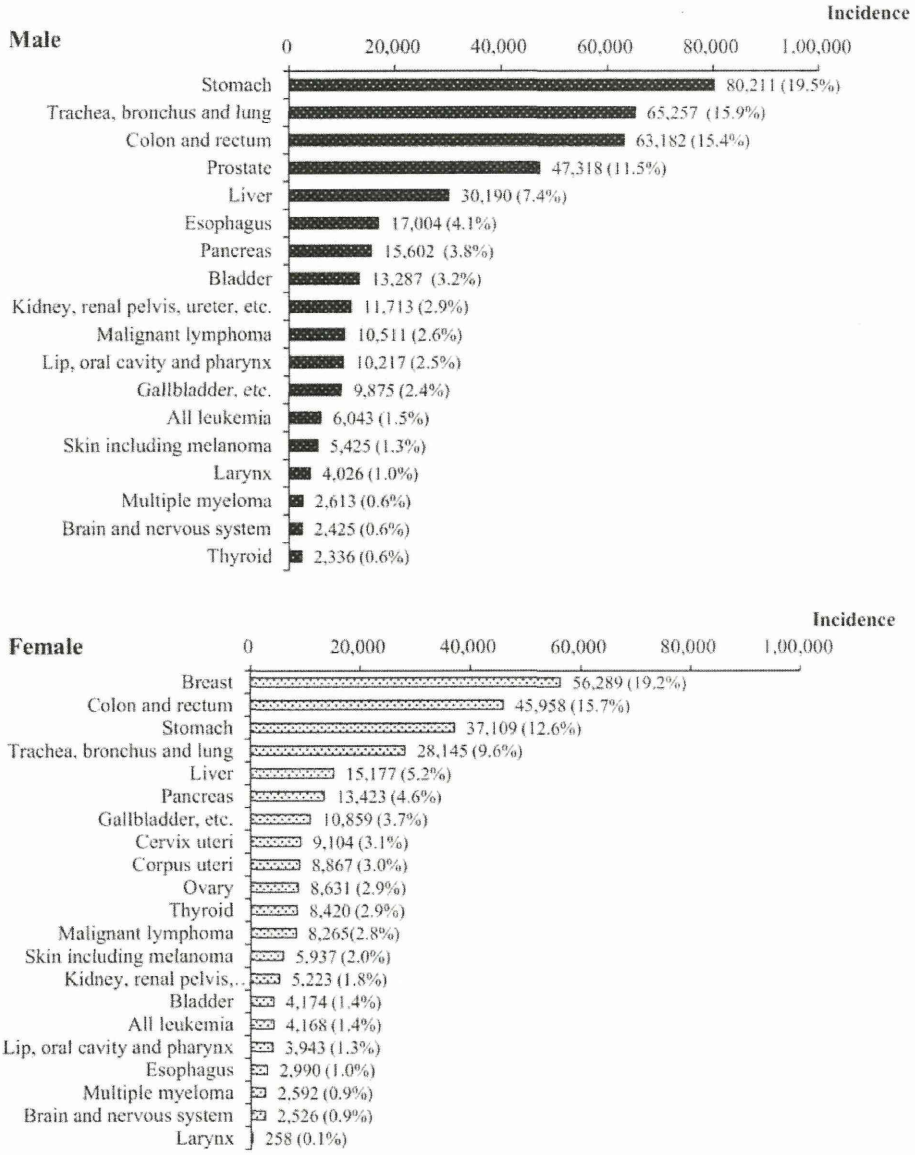

Figure 1. Incidence of cancer (only invasive) in Japan in 2007, according to the primary site, in males (upper panel) and females (lower panel). Data are expressed as number (%).

site in females was of breasts (19.2%), followed by the colon and rectum (15.7%) and stomach (12.6%), which was similar to 2006 (7). The leading five primary sites constituted 69.7% of the total incidence in males and 62.3% in females. These proportions increase to 86.3% in males and 79.6% in females, when the leading 10 primary sites are considered.

Age-specific incidence rates for five major cancer sites for each sex are presented in Fig. 2. Among males, the age-specific incidence trend increased with age for stomach, colon and lung cancers. In these sites, incidence rates increased in the fifth decade. For liver and prostate cancers, the incidence rate increased by the seventh decade, and remained almost flat until the highest age group. In females, trends of the age-specific incidence increased with age for stomach, colon and rectum and lung cancers. Incidence rates peaked at approximately the fourth decade for breast and cervical cancers, and at the fifth decade for corpus uteri cancer, which was clearly younger compared with the other primary sites.

The estimated cancer incidence data in Japan according to sex, cancer site, 5-year age groups and calendar year during the period of 1975–2007 are available in a booklet format (only available in Japanese), as well as via an electronic database on the following website: http://ganjoho.jp/pro/statistics/en/table_download.html. Additionally, the results from the trend analyses of cancer incidence and mortality in Japan are presented in another article in this issue (12).

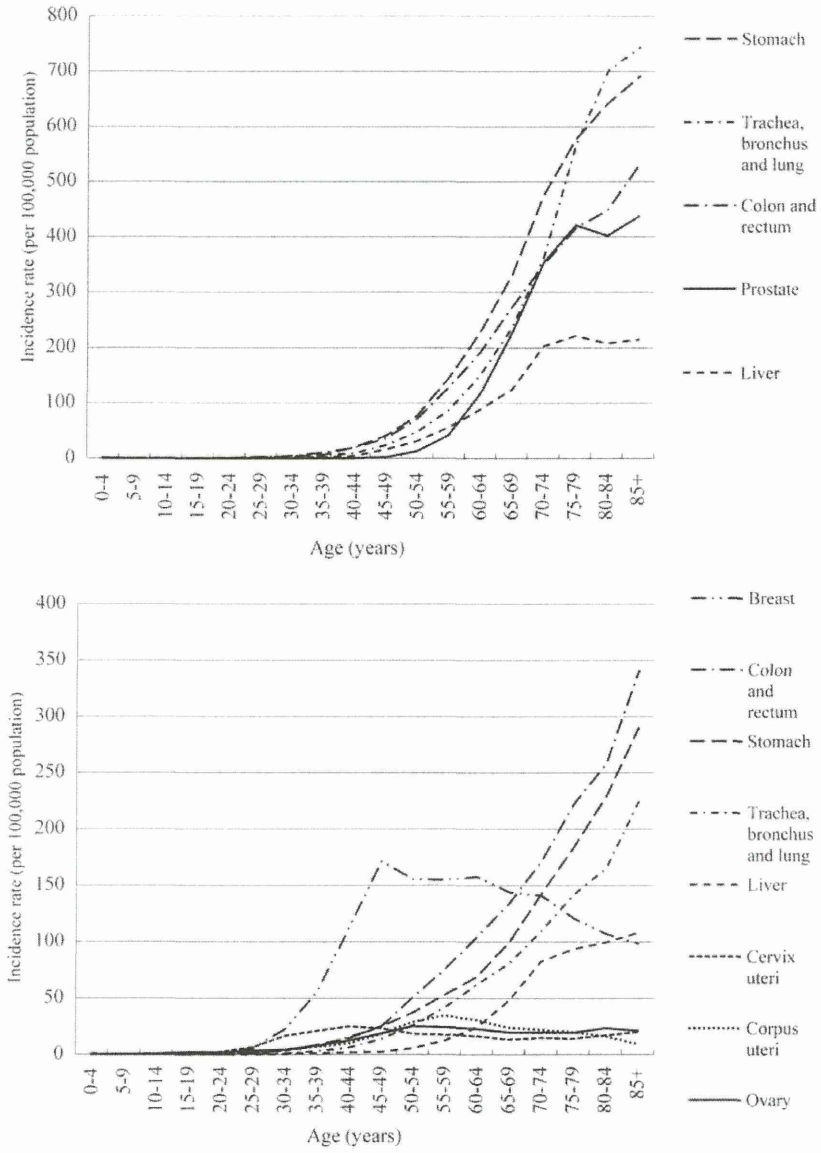

Figure 2. Age-specific incidence rate per population of 100 000 in 2007 for major cancer sites (only invasive) in males (upper panel) and females (lower panel).

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Conflict of interest statement

None declared.

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Cancer Statistics Digest

The 5-Year Relative Survival Rate of Stomach Cancer in the USA, Europe and Japan

In order to compare survival rates in Japan with those in the USA and European countries, we abstracted the 5-year relative survival rate from several data sources. Survival rates of cancer diagnosed in 1995–99 in the USA were abstracted from 18 cancer registries in the Surveillance, Epidemiology and End Results (SEER) data (1). Survival rates of cancer diagnosed in 1995–99 in the UK and Norway were obtained from three cancer registries (Norway, the UK: Northern Ireland, the UK: Scotland and the UK: Wales) in the European Network of Cancer Registries data (2), and the rate of cancer diagnosed in 2000–02 in Japan was reported from six cancer registries (Miyagi, Yamagata, Niigata, Fukui, Osaka and Nagasaki) in the monitoring of cancer incidence in Japan (MCIJ) project (3). Here, we compared the survival rate of stomach cancer coded as C16 (ICD10). Figure 1 shows the 5-year relative survival rate of stomach cancer by age category for males; Fig. 2 shows these data for females.

