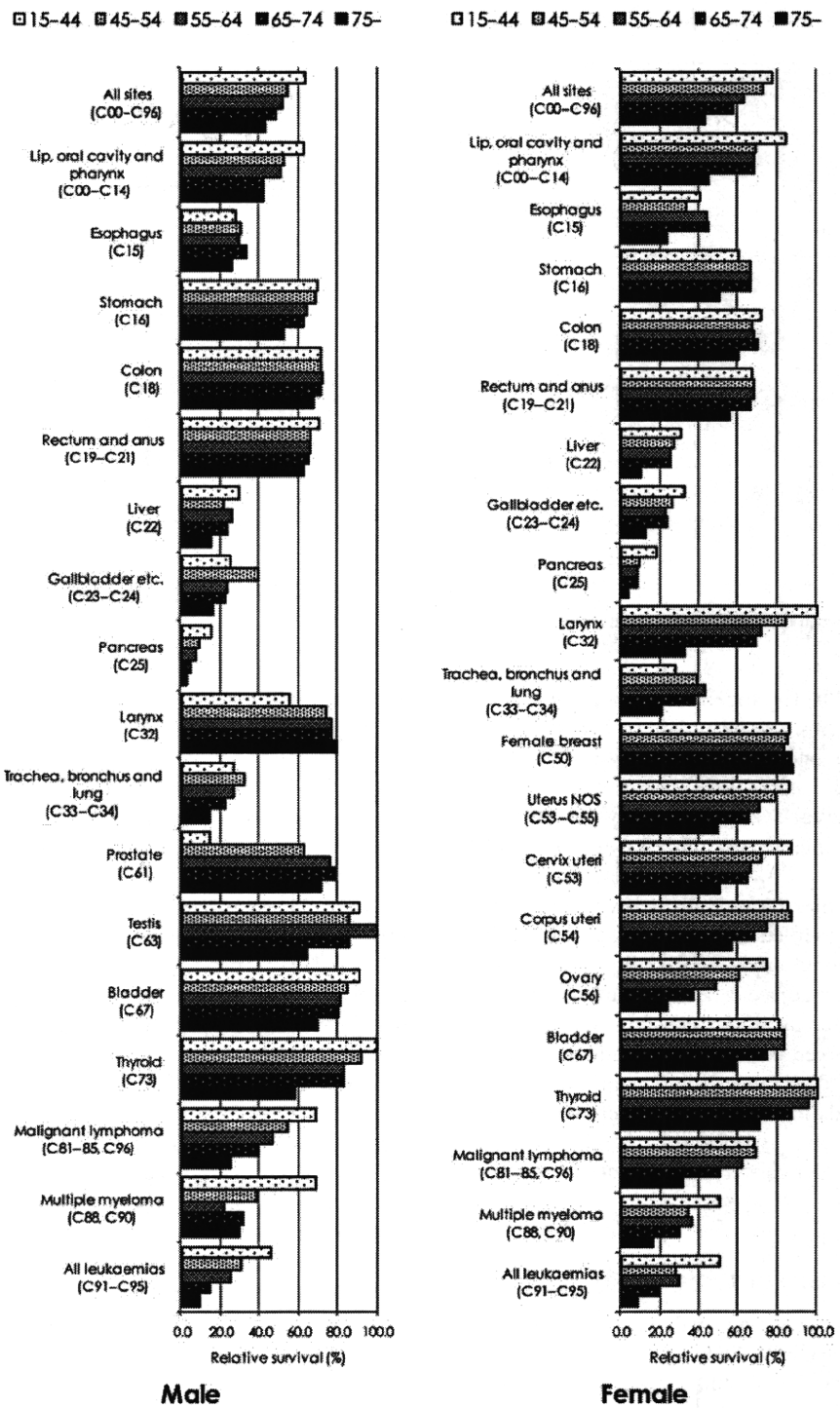

Figure 1. Relative 5-year survival for major sites of cancer by sex and age at diagnosis (1997–99, Subject 2).

regional study (18). Unfortunately, no change was seen in survival of cancers with distant metastases.

There were particularly marked improvements in survival for cancers of the esophagus, liver and female breast, which might be mainly due to diffusion of organized screening programs in the society or development of early detection systems in cases of opportunistic screening (19–22). Treatment has also evolved during these two observational periods. Yamanaka et al. (23) reported, for example, that the establishment of indication criteria for hepatectomy and the

Table 4. Relative 5-year survival for major sites of cancer by extent of tumor at diagnosis (Subjects 2)

Primary sites	Localized		Regional lymph node metastases, adjacent organ metastases		Distant metastasis	
	%	SE	%	SE	%	SE
1993–96						
All sites (C00–C96)	84.6	0.2	43.2	0.2	10.3	0.2
Lip, oral cavity and pharynx (C00–C14)	75.0	1.5	39.4	1.4	16.5	2.8
Esophagus (C15)	55.2	1.6	19.1	0.9	3.7	0.6
Stomach (C16)	94.4	0.3	40.2	0.5	3.1	0.2
Colon (C18)	96.6	0.5	64.8	0.8	8.2	0.5
Rectum and anus (C19–C21)	93.0	0.6	55.3	0.9	8.1	0.7
Liver (C22)	30.3	0.6	8.6	0.8	4.0	0.5
Gallbladder etc. (C23–C24)	61.5	1.8	12.6	0.8	1.6	0.3
Pancreas (C25)	37.1	2.5	4.5	0.5	1.1	0.2
Larynx (C32)	89.3	1.6	51.8	3.2	14.2	5.4
Trachea, bronchus and lung (C33–C34)	65.8	0.9	16.0	0.5	2.5	0.2
Female breast (C50)	96.6	0.3	78.3	0.7	25.3	1.7
Uterus (C53–C55)	93.1	0.6	54.1	1.4	15.2	2.0
Cervix uteri (C53)	93.6	0.8	52.8	1.6	9.8	2.1
Corpus uteri (C54)	92.9	1.0	63.4	3.1	22.7	3.7
Ovary (C56)	89.6	1.6	40.5	2.0	15.4	1.6
Prostate (C61)	96.5	1.7	71.0	2.9	35.2	1.7
Testis (C63)	99.5	1.1	86.3	6.3	60.9	6.1
Bladder (C67)	91.4	1.0	35.1	2.7	7.6	1.9
Thyroid (C73)	98.6	0.8	94.0	0.9	40.7	4.3
Malignant lymphoma (C81–85, C96)	75.3	2.0	55.4	2.4	36.2	1.4
Multiple myeloma (C88, C90)	56.4	11.5	55.0	15.6	25.3	2.2
All leukemias (C91–C95)	–	–	–	–	–	–
1997–99						
All sites (C00–C96)	85.2	0.2↑*	43.7	0.3	10.1	0.2
Lip, oral cavity and pharynx (C00–C14)	76.1	1.7	39.2	1.6	12.7	2.9
Esophagus (C15)	64.9	1.6↑**	21.0	1.0	4.8	0.8
Stomach (C16)	95.2	0.3	39.8	0.6	2.9	0.3
Colon (C18)	95.7	0.5	65.0	0.9	9.3	0.6
Rectum and anus (C19–C21)	94.0	0.7	56.4	1.0	9.7	0.8
Liver (C22)	33.2	0.7↑**	10.4	0.9	3.2	0.5
Gallbladder etc. (C23–C24)	57.4	2.0	14.0	0.9	0.8	0.2↓*
Pancreas (C25)	34.7	2.7	6.1	0.6↑*	1.0	0.2
Larynx (C32)	90.0	1.9	37.5	3.5↓**	5.7	2.7
Trachea, bronchus and lung (C33–C34)	68.7	0.9↑*	18.6	0.6↑**	2.8	0.2
Female breast (C50)	97.7	0.3↑**	78.4	0.7	27.6	1.8
Uterus (C53–C55)	92.2	0.7	52.4	1.6	12.8	2.0
Cervix uteri (C53)	92.3	1.1	53.1	2.0	10.2	2.4
Corpus uteri (C54)	92.4	1.1	53.7	3.1↓*	17.2	3.2

Continued

Table 4. *Continued*

Primary sites	Localized		Regional lymph node metastases, adjacent organ metastases		Distant metastasis	
	%	SE	%	SE	%	SE
Ovary (C56)	86.0	1.8	43.6	2.1	20.3	2.1
Prostate (C61)	97.6	1.3	79.2	2.9↑*	39.6	1.8
Testis (C63)	97.8	1.8	100.0	0.0↑*	70.7	6.3
Bladder (C67)	88.1	1.1↓*	34.3	2.8	8.8	2.4
Thyroid (C73)	99.6	0.8	93.6	1.1	41.7	4.9
Malignant lymphoma (C81–85, C96)	79.8	2.1	58.4	2.7	34.1	1.6
Multiple myeloma (C88, C90)	51.2	10.2	52.7	15.7	24.4	2.8
All leukemias (C91–C95)	–	–	–	–	–	–

