Calendar year[a]	2) Number of deaths from cancer of the adrenal gland[c]				
	0–14 years	<1 year	1–4 years	5–9 years	10–14 years		0–14 years	<1 year	1–4 years	5–9 years	10–14 years
1980–1982	381	28	209	119	25	1980–1982	338	22	194	103	19
1983–1985	329	31	174	102	22	1983–1985	294	28	150	94	22
1986–1988	280	15	132	101	32	1986–1988	249	15	119	88	27
1989–1991	221	10	109	81	21	1989–1991	207	8	106	74	19
1992–1994	178	11	72	77	18	1992–1994	171	8	68	76	19
1995–1997	185	16	67	78	24	1995–1997	181	14	65	79	23
1998–2000	147	9	55	59	24	1998–2000	139	8	53	56	22
2001–2003	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	2001–2003	118	6	49	42	21
2004–2006	(N.A.)	(N.A.)	(N.A.)	(N.A.)	(N.A.)	2004–2006	123	7	55	45	16
2001, 2006	86	4	38	29	15	2001, 2006	84	4	38	27	15

[a]Consecutive 3-year periods from 1980 to 2006 were pooled. Two years (2001 and 2006) were also pooled.
[b]The numbers of NB deaths between 1980 and 2001 were obtained from previous reports (Hanawa et al, 1990 and Hayashi et al, 2004), and the numbers of NB deaths in 2006 were counted by one of the authors (K. K.).
[c]Deaths due to cancer of the adrenal gland were defined by codes in the ICD: 194.0 for 1980–1994, C74.0, C74.1, and C74.9 for 1995–2006.
N.A.: Not available

Table 2. Results of joinpoint regression analysis for the secular trends in adrenal gland cancer mortality

A) Age-specific mortality rate, by calendar year

	Number of joinpoints	Line segment		Annual % change	95% confidence interval	
		Start	End		Lower	Upper
0 year old	0	1980	2006	−3.6[a]	−5.8	−1.4
1–4 years old	0	1980	2006	−4.1[a]	−5.0	−3.3
5–9 years old	0	1980	2006	−1.1[a]	−2.0	−0.1
10–14 years old	0	1980	2006	1.4	−0.4	3.2

B) Cumulative mortality rate, by birth year[b]

	Number of joinpoints	Line segment		Annual % change	95% confidence interval	
		Start	End		Lower	Upper
<1 year old	0	1980	2005	−3.0[a]	−5.4	−0.5
<2 years old	0	1980	2004	−3.4[a]	−5.3	−1.4
<3 years old	0	1980	2003	−4.3[a]	−5.7	−2.8
<4 years old	0	1980	2002	−4.1[a]	−5.2	−2.9

[a]Annual % change is statistically significant from zero.
[b]The analyzed most recent birth year was 2005 for age <1 year, 2004 for <2 years, 2003 for age <3 years, and 2002 for age <4 years.

decreased from the 1980 birth cohort. Figure 1 shows the trends in the age-specific mortality rate. The mortality rates for 1 to 4 years of age in 2004 and 2006 were high, but no significant increase or joinpoint was detected around this time. Figure 2 shows the trends in the cumulative mortality rate. The cumulative mortality rate under the age of 2 for the 2004 birth cohort was considerably higher than the cumulative mortality rate for the past several birth cohorts. However, this change was not detected as a significant joinpoint.

DISCUSSION

We examined the secular trends in the mortality rate for NB, using mortality for cancer of the adrenal gland as a surrogate index, and found no significant increase before or after the cessation of the Japanese national mass screening program. We confirmed the validity of this surrogate method by examining the correlation between the numbers of deaths from the 2 cancers. Nationwide mass screening had previously been performed for infants aged 6 months, and the participation level was high (ranging from 84% to 90% in the period from 1990 through 2001). Because the most recent year of death that we analyzed was 2006, any increase in the age-specific mortality rate associated with the cessation of mass screening in 2003 would have been expected to occur among children aged 1 to 4 years. However, we did not observe any significant increase or joinpoint in the mortality rate among this age group around this time. It is possible that the time elapsed since the cessation of mass screening was still too short to detect any increase in mortality for this age group, which