The 5-year relative survival rates for males across all age groups were about the same as those for females. The rates for both sexes slightly decrease as the patients age. Males and females showed different trends. The survival rates declined constantly according to age for males, while the survival rates for females remain at the same level until the age group 65–74 years, then fell rapidly after the age 75 years. The survival rate in Japan was clearly higher than those in the other countries for both sexes; the rates ranged from 50% to 70%. The other countries showed a similar trend; the rates ranged from 10% to 30%.

The high survival rate for Japanese patients could be related to the organized stomach cancer screening and abundant experience in treatment according to the high incidence rate in the country.

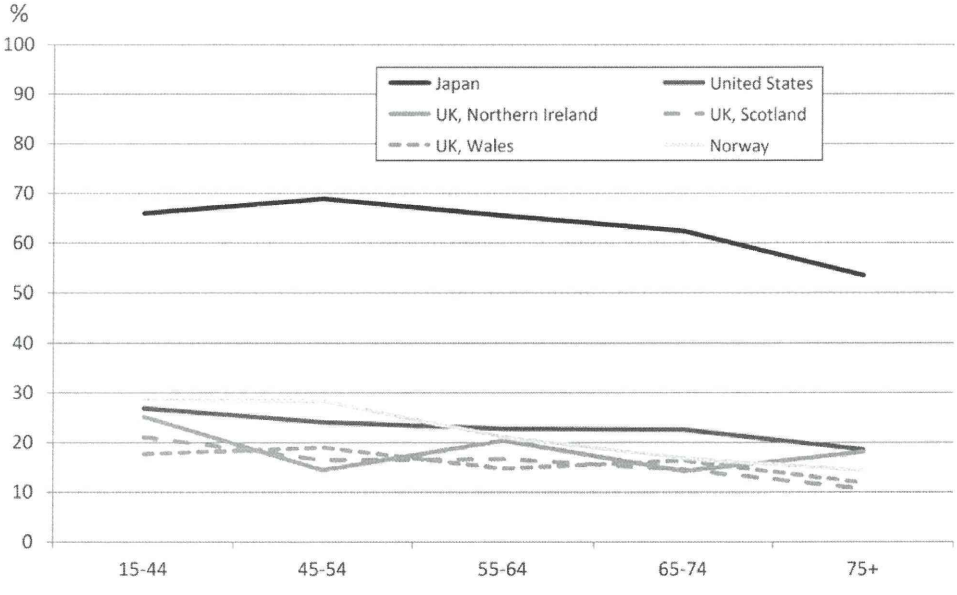

Figure 1. Five-year relative survival rate for stomach cancer (males).

Note: Data were downloaded from the SEER Program (www.seer.cancer.gov) SEER*Stat Database, IARC CANCER Mondial Statistical Information System (http://www-dep.iarc.fr/) and MCIJ database. Responsibility for this presentation and interpretation lies with the authors of this article.

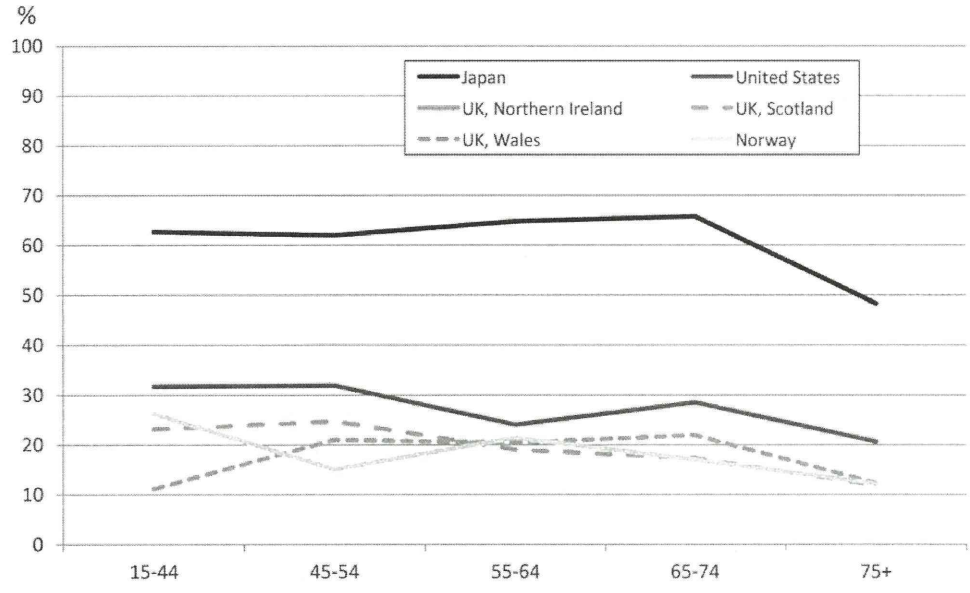

Figure 2. Five-year relative survival rate for stomach cancer (females).

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bjh research paper

Differences in incidence and trends of haematological malignancies in Japan and the United States

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Summary

The incidence of a malignant disease reflects the genetic and cumulative exposure to the environment of a population. Therefore, evaluation of the incidence and trends of a disease in different populations may provide insights into its aetiology and pathogenesis. To evaluate the incidence of haematological malignancies according to specific subtypes, we used population-based registry data in Japan (N = 125 148) and the United States (US; N = 172 925) from 1993 to 2008. The age-adjusted incidence of haematological malignancies in Japan was approximately one-half that in the US but has been increasing significantly, whereas no significant change was seen in the US [annual percent change (95% C confidence interval): Japan, +2·4% (1·7, 3·1); US, +0·1% (−0·1, 0·2)]. Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL) showed the largest differences in incidence, with the most remarkable differences observed for chronic lymphocytic leukaemia, HL-nodular sclerosis, mycosis fungoides and cutaneous T-cell lymphoma. HL and NHL are increasing substantially in Japan but not in the US, suggesting that environmental exposures, such as Westernization of the life style may be causing this increase. Differences in the incidence and trends for specific subtypes also showed a marked contrast across subtypes, which, in turn, may provide significant new insights into disease aetiology in the future.

Keywords: incidence, trend, haematological malignancies, surveillance epidemiology and end results, Japan.

The incidence of a malignant disease in a certain population reflects the genetic and cumulative exposure to the environment of that population. Evaluation of the incidence and secular trends of a disease in various populations may, therefore, be helpful in providing insights into the aetiology and pathogenesis of that disease (Parkin, 2006; Morton *et al*, 2008). Trends in cancer incidence are reported by the International Agency for Research on Cancer (IARC) of the World Health Organization (WHO) (Ferlay *et al*, 2010). Although these data are useful in comparing the incidence of cancers between countries, statistics for haematological malignancies are estimated by general categories such as 'leukaemia,' which includes all leukaemic diseases (Ferlay *et al*, 2010). The haematological malignancies are a collection of heterogeneous disease entities with diverse epidemiological features, and their classification has evolved dramatically into highly-specific disease subtypes (Swerdlow *et al*, 2008). Although detailed epidemiological data for these disease subtypes are available from Western countries (Morton *et al*, 2006; Sant *et al*, 2010; Dores *et al*, 2012), and several

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studies have evaluated the incidence of haematological malignancies among Asians living in the US (Carreon *et al*, 2008; Yamamoto & Goodman, 2008; Clarke *et al*, 2011), no population-based data from Asia is currently available. This lack of data severely hampers efforts to evaluate the differences in incidence and trends for each disease subtype among different populations.

One major purpose of a specialized registry code, such as the International Classification of Diseases – Oncology (ICD-O), is to collect epidemiological data on well-defined disease entities. Comparison of the incidence of haematological malignancies across countries and over time has been complicated by changes in disease classification systems. However, the most recent ICD-O-3 classification, published in 2000, is closely linked to the WHO classification of haematological malignancies (Jaffe *et al*, 2001; Swerdlow *et al*, 2008), and this has enabled the comparison of various disease entities encoded by ICD-O-3 between different population-based registries. The present study aimed to evaluate the differences in incidence and time trends of various haematological malignancies in Japan and the United States (US).

Material and methods

Populations

We used population-based cancer registry data from Japan and the US. The Japanese data came from of 16 prefectures (Fig S1) included in the Monitoring of Cancer Incidence in Japan (MCIJ) project (Matsuda *et al*, 2013), and the US data came from the Surveillance Epidemiology and End Results (SEER) nine database including nine registries (Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco-Oakland, Seattle-Puget Sound, and Utah) (http://www.seer.cancer.gov/, http://www.seer.cancer.gov/popdata/). The period covered in this analysis is 1993–2008, and the population covered is 33·1% of Japan (includes both metropolitan and rural areas) and 9·4% of the US. Our analysis was begun in 1993 because this was the point at which the Japanese cancer registries began to achieve an acceptable degree of organization, and underwent significant expansion thereafter.