↑ improved significantly between the two observation periods $^{**}P < 0.01$, $^{*}P < 0.05$.
↓ deteriorated significantly between the two observation periods ** $P < 0.01$, * $P < 0.05$.

introduction of multimodal treatment for recurrence were contributory factors. Lung cancer patients, particularly those with early stage disease, also benefit from improvements in surgical technique (24). The increase in breast cancer survival likely results from development of new treatments. The breast conserving treatment with or without axillary dissection has been developed and replaced Halsted radical mastectomy in early 1990s in Japan. At the same time, endocrine therapy has progressed remarkably with acceptance of tamoxifen use in 1981. Since then LHRH agonist and aromatase inhibitors were approved one after another in the mid-1990s, and effective chemotherapy regimens in premenopausal women have also been developed: the majority of the university hospitals and clinics employed these new treatment strategies. We have to be cautious when considering prostate cancer survival because the early detection of micro tumors by PSA screening has been evident for more than a decade. However, considering that survival was particularly improved for cases with metastasis to regional lymph nodes or adjacent organs, the introduction of more effective radiation therapy might have contributed to the survival of older patients with prostate cancer (25).

We found that the overall survival of cancer patients in Japan is comparable with that in Europe (51.9%), although survival for some cancer types, particularly prostate cancer, lymphoma and leukemia, is much lower than in these Western countries. In contrast, the overall survival in the USA was much higher than Japan. This is probably due to the large difference of weights on breast and prostate cancer in cancer incidence. Survival for digestive organ and hepatobiliary cancers was better in Japan than in Western countries. For specific types of cancer, greater survival in a particular country tends to be correlated with higher incidence in that country (8). A high survival rate might result from greater surgical volume for these primary sites (26). In other words, compared with their Western counterparts, Japanese oncologists are usually more aware of digestive organ and hepatobiliary cancers and have greater experience in treatment of these cancers. Conversely, tumors that are sensitive to chemotherapy seem to be treated less effectively by Japanese oncologists. This slow progress in chemo-sensitive malignancies may demonstrate weaknesses of the system of oncology in Japan; serious shortage of oncologists specialized in chemotherapy and less centralized primary cancer treatment.

Changes over time in Japan were similar to those in the international studies examined. For example, considering changes in lung cancer and breast cancer, the time trends identified in Japan were very similar to those seen when comparing EUROCARE 3 and EUROCARE 4 (27).

Limitations

To perform survival analyses in Japan, it is a priority to improve the quality of cancer registry data, because the high proportion of patients not registered will diminish the accuracy of survival estimates according to international criteria (28). In this study, we required each registry to meet the necessary standards for participating in nationwide estimates of incidence (8). It would be reasonable to assume, therefore, that the current study has been conducted on the basis of fairly accurate data from population-based cancer registries.

In the three prefectures where the vital status of patients was checked after 5 years from diagnosis, the proportion of unknown cases for vital status was only 2%, which implies that the assessment of outcome was highly accurate. The other three prefectures did not have the resources to check the vital status of patients in the resident registry. Table 2 shows that the survival proportion from these three registries was higher than that from the other three referring resident registries. The best way to collect more accurate survival

Table 5. Comparison of the survival between the SEER (96-03), the EUROCARE 4 and the present study

Primary sites	Present study (Subjects 2) 1997–99		SEER 1996–2003	EUROCARE4 1995–99
	All ages	Age standardized rate	All ages	Age standardized rate
All sites (C00–C96)	54.3	53.3	64.9	51.9
Lip, oral cavity and pharynx (C00–C14)	52.9	51.6	59.1	–
Esophagus (C15)	31.6	30.6	15.6	12.3
Stomach (C16)	62.1	61.4	24.3	24.1
Colon (C18)	68.9	68.7	63.5	53.9
Rectum and anus (C19–C21)	65.2	64.7	65.0	53.5
Liver (C22)	23.1	22.0	10.8	8.6
Gallbladder etc. (C23–C24)	20.2	22.1	15.1[a]; 18.6[b]	14.1
Pancreas (C25)	6.7	7.2	5.0	5.5
Larynx (C32)	76.1	75.2	62.9	63.1
Trachea, bronchus and lung (C33–C34)	25.6	25.8	15.0	12.6
Female breast (C50)	85.5	86.1	88.6	81.1
Cervix uteri (C53)	71.5	70.6	71.6	66.5
Corpus uteri (C54)	76.8	69.9	83.9	78.3
Ovary (C56)	52.0	41.3	44.9	41.6
Prostate (C61)	75.5	69.7	98.1	77.0
Testis (C63)	92.0	88.4	98.4	93.8
Bladder (C67)	76.5	77.5	79.5	65.8
Thyroid (C73)	92.4	91.2	93.9	86.5
Malignant lymphoma (C81–85, C96)	49.9	45.6	66.8	–
Hodgkin's lymphoma	68.3	71.8	84.9	83.0
Non-Hodgkin's lymphoma	49.1	45.5	63.4	54.6
Multiple myeloma (C88, C90)	29.8	30.7	33.7	34.4
All leukemias (C91–C95)	32.9	20.6	49.6	–
Acute lymphocytic leukemia	50.0	25.3	64.0	30.0
Acute myelogenous leukemia	26.6	17.1	21.2	19.0
Chronic myelogenous leukemia	44.0	32.5	47.5	39.5

[a]Gallbladder.
[b]Intrahepatic bile duct.

data are to assess patient outcome by referring to resident registries. However, the fact that these registries do not check the survival of patients appears to have a modest effect on the overestimation of survival, because death information is very precise in Japan, and collation could be done with high accuracy in these three prefectures. Further, the frequency of patients moving to different prefectures is considered to be relatively low.

Mucosal cancers of the large bowel should have been excluded from the survival analysis, since they are regarded as *in situ* cancers according to the agreement of the International Union Against Cancer (UICC) (29). However, some population-based cancer registries in Japan still do not distinguish them. In this study, it seems that the proportions of mucosal cancer of the large bowel and of multiple primary cancers (except the first-diagnosed tumor) were negligible; it is therefore reasonable to think that they did not greatly affect survival results.

Future of Survival Analysis in Japan

The EUROCARE study is one of the most important collaborative studies of the European Union (9), currently involving 67 population-based cancer registries operating in 22 European countries (11). Furthermore, the CONCORD study extends the EUROCARE study to include North America

(the USA and Canada), Australia and Asian countries, involving 101 population-based cancer registries in 31 countries (30). The International Agency for Research on Cancer has published an article on cancer survival in Africa, Asia and Central America recently including nine Asian countries (31), in addition, a similar international project on survival is ongoing in the Asia region; an Asian cancer registry network is being formed (32).

We confirmed the importance of calculating a comparable population-based survival as a measure of cancer control programs through the present study. Comparing the data chronologically and internationally, we figured out current situation, progress and international position of cancer screening and treatments in Japan. Drawing up a project or evaluating outcomes based on such a useful index is undoubtedly the basic principle of cancer control. Currently, it is highly recommended to analyze incidence, mortality and survival together in order to more fully understand the characteristics of cancer in a country (27,33). The Japanese research group is also conducting the MCIJ to monitor incidence, mortality and survival as the index of the progress of the cancer control routinely in Japan (34), and we hope to show the results to the world in the near future.

Conclusion

The study suggests an improvement in cancer survival in Japan in several primary sites during a relatively short period, which is consistent with the development of treatments and early detection. We confirmed that the overall survival of cancer patients in Japan is comparable with that in Europe. In contrast, the overall survival in the USA was much higher than Japan, but this is probably due to the difference of cancer incidence proportion.

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Conflict of interest statement

None declared.

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Cancer Incidence and Incidence Rates in Japan in 2005: Based on Data from 12 Population-based Cancer Registries in the Monitoring of Cancer Incidence in Japan (MCIJ) Project

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The Japan Cancer Surveillance Research Group estimated the cancer incidence in 2005 as part of the Monitoring of Cancer Incidence in Japan (MCIJ) project, on the basis of data collected from 12 of 30 population-based cancer registries. The total number of incidences in Japan for 2005 was estimated as 646 802 (C00–C96). The leading cancer site was the stomach for men and the breast for women. Age-standardized incidence rates remained almost the same level as the previous 2 years.