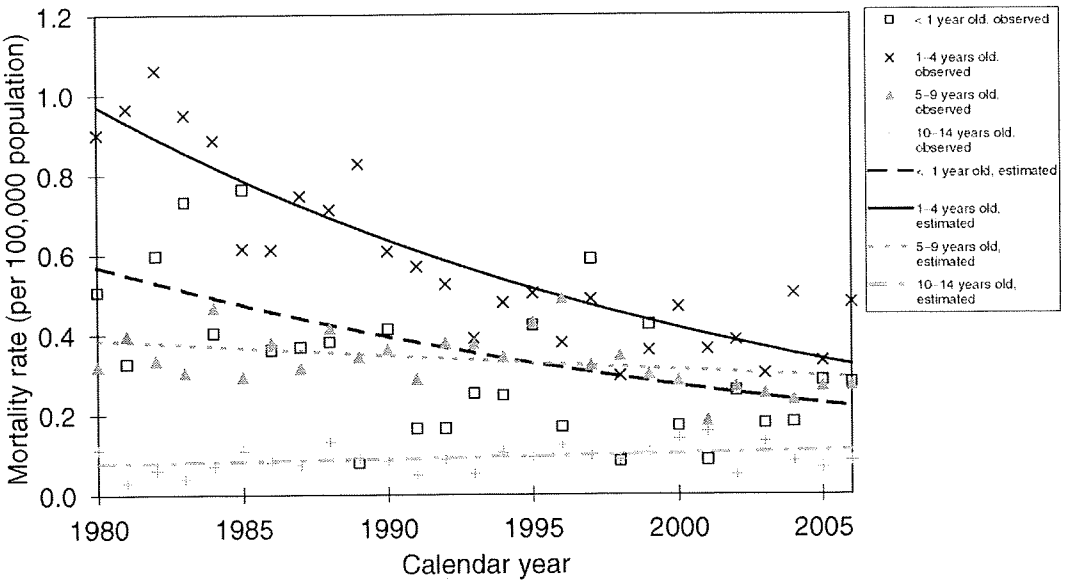

Figure 1. Annual trends in age-specific mortality rate for cancer of the adrenal gland, by calendar year

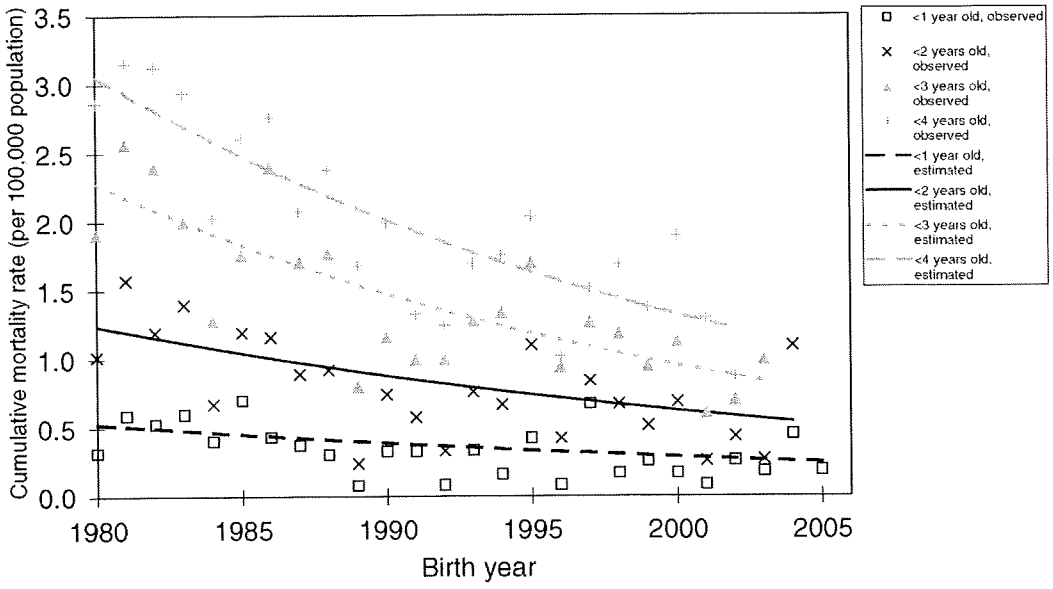

Figure 2. Annual trends in cumulative mortality rate for cancer of the adrenal gland, by birth year. Note: The most recent analyzed birth year was 2005 for age <1 year, 2004 for age <2 years, 2003 for age <3 years, and 2002 for age <4 years

included both screened and unscreened individuals, even at the end of our observation period.

The cumulative mortality rate according to birth year was a more direct index to examine the effect of the cessation of the mass screening program. It decreased significantly throughout the observed birth years, and the birth year 2003 was not detected as a significant joinpoint. However, these results should be interpreted with caution because the analyzed range of birth years and ages was limited after the cessation of the mass screening program. In consideration of the time from diagnosis to death, we should assume that any increase in the mortality rate for infants born after the cessation could occur later than the end of our observation period.

There are several Japanese municipalities that continued mass screening for NB after 2003. However, the number of such municipalities is very small, and our results did not change when we excluded the prefectures to which these municipalities belong (ie, Hokkaido, Kanagawa, Niigata, Shizuoka, Kyoto, Osaka, and Kumamoto).

We found a high correlation between the number of deaths from NB and the number of deaths from adrenal gland cancer, with the former slightly and consistently higher than the latter (Table 1). This tendency was in agreement with a previous report, in which approximately 90% of NB deaths were attributable to cancer of the adrenal gland, and almost all of the cancers that occurred at this site were NB.[16] One death due

to non-NB cancer in the adrenal gland was included among the data for 2006, but this was considered to be an unusual case.

The effect of the cessation of the mass screening program for NB should be verified by monitoring the trend in incidence.[22] Studies have reported the trends in NB incidence and mortality before and after the start of a national mass screening program, based on data from a population-based cancer registry.[3,5] Additional similar studies need to be conducted, and should include a sufficient observation period after the cessation of the program.

In conclusion, no significant increase in the NB mortality rate was detected after the cessation of the national mass screening program in Japan. However, continuous monitoring is still needed to evaluate further this health policy decision.

ACKNOWLEDGMENTS

This work was supported by Grants-in-aid for the Third-Term Comprehensive Ten-Year Strategy for Cancer Control from the Ministry of Health, Labour, and Welfare, Japan. The authors thank Dr. M. Nishi for his useful suggestions.