Disease coding

In the Japanese cancer registry system, incidence data are collected according to the ICD-O criteria. ICD-O-3 codes have been used since 2002 and all diseases coded by ICD-O-2 before 2002 have been re-coded in ICD-O-3. ICD-O-3 coding has been used since 2001 by SEER and all cases in ICD-O-2 have also been re-coded. As myeloproliferative neoplasms (MPN) and myelodysplastic syndromes (MDS) were not considered as malignant diseases in ICD-O-2, we excluded these diseases from this study. The ICD-O-3 code assignment for each disease is summarized in Table I.

Table I. Disease coding of haematological malignancies.

Disease	ICD-O-3 code
Leukaemia	9800–9948
Acute myeloid leukaemia (AML)	9840, 9861, 9866, 9867, 9871–9874 9895–9897, 9910, 9920
Acute lymphoblastic leukaemia (ALL)	9826, 9835–9837
Chronic myelogenous leukaemia (CML)	9863, 9875, 9876
Malignant lymphoma (ML)	9590–9729
Hodgkin lymphoma (HL)	9650–9667
Nodular sclerosis (HL-NS)	9663–9667
Mixed cellularity (HL-MC)	9652
Non-Hodgkin lymphoma (NHL)	9670–9729, 9591, 9823
Diffuse large B-cell lymphoma (DLBCL)	9680, 9684
Follicular lymphoma (FL)	9690–9698
Chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL)	9823, 9670
Mantle cell lymphoma (MCL)	9673
Burkitt lymphoma (BL)	9687
Marginal zone B-cell lymphoma (MZBCL)	9699
Mycosis fungoides (MF)	9700
Peripheral T-cell lymphoma-NOS (PTCL-NOS)	9702, 9675
Angioimmunoblastic T-cell lymphoma (AITL)	9705
Cutaneous T-cell lymphoma (CTCL)	9709
Anaplastic large T/null-cell lymphoma (ALCL)	9714
NK/T-cell lymphoma, nasal type (NKTCL)	9719
Adult T-cell leukaemia/lymphoma (ATLL)	9827
Non-Hodgkin lymphoma-NOS (NHL-NOS)	9591, 9675, 9684
Multiple myeloma (MM)	9731–9734

ICD-O, International Classification of Diseases – Oncology; NOS, not otherwise specified.

Statistical methods

Rates of sex-specific disease incidence and 95% confidence intervals (CI) were estimated and standardized by age-adjustment according to the world standard population (Bray *et al*, 2002). Incidence rates for Japan were additionally age-adjusted to the 1985 Japanese population, and those for the US were age-adjusted to the 2000 US population. Incidence rates were calculated for newly-diagnosed cases of each disease per 100 000 person-years. We calculated incidence rate ratios (IRR; US/Japan with 95% CI) for 2008 to compare incidence rates in the latest year between Japan and the US. We also calculated the annual percent change using Joinpoint regression analysis and estimated the annual percent change (APC), as well as the significance of the trend as described in detail elsewhere (Kim *et al*, 2000). Standard error of the age-standardized rates was estimated for each year. All computations were

performed with STATA version 11 (STATA Corporation, College Station, TX, USA), except for the Joinpoint regression analysis for which we used the Joinpoint Regression Program version 3.3 (US National Cancer Institute, Bethesda, MD, USA). For Joinpoint regression analysis, two-sided *P* values <0·05 were considered statistically significant.

Results

Major classification

The data for Japan included 125 148 cases and the data from SEER included 172 925 cases. Overall age-standardized incidence rates for all haematological malignancies per 100 000 in 2008 were 18·0 for males and 12·2 for females in Japan, and 34·9 for males and 23·6 for females in the US. The age-standardized incidence rates of males and females combined for acute myeloid leukaemia (AML), acute lymphoblastic leukaemia (ALL), chronic myeloid leukaemia (CML), Hodgkin lymphoma (HL), non-Hodgkin lymphoma (NHL), and multiple myeloma (MM) from 1993 to 2008 are shown in Fig 1. The crude numbers for incidence and the sex-specific, age-standardized incidence rates of these diseases, which are the basis for Fig 1, are shown in Tables S1–S4. The age-adjusted incidences of AML, ALL, CML, HL, NHL, and MM per 100 000 in 2008 were 2·5, 1·7, 0·9, 2·7, 15·7 and 3·8 in the US and 1·9, 1·1, 0·5, 0·5, 5·9 and 1·5 in Japan, respectively. The most frequent haematological malignancy in both countries is NHL, which consists of 39·6% of all haematological malignancies in Japan and 54·5% in the US. The lowest incidence was seen for CML, at only 3·4% of all haematological malignancies in Japan and 3·0% in the US. The IRR between Japan and the US for each disease is shown in Table II. In total, there are twice as many haematological malignancies per 100 000 in the US than Japan. The difference in the incidence is substantial for HL, NHL and MM (2·5- to 5-fold), whereas the leukaemias (AML, ALL and CML) have a more similar incidence. The trends in incidence during this period, as estimated by Joinpoint regression analysis, are also shown in Table II. The total number of

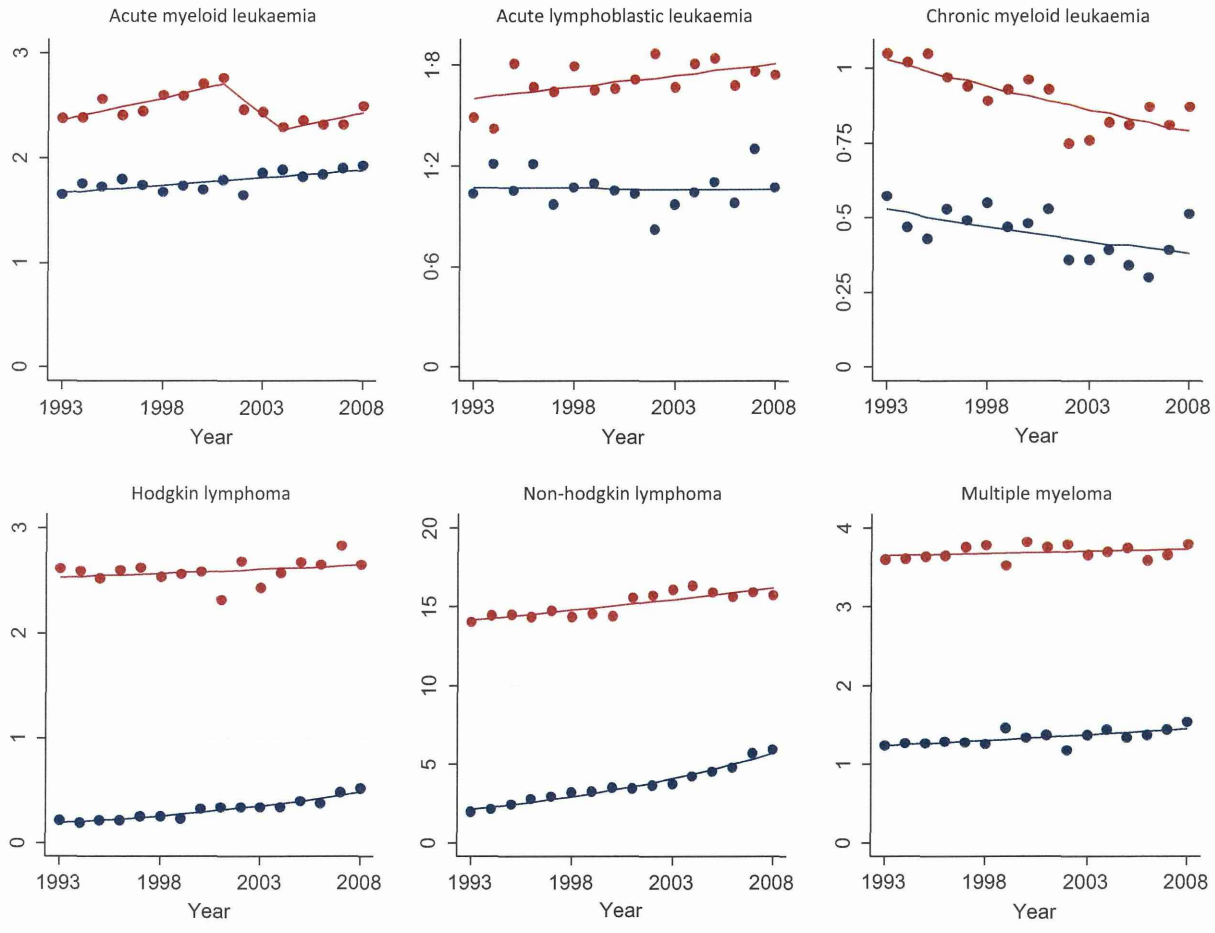

Fig 1. Incidence and trends for haematological malignancies from 1993 to 2008 in Japan and the US. Data for the US are shown in red and Japan in blue. Circles indicate the observed age-standardized incidence rates of males and females combined, and lines indicate the age-standardized incidence rates estimated by Joinpoint regression analysis. Axis indicates the annual incidence /100 000.