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

The Japan Cancer Surveillance Research Group is involved in cancer monitoring in Japan since 2000 (1–5). This group estimated the cancer incidence in 2005 as part of the Monitoring of Cancer Incidence in Japan (MCIJ) project, on the basis of data collected from 12 of 30 population-based cancer registries: Miyagi, Yamagata, Chiba, Kanagawa, Niigata, Fukui, Shiga, Tottori, Okayama, Hiroshima, Nagasaki and Kumamoto. If data from all 30 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 (6–8). We maintained the same methodology since the MCIJ2003: (i) we invited all 30 population-based cancer registries in Japan to participate, and from these, we selected the 12 cancer registries with high-quality data in order to estimate the national incidence, and (ii) we used 2005 data alone for the national estimation. For this year, data from Osaka and Saga prefectures, regularly considered as one of the registries with high quality, were not available for the MCIJ project. The other registries remained since the previous estimation in 2004.

The number of incidences, crude rates, age-standardized rates and quality indicators of registration in 2005 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 2005 was estimated as 646 802 (C00–C96). The time trends of age-standardized incidence rates for the five major sites and male- and female-specific sites in 1975–2005 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 since the research group took over national estimation of incidence, as shown in Figs 1 and 2. Age-standardized incidence rates remained almost the same level as the previous 2 years. It is thought to be partly due to that the development of hospital-based cancer registry in designated cancer care hospitals was calmed down in 2005. The estimated cancer incidence data in Japan by sex, site, 5-year age group and calendar year during the period 1975–2005 are available as a booklet and as an electronic database

Table 1. Incidence, completeness of reporting and accuracy of diagnosis in Japan according to sex and primary site, 2005

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	390 835	626.9	288.5	408.4	14.9	1.99	74.8
All sites	C00–C96	379 436	608.6	279.7	396.1	15.2	1.93	74.3
Lip, oral cavity and pharynx	C00–C14	7417	11.9	6.0	8.2	12.8	1.79	80.6
Esophagus	C15	14 818	23.8	11.1	15.5	13.1	1.57	80.0
Stomach	C16	80 102	128.5	59.3	83.9	12.1	2.45	84.0
Colon	C18	37 126	59.5	27.1	38.7	10.3	2.76	84.1
Rectum	C19–C20	22 344	35.8	17.5	24.2	10.3	2.57	85.3
Colon and rectum	C18–C20	59 470	95.4	44.6	62.9	10.3	2.69	84.6
Liver	C22	28 729	46.1	21.4	30.1	23.5	1.24	31.3
Gallbladder etc.	C23–C24	9237	14.8	6.1	9.1	25.3	1.18	48.8
Pancreas	C25	13 108	21.0	9.5	13.5	26.5	1.07	35.9
Larynx	C32	3903	6.3	2.9	4.0	6.1	3.88	89.3
Trachea, bronchus and lung	C33–C34	58 264	93.4	39.4	58.5	21.7	1.29	68.8
Melanoma of skin etc.	C43–C44	4798	7.7	3.5	5.0	4.2	7.64	92.5
Prostate	C61	42 997	69.0	28.2	42.0	10.3	4.64	83.5
Bladder	C67	12 619	20.2	8.8	12.9	10.3	3.05	83.2
Kidney, renal pelvis, ureter etc.	C64–C66, C68	9758	15.7	7.7	10.6	13.2	2.43	76.1
Brain and nervous system	C70–C72	2496	4.0	2.8	3.3	25.3	2.71	68.2
Thyroid	C73	2126	3.4	2.0	2.6	4.5	4.77	91.0
Malignant lymphoma	C81–C85, C96	9667	15.5	8.0	10.9	12.4	1.99	86.1
Multiple myeloma	C88, C90	2242	3.6	1.5	2.3	23.2	1.14	67.4
All leukaemias	C91–C95	5200	8.3	5.3	6.3	21.6	1.21	85.9

Female								
All sites (incl. CIS)	C00–C96, D00–D09	285 240	436.0	202.6	271.1	15.0	2.21	74.9
All sites	C00–C96	267 366	408.7	183.8	247.7	15.8	2.07	73.7
Lip, oral cavity and pharynx	C00–C14	3498	5.3	2.3	3.1	14.6	2.29	80.4
Esophagus	C15	2678	4.1	1.5	2.1	20.9	1.56	71.6
Stomach	C16	37 035	56.6	21.8	30.7	15.6	2.10	80.2
Colon	C18	31 069	47.5	17.9	25.1	14.3	2.27	79.5
Rectum	C19–C20	13 517	20.7	8.9	12.1	11.0	2.70	83.8
Colon and rectum	C18–C20	44 586	68.2	26.8	37.2	13.3	2.39	80.7
Liver	C22	13 465	20.6	6.9	10.1	27.6	1.22	26.7
Gallbladder etc.	C23–C24	9399	14.4	4.0	6.1	30.9	1.08	38.4
Pancreas	C25	11 691	17.9	5.8	8.4	28.8	1.10	30.7
Larynx	C32	214	0.3	0.1	0.2	16.2	2.55	73.7
Trachea, bronchus and lung	C33–C34	25 617	39.2	14.3	20.2	23.3	1.52	68.0
Melanoma of skin etc.	C43–C44	4342	6.6	2.3	3.2	8.2	7.50	90.1
Breast (incl. CIS)	C50, D05	50 695	77.5	47.5	61.4	5.0	4.73	90.4
Breast (only invasive)	C50	47 583	72.7	44.4	57.4	5.3	4.44	89.9
Uterus (incl. CIS)	C53–C55, D06	25 424	38.9	27.5	34.3	5.5	4.73	89.9
Uterus (only invasive)	C53–C55	17 476	26.7	16.4	21.1	7.4	3.25	87.2
Cervix uteri	C53	8474	13.0	8.7	11.0	6.1	3.44	88.6
Corpus uteri	C54	8189	12.5	7.3	9.5	3.2	5.61	92.1
Ovary	C56	8304	12.7	7.4	9.4	13.4	1.86	77.7
Bladder	C67	3858	5.9	1.8	2.7	19.8	2.04	71.7
Kidney, renal pelvis, ureter etc.	C64–C66, C68	4884	7.5	3.1	4.2	16.8	2.31	71.4
Brain and nervous system	C70–C72	2567	3.9	2.3	2.7	28.2	3.49	64.6
Thyroid	C73	7093	10.8	6.7	8.5	7.5	6.93	88.5
Malignant lymphoma	C81–85 C96	7324	11.2	5.0	6.6	13.7	1.97	83.7
Multiple myeloma	C88 C90	2171	3.3	1.2	1.7	26.3	1.13	66.8
All leukaemias	C91–C95	3832	5.9	3.4	4.0	22.6	1.29	83.5

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, 2005

Primary sites	ICD-10th	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	411	251	264	325	694	915	1592	2633	4640	7543	17 618	34 039	47 157	60 310	73 404	69 067	40 247	29 725
All sites	C00–C96	411	247	264	320	694	895	1577	2540	4422	7221	16 847	32 892	45 627	58 269	71 267	67 254	39 392	29 297
Lip, oral cavity and pharynx	C00–C14	1	7	14	2	36	39	58	71	123	261	543	1125	1157	1040	1060	1054	494	332
Esophagus	C15	0	2	0	0	0	0	0	22	61	304	717	1779	2364	2846	2604	2304	1196	619
Stomach	C16	4	0	0	6	46	66	168	435	1060	1708	4174	7786	10 330	12 802	14 933	13 373	7552	5659
Colon	C18	0	0	0	6	1	62	115	311	456	658	1786	3257	4635	5947	6828	6253	3979	2832
Rectum	C19–C20	0	0	0	5	4	20	120	171	406	734	1437	2830	3320	3508	3825	3184	1640	1140
Colon and rectum	C18–C20	0	0	0	11	5	82	235	482	862	1392	3223	6087	7955	9455	10 653	9437	5619	3972
Liver	C22	15	0	0	0	6	22	56	160	271	501	1523	2795	4111	4824	5840	4716	2448	1441
Gallbladder etc.	C23–C24	0	0	0	0	11	1	0	41	24	77	282	481	877	1241	1541	1908	1481	1272
Pancreas	C25	0	0	1	0	0	10	7	59	114	181	698	1216	1625	2214	2301	2049	1503	1130
Larynx	C32	0	0	0	0	0	0	0	12	23	28	160	454	723	690	550	721	343	199
Trachea, bronchus and lung	C33–C34	0	0	5	0	0	46	71	205	388	802	1889	4084	6049	7396	11 080	12 646	7755	5848
Melanoma of skin etc.	C43–C44	0	0	1	6	8	16	28	83	103	75	169	330	338	737	866	701	602	735
Prostate	C61	0	0	0	0	0	0	8	0	7	66	487	1844	4333	7797	10 615	9458	4869	3513
Bladder	C67	5	0	0	0	0	10	46	49	188	254	402	1051	1286	1506	2280	2461	1687	1394
Kidney, renal pelvis, ureter etc.	C64–C66 C68	16	23	0	0	1	23	29	85	262	306	649	1149	984	1565	1903	1462	765	536
Brain and nervous system	C70–C72	31	44	89	48	129	63	85	59	114	100	126	194	269	293	285	294	178	95
Thyroid	C73	0	0	0	18	36	58	81	105	65	123	215	361	247	245	221	217	106	28
Malignant lymphoma	C81–85 C96	9	43	22	77	48	69	141	228	264	381	597	674	1046	1302	1604	1521	892	749
Multiple myeloma	C88 C90	0	0	0	0	3	0	2	5	5	44	75	160	239	270	478	421	297	243
All leukaemias	C91–C95	162	84	48	64	112	82	156	149	117	164	275	365	439	671	777	750	478	307