REFERENCES

1. Schilling FH, Spix C, Berthold F, Erttmann R, Fehse N, Hero B, et al. Neuroblastoma screening at one year of age. N Engl J Med. 2002;346:1047–53.
2. Woods WG, Gao RN, Shuster JJ, Robison LL, Bernstein M, Weitzman S, et al. Screening of infants and mortality due to neuroblastoma. N Engl J Med. 2002;346:1041–6.
3. Ajiki W, Tsukuma H, Oshima A, Kawa K. Effects of mass screening for neuroblastoma on incidence, mortality, and survival rates in Osaka, Japan. Cancer Causes Control. 1998;9:631–6.
4. Hiyama E, Ichara T, Sugimoto T, Fukuzawa M, Hayashi Y, Sasaki F, et al. Effectiveness of screening for neuroblastoma at 6 months of age: a retrospective population-based cohort study. Lancet. 2008;371:1173–80.
5. Honjo S, Doran HE, Stiller CA, Ajiki W, Tsukuma H, Oshima A, et al. Neuroblastoma trends in Osaka, Japan, and Great Britain 1970–1994, in relation to screening. Int J Cancer. 2003;103:538–43.
6. Nishi M, Miyake H, Takeda T, Hanai J, Kikuchi Y, Takasugi N. Mass screening for neuroblastoma and mortality in birth cohorts. Int J Cancer. 1997;71:552–5.
7. Suita S, Tajiri T, Akazawa K, Sera Y, Takamatsu H, Mizote H, et al. Mass screening for neuroblastoma at 6 months of age: difficult to justify. J Pediatr Surg. 1998;33:1674–8.
8. Yamamoto K, Ohta S, Ito E, Hayashi Y, Asami T, Mabuchi O, et al. Marginal decrease in mortality and marked increase in incidence as a result of neuroblastoma screening at 6 months of age: cohort study in seven prefectures in Japan. J Clin Oncol. 2002;20:1209–14.
9. Matsumura M, Tsunoda A, Nishi T, Nishihira H, Sasaki Y. Spontaneous regression of neuroblastoma detected by mass screening. Lancet. 1991;338:447–8.
10. Nishihira H, Toyoda Y, Tanaka Y, Ijiri R, Aida N, Takeuchi M, et al. Natural course of neuroblastoma detected by mass screening: s 5-year prospective study at a single institution. J Clin Oncol. 2000;18:3012–7.
11. Okazaki T, Kohno S, Mimaya J, Hasegawa S, Urushihara N, Yoshida A, et al. Neuroblastoma detected by mass screening: the Tumor Board's role in its treatment. Pediatr Surg Int. 2004;20:27–32.
12. Oue T, Inoue M, Yoneda A, Kubota A, Okuyama H, Kawahara H, et al. Profile of neuroblastoma detected by mass screening, resected after observation without treatment: results of the Wait and See pilot study. J Pediatr Surg. 2005;40:359–63.
13. Yamamoto K, Hanada R, Kikuchi A, Ichikawa M, Aihara T, Oguma E, et al. Spontaneous regression of localized neuroblastoma detected by mass screening. J Clin Oncol. 1998;16:1265–9.
14. Yoneda A, Oue T, Imura K, Inoue M, Yagi K, Kawa K, et al. Observation of untreated patients with neuroblastoma detected by mass screening: a "wait and see" pilot study. Med Pediatr Oncol. 2001;36:160–2.
15. Tsubono Y, Hisamichi S. A halt to neuroblastoma screening in Japan. N Engl J Med. 2004;350:2010–1.
16. Hanawa Y, Sawada T, Tsunoda A. Decrease in childhood neuroblastoma death in Japan. Med Pediatr Oncol. 1990;18:472–5.
17. Nishi M, Takeda T, Hatae Y, Hanai J, Fujita K, Ichimiya H, et al. Contribution of HPLC mass screening for neuroblastoma to a decrease in mortality. J Exp Clin Cancer Res. 2002;21:73–8.
18. Hayashi K, Fujita T, Katanoda K, Sobue T, Sato T, Nishi M, et al. Effectiveness of mass-screening program on neuroblastoma mortality in 1995–2000 birth cohort of Japan: Nationwide Neuroblastoma Mortality Study. Advances in Neuroblastoma Research 2004, Genoa, Italy.
19. Hayashi K. Epidemiologic evaluation of mass screening program for neuroblastoma. In: Kuroda Y, ed. Research on effective implementation and development of mass screening, Research on Measures for Intractable Diseases, Health and Labour Sciences Research Grants, 2004: 109–165.
20. Day N. Cumulative rate and cumulative risk. In: Muir C, Waterhouse J, Mack T, Powell J, Whelan S, editors. Cancer Incidence in Five Continents Volume V. Lyon: International Agency for Research on Cancer; 1987. p. 787–789.
21. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. Stat Med. 2000;19:335–51.
22. Panel on Mass Screening Program for Neuroblastoma Ministry of Health, Labour and Welfare. A report on the mass screening program for neuroblastoma, 2003.