Table II. Trends in age-standardized incidence rates and incidence rate ratios for 2008, for haematological malignancies in the United States and Japan.

	Trend		Trend		
	Year	APC (95% CI)	Year	APC (95% CI)	IRR in 2008 (US/Japan)
Disease	United States		Japan		IRR (95% CI)
All haematological malignancies	1993–2008	0·1 (−0·1, 0·2)	1993–2008	2·4 (1·7, 3·1)*	1·94 (1·87–2·00)
Acute myeloid leukaemia (AML)	1993–2001	1·7 (0·6, 2·8)*	1993–2008	0·8 (0·4, 1·2)*	1·30 (1·28–1·32)
	2001–04	−5·7 (−14·2, 3·8)			
	2004–08	1·7 (−1·3, 4·7)			
Acute lymphoblastic leukaemia (ALL)	1993–2008	0·8 (0·1, 1·5)*	1993–2008	−0·0 (−1·3, 1·2)	1·63 (1·60–1·65)
Chronic myeloid leukaemia (CML)	1993–2008	−1·7 (−2·5, −1·0)*	1993–2008	−2·2 (−4·0, −0·4)*	1·71 (1·69–1·72)
All malignant lymphoma	1993–2008	0·2 (−0·0, 0·4)	1993–2008	3·2 (2·7, 3·8)*	2·25 (2·21–2·30)
Hodgkin lymphoma (HL)	1993–2008	0·3 (−0·2, 0·8)	1993–2008	6·5 (5·4, 7·7)*	5·10 (5·08–5·12)
Non-Hodgkin lymphoma (NHL)	1993–2008	0·9 (0·6, 1·2)*	1993–2008	6·8 (6·1, 7·6)*	2·65 (2·61–2·70)
Multiple myeloma (MM)	1993–2008	0·1 (−0·1, 0·4)	1993–2008	1·1 (0·4, 1·7)*	2·48 (2·46–2·50)

APC, annual percent change (age-standardized to the world population); CI, confidence interval; IRR, incidence rate ratio.
*APC is statistically significantly different from zero (two-sided $P < 0·05$, calculated using the *t*-test.)

haematological malignancies was found to have increased significantly in Japan, whereas no obvious change was seen in the US [APC (95% CI) in Japan, +2·4% (1·7 to 3·1); US, +0·1% (−0·1 to 0·2)]. By subtype, AML and the lymphoid malignancies (HL, NHL and MM) have increased significantly in Japan [APC (95% CI) for HL, +6·5% (5·4–7·7); NHL, +6·8% (6·1–7·6); MM: +1·1% (0·4–1·7)], but only a slight increase was seen for NHL in the US [APC (95% CI) for NHL, +0·9% (0·6–·2)]. In contrast, ALL has increased significantly in the US but shown no change in Japan. Interestingly, the incidence of CML has decreased during this period in both countries [APC (95% CI) in Japan, −2·2% (−4·0 to −0·4); US, −1·7% (−2·5 to −1·0)].

Malignant lymphoma

As HL and NHL consist of diverse entities, we evaluated these diseases further to determine which subtypes contributed to the large IRRs between the two countries. For HL, the dominant subtypes of nodular sclerosis (HL-NS) and mixed cellularity (HL-MC) were evaluated. For NHL, we evaluated the subtypes for which we had enough cases to calculate the trend. Table III shows the distribution of lymphoma subtypes diagnosed in the last 5 years (2003–2008, excluding cases coded as lymphoma, not otherwise specified). Due to the skewed distribution of human T-lymphotropic virus-1 carriers, the proportion of lymphoma subtypes in Japan differs significantly between areas endemic for Adult T-cell leukaemia/lymphoma (ATLL) (Kyushu) and non-endemic areas (Honshu) (Table III). The most common subtype in the US was diffuse large B-cell lymphoma (DLBCL, 27·9%) followed by chronic lymphocytic leukaemia/small lymphocytic leukaemia (CLL/SLL, 24·1%) and follicular lymphoma (FL, 15·1%). The most common subtype in Japan was DLBCL (45·3%) followed by FL (13·5%) and ATLL (8·3%). DLBCL was the most common subtype in both countries, but differed significantly by proportion. The largest difference in proportion between the US and Japan was seen in CLL/SLL (Japan, 3·2%; US, 24·1%). Consistent with previous results (Anderson *et al*, 1998), the proportion of T-cell lymphoma (TCL, excluding ATLL) was higher in Japan than the US (Japan, 9·8%; US, 6·6%), and this was

Table III. Proportion of malignant lymphoma diagnosed in 2003–08 in the US and Japan.

Subtype	US (%)	Japan (%)	Honshu (%)	Kyushu (%)
HL	11·6	5·9	7·4	3·4
DLBCL	27·9	45·3	46·2	27·3
FL	15·1	13·5	13·8	7·7
CLL/SLL	24·1	3·2	4·6	4·6
BL	1·5	1·3	1·9	0·7
MCL	3·0	2·0	1·9	1·3
MZBCL	6·8	7·2	6·1	5·4
PTCL-NOS	1·7	4·1	4·0	3·8
MF	2·2	1·0	1·2	0·9
CTCL	1·0	0·4	0·5	0·7
ALCL	1·0	1·1	1·0	1·2
AITL	0·5	2·0	1·7	1·7
NKTCL	0·2	1·2	1·0	0·5
ATLL	0·2	8·3	5·5	36·8
Others	3·6	3·8	3·8	3·9

HL, Hodgkin lymphoma; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; CLL/SLL, chronic lymphocytic leukaemia/small lymphocytic lymphoma; BL, Burkitt lymphoma; MCL, mantle cell lymphoma; MZBCL, marginal zone B-cell lymphoma; PTCL-NOS, peripheral T-cell lymphoma, not otherwise specified; MF, mycosis fungoides; CTCL, cutaneous T-cell lymphoma; ALCL, anaplastic large T/null-cell lymphoma; AITL, angioimmunoblastic T-cell lymphoma; NKTCL, NK/T-cell lymphoma; ATLL, adult T-cell leukaemia/lymphoma.

even more profound when ATLL is included in TCL (Japan, 18·1%; US, 6·8%).

The age-standardized incidence rates of the various subtypes of HL and NHL are shown in Fig 2. The crude numbers for incidence and sex-specific, age-standardized incidence rates are shown in Tables S5–S8. The age-adjusted incidences of HL-NS, HL-MC, DLBCL, FL, CLL/SLL, mantle cell lymphoma (MCL), Burkitt lymphoma (BL), marginal zone B-cell lymphoma (MZBCL), mycosis fungoides (MF), peripheral T-cell lymphoma not otherwise specified (PTCL-NOS), angioimmunoblastic T-cell lymphoma (AITL), cutaneous T-cell lymphoma (CTCL), anaplastic large T/null-cell lymphoma (ALCL), Natural killer/T-cell lymphoma, nasal type (NKTCL) and ATLL per 100 000 in 2008 were 1·5, 0·2, 4·5, 2·6, 3·5, 0·5, 0·4, 1·2, 0·4, 0·3, 0·1, 0·2, 0·2, 0·04 and 0·02 in the US and 0·2, 0·1, 2·5, 1·1, 0·2, 0·1, 0·1, 0·5, 0·1, 0·3, 0·1, 0·02, 0·1, 0·1 and 0·3 in Japan, respectively. The IRRs between Japan and the US for each of the various subtypes are summarized in Table IV. Most of the subtypes had a higher incidence in the US than in Japan, with the highest IRR seen for CLL/SLL (IRR: 21·0), followed by MF (IRR: 8·1), HL-NS (IRR: 6·8) and CTCL (IRR: 6·4). Some subtypes of TCL, such as ATLL and NKTCL, had a higher incidence in Japan, but the most common subtypes of TCL, PTCL-NOS and AITL, showed similar incidence rates in the two countries. The trends in incidence during this period are summarized in Table IV. With regard to Japan, all subtypes except CLL/SLL, CTCL and ATLL showed a substantial increase during this period. In the US, several NHL subtypes, such as FL, BL, MCL, MZBCL, PTCL-NOS, AITL and NKTCL, also showed a significant increase, whereas HL-MC showed a significant decrease (Fig 2, Table IV).