Female																			
All sites (incl. CIS)	C00–C96 D00–D09	248	178	209	298	972	2407	4945	6920	10 446	14 101	18 686	26 896	28 609	30 500	35 638	36 211	31 284	36 692
All sites	C00–C96	248	178	209	285	596	1372	3149	5140	8819	12 773	17 301	25 607	27 125	29 124	34 121	34 887	30 392	36 040
Lip, oral cavity and pharynx	C00–C14	0	2	14	4	21	28	80	30	53	144	124	280	362	440	520	508	346	542
Esophagus	C15	0	0	0	0	0	0	4	2	10	81	147	258	279	328	329	378	395	467
Stomach	C16	0	0	0	4	0	41	281	399	781	1087	1644	2922	3333	4238	5397	5993	5080	5835
Colon	C18	0	0	17	0	7	25	117	173	356	703	1560	2313	3030	4278	4351	4720	4273	5146
Rectum	C19–C20	0	0	0	0	0	6	63	189	324	474	926	1361	1635	1773	1764	1761	1408	1833
Colon and rectum	C18–C20	0	0	17	0	7	31	180	362	680	1177	2486	3674	4665	6051	6115	6481	5681	6979
Liver	C22	23	0	0	0	4	5	30	18	81	62	250	707	1122	1806	2569	2787	2060	1941
Gallbladder etc.	C23–C24	0	0	0	0	5	0	6	24	30	68	209	262	512	801	1265	1553	1987	2677
Pancreas	C25	0	0	0	0	2	8	12	20	73	160	295	762	891	1171	1734	2006	1873	2684
Larynx	C32	0	0	0	0	0	0	0	0	7	14	4	14	31	11	23	10	43	57
Trachea, bronchus and lung	C33–C34	0	0	0	0	0	47	93	73	261	449	978	2186	2686	3021	3871	4159	3418	4375
Melanoma of skin etc.	C43–C44	0	0	17	7	26	17	71	22	81	99	91	193	290	303	492	689	755	1189
Breast (incl. CIS)	C50 D05	0	0	0	7	19	159	805	2092	4374	6139	6244	7245	6667	4930	4573	3352	2336	1753
Breast (only invasive)	C50	0	0	0	7	19	146	761	1973	4038	5732	5751	6903	6246	4629	4275	3179	2218	1706
Uterus (incl. CIS)	C53–C55 D06	0	0	6	28	413	1397	2412	2697	2455	2156	2446	3031	2157	1566	1589	1338	836	897
Uterus (only invasive)	C53–C55	0	0	6	19	64	402	726	1142	1309	1439	1966	2676	1915	1378	1464	1286	804	880
Cervix uteri	C53	0	0	0	19	50	334	553	908	920	704	857	1018	566	562	625	590	357	411
Corpus uteri	C54	0	0	6	0	14	67	171	226	361	709	1088	1579	1298	764	797	585	313	211
Ovary	C56	0	11	22	45	111	166	203	289	348	663	969	1186	985	805	757	629	513	602
Bladder	C67	0	0	0	0	0	13	9	23	17	55	143	156	242	293	553	621	748	985
Kidney, renal pelvis, ureter etc.	C64–C66 C68	15	35	2	10	9	29	17	32	83	93	281	433	474	521	812	725	662	651
Brain and nervous system	C70–C72	46	32	51	17	28	21	88	56	76	96	191	177	258	317	258	247	279	329
Thyroid	C73	0	0	4	22	110	200	279	313	451	626	672	935	857	767	663	522	361	311
Malignant lymphoma	C81–85 C96	5	14	14	84	32	125	58	94	158	217	382	724	676	812	1076	981	895	977
Multiple myeloma	C88 C90	0	0	0	0	0	0	0	4	13	55	44	183	224	269	330	293	400	356
All leukaemias	C91–C95	60	66	37	35	58	47	174	77	93	180	196	343	388	387	393	498	388	412

Table 3. Age-specific incidence rate per 100 000 population in Japan according to sex and primary site, 2005

Primary sites	ICD-10th	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	14.4	8.3	8.6	9.6	18.5	21.8	32.3	59.8	114.1	195.0	401.9	670.4	1135.1	1701.3	2414.8	3061.1	3291.8	3665.7
All sites	C00–C96	14.4	8.1	8.6	9.5	18.5	21.3	32.0	57.7	108.8	186.7	384.4	647.8	1098.2	1643.7	2344.5	2980.7	3221.9	3612.9
Lip, oral cavity and pharynx	C00–C14	0.0	0.2	0.5	0.1	1.0	0.9	1.2	1.6	3.0	6.7	12.4	22.2	27.8	29.3	34.9	46.7	40.4	40.9
Esophagus	C15	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.5	1.5	7.9	16.4	35.0	56.9	80.3	85.7	102.1	97.8	76.3
Stomach	C16	0.1	0.0	0.0	0.2	1.2	1.6	3.4	9.9	26.1	44.2	95.2	153.3	248.6	361.1	491.3	592.7	617.7	697.9
Colon	C18	0.0	0.0	0.0	0.2	0.0	1.5	2.3	7.1	11.2	17.0	40.7	64.1	111.6	167.8	224.6	277.1	325.4	349.2
Rectum	C19–C20	0.0	0.0	0.0	0.1	0.1	0.5	2.4	3.9	10.0	19.0	32.8	55.7	79.9	99.0	125.8	141.1	134.1	140.6
Colon and rectum	C18–C20	0.0	0.0	0.0	0.3	0.1	2.0	4.8	10.9	21.2	36.0	73.5	119.9	191.5	266.7	350.5	418.2	459.6	489.8
Liver	C22	0.5	0.0	0.0	0.0	0.2	0.5	1.1	3.6	6.7	13.0	34.7	55.0	99.0	136.1	192.1	209.0	200.2	177.7
Gallbladder etc.	C23–C24	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.9	0.6	2.0	6.4	9.5	21.1	35.0	50.7	84.6	121.1	156.9
Pancreas	C25	0.0	0.0	0.0	0.0	0.0	0.2	0.1	1.3	2.8	4.7	15.9	23.9	39.1	62.5	75.7	90.8	122.9	139.4
Larynx	C32	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.6	0.7	3.7	8.9	17.4	19.5	18.1	32.0	28.1	24.5
Trachea, bronchus and lung	C33–C34	0.0	0.0	0.2	0.0	0.0	1.1	1.4	4.7	9.5	20.7	43.1	80.4	145.6	208.6	364.5	560.5	634.3	721.2
Melanoma of skin etc.	C43–C44	0.0	0.0	0.0	0.2	0.2	0.4	0.6	1.9	2.5	1.9	3.9	6.5	8.1	20.8	28.5	31.1	49.2	90.6
Prostate	C61	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.0	0.2	1.7	11.1	36.3	104.3	219.9	349.2	419.2	398.2	433.2
Bladder	C67	0.2	0.0	0.0	0.0	0.0	0.2	0.9	1.1	4.6	6.6	9.2	20.7	31.0	42.5	75.0	109.1	138.0	171.9
Kidney, renal pelvis, ureter etc.	C64–C66, C68	0.6	0.8	0.0	0.0	0.0	0.5	0.6	1.9	6.4	7.9	14.8	22.6	23.7	44.1	62.6	64.8	62.6	66.1
Brain and nervous system	C70–C72	1.1	1.4	2.9	1.4	3.4	1.5	1.7	1.3	2.8	2.6	2.9	3.8	6.5	8.3	9.4	13.0	14.6	11.7
Thyroid	C73	0.0	0.0	0.0	0.5	1.0	1.4	1.6	2.4	1.6	3.2	4.9	7.1	5.9	6.9	7.3	9.6	8.7	3.5
Malignant lymphoma	C81–85, C96	0.3	1.4	0.7	2.3	1.3	1.6	2.9	5.2	6.5	9.9	13.6	13.3	25.2	36.7	52.8	67.4	73.0	92.4
Multiple myeloma	C88, C90	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.1	0.1	1.1	1.7	3.2	5.8	7.6	15.7	18.7	24.3	30.0
All leukaemias	C91–C95	5.7	2.8	1.6	1.9	3.0	2.0	3.2	3.4	2.9	4.2	6.3	7.2	10.6	18.9	25.6	33.2	39.1	37.9