タバコと発がん

片野田耕太*

要　旨

・タバコは，予防可能な最大のがんのリスク要因である。
・タバコの煙に含まれる発がん物質は，体内の代謝過程で活性化され，DNA 付加体を形成し，遺伝子変異を引き起こす。
・タバコとがんとの関連について，能動喫煙によるリスク上昇だけでなく，禁煙後のリスク低下，受動喫煙など，さまざまな側面から疫学的な証拠が蓄積されてきた。
・能動喫煙と因果関係が確立されているがん種は，口腔，鼻腔・副鼻腔，咽頭，食道，胃，肝臓，膵臓，喉頭，肺，子宮頸部，膀胱，腎臓（腎盂，腎細胞）のがん，および骨髄性白血病である。これらの多くは，継続的な禁煙によりリスクが低下する。
・日本人において，非喫煙者に対する現在喫煙者のリスクは，肺がんでは男女とも 3〜4 倍，喉頭および尿路のがんでは男性で 5 倍以上である。
・日本人のがん死亡に占める喫煙の寄与（人口寄与危険割合）は，男性で 30%強，女性で 5%前後である。
・受動喫煙と肺がんとの因果関係は確立されており，リスク上昇は 20〜30%である。

はじめに

タバコは，予防可能な最大のがんのリスク要因である。1950 年代に喫煙と肺がんとの関連を示す疫学研究の結果が初めて報告されて以来，タバコとがんとの関連については，能動喫煙だけでなく，禁煙によるリスク低下，受動喫煙など，さまざまな側面から研究が行われてきた。今日では，タバコとの因果関係が確立されているがん種は 10 を超える。

以下，タバコとがんとの関連について，トピックごとに最近の知見をまとめる。

タバコによる発がんの仕組み

タバコの煙の中には，タバコ自体に含まれるものだけでなく，不完全燃焼に伴って生じる化合物を含めて約 4,000 種類の化学物質が含まれているといわれる。その中には，多環芳香族炭化水素化合物やニトロソアミン類をはじめとする発がん物質が 60 種類以上含まれている[1]。発がん物質の多くは，体内で代謝される際に活性型に変化した後，DNA と共有結合をして DNA 付加体を形成する。この DNA 付加体が，DNA 複製の際に遺伝子の変異を引き起こす。こうした遺伝子変異が，がん遺伝子やがん抑制遺伝子などに蓄積することによって，細胞ががん化すると考えられている[2]。

*KATANODA Kota　国立がんセンターがん対策情報センターがん情報・統計部〔〒104-0045 東京都中央区築地 5-1-1〕

表1　日本人における喫煙者のがんの相対リスク

がん種	日本の三つのコホート研究の併合解析による相対リスク*		日本の疫学研究のメタアナリシスによる相対リスク†	
	男　性	女　性	男　性	女　性
全がん	2.0 [1.8：2.1]	1.6 [1.4：1.8]	1.6 [1.6：1.7]	1.3 [1.2：1.4]
口唇・口腔・咽頭	2.7 [1.5：4.8]	2.0 [0.7：5.7]	—	—
食道	3.4 [2.3：5.1]	1.9 [0.7：4.9]	—	—
胃	1.5 [1.3：1.8]	1.2 [0.9：1.6]	1.8 [1.5：2.1]	1.2 [1.1：1.4]
肝・肝内胆管	1.8 [1.5：2.2]	1.7 [1.2：2.5]	—	—
膵臓	1.6 [1.2：2.1]	1.8 [1.3：2.6]	—	—
喉頭	5.5 [1.3：23.1]	N. A.	—	—
肺	4.8 [3.9：5.9]	3.9 [3.1：4.9]	4.4 [3.9：4.9]	2.8 [2.4：3.2]
子宮頸部	—	2.3 [1.3：4.1]	—	—
腎盂を除く腎臓	1.6 [0.8：3.1]	0.6 [0.1：4.5]	—	—
膀胱	6.7 [2.4：18.5]	1.7 [0.7：4.2]	—	—
腎盂・尿管・膀胱	5.4 [2.5：11.6]	1.9 [0.8：4.1]	—	—
骨髄性白血病	1.5 [0.7：2.8]	1.0 [0.3：3.1]	—	—

*：現在喫煙者の非喫煙者に対する死亡相対リスク（年齢調整），出典；文献[4,5]，†：出典；文献[6~8]
N. A.：死亡数が少数のため算出不可
［ ］内は95%信頼区間

能動喫煙とがん

1．喫煙によるリスク上昇

2002年，国際がん研究機関（IARC）は「ヒトへの発がんリスク評価に関するモノグラフ」（以下，モノグラフ）第83巻において，喫煙とタバコ煙のヒトに対する発がん性を評価した[1]。その結果，喫煙とタバコ煙は，もっとも強い「グループ1：ヒトに対して発がん性がある」と判定された。この報告書は，喫煙と因果関係が認められるがん種として，口腔，鼻腔・副鼻腔，咽頭，食道，胃，肝臓，膵臓，喉頭，肺，子宮頸部，膀胱，腎臓（腎盂，腎細胞）のがん，および骨髄性白血病をあげている。これらの因果関係の評価は，2004年にまとめられた米国公衆衛生総監（Surgeon General）報告書でも，ほぼ同じ内容となっている[3]。

表1は，これらのがん種について，日本の三つのコホート研究の併合解析[4,5]，および日本の疫学研究のメタアナリシスによる[6~8]，喫煙による各種がんの相対リスクをまとめたものである。現在喫煙者の非喫煙者に対する全がんのリスクは，男性で1.5～2倍，女性で1.5倍前後である。男性では肺，喉頭，および尿路のがんで4～7倍と高く，次いで口唇・口腔・咽頭および食道がんが3倍前後である。女性では男性より全体的に相対リスクが低く，現在喫煙者の非喫煙者に対するリスクは肺がんで3～4倍，口唇・口腔・咽頭および子宮頸部のがんで約2倍，その他のがん種では2倍未満である。