Discussion

Although some studies have evaluated the incidence of haematological malignancies in Asians living in the US (Carreon *et al*, 2008; Yamamoto & Goodman, 2008; Clarke *et al*, 2011), they were conducted with relatively small numbers of cases and the incidence of disease in Asians may reflect their lifestyle in the US. In this study, we evaluated the incidence of haematological malignancies in Japanese using population-based data, and show the differences in incidence of haematological malignancies and trends between Japan and the US. Consistent with previous reports, the incidence varies greatly between diseases, with CML showing the lowest incidence and NHL showing the highest incidence in both Japan and the US (Morton *et al*, 2006, 2007; Sant *et al*, 2010). As shown in Fig 1, the incidence of all major diseases was higher in the US. Furthermore, the incidence of lymphoid malignancies, such as HL, NHL and MM, showed impressive differences between the US and Japan, whereas the differences in AML, ALL, and CML were smaller.

This significant difference in the incidences of malignant lymphoma (ML) is partially explained by the difference in the prevalence of the human immunodeficiency virus (HIV) between countries. Although the prevalence of HIV in the US is low among the general population (0·4% in 2008) (Centers for Disease Control and Provention (CDC), 2011), HIV significantly increases the risk of NHL and HL (NHL: 77-fold, HL: 11-fold) (Grulich *et al*, 2007). The prevalence rate of HIV in Japan is extremely low, i.e., around 0·01–0·02%, indicating that there is a large difference in the incidence of HIV-related ML between countries.

Among the subtypes of ML, CLL/SLL, MF, HL-NS, CTCL and ATLL showed the largest differences in incidence, which is consistent with previous studies except for the new findings for CTCL (Carreon *et al*, 2008; Clarke *et al*, 2011). In these previous studies, Asians living in the US showed a significantly lower incidence of CLL/SLL and HL-NS than US whites, which points to the importance of genetic background in defining the risk of disease. Clarke *et al* (2011) also showed significantly higher incidence rates of CLL/SLL and HL-NS in US-born Asians compared to foreign-born Asians, which suggests that environmental risk factors also exist for Asians who emigrate to the US. However, the magnitude of these two factors (genetic and environmental) and their contribution to the differences in incidence between populations may vary across the subtypes (Morton *et al*, 2008). For example, the effect of HIV is more profound in the incidence of DLBCL, BL and central nervous system lymphoma (Engels *et al*, 2006). Although we cannot accurately compare the incidence rates in our study to those of previous studies (Morton *et al*, 2006; Carreon *et al*, 2008) because previous studies were not standardized to the world standard population, we can speculate that environmental factors have less effect on the risk of HL-NS than CLL/SLL because the incidence of HL-NS in Asians in the US is more similar to the incidence in Japanese in our study. MF and CTCL are more prevalent among African Americans (Morton *et al*, 2006; Imam *et al*, 2013), suggesting genetic susceptibility in their population. Our findings and those of previous studies strongly suggest that there is aetiological heterogeneity among these diseases and that not only environmental factors, but also genetic background, are important in defining the risk of disease. Considering the differences in incidence in different places and among different populations would be important when investigating the aetiology of these diseases and subtypes.

Not surprisingly, for the major subtypes of nodal T-cell lymphoma, such as PTCL-NOS and AITL, the incidence was similar in Japan and the US. As Japan has significantly fewer cases of B-cell lymphoma and more cases of ATLL, the proportion of TCL is much higher in Japan than in the US (Fig 2; Japan, 18·2%; US, 6·4%). Historically, such information gave the impression that the incidence of TCL is also higher in Asia, but the more accurate incidence calculated using the population-based registry data suggests that this is incorrect, as previously described (Morton *et al*, 2006). NKTCL and ATLL are the only two diseases in Japan with a

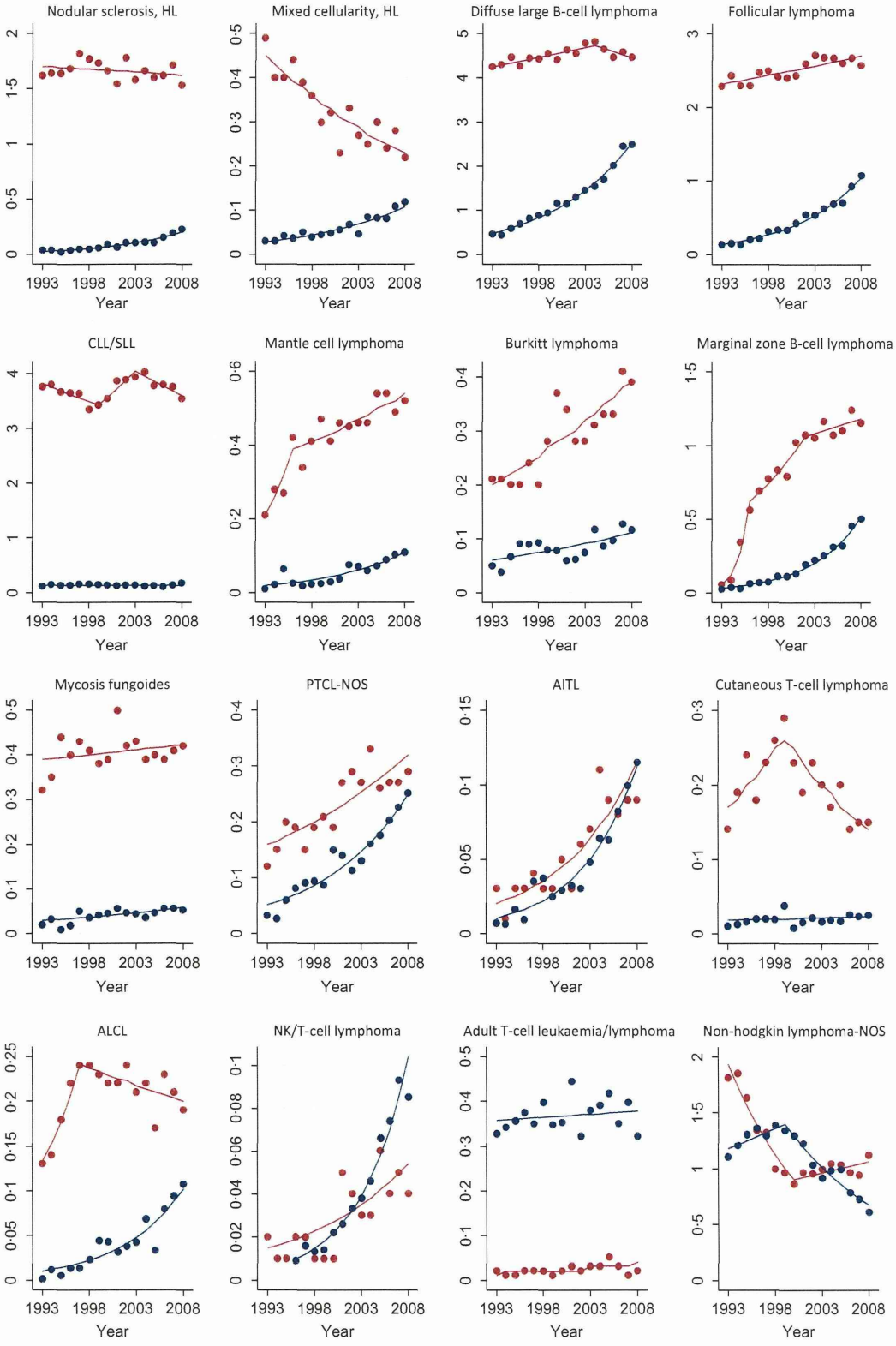

Fig 2. Incidence and trends for malignant lymphoma from 1993 to 2008 in Japan and the US. Data for the US are shown in red and Japan in blue. Circles indicate the observed age-standardized incidence rates of males and females combined, and lines indicate the age-standardized incidence rates estimated by Joinpoint regression analysis. Axis indicates the annual incidence /100 000.

Table IV. Trends in age-standardized incidence rates and incidence rate ratio for 2008, for lymphoid malignancies in the United States and Japan.