Female

All sites (incl. CIS)	C00–C96, D00–D09	9.1	6.2	7.1	9.3	27.0	59.0	102.6	159.7	260.2	365.5	423.4	519.4	651.7	784.5	990.6	1204.4	1428.7	1734.2
All sites	C00–C96	9.1	6.2	7.1	8.9	16.6	33.6	65.3	118.6	219.6	331.0	392.0	494.6	617.9	749.2	948.4	1160.4	1387.9	1703.4
Lip, oral cavity and pharynx	C00–C14	0.0	0.1	0.5	0.1	0.6	0.7	1.7	0.7	1.3	3.7	2.8	5.4	8.2	11.3	14.5	16.9	15.8	25.6
Esophagus	C15	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.2	2.1	3.3	5.0	6.4	8.4	9.1	12.6	18.0	22.1
Stomach	C16	0.0	0.0	0.0	0.1	0.0	1.0	5.8	9.2	19.5	28.2	37.3	56.4	75.9	109.0	150.0	199.3	232.0	275.8
Colon	C18	0.0	0.0	0.6	0.0	0.2	0.6	2.4	4.0	8.9	18.2	35.3	44.7	69.0	110.0	120.9	157.0	195.1	243.2
Rectum	C19–C20	0.0	0.0	0.0	0.0	0.0	0.1	1.3	4.4	8.1	12.3	21.0	26.3	37.2	45.6	49.0	58.6	64.3	86.6
Colon and rectum	C18–C20	0.0	0.0	0.6	0.0	0.2	0.8	3.7	8.4	16.9	30.5	56.3	71.0	106.3	155.6	170.0	215.6	259.4	329.9
Liver	C22	0.8	0.0	0.0	0.0	0.1	0.1	0.6	0.4	2.0	1.6	5.7	13.7	25.6	46.5	71.4	92.7	94.1	91.7
Gallbladder etc.	C23–C24	0.0	0.0	0.0	0.0	0.1	0.0	0.1	0.6	0.7	1.8	4.7	5.1	11.7	20.6	35.2	51.7	90.7	126.5
Pancreas	C25	0.0	0.0	0.0	0.0	0.1	0.2	0.2	0.5	1.8	4.1	6.7	14.7	20.3	30.1	48.2	66.7	85.5	126.9
Larynx	C32	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.4	0.1	0.3	0.7	0.3	0.6	0.3	2.0	2.7
Trachea, bronchus and lung	C33–C34	0.0	0.0	0.0	0.0	0.0	1.2	1.9	1.7	6.5	11.6	22.2	42.2	61.2	77.7	107.6	138.3	156.1	206.8
Melanoma of skin etc.	C43–C44	0.0	0.0	0.6	0.2	0.7	0.4	1.5	0.5	2.0	2.6	2.1	3.7	6.6	7.8	13.7	22.9	34.5	56.2
Breast (incl. CIS)	C50, D05	0.0	0.0	0.0	0.2	0.5	3.9	16.7	48.3	108.9	159.1	141.5	139.9	151.9	126.8	127.1	111.5	106.7	82.9
Breast (only invasive)	C50	0.0	0.0	0.0	0.2	0.5	3.6	15.8	45.5	100.6	148.6	130.3	133.3	142.3	119.1	118.8	105.7	101.3	80.6
Uterus (incl. CIS)	C53–C55, D06	0.0	0.0	0.2	0.9	11.5	34.2	50.0	62.2	61.1	55.9	55.4	58.5	49.1	40.3	44.2	44.5	38.2	42.4
Uterus (only invasive)	C53–C55	0.0	0.0	0.2	0.6	1.8	9.8	15.1	26.4	32.6	37.3	44.5	51.7	43.6	35.4	40.7	42.8	36.7	41.6
Cervix uteri	C53	0.0	0.0	0.0	0.6	1.4	8.2	11.5	21.0	22.9	18.2	19.4	19.7	12.9	14.5	17.4	19.6	16.3	19.4
Corpus uteri	C54	0.0	0.0	0.2	0.0	0.4	1.6	3.5	5.2	9.0	18.4	24.7	30.5	29.6	19.7	22.2	19.5	14.3	10.0
Ovary	C56	0.0	0.4	0.7	1.4	3.1	4.1	4.2	6.7	8.7	17.2	22.0	22.9	22.4	20.7	21.0	20.9	23.4	28.5
Bladder	C67	0.0	0.0	0.0	0.0	0.0	0.3	0.2	0.5	0.4	1.4	3.2	3.0	5.5	7.5	15.4	20.7	34.2	46.6
Kidney, renal pelvis, ureter etc.	C64–C66, C68	0.6	1.2	0.1	0.3	0.3	0.7	0.4	0.7	2.1	2.4	6.4	8.4	10.8	13.4	22.6	24.1	30.2	30.8
Brain and nervous system	C70–C72	1.7	1.1	1.7	0.5	0.8	0.5	1.8	1.3	1.9	2.5	4.3	3.4	5.9	8.2	7.2	8.2	12.7	15.5
Thyroid	C73	0.0	0.0	0.1	0.7	3.1	4.9	5.8	7.2	11.2	16.2	15.2	18.1	19.5	19.7	18.4	17.4	16.5	14.7
Malignant lymphoma	C81–C85, C96	0.2	0.5	0.5	2.6	0.9	3.1	1.2	2.2	3.9	5.6	8.7	14.0	15.4	20.9	29.9	32.6	40.9	46.2
Multiple myeloma	C88, C90	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.3	1.4	1.0	3.5	5.1	6.9	9.2	9.7	18.3	16.8
All leukaemias	C91–C95	2.2	2.3	1.3	1.1	1.6	1.2	3.6	1.8	2.3	4.7	4.4	6.6	8.8	10.0	10.9	16.6	17.7	19.5

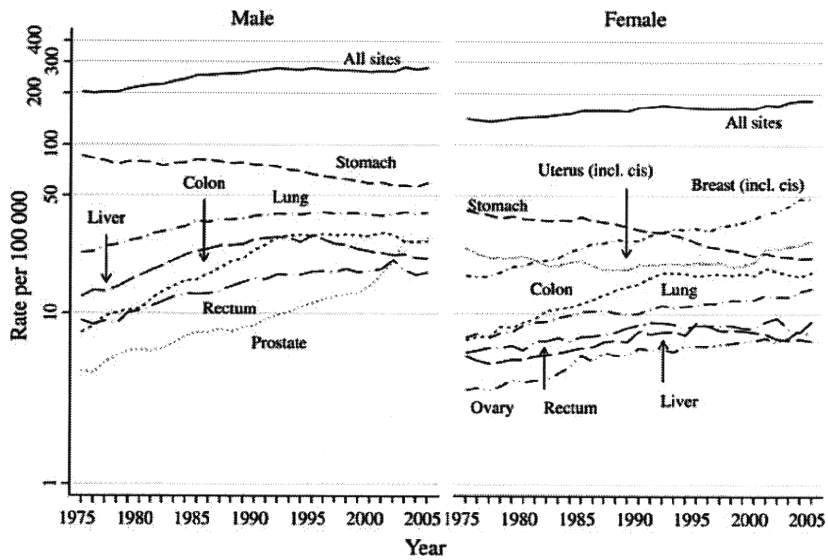

Figure 1. Trends of age-standardized cancer incidence rates for five major sites and specific sites for each sex (standard population: world population).