全がん死亡に占める喫煙（現在喫煙および過去喫煙）の人口寄与危険割合（当該死因の死亡のうち喫煙が原因だと考えられる割合）は，年齢調整では男性39%，女性5%[4]，多変量調整では男性33%，女性3%（女性は現在喫煙のみ）であり[9]，男性の全がん死亡の30%強，女性の全がん死亡の5%前後は喫煙が原因だと考えられる。同様に肺がんでは，男性肺がん死亡の約70%，女性肺がん死亡の約20%は喫煙が原因だと推計されている[4]。

日本人における現在喫煙者の非喫煙者に対する相対リスクは肺がんでも3～5倍だが，欧米人を対象とした研究では10倍を超える相対リスクが報告されている[10]。喫煙による日本人の肺がん相対リスクが欧米人に比べて低い理由には，①日本人の方が喫煙者の曝露量が小さい（喫煙開始年齢が遅い，1日喫煙本数が少ないなど），②喫煙によるリスク増加が比較的小さい腺がんの割合が日本人で大きい，③日本人の方が非喫煙者の肺がん死亡率が高い（受動喫煙レベルが高い，非喫煙者に喫煙経験者が誤分類されているなど），④遺伝的な感受性が異なる，などが指摘されている。ただし，②については，近年米国の肺がん罹患率は男女とも扁平上皮がんの減少傾向が顕著で腺がんの割合が増加している[11]。

喫煙との関連が明らかではないがん種として，大腸がんがある。IARCモノグラフおよび米国公衆衛生総監報告書とも，喫煙と大腸がんとの間に因果関係があると判定するための科学的証拠は不十分であると結論づけている[1,3]。一方，2008年に能動喫煙と大腸がんとの関連について，大規模なメタアナリシスの結果が報告された[12]。この論文は，喫煙と大腸がん罹患および死亡との間に有意な関連を認め，大腸がんのリスク上昇が有意になるには喫煙年数が30年以上必要であると報告している。

日本人を対象とした疫学研究の系統的レビューでは，喫煙と大腸がんとの関連は「可能性がある（possible）」という弱い評価となっている（4段階中，「確実である」，「ほぼ確実である」に次ぐ3番目）[13]。この結果は上記のメタアナリシスの結果と一見矛盾するようではあるが，上記のメタアナリシスでも，対象地域別の解析においてアジアではリスク比が1に近い[12]。また，結腸がんより直腸がんが強く喫煙と関連しているという結果において両研究は一致している。

喫煙による大腸がんリスク上昇の生物学的機序としては，ポリープの発生過程，進行過程，およびがん化過程にそれぞれ関与する*APC*（*adenomatous polyposis coli*），*ras*，*p53*などの遺伝子が喫煙により変異を起こす可能性が考えられている。

喫煙との関連が否定的とされているがん種として乳がんがある。IARCモノグラフおよび米国公衆衛生総監報告書とも，喫煙と乳がんとの関連に否定的な結論を出している[1,3]。日本の疫学研究の系統的レビューの結果でも，喫煙と乳がんとの関連は「可能性がある」という弱い評価にとどまる[14]。タバコ煙に含まれる物質やその影響が喫煙者の乳腺組織に到達する可能性が指摘されている一方，喫煙者ではエストロゲンレベルが低下するという報告もあり，喫煙と乳がんとの関連についてはリスクの上昇と低下の双方の生物学的機序が考えられ，いずれも確定的ではない。

2．禁煙によるリスク低下

表2は，IARCが2007年に行った禁煙後のリスク低下についての評価をまとめたものである[15]。禁煙後リスクが低下するとされたがん種は，口腔，食道，胃，膵臓，喉頭，肺，子宮頸部，腎細胞，膀胱のがんで，うち喉頭および子宮頸部のがんは禁煙後のリスク低下が早い。子宮頸部のがんは禁煙後非喫煙者のレベルまでリスクが急速に下がるが，他の多くのがん種では非喫煙者のレベルまでリスクが下がるのに20年以上かかる。

また，肺がんは禁煙後長期間経っても非喫煙者のレベルまでリスクが下がらない。ただ，禁煙後の肺がんリスクの低下は，40歳代および50歳代はもちろん，60歳代で禁煙した場合でも認められるため[16]，比較的高齢の喫煙者においても禁煙によるメリットは確実にある。

禁煙後に疾病リスクが低下するかどうかは，喫煙と疾病との因果関係の判定に重要である。ただ，もし喫煙による遺伝子変異が発がん過程の初期に関与していた場合，喫煙をやめた後に他の要因でがん化の過程が進むことも考えられる。

受動喫煙とがん

1．国際機関などの報告

1980年代後半以降，IARC，米国学術会議（National Research Council；NRC），米国環境保護庁（Environmental Protection Agency；EPA）などが科学的証拠に基づいて受動喫煙を肺がんのリスク要因として認め始めた。2002年のIARCモノグラフ第83巻は，受動喫煙について，もっとも強い「グループ1：ヒトに対して発がん性がある」と判定している[1]。受動喫煙と疾患との関連について比較的最近まとめられた報告書