	Trend		Trezbnd		
	Year	APC (95% CI)	Year	APC (95% CI)	IRR in 2008 (US/Japan)
Disease	United States		Japan		IRR (95% CI)
Hodgkin lymphoma; nodular sclerosis (NS)	1993–2008	−0·3 (−0·9, 0·3)	1993–2008	14·2 (11·8, 16·6)*	6·77 (6·75–6·79)
Hodgkin lymphoma; mixed cellularity (MC)	1993–2008	−4·4 (−5·7, −3·1)*	1993–2008	9·3 (7·0, 11·7)*	1·85 (1·84–1·86)
Diffuse large B-cell lymphoma (DLBCL)	1993–2004	1·0 (0·6, 1·4)*	1993–2008	11·8 (10·9, 12·7)*	1·79 (1·76–1·81)
	2004–08	−1·5 (−3·3, 0·3)			
Follicular lymphoma (FL)	1996–2008	1·0 (0·6, 1·4)*	1993–2008	14·4 (13·2, 15·6)*	2·40 (2·39–2·42)
Chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL)	1993–99	−1·8 (−3·2, −0·3)*	1993–2008	0·2 (−1·5, 2·0)	20·95 (20·93–20·96)
	1999–2003	4·2 (−0·0, 8·6)			
	2003–08	−2·3 (−3·9, −0·6)*			
Mantle cell lymphoma (MCL)	1993–96	22·2 (2·1, 46·3)*	1993–2008	12·3 (8·0, 16·8)*	4·81 (4·81–4·82)
	1996–2008	2·7 (1·3, 4·2)*			
Burkitt lymphoma (BL)	1993–2008	4·5 (2·8, 6·2)*	1993–2008	10·1 (4·8, 15·6)*	3·36 (3·35–3·37)
Marginal zone B-cell lymphoma (MZBCL)	1993–96	128·4 (54·3, 237·9)*	1993–2008	20·8 (18·9, 22·8)*	2·56 (2·55–2·57)
	1996–2002	9·4 (3·0, 16·3)*			
	2002–08	1·8 (−1·8, 5·7)			
Mycosis fungoides (MF)	1993–2008	0·6 (−0·6, 1·7)	1993–2008	4·9 (2·0, 7·9)*	8·08 (8·07–8·08)
Peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS)	1993–2008	4·8 (2·9, 6·7)*	1993–2008	11·2 (8·7, 13·8)*	1·15 (1·14–1·16)
Angioimmunoblastic T-cell lymphoma (AITL)	1993–2008	12·6 (7·9, 17·5)*	1993–2008	17·6 (14·3, 21·0)*	0·80 (0·79–0·80)
Cutaneous T-cell lymphoma (CTCL)	1993–99	7·3 (−0·1, 15·3)	1993–2008	1·6 (−2·3, 5·7)	6·42 (6·41–6·42)
	1999–2008	−6·6 (−10·0, −3·1)*			
Anaplastic large T/null-cell lymphoma (ALCL)	1993–97	16·6 (5·9, 28·4)*	1993–2008	16·5 (11·7, 21·5)*	1·78 (1·77–1·78)
	1997–2008	−1·7 (−3·4, −0·0) *			
NK/T-cell lymphoma, nasal type (NKTCL)	1993–2008	9·1 (4·7, 13·6)*	1996–2008	21·4 (17·9, 25·1)*	0·52 (0·51–0·52)
Adult T-cell leukaemia/lymphoma (ATLL)	1993–2008	6·2 (1·5, 11·1)*	1993–2008	0·4 (−0·8, 1·6)	0·07 (0·07–0·08)

APC, annual percent change (age-standardized to the world population); CI, confidence interval; IRR, incidence rate ratio.
*APC is statistically significantly different from zero (two-sided $P < 0·05$, calculated using the t-test.)

higher incidence than in the US. Among a total of 167 patients diagnosed with NKTCL in this period in the US, 112 patients (67%) were white, 40 (24%) were Asian and 15 (9%) were other races. Given that Asians account for only 5% of the US population, it seems that Asians are more prone to develop this disease. ATLL and NKTCL are both associated with viral infections and numerous studies have reported associations between polymorphisms in immune-related genes and risk of NHL (Purdue *et al*, 2009; Skibola *et al*, 2010; Wang *et al*, 2010; Hosgood *et al*, 2011; Lan *et al*, 2011). There seems to be a difference in the immune response to Epstein-Barr virus among Japanese (Kimura, 2006), and it would be interesting to evaluate polymorphisms in immune-related genes to better understand this phenomenon. Unfortunately, however, there is little data evaluating these associations in Asians and this should be investigated in the future.

As well as the differences in incidence, trends in incidence also differ significantly between Japan and the US. Among all haematological malignancies, the differences in the trend for HL and NHL were more striking than for other diseases. ML showed a substantial increase in Japan but there was little change in incidence in the US, as described in a recent study (Shiels *et al*, 2013). The trend of NHL in the US has been affected by HIV, with increases through the early-2000s and subsequent decline after the introduction of highly-active anti-retroviral therapy (HAART) (Shiels *et al*, 2013). Shiels *et al* (2013) showed that the incidence of NHL has plateaued over the last several years in the HIV-uninfected population. Although we found a gradual increase in the incidence of NHL in the US, this difference in trend could be explained by the difference in the study population and period, and a similar trend was also seen in DLBCL in our study. The increasing trend in ML in Japan may be explained by changes in lifestyle and dietary habits to some extent. According to previous studies, vegetable, fish and alcohol intake have been shown to reduce the risk of NHL, whereas meat and fat intake and obesity are thought to increase the risk (Morton *et al*, 2005; Lim *et al*, 2007; Skibola, 2007; Kanda *et al*, 2010a,b). According to the Ministry of Health, Labour and Welfare and Ministry of Agriculture, Forestry and Fisheries in Japan, vegetable, fish and alcohol intake are constantly decreasing, whereas meat and fat intake and the proportion of people with obesity are constantly increasing (http://www.mhlw.go.jp/, http://www.maff.go.jp/). Although this Westernization in lifestyle has probably increased the incidence of NHL in Japan, there are almost certainly other risk factors that have not been identified. All TCLs, except ALCL, MF and CTCL in the US, and CTCL and ATLL in Japan, are significantly increasing in the two countries. Little is known about the risk factors for TCL and this should be investigated. Comparing the differences in trends and the exposures across countries would be useful to identify new risk factors. When we consider conducting such studies, standardization of exposure information is essential. International epidemiological consortiums, such as the International Lymphoma Epidemiology Consortium (InterLymph) can play a substantial role in these efforts. The availability of comprehensive data through such consortiums to evaluate genetic information, environmental exposures and lifestyles will facilitate new studies on the aetiology of these diseases.

Interestingly, decreasing trends were seen for CML in both countries, and for HL-MC in the US. Previous studies have suggested an inverse association between socioeconomic status and the risk of HL-MC (McNally *et al*, 2003), and a positive association with an immunosuppressed status, such as HIV infection, and HL-MC (Glaser *et al*, 2003; Clifford *et al*, 2005). Although the effect of HAART on the incidence of HL remains controversial (Clifford *et al*, 2005), the decrease in the incidence of HL-MC may be related to improvements in public health and socioeconomic status, as well as treatment for HIV, in the US. With regard to CML, aside from the possibility that this decreasing trend is real, several other possibilities warrant discussion (Chihara *et al*, 2012). Most important might be a change in disease definition and classification. A more stringent requirement for the *BCR/ABL1* translocation was introduced in the WHO classification during the study period (Jaffe *et al*, 2001). Also, there was no code for MPN in ICD-O-2, and MPNs other than CML may have been misdiagnosed as CML in the pre-ICD-O-3 era. The trend in the incidence of other MPNs cannot be estimated properly, which hampers the confirmation of this hypothesis.

Several limitations should be considered. One is the problem of diagnostic accuracy and introduction of new diagnostic criteria. Figure 2 shows a marked increase in the incidence of MCL, MZBCL and ALCL in the early 1990s. These changes are probably due to improvements in the diagnosis of these lymphomas, as described in a recent study (Shiels *et al*, 2013). When a significant development changes a disease definition, the incidence will change significantly in registry data, as shown in Table III. Another problem is the 'not otherwise specified' (NOS) cases of ML in registry data. The registry data of Japan includes more NHL-NOS and ML-NOS cases than the US data (Japan, 22·1%; US, 9·6%). Given that these cases would allocate to more specific subtypes, the incidence of specific subtypes in Japan tends to be underestimated. Clarke *et al* (2006) evaluated the diagnosis of unclassifiable ML in the SEER database and compared the results with a review of pathology reports. They were able to provide a more accurate diagnosis to the unclassified cases after pathology review and found that the unclassifiable cases tended to be minor subtypes, such as BL, TCL and NKTCL, and were less likely to be major subtypes, such as DLBCL or FL. On this basis, the incidence of minor subtypes is probably underestimated in Japan as the proportion of NOS cases in Japan is over two-fold higher than in the US. The number of NOS cases was higher in the past in both countries (Fig 2). Because of this, the marked increase in trends of specific lymphoma subtypes in Japan and the US (Table IV)

should be interpreted with caution, as this might be partially due to the impact of improvements in diagnosis and coding of registry data. The striking increase in TCLs, such as PTCL-NOS, AITL and NKTCL, in Japan and the US could be a real increase, but should be interpreted with caution given the possibility of a change in diagnostic accuracy of TCL. Centralized review of past cases by haematopathologists would improve the quality of this data, but is unrealistic in population-based registry data. Nevertheless, our results are worthwhile in evaluating the differences in incidence and proportion of diseases between Asia and the US, and in providing clues toward an understanding of aetiology.