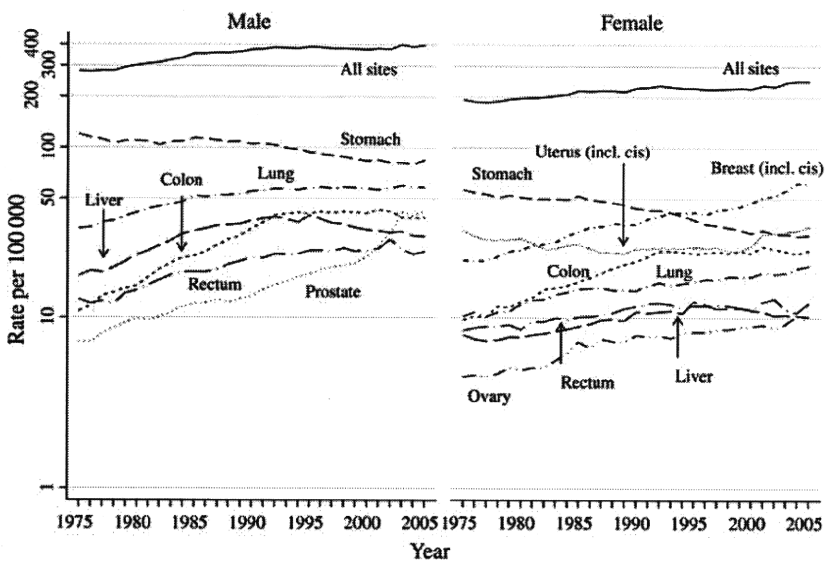

Figure 2. Trends of age-standardized cancer incidence rates for five major sites and specific sites for each sex (standard population: 1985 Japanese model population).

on the website (only available in Japanese, http://ganjoho.jp/professional/statistics/monita.html).

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Conflict of interest statement

None declared.

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Fresh and pickled vegetable consumption and gastric cancer in Japanese and Korean populations: A meta-analysis of observational studies

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It is widely known that vegetable consumption contributes to reducing the risk of gastric cancer (GC). However, the incidence rates of GC remain high in both Japanese and Korean populations, even though they have a high consumption of total vegetables. This may be due to the fact that Japanese and Koreans mainly consume processed vegetables, such as cooked, salted, or pickled vegetables, rather than fresh vegetables. To determine whether the intakes of fresh and pickled vegetables have different effects on the risk of GC in Japanese and Korean populations, we carried out a meta-analysis of published epidemiological reports. Eight studies on the consumption of fresh vegetables and 14 studies on the consumption of pickled vegetables related to GC risk were included in this meta-analysis. Four studies exploring differences in GC risk in men and women were considered separately. We observed that a high intake of fresh vegetables was significantly associated with a decreased risk of GC (overall summary OR = 0.62, 95% CI = 0.46–0.85) but that a high intake of pickled vegetables was significantly associated with an increased risk of GC (overall summary OR = 1.28, 95% CI = 1.06–1.53). The results of this meta-analysis provide evidence that a high intake of pickled vegetables may increase GC risk and suggest that a high consumption of fresh vegetables, rather than a large total amount of vegetables including pickled vegetables, is important to reduce GC risk. (*Cancer Sci* 2010; 101: 508–516)

Vegetable consumption is known to contribute to a reduction of gastric cancer (GC) risk.[1–6] The mean daily intake of vegetables in Korea (327.0 g/day)[7] and Japan (253.9 g/day)[8] is higher than that of the USA (189 g/day)[9] and northern Europe (104.6–119.1 g/day in men and 119.4–131.0 g/day in women),[10] all regions characterized by low rates of GC incidence (<15/100 000).[11] However, the age-standardized incidence rate of GC remained high in Korea (67–73/100 000 men and 20–30/100 000 women) and Japan (60–92/100 000 men and 24–39/100 000 women) during the 1990s.[12] Moreover, the seroprevalence of *Helicobacter pylori* infection, considered as a major risk factor for GC, is also high in Japan (60.0%) and Korea (59.6%).[13,14]

This paradox might be explained by the fact that Japanese and Korean people consume more pickled vegetables than fresh vegetables. Vegetables are the main source of various antioxidants (such as carotenoids, vitamin C, folate, and selenium), fiber, and phytochemicals that play an important role in the etiology of cancer.[15–17] However, vegetables have varying effects on GC risk, depending on how they are prepared and preserved. Fresh vegetables contain greater amounts of these nutrients because there is no nutrient loss due to preparation, so fresh vegetable consumption appears to be a stronger protective factor against GC than total vegetable consumption.[16] Unfortunately, Japanese and Korean people often consume processed vegetables, such as cooked, salted, or pickled vegetables, rather than fresh vegetables.[7] Pickling, also known as brining or corning, is the process of preserving food by soaking and storing it in vinegar or brine.[18] Although pickled vegetables may offer health benefits due to the fermentation process,[19] they may have adverse effects on GC risk due to the addition of large amounts of salt and the loss of key nutrients contained in vegetables under acidic and oxygenic conditions.[15,20,21] In addition, pickled vegetables are a possible source of nitroso compounds that may contribute to gastric carcinogenesis.[22,23]

Although the evidence from case–control studies supporting the protective effects of vegetables against GC risk remains strong, evidence about the effects of vegetable consumption on GC risk from cohort studies is equivocal,[16,24–26] and meta-analyses of the relationships between pickled vegetable intake and GC risk have not been carried out. Therefore, we examined the relationships between the consumption of fresh vegetables and pickled vegetables and GC risk through a meta-analysis of studies carried out in Japanese and Korean populations that indicated a high risk of GC but also a high intake of vegetables.

Materials and Methods

Selection of studies for meta-analysis. Case–control studies and cohort studies evaluating the relationships between vegetable intake and GC risk published before November 2008 were identified using databases including PubMed (http://www.ncbi.nlm.nih.gov/pubmed/), KoreaMed (http://www.koreamed.org/SearchBasic.php), and Ichushi (Japana Centra Revuo Medicina, http://www.jamas.or.jp). The keywords used in these searches were (''gastric cancer'' or ''stomach cancer''), (''vegetable'' or ''pickled vegetable''), and (''Japan'' or ''Korea''). We also reviewed the references cited in the articles to identify additional studies for inclusion. We included published works written in Japanese, Korean, and English.

Inclusion/exclusion criteria. Inclusion/exclusion criteria for this meta-analysis were as follows.

1 To examine the relationships between overall fresh or pickled vegetables intake and GC risk, we included only the results that specified the food item to be ''fresh vegetables,'' ''raw vegetables,'' ''pickled vegetables,'' ''pickles,'' or ''pickled food'' in each study, and the results obtained from single food item questions have been excluded.

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2 Subjects were of Japanese or Korean ethnicities. Migrant studies were also included.
3 Cohort or case–control studies were included. Review or meta-analysis articles were excluded.
4 The studies that presented adjusted 95% confidence intervals (CI) as well as relative risks (RR) or odds ratios (OR) were included for meta-analysis in order to use adjusted values. Studies that did not report adjusted 95% CI or that presented regression coefficient values were excluded even if the number of cases and controls were presented.
5 In cases of multiple publications drawn from studies of the same population, only the most recent study was included.
6 Case–control studies that evaluated mortality instead of GC incidence were excluded.

Data abstraction. The studies were reviewed independently by two reviewers using the same inclusion/exclusion criteria, with disagreements between the reviewers resolved by consensus. The following information was collected from each study: the study design; author; publication year; nation; study period; study subjects (type and sources, definition, and numbers of subjects); measure unit of food intake (consumption frequency or quantitative intake amount); category of food intake; RR/OR and 95% CI; *P* for trend; and confounding variables.

Statistical analysis. To consider the values adjusted for the confounding factors and to include the studies that did not present each cell number (cross-tabulation) in the tables,[6,27] we used the values of RR or OR with its 95% CI. Statistical heterogeneity across the studies was assessed by calculating the between-study variation (τ^2) from the Q statistic.[28] In addition to Q, the I^2 statistic describing the percentage of variation attributable to heterogeneity across the studies was also calculated from Q values because it is easily interpretable. It has been suggested that I^2 values of 25%, 50%, and 75% is assigned to low, moderate, and high heterogeneity, respectively.[29] Depending on these results for heterogeneity, we decided whether a fixed-effect or random-effect model would be used to calculate the summary OR and its 95% CI. Additionally, we discovered sources of heterogeneity between studies through a meta-regression analysis including nationality (Japanese *vs* Korean), study design (cohort *vs* case–control study), sex (total, men, *vs* women), and the year the study started. To assess the degree of publication bias, we tested asymmetry in the funnel plot using Begg's test.[30] *P*-values less than 0.05 were considered statistically significant. All analyses were carried out using STATA 10 software (STATA, College Station, TX, USA).