表2　国際がん研究機関(IARC)による禁煙とリスク低下に対する評価

がん種	①禁煙した人のリスクが現在喫煙者より低いか	②禁煙継続によるリスクの低下	③非喫煙者のレベルまでのリスクの低下	備　考
口腔	◎	○	○(20年以上)	一般に禁煙期間の増加に伴いリスクも低下。
鼻咽頭・副鼻腔	○	—	—	
食道	◎	○	○(20年以上)	リスク低下は扁平上皮がんで認められる。禁煙後長期間(20年以上)リスクは高い。禁煙後10年で非喫煙者の2倍までリスクが下がる。腺癌に関する研究結果は少なく，関連を判断するには不十分。
胃	◎	○		禁煙期間の増加に伴いリスクも低下し，禁煙した年齢が若いほど大きく低下する。
肝	○	—	—	リスクは低下すると思われるが，地域によって研究結果に違いがある。
膵臓	◎	○	○(15年以上)	研究報告が少ない。
喉頭	◎	◎	○(20年以上)	禁煙後，急速にリスクは低下する。10〜15年で約60%低下。20年以上かけて非喫煙者レベルに達する。
肺	◎	○	△	リスクは5〜9年で低下を始め，長い期間かかり徐々に低下，禁煙後長期間経っても非喫煙者レベルより高い。
子宮頸部	◎	◎	◎	リスク低下は扁平上皮がんで認められる。禁煙によって非喫煙者のリスクレベルまで急速に下がる。
腎細胞	◎	○	○(20年以上)	研究報告が少ない。
膀胱	◎	○	○(25年以上)	
骨髄性白血病	○	—	—	リスクは低下すると思われるが，研究結果が一致していない。

①禁煙した人のリスクが現在喫煙者より低いか
　◎：禁煙した人のリスクは現在喫煙者より低い
　○：禁煙した人のリスクは現在喫煙者より低いと考えられる
②禁煙継続によるリスクの低下
　◎：禁煙後，急速にリスクが低下する
　○：禁煙期間の増加に伴いリスクが低下する
　—：情報が不十分
③非喫煙者のレベルまでのリスクの低下
　◎：禁煙後，非喫煙者のレベルまでリスクが下がる
　○：禁煙後，非喫煙者のレベルまでリスクが下がるが，長期間かかる。(　)内はかかる年数
　△：禁煙後，非喫煙者のレベルまでリスクが下がらない
　—：情報が不十分
(空白)：記載なし

出典：国際がん研究機関がん予防ハンドブック，たばこ対策，第11巻，2007年[15]

に，カリフォルニア州環境保護庁の報告書(2005年)[17]と，米国公衆衛生総監報告書(2006年)[18]がある。これら二つの報告書においても，受動喫煙は，タバコを吸わない大人と子どもの両方に，さまざまな病気や早期死亡を引き起こすと結論づけている。

表3は，これら三つの報告書の評価結果をまとめたものである。肺がんについては，三つの報告

表3　非喫煙者における受動喫煙とがんとの関連についての評価結果

がん種	①IARCモノグラフ 83巻 (2002年)	②カリフォルニア州環境保護庁報告書 (2005年)	③米国公衆衛生総監報告書 (2006年)	各報告書のその他の記述
肺がん	○	○	○	①配偶者の喫煙による受動喫煙で肺がんリスクは女性で約1.2倍，男性で約1.3倍。職場での受動喫煙で肺がんリスクは1.12〜1.19倍。 ③同居者の喫煙による受動喫煙で肺がん死亡リスクは1.2〜1.3倍。
頭頸部がん	—	関連を示唆する研究はあるが結論は出せない	—	
鼻腔がん	×	○	△	
鼻咽頭がん	×		データが不十分	
乳がん	×	○*	△	①能動喫煙と乳がんとの間の関連が十分でないことから，受動喫煙との関連の可能性は低い。
子宮頸がん	×	受動喫煙が病因の一つである可能性がある	—	
小児がん	関連が示唆されるが他の要因の影響を否定できない	△‡	△†	
全がん	×	△	—	

○：因果関係がある，△：因果関係が示唆される，×：データが一致しない，—：(評価なし)
＊：閉経前若年女性について，†：白血病・リンパ腫・脳腫瘍について，‡：リンパ腫と脳腫瘍について

書とも，受動喫煙との因果関係があると判定している。同居者の喫煙による受動喫煙による非喫煙者の肺がんリスクは1.2〜1.3倍であり，職場での受動喫煙による非喫煙者の肺がんリスクは1.1〜1.2倍である。鼻腔がんおよび乳がんは，カリフォルニア州環境保護庁報告書のみが因果関係ありと判定している。乳がんについては，前述の通り能動喫煙との関連が否定的であるため，米国公衆衛生総監報告書では，「因果関係が示唆される」という評価にとどまった。小児がんおよび全がんについては，いずれの報告書も因果関係があるとは判定していない。

2．日本人を対象とした研究

日本人を対象とした受動喫煙とがんとの関連は，平山によって夫の喫煙と非喫煙女性の肺がんとの関連が最初に報告された[19]。以後，受動喫煙に関する日本人を対象とした疫学研究は，配偶者など同居者の喫煙による受動喫煙を対象としたものが比較的多い。