In conclusion, this is the first large study to evaluate the incidence of haematological malignancies in Asians using population-based data, and we identified some marked differences in disease incidence and trends between Japan and the US. The incidence of haematological malignancies is lower in Japan than the US, but is still increasing significantly, especially for ML. Aetiological heterogeneity is suggested for these diseases, and epidemiological study by disease subtypes, considering differences in genetics and exposures, will be helpful in understanding tumourigenesis. Improvement in the quality of cancer registries, including information on exposure and genetics across countries, will enable the evaluation of data worldwide and, in turn, provide significant new insights into disease trends and aetiologies in the future.

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Authorship

T.M., A.S., and T.S. prepared MCIJ data for analysis. M.K., and T.S. played an administrative role in conduct of the study. D.D.W., S.N. and A.K. gave advice on pathological and clinical aspects. D.C., H.I. and K.M. analyzed data. D.C., D.D.W, L.M.M and K.M. wrote draft of the paper and all authors reviewed and finalized the paper.

Disclosures of conflict of interest

The authors declare no conflict of interest.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Incidence of hematologic malignancies in the United States: Male.

Table S2. Incidence of hematologic malignancies in the United States: Female.

Table S3. Incidence of hematologic malignancies in Japan: Male.

Table S4. Incidence of hematologic malignancies in Japan: Female.

Table S5. Incidence of lymphoid malignancies in the United States: Male.

Table S6. Incidence of lymphoid malignancies in the United States: Female.

Table S7. Incidence of lymphoid malignancies in Japan: Male.

Table S8. Incidence of lymphoid malignancies in Japan: Female.

Fig S1. The prefectures included in this study in Japan.

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ORIGINAL ARTICLE

Association between decreasing trend in the mortality of adult T-cell leukemia/lymphoma and allogeneic hematopoietic stem cell transplants in Japan: analysis of Japanese vital statistics and Japan Society for Hematopoietic Cell Transplantation (JSHCT)

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Adult T-cell leukemia/lymphoma (ATLL) is a peripheral T-cell neoplasm with a very poor outcome. However, several studies have shown a progress in the treatment. To evaluate the effect of the progress in the treatment of ATLL in a whole patient population, we used vital statistics data and estimated age-adjusted mortality and trends in the mortality from 1995 to 2009. Since allogeneic hematopoietic stem-cell transplantation (allo-HSCT) has been introduced as a modality with curative potential during study period, we also evaluated the association of the annual number of allo-HSCT and the trend of the mortality of ATLL. Endemic (Kyushu) and non-endemic areas (others) were evaluated separately. Significance in the trend of mortality was evaluated by joinpoint regression analysis. During the study period, a total of 14 932 patients died of ATLL in Japan, and mortality decreased significantly in both areas (annual percent change (95% confidence interval (CI)): Kyushu, −3.1% (−4.3, −1.9); others, −3.4% (−5.3, −1.5)). This decreasing trend in mortality seems to be associated with an increase in the number of allo-HSCTs (Kyushu, R-squared = 0.70, $P = 0.003$; and others, R-squared = 0.55, $P = 0.058$). This study reveals that the mortality of ATLL is now significantly decreasing in Japan and this decreasing trend might be associated with allo-HSCT.

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Keywords: adult T-cell leukemia/lymphoma; ATLL; mortality; allogeneic transplant; trend

INTRODUCTION

Adult T-cell leukemia/lymphoma (ATLL) is a peripheral T-cell neoplasm that is associated with infection by the human T-cell leukemia virus type I.[1,2] Infection with human T-cell leukemia virus type I and cases of ATLL are endemic in several regions of the world, with the south-west area of Japan (Kyushu) being a well-known example. Although the total number of carriers in Japan has decreased by 10% over the past two decades,[3] the incidence of this fatal disease has nevertheless significantly increased due to the aging of carriers.[4]

Recent advances in the treatment of ATLL include several combination chemotherapies and allogeneic hematopoietic stem-cell transplantation (allo-HSCT).[5–13] Allo-HSCT was deemed to show a successful outcome, in that around 30% of patients achieved long-term survival.[6] Dose-intensified chemotherapy also showed a survival benefit, however, the usual outcome in patients with acute and lymphoma-type ATLL, for which allo-HSCT is not indicated, is markedly poor, with essentially no chance of prolonged remission.[8] Another advance in the treatment of ATLL is an improvement in the infection control, which frequently strikes patients during the treatment. Despite these advances in treatment, however, the survival benefit in whole patient population had not been presented.

Here, to evaluate the progress in the treatment of ATLL, we estimated the age-standardized mortality and trends in the age-standardized mortality of ATLL. Since allo-HSCT has been introduced as a modality with curative potential during study period, we also evaluated the correlation of the annual number of allo-HSCT and the trend of the mortality of ATLL.

PATIENTS AND METHODS

We used the data of vital statics of Japan for 47 prefectures during 1995–2009,[14] and estimated the ATLL-specific age-standardized mortality rate adjusted by world standard population. Since the incidence of ATLL differs significantly between endemic (Kyushu) and non-endemic areas in Japan (others), age-standardized mortality rates for these two areas were estimated separately. Data for the number of allo-HSCTs administered in Japan for ATLL were obtained from the Japan Society for Hematopoietic Cell Transplantation.

To assess the secular trend in the age-standardized mortality rate, we used joinpoint regression analysis, as described in detail elsewhere.[15] The association between mortality rates of ATLL and annual numbers of allo-HSCT was evaluated by a regression framework.[16] In this analysis, we explored zero-, one- or two-year time lags from the numbers of allo-HSCT to mortality rate to evaluate whether the number of transplants was associated with a later decrease in mortality. We examined R-squared to evaluate the strength of the association and interpreted the result such that for every increase in the annual number of allo-HSCTs, we expect a certain degree (coefficient) decrease in the mortality of ATLL.

All computations were performed with STATA version 11 (StataCorp, College Station, TX, USA), except for the joinpoint regression analysis,

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for which we used the Joinpoint Regression Program version 3.3 (US National Cancer Institute, Bethesda, MD, USA).

RESULTS

During the study period, a total of 14 932 patients died of ATLL in Japan. Estimated age-standardized mortalities of ATLL from 1995 to 2009 in Kyushu and others are shown as circles in Figure 1 and the exact rates with 95% confidence intervals (95% CIs) in both areas, which are the basis of Figure 1, are summarized in Supplementary Table 1. The solid line shows the age-standardized modeled mortality estimated by joinpoint regression analysis and the dotted line shows the annual numbers of allo-HSCT administered in each area. As depicted in Figure 1, the trend in age-standardized mortality changed significantly in 2000 in Kyushu and in 2003 in others (Table 1). Mortality decreased significantly after that period in both areas (annual percent change (95% CI); Kyushu: −3.1% (−4.3, −1.9), others: −3.4% (−5.3, −1.5)).

A total of 929 allo-HSCTs were performed in Japan during the study period. Median age at the allo-HSCT was 53 years old (range: 18–79). Table 2 summarizes the association between mortality and annual numbers of allo-HSCT. The increasing trend in allo-HSCT was negatively associated with the mortality of ATLL in Japan (Table 2). The association was strongest when no time lag was set in years from the number of transplants to mortality, indicating that the number of allo-HSCTs was directly associated with mortality in that year.

We also evaluated the association of the numbers of allo-HSCT with the decreasing trend of the mortality according to the age group. The increase in the numbers of allo-HSCT was associated with the decrease in the mortality in both patients aged younger than 55 years old and aged 55 years or older (<55 years old, R-squared = 0.62, $P = 0.007$; ⩾55 years old, R-squared = 0.65, $P = 0.028$).

DISCUSSION

We previously reported that the incidence of ATLL is significantly increasing in Honshu (representative non-endemic area in Japan) but has shown no change in Kyushu.[4] Although this increasing trend in Honshu might be due to an improvement in diagnostic accuracy, these findings show that the incidence of ATLL is at least not decreasing in the endemic areas of Japan where the disease is well known and would not be missed in the registry data. The significant decrease in the trend in mortality observed in the present study is therefore likely to have resulted from an improvement in treatment. The present findings show that the number of allo-HSCTs administered in Japan might be associated with this decreasing trend in mortality.

Utsunomiya *et al.*[13] reported the first case series of patients with ATLL who received allo-HSCT in 2001. In their study, 5 of 10 patients showed long-term survival, which appeared to plateau after a median leukemia-free survival of 17.5 months. This aggressive but curative approach has now become the standard treatment for eligible patients, and the number of allo-HSCTs administered in Japan has increased rapidly, with >100 patients now receiving allo-HSCT annually. A nationwide retrospective analysis of patients who received allo-HSCT for ATLL in Japan reported a 3-year overall survival of 33%,[6] which is the best treatment outcome in the eligible patients to this day. The rapid increase in the numbers of allo-HSCT reflects the introduction of the allo-HSCT to elderly patients with reduced-intensity conditioning regimen which has also been shown to be effective in ATLL.[10,17] In our analysis, allo-HSCT in patients aged 55 years or older showed an association with the decrease in the mortality suggesting that increasing the candidate of allo-HSCT in this population may improve the outcome of ATLL.