Results

We identified a total of 75 articles through an initial computerized search of published work. By screening the articles according to title and abstract, 54 articles (11 review papers, 1 meta-analysis study, 9 experiment studies or clinical trials, 9 studies of populations from other countries, 23 studies on other foods or vegetables or non-dietary factors, and 1 study on atrophic gastritis) were excluded. We added 11 articles through citation searches, and then 32 original articles related to the relationships between the consumption of fresh and/or pickled vegetables and GC risk were included. Among these articles, the number of studies on the relationships between fresh vegetable intake and GC risk was 14 (2 cohort studies[31,32] and 12 case–control studies[6,27,33–42]), and the number of studies on the relationships between pickled vegetable intake and GC risk was 25 (15 cohort studies[23,31,32,43–54] and 10 case–control studies[27,33,34,36,41,55–59]). Based on the exclusion criteria, three case–control studies that did not report adjusted 95% CI values,[33,55,56] one cohort study that presented the regression coefficient values,[43] one cohort study that compared the mean intake times per week,[44] nine publications presenting multiple studies of the same population,[31,35,37–39,45,47,48,54] and one case–control study using death cases[57] were excluded. Finally, a total of eight articles (one cohort study[32] and seven case–control studies[6,27,34,36,40–42]) on the effects of consuming fresh vegetables and 14 articles (eight cohort studies[23,32,46,49–53] and six case–control studies[27,34,36,41,58,59]) on the effects of consuming pickled vegetables were included in this meta-analysis. Four articles[34,50,51,53] that presented results separately for men and women were considered in the separate articles for meta-analysis.

The details of the eligible studies are presented in Tables 1 and 2 by vegetable type (fresh or pickled). Confounding factors, including typical confounders such as age and sex, were adjusted for in most studies. We obtained statistically significant results in tests of heterogeneity between studies of fresh vegetables (Q = 28.369 on 8 degrees of freedom, $P < 0.001$; $I^2 = 71.8\%$) and pickled vegetables (Q = 45.292 on 16 degrees of freedom, $P < 0.001$; $I^2 = 64.7\%$). Therefore, we selected a random-effect model to present the summary statistics. The results of the meta-analysis of the relationships between fresh and pickled vegetable intake and GC risk are presented in Figures 1 and 2, respectively. A high intake of fresh vegetables was significantly associated with a decreased risk of GC (overall summary OR = 0.62, 95% CI = 0.46–0.85), whereas a high intake of pickled vegetables was significantly associated with an increased risk of GC (overall summary OR = 1.28, 95% CI = 1.06–1.53). The adjusted RR/OR for the highest category of fresh vegetable intake were skewed in the negative direction (RR/OR range, 0.20–0.92) except for one study (OR = 1.20),[36] whereas the adjusted RR/OR for the highest category of pickled vegetable intake varied (RR/OR range, 0.60–3.80). After excluding two studies by Lee JK *et al.*[36] and Lee SA *et al.*,[40] which reported excessive right- or left-sided skew in their associations between fresh vegetable intake and GC risk, the level of heterogeneity became low (Q = 13.074 on 6 degrees of freedom, $P = 0.042$; $I^2 = 54.1\%$; data not shown). However, the significance levels of the overall summary estimate of the effect of the consumption of fresh vegetables on GC risk did not change (overall summary OR = 0.64, 95% CI = 0.49–0.83; data not shown).

To explore the possible variables that explain why the results varied from study to study, a meta-regression analysis was carried out that included nationality (Japanese *vs* Korean), study design (cohort *vs* case–control study), sex (total, men *vs* women), and the year the study started. Of these variables, nationality ($P = 0.043$ for fresh vegetables and $P < 0.001$ for pickled vegetables) was observed as a source of heterogeneity. However, study design ($P = 0.690$ for fresh vegetables and $P = 0.126$ for pickled vegetables), sex ($P = 0.449$ for fresh vegetables and $P = 0.567$ for pickled vegetables), and the year the study started ($P = 0.081$ for fresh vegetables and $P = 0.512$ for pickled vegetables) were not significant sources of heterogeneity between studies. Therefore, we carried out a subgroup analysis according to nationality. The protective effects of fresh vegetables on GC risk from Japanese studies (OR = 0.56, 95% CI = 0.45–0.69) was stronger than that of the overall analysis, and the heterogeneity between studies disappeared (Q = 3.609 on four degrees of freedom, $P = 0.461$, $I^2 = 0\%$). However, the heterogeneities between Korean studies on fresh vegetables as well as Japanese studies on pickled vegetables remained after the subgroup analysis according to nationality (data not shown).

Begg's funnel plots for assessment of publication bias are presented in Figure 3. Begg's test and funnel plots did not detect publication bias in the meta-analyses of the effect of fresh ($Z = 0.94$, $P = 0.348$) or pickled vegetables ($Z = 0.78$, $P = 0.434$) on GC risk.

Table 1. Intake of fresh vegetables and gastric cancer (GC) risk: cohort and case–control studies among Japanese and Korean populations

Author (year), country[Ref.]	Study period	Study subjects: Source of subjects	Study subjects: No. of subjects	Study subjects: Event followed	Study subjects: No. of incident cases or deaths	Measure unit of food intake	Category	RR/OR (95% CI)	*P* for trend	Confounding variables considered
Cohort studies										
Inoue *et al.* (1996), Japan[32]	1985–1995	Patients who received gastroscopy (Aichi Cancer Center)	5373	Incidence	69 (51 men, 18 women)	Frequency	Rarely Occasionally Daily	1.0 0.73 (0.34–1.55) 0.67 (0.29–1.57)†	NA	Adjusted for sex and age
Case–control studies										
Kato *et al.* (1990), Japan[34]	1985–1989	Cases: histologically confirmed cases/Controls: patients with normal gastric mucosa (Aichi Cancer Center)	Cases: 289 men/ Controls: 1247 men			Frequency	≤1–2/month 2–3/week Daily	1.0 0.77 (0.51–1.15) 0.59 (0.37–0.93)	NA	Adjusted for age and residence
			Cases: 138 women/ Controls: 1767 women				≤1–2/month 2–3/week Daily	1.0 1.04 (0.62–1.74) 0.84 (0.47–1.51)	NA	
Hoshiyama *et al.* (1992), Japan[27]	1984–1990	Cases: newly histologically confirmed cases/Controls: residents in the study area (Saitama Cancer Center)	Cases: 294 (206 men, 88 women)/ Controls: 294 (206 men, 88 women)			Frequency	≤1/week 2–5/week ≥6/week	1.0 0.5 (0.3–0.8) 0.4 (0.2–0.7)‡	<0.0100	Matched for sex, age, administrative division, and smoking status
Lee *et al.* (1995), Korea[36]	1990–1991	Cases: histologically confirmed cases/Controls: hospitalized patients (Hanyang University Hospital and Asan Medical Center)	Cases: 213 (132 men, 81 women)/ Controls: 213 (132 men, 81 women)			Quantitative amount	Tertile 1 Tertile 2 Tertile 3	1.0 1.1 (0.7–1.9) 1.2 (0.8–1.9)	0.6400	Matched for sex and age (±2 years)/Adjusted for age, sex, education, economic status and residence
Kim *et al.* (2002), Korea[6]	1997–1998	Cases: newly histologically confirmed cases/Controls: patients without GC of the same hospital (Hanyang University Hospital and Hallim University Hospital)	Cases: 136 (93 men, 43 women)/ Controls: 136 (93 men, 43 women)			Quantitative amount	Quartile 1 Quartile 2–3 Quartile 4	1.0 0.61 (0.34–1.09) 0.55 (0.28–1.09)	0.1579	Matched for sex, age (±2 years), and hospital/ Adjusted for age, sex, socioeconomic status, family history of GC, and refrigerator use
Ito *et al.* (2003), Japan[41]	1988–1998	Cases: histologically confirmed cases/Controls: cancer-free first visit outpatients at the center (Aichi Cancer Center)	Cases: 508 women/ Controls: 36 490 women			Frequency	Almost never Occasionally 3–4 times/week Everyday	1.00 0.68 (0.48–0.97) 0.74 (0.52–1.05) 0.50 (0.36–0.71)	<0.0010	Adjusted for age, year and season of first hospital visit, smoking, and family history of GC
Lee *et al.* (2003), Korea[40]	2000	Cases: newly histologically confirmed cases/Controls: outpatients without GC (Asan Medical Center)	Cases: 69 (50 men, 19 women)/ Controls: 199 (116 men, 83 women)			Frequency	<4/week 4–6/week >6/week	1.0 0.2 (0.1–0.5) 0.2 (0.1–0.5)	<0.0100	Adjusted for age, sex, and *Helicobacter pylori* infection
Nan *et al.* (2005), Korea[42]	1997–2003	Cases: histologically confirmed cases/Controls: patients of the same hospital (Chungbuk National University Hospital and Eulji University Hospital)	Cases: 421 (276 men, 145 women)/ Controls: 632 (414 men, 218 women)			Quantitative amount	Low High	1.0 0.92 (0.72–1.17)	NA	Matched for sex, age (±3 years), and hospital

†Compared with subjects without atrophic gastritis. ‡Compared with general population controls. CI, confidence interval; NA, not available; OR, odds ratio; RR, relative risk.