表4は，主に非喫煙女性について夫の喫煙による受動喫煙の健康影響を調べた疫学研究のまとめである。肺がんについては，平山研究以後の疫学研究で報告された非喫煙女性の夫からの受動喫煙の相対リスクはおおむね1.3〜2.0に分布しており，平山研究や国際機関などの報告と大きな相違はない。組織型別では，近年肺腺がんが受動喫煙とより関連が強いとの報告があり，副流煙が主流煙より肺末梢に到達しやすいこと，腺がんとの関連が指摘されている4-(N-ニトロソメチルアミノ)-1-(3-ピリジル)-1-ブタノン(NNK)の関与などが機序として考えられている(Kurahashi N, et al)。

肺がん以外のがんでは，2000年以降，乳がんを対象としたコホート研究が三つある。これらの結

表4　夫の喫煙または家庭での受動喫煙に関する日本の疫学研究のまとめ

文　献	研究手法	調査年	対象者	エンドポイント	曝露レベル把握方法	調整変数・マッチングなど	曝露形態	疾患・組織型など	曝露レベル・層別など	相対リスク［95%信頼区間］*
Hirayama T BMJ 282： 183-185, 1981	コホート	1965	非喫煙女性 91,540 名	死亡	質問票	年齢，職業	夫の喫煙	肺がん 肺気腫・喘息 子宮頸がん 胃がん 虚血性心疾患	現在喫煙 （20 本/日以上）	2.08（p=0.001） 1.49（p=0.474） 1.14（p=0.249） 0.99（p=0.720） 1.03（p=0.393）
Hirayama T Prev Med 13： 680-690, 1984	コホート	1965	非喫煙女性 91,540 名	死亡	質問票	年齢，職業	夫の喫煙	肺がん 胃がん 鼻腔がん 脳腫瘍 全がん	現在喫煙 （20 本/日以上）	1.91［1.34～2.71］ 1.01［0.86～1.19］ 2.55［1.04～6.27］ 4.32［1.53～12.19］ 1.23［1.12～1.35］
Akiba S Can Res 46： 4804-4807, 1986	コホート内ケースコントロール	1982	原爆生存者男女。 症例 428 名， 対照 957 名	肺がん罹患	インタビュー	出生年，居住地，性，健診対象者か否かをマッチング	夫の喫煙		非喫煙男性 非喫煙女性	1.80［0.50～5.60］ 1.50［1.00～2.50］
Inoue R & Hirayama T Smoking and Health 283-285, 1987	ケースコントロール（病院対照）	1980～1983， 1973～1981	女性。症例 37 名， 対照（脳血管疾患） 74 名	肺がん死亡	インタビュー	出生年，死亡年，地域をマッチング	夫の喫煙		非喫煙女性	2.25［0.91～7.10］
Shimizu H, et al Tohoku J Exp Med 154： 389-397, 1988	ケースコントロール（病院対照）	1982～1985	非喫煙女性 （症例 90 例， 対照 163 例）	肺がん罹患	質問票	病院，年齢，入院日をマッチング	夫の喫煙			1.1（NS）
Sobue T Int J Epi 19： S62-S66, 1990	ケースコントロール（病院対照）	1986～1988	非喫煙女性 （症例 144 例， 対照 713 例）	肺がん罹患		年齢階級と教育歴調整	夫の喫煙			1.13［0.78～1.63］
Nishino Y, et al Can Causes Cont 12： 797-802, 2001	コホート	1984	非喫煙女性 9,675 名	がん罹患	質問票	年齢，地域，飲酒，緑黄色野菜摂取，果物摂取 十肉摂取，肺疾患既往 十肉摂取 十肉摂取 十初産年齢，出産回数，初経年齢，BMI	夫の喫煙	全がん 肺がん 結腸がん 直腸がん 乳がん		1.1［0.91～1.4］ 1.8［0.67～4.6］ 1.1［0.54～2.4］ 1.9［0.87～4.2］ 0.58［0.32～1.1］
Hanaoka T, et al Int J Can 114： 317-322, 2005	コホート	1990～1992	非喫煙女性 20,193 名	乳がん罹患	質問票	年齢，地域，就労状況，教育歴，BMI，乳がん家族歴，良性乳腺腫瘍既往，飲酒，初経年齢，出産回数，ベースライン閉経状態，女性ホルモン使用	家庭 家庭または，職場 and/or 公共の場所		ベースライン時閉経前 ベースライン時閉経後 全例 ベースライン時閉経前 ベースライン時閉経後 全例	1.6［0.9～2.7］ 0.7［0.4～1.1］ 1.0［0.7～1.4］ 2.6［1.3～5.2］ 0.7［0.4～1.0］ 1.1［0.8～1.6］
Ozasa K Asian Pacif J Can Prev 8： 89-96, 2007	コホート	1988～1990	非喫煙男性 67,997 人年 非喫煙女性 420,201 人年	肺がん死亡	質問票	年齢，地域	家庭		ほぼ毎日 3 時間/日以上 時々，1～4 時間/週 ほぼ毎日 3 時間/日以上 時々，1～4 時間/週	0.45［0.09～2.22］ 5.29［1.03～27.20］ 1.48［0.57～3.84］ 1.06［0.68～1.64］ 1.12［0.55～2.28］ 0.84［0.49～1.46］
Lin Y, et al J Epi 18： 77-83, 2008	コホート	1988～1990	非喫煙女性 32,023 名	乳がん罹患	質問票	年齢，地域，BMI，乳がん家族歴，飲酒，日常歩行，初経年齢，初産年齢，出産回数，ベースライン閉経状態，女性ホルモン使用	家庭		時々 ほぼ毎日	0.59［0.33～1.05］ 0.71［0.48～1.05］
Kurahashi N, et al Int J Can 122： 653-657, 2008	コホート	1990，1993	非喫煙女性 28,414 名	肺がん罹患	性・姓・住所・年齢（差 16 歳未満）で夫婦同定，夫の喫煙状況は質問票に基づく	年齢，地域，飲酒，肺がん家族歴，閉経状態	夫の喫煙	肺がん全体 肺腺がん	現在喫煙 現在喫煙	1.34［0.81～2.21］ 2.03［1.07～3.86］