Recently, the new drug mogamulizumab, an anti-CCR4 antibody, has shown a clear benefit in the treatment for ATLL.[18] Overall response rate to mogamulizumab on single agent use in a phase II study in relapsed patients was 50% (95% CI: 30–70%),

Table 1. Trends in age-standardized mortality of adult T-cell leukemia/lymphoma

Trend 1		*Trend 2*	
Year	*APC (95% CI)*	*Year*	*APC (95% CI)*
		Mortality	
Kyushu			
1995–2000	1.3 (−1.7, 4.3)	2000–2009	−3.1 (−4.3, −1.9)[a]
Others			
1995–2003	1.2 (−0.1, 2.6)	2003–2009	−3.4 (−5.3, −1.5)[a]

Abbreviations: APC, annual percent change; CI, confidence interval. [a]APC is statistically significantly different from zero (two-sided $P<0.05$, calculated using the *t*-test).

Table 2. Relationship between the number of allogeneic transplantations and ATLL mortality

Area	*Changing trend in mortality (year)*	*Coef* $\times 10^{-3}$ *(95% CI)*	*R-squared*	*P-value*
Kyushu	2000	−9.34 (−14.3, −4.36)	0.70	0.003
Others	2003	−2.49 (−5.10, 0.12)	0.55	0.058

Abbreviations: ATLL, adult T-cell leukemia/lymphoma; Coef, coefficient; CI, confidence interval.

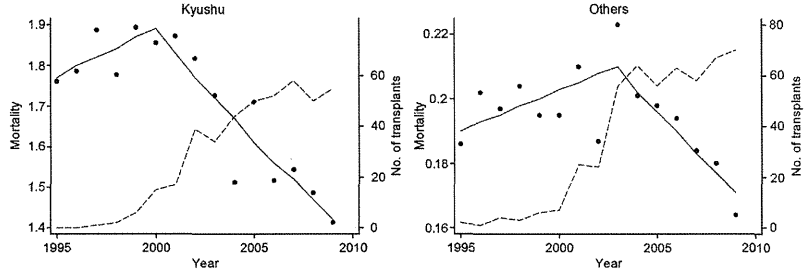

Figure 1. The mortality of adult T-cell leukemia/lymphoma and the number of allogeneic transplants administered in Kyushu and others. Circles indicate the observed age-standardized mortality rates and the solid line indicates the age-standardized mortality rates estimated by joinpoint regression analysis. The dashed line indicates the number of allogeneic transplants.

which suggests the promising possibility of combined use with existing regimens as a new chemotherapy protocol. Patients who received allo-HSCT while in complete remission had a higher probability of survival than those who received when not in complete remission.[6] Improvement in induction chemotherapy will increase the number of patients in remission, and thus the number of candidates for allo-HSCT beneficially impacting outcomes.

The association between decreased mortality and number of allo-HSCTs seems to be stronger in Kyushu than in other areas. This difference might be due to differences in indications for allo-HSCT, based on differences in the understanding of ATLL. Hematologists in Kyushu are well experienced with ATLL, and it is possible that their indications for allo-HSCT are well organized and they proceed to allo-HSCT with good patient's condition during the treatment. In any case, this issue is difficult to analyze using registry data alone.

Although the potential for prolonged remission without allo-HSCT appears to be limited, other factors might have contributed to this decrease in mortality. The Japanese Clinical Oncology Group has conducted several clinical trials to improve survival with chemotherapy. Results have been shown to be effective on long-term follow-up and might have improved the survival of patients who were unable to proceed to transplantation. A dose-intensified multi-agent chemotherapy protocol named modified LSG15 improved 3-year overall survival of aggressive ATLL over bi-weekly CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) to 24% from 13%.[8] The more general improvement seen in the management of ATLL, such as with regard to infection control, might also have prolonged survival. Considering the dismal outcome by general treatments that have not progressed significantly during the study period, however, we speculate that the decreasing trends in the mortality would have been mostly achieved by allo-HSCT. Nevertheless, this study is conducted in two independent data sets that lack the information about the treatment of individual patient. We cannot evaluate the association between the decreasing in the mortality and other unmeasured variables which potentially could limit the clinical relevance of our results. We need to emphasize that it is difficult completely to rule out the possibility that our finding is not causal association. Further studies to assess the association of other factors with the decreased mortality are required.

In conclusion, this study showed that the mortality of ATLL in Japan is significantly decreasing, and this decreasing trend might be associated with the increasing number of allo-HSCTs. Nevertheless, allo-HSCT is associated with a significant toxicity, and further studies are needed to identify patients at high risk for treatment-related morbidity or mortality to improve the feasibility of allo-HSCT. Although ATLL remains a highly aggressive and still fatal disease, new drugs such as mogamulizumab and approaches such as reduced-intensity conditioning for elderly patients are promising treatment. A combined modality of improved induction chemotherapy followed by allo-HSCT may change the outcome of ATLL, and future studies may better focus on improving induction chemotherapy to allow an eventual increase in the number of candidates for allo-HSCT.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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大阪府がん対策推進計画の立案・評価における各種がん統計資料の活用

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要旨：

大阪府におけるがん対策に関して、がん対策の基礎となる喫煙対策、肝炎対策、がん検診、がん医療の４分野について、ストラクチャ、プロセス、アウトカム指標の抽出を行い、既存統計資料により提示可能な評価指標を整理し示した。また、現状では入手できないいくつかの重要な指標について整理し、今後のがん対策の推進に必要な資料として提示した。いくつかの指標についてはがん対策の評価を行う上での可視化例を示すとともに、実際に第二期大阪府がん対策推進計画において、地域がん登録資料をはじめとしたがん統計資料が活用された事例を紹介する。

１．はじめに

平成24年度、大阪府におけるがん対策推進計画の中間評価および第二期計画の策定に際し、大阪府立成人病センターがん予防情報センターは大阪府健康医療部保健医療室健康づくり課がん対策グループと週一回のミーティングを行い、がん対策の進捗評価に係る各種資料を提供し、計画の考え方や提示する資料の解釈、計画本文の構成までを、緊密な協力の下、実施した。

本報告は、大阪府におけるがん対策に関して、がん対策の基礎となる喫煙対策、肝炎対策、がん検診、がん医療の４分野について、ストラクチャ、プロセス、アウトカム指標の抽出を行い、既存統計資料により提示可能な評価指標を整理し、いくつかの指標についてはがん対策の評価を行う上での可視化例を示すとともに、実際に第二期大阪府がん対策推進計画において、地域がん登録資料をはじめとしたがん統計資料が活用された事例を紹介するものである。

２．がん対策進捗評価指標のマトリックス

入手可能な既存統計資料である人口動態統計、国民生活基礎調査、大阪府における成人病（精密死因）統計、大阪府がん登録資料、健康おおさか21中間評価実態調査、拠点病院腫瘍データ収集調査、等をもとに、「タバコ対策」、「肝炎対策」、「がん検診」、「がん医療」のがん対策の

施策４分野別に「ストラクチャ指標」、「プロセス指標」、「アウトカム指標」となり得る項目を洗い出し、整理した（表１）。

表１において、斜体文字になっている項目は平成24年度時点では入手できなかった項目である。大阪府においては地域がん登録資料が整備されており、がん対策評価時点の適時性の問題はあるものの、アウトカム指標については提示できない項目はなかった。しかしながら、がん対策の進捗を評価する上で重要ないくつかの指標については、入手できない項目があった。たとえば、飲食店の禁煙化の割合（TC-ST2）、市町村がん検診における受診勧奨（call-recall）の実施の有無（SC-ST2）や検診費用（SC-ST3）、肝炎に関するあらゆるプロセス指標（HP-PR1-4）などである。

表1. 既存統計資料を用いたがん対策の進捗評価のための評価指標

	Tobacco Control (TC) タバコ対策	Hepatitis Virus Control (HP) 肝炎対策	Cancer Screening (SC) がん検診	Cancer Treatment (TR) がん医療
Structure (ST) ストラクチャ指標	TC-ST 1. 公的施設（官公庁、病院、学校）の敷地内禁煙実施数（割合） *2. 飲食店に対する禁煙・分煙化の指導について、指導を実施した飲食店数（割合）* 3. 禁煙治療実施施設数 資料：大阪府および府内市町村のたばこ規制・対策実態調査報告書	HP-ST 1. 肝炎検査実施状況 2. 肝炎治療施設数 資料：肝炎対策に関するアンケート