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Table 2. Intake of pickled vegetables and gastric cancer (GC) risk: cohort and case–control studies among Japanese or Korean populations

Author (year), country[Ref.]	Study period	Study subjects: Source of subjects	Study subjects: No. of subjects	Study subjects: Event followed	Study subjects: No. of incident cases or deaths	Measure unit of food intake	Category	RR/OR (95% CI)	*P* for trend	Confounding variables considered
Cohort studies										
Kato *et al.* (1992), Japan[23]	1985–1991	Population-based subjects (Aichi prefectures)	9753	Death	57 (35 men, 22 women)	Frequency	≤1–2/week	1.0	0.593	Adjusted for age and sex
							3–4/week	0.51 (0.18–1.48)		
							Daily	0.75 (0.38–1.49)		
Inoue *et al.* (1996), Japan[32]	1985–1995	Patients who received gastroscopy at Aichi Cancer Center	5373	Incidence	69 (51 men, 18 women)	Frequency	Rarely	1.0	NA	Adjusted for sex and age
							Occasionally	2.40 (0.91–6.34)		
							Daily	2.31 (0.87–6.10)†		
Galanis *et al.* (1998), Japan[46]	1975–1994	Japanese-American residents of Hawaii	11 907 (5610 men, 6297 women)	Incidence	108 (64 men, 44 women)	Frequency	None	1.0	0.750	Adjusted for sex, age, years of education, and Japanese place of birth
							1–6/week	1.3 (0.8–2.2)		
							≥7/week	1.1 (0.7–1.8)		
Ngoan *et al.* (2002), Japan[49]	1986–1999	Population-based subjects (Fukuoka prefectures)	13 250 (5917 men, 7333 women)	Death	116 (77 men, 39 women)	Frequency	≤2–4/week	1.0	≥0.050	Adjusted for age, sex, smoking, processed meat, liver, cooking or salad oil, suimono soup
							Once/day	1.3 (0.7–2.5)		
							≥2/day	1.5 (0.7–3.2)		
Khan *et al.* (2004), Japan[50]	1984–2002	Population-based subjects (Hokkaido prefectures)	1524 men	Death	36 men	Frequency	≤Several/month	1.0	NA	Adjusted for age and smoking
							≥Several/week	0.9 (0.3–3.1)‡		
Tsugane *et al.* (2004), Japan[51]	1990–2001	Participants in JPHC cohort I (four prefectures; Iwate, Akita, Nagano, Okinawa)	18 684 men	Incidence	358 men	Frequency	Almost none	1.0	<0.001	Adjusted for age, smoking, fruit and non green-yellow vegetable intake
							1–2 days/week	1.54 (0.97–2.46)		
							3–4 days/week	2.71 (1.76–4.19)		
							Almost every day	2.35 (1.57–3.54)		
			20 381 women	Incidence	128 women		Almost none	1.0	0.050	
							1–2 days/week	1.01 (0.44–2.31)		
							3–4 days/week	2.20 (1.05–4.58)		
							Almost every day	1.74 (0.89–3.41)		
Sauvaget *et al.* (2005), Japan[52]	1980–1999	Participants in LSS cohort§ (two prefectures; Hiroshima and Nagasaki)	38 576 (14 885 men, 23 691 women)	Incidence	1270 (719 men, 551 women)	Frequency	<2/week	1.0	0.025	Adjusted for age, sex, city, radiation dose, sex-specific smoking habit, and education
							2–4/week	0.91 (0.77–1.07)		
							≥5/week	1.11 (0.98–1.26)		
Tokui *et al.* (2005), Japan[53]	1988–1999	Participants in JACC study (45 areas)	110 792	Death	574 men	Frequency	≤1–2/month	1.0	0.480	Adjusted for age
							1–2/week	1.04 (0.72–1.51)		
							3–4/week	1.00 (0.70–1.42)		
							≥1/day	1.09 (0.82–1.47)		
					285 women		≤1–2/month	1.0	0.260	
							1–2/week	1.56 (0.87–2.81)		
							3–4/week	1.32 (0.74–2.36)		
							≥1/day	1.47 (0.90–2.39)		
Case–control studies										
Kato *et al.* (1990), Japan[34]	1985–1989	Cases: histologically confirmed cases/Controls: patients with normal gastric mucosa (Aichi Cancer Center)	Cases: 289 men/ Controls: 1247 men			Frequency	≤1–2/month	1.0	NA	Adjusted for age and residence
							2–3/week	1.54 (1.00–2.39)		
							Daily	1.37 (0.88–2.13)		
			Cases: 138 women/ Controls: 1767 women				≤1–2/month	1.0	NA	
							2–3/week	1.16 (0.71–1.90)		
							Daily	0.75 (0.45–1.27)		

Table 2. (continued)

Author (year), country[Ref.]	Study period	Study subjects: Source of subjects	Study subjects: No. of subjects	Study subjects: Event followed	Study subjects: No. of incident cases or deaths	Measure unit of food intake	Category	RR/OR (95% CI)	*P* for trend	Confounding variables considered
Hoshiyama *et al.* (1992), Japan[27]	1984–1990	Cases: newly histologically confirmed cases/Population controls: residents in the study area (Saitama Cancer Center)	Cases: 294 (206 men, 88 women)/ Controls: 294 (206 men, 88 women)			Frequency	≤1/week 2–9/week ≥10/week	1.0 0.8 (0.4–1.5) 1.3 (0.7–2.6)¶	0.030	Matched for sex, age, administrative division, and smoking status
Lee *et al.* (1995), Korea[36]	1990–1991	Cases: histologically confirmed cases/Controls: hospitalized patients (Hanyang University Hospital and Asan Medical Center)	Cases: 213 (132 men, 81 women)/ Controls: 213 (132 men, 81 women)			Quantitative amount	Tertile 1 Tertile 2 Tertile 3	1.0 2.9 (1.6–5.2) 3.8 (2.3–6.5)	<0.001	Matched for sex and age (±2 years)/Adjusted for age, sex, education, economic status and residence
Watabe *et al.* (1998), Japan[58]	1996–1997	Cases: histologically confirmed cases/Controls: randomly selected from the telephone book (Sapporo Medical University Hospital)	Cases: 242 (180 men, 62 women)/ Controls: 484 (360 men, 124 women)			Frequency	≤3–6/week Daily	1.0 1.10 (0.78–1.55)	NA	Matched for sex, age (±3 years), and registered residence
Ito *et al.* (2003), Japan[41]	1988–1998	Cases: histologically confirmed cases/Controls: cancer- free first visit outpatients (Aichi Cancer Center)	Cases: 508 women/ Controls: 36 490 women			Frequency	<1/week 1–2/week 3–4/week ≥5/week	1.00 0.92 (0.72–1.18) 1.36 (1.02–1.81) 1.04 (0.74–1.47)	NS	Adjusted for age, year and season of first hospital visit, smoking, and family history of GC
Machida-Montani *et al.* (2004), Japan[59]	1998–2002		Cases: 122 (82 men, 40 women)/ Controls: 235 (159 men, 76 women)			Quantitative amount	Tertile 1 Tertile 2 Tertile 3	1.0 0.6 (0.3–1.2) 0.6 (0.3–1.3)	0.17	

†Compared with subjects without atrophic gastritis. ‡Only for men (relative risk [RR] in women was not estimated due to zero cases in both intake groups). §Life Span Study (LSS) cohort includes atomic bomb survivors and unexposed subjects in Hiroshima and Nagasaki. ¶Compared with general population control. CI, confidence interval; JACC, Japan Collaborative Cohort Study for Evaluation of Cancer Risk; JPHC cohort, Japan Public Health Center-based prospective study; NA, not available; NS, not significant; OR, odds ratio.

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