NS：有意でない，*：Hirayama は 90%信頼区間

199

果は一致していないが，前述のカリフォルニア州環境保護庁報告書での乳がんの評価には，閉経前女性で受動喫煙との有意な関連がみられた日本の研究が影響している。平山研究では鼻腔がん，脳腫瘍，および全がんでも有意なリスク上昇を観察したが，その後同様の報告はない。

おわりに

喫煙の健康影響については，過去半世紀近くにわたって研究が蓄積し，因果関係が認められる疾患や症状が一貫して増えてきた。今日，能動喫煙はがんだけでなく，循環器疾患，呼吸器疾患など，さまざまな疾患との因果関係が科学的に確立され，最近では大規模なメタアナリシスにより糖尿病との関連も確立されつつある。今後も，受動喫煙を含めて，タバコとの関連が科学的に確立される疾患や症状は増え続けることが予想される。

文　献

1) Tobacco smoke and involuntary smoking. IARC Monograph on the Evaluation of Carcinogenic Risks to Humans, Vol. 83, World Health Organization International Agency for Research on Cancer, Lyon, 2002
2) Hecht SS : Tobacco smoke carcinogens and lung cancer. J Natl Cancer Inst **91** : 1194-1210, 1999
3) The health consequences of smoking. A Report of the Surgeon General, U. S. Public Health Service (ed), 2004
4) Katanoda K, Marugame T, Saika K, et al : Population attributable fraction of mortality associated with tobacco smoking in Japan : a pooled analysis of three large-scale cohort studies. J Epidemiol **18** : 251-264, 2008
5) 祖父江友孝：「たばこに関する科学的知見の収集に係る研究」平成19年度報告書，厚生労働省科学研究補助金循環器疾患等生活習慣病対策総合研究事業，2008
6) Inoue M, Tsuji I, Wakai K, et al : Evaluation based on systematic review of epidemiological evidence among Japanese populations : tobacco smoking and total cancer risk. Jpn J Clin Oncol **35** : 404-411, 2005
7) Nishino Y, Inoue M, Tsuji I, et al : Tobacco smoking and gastric cancer risk : an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol **36** : 800-807, 2006
8) Wakai K, Inoue M, Mizoue T, et al : Tobacco smoking and lung cancer risk : an evaluation based on a systematic review of epidemiological evidence among the Japanese population. Jpn J Clin Oncol **36** : 309-324, 2006
9) Inoue M, Hanaoka T, Sasazuki S, et al : Impact of tobacco smoking on subsequent cancer risk among middle-aged Japanese men and women : data from a large-scale population-based cohort study in Japan—the JPHC study. Prev Med **38** : 516-522, 2004
10) Thun MJ, Day-Lally C, Myers DG, et al : Trends in tobacco smoking and mortality from cigarette use in Cancer Prevention Studies I (1959-1965) and II (1982-1988). National Cancer Institute, Smoking and Tobacco Control, Monograph 8. NIH Publication, Washington DC, 1997, pp305-382
11) Jemal A, Travis WD, Tarone RE, et al : Lung cancer rates convergence in young men and women in the United States : analysis by birth cohort and histologic type. Int J Cancer **105** : 101-107, 2003
12) Botteri E, Iodice S, Bagnardi V, et al : Smoking and colorectal cancer : a meta-analysis. JAMA **300** : 2765-2778, 2008
13) Mizoue T, Inoue M, Tanaka K, et al : Tobacco smoking and colorectal cancer risk : an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol **36** : 25-39, 2006
14) Nagata C, Mizoue T, Tanaka K, et al : Tobacco smoking and breast cancer risk : an evaluation based on a systematic review of epidemiological evidence among the Japanese population. Jpn J Clin Oncol **36** : 387-394, 2006
15) Reversal of risk after quitting smoking. IARC Handbooks of Cancer Prevention, Tabacco Control, Volume 11, IARC (ed), Lyon, 2007
16) Wakai K, Marugame T, Kuriyama S, et al : Decrease in risk of lung cancer death in Japanese men after smoking cessation by age at quitting : pooled analysis of three large-scale cohort studies. Cancer Sci **98** : 584-589, 2007
17) Proposed identification of environmental tobacco smoke as a toxic air contaminant. California Environmental Protection Agency, 2005
18) The health consequences of involuntary exposure to tobacco smoke. A Report of the Surgeon General. U. S. Department of Health and Human Services, 2006
19) Hirayama T : Non-smoking wives of heavy smokers have a higher risk of lung cancer : a study from Japan. Br Med J (Clin Res Ed) **282** : 183-185, 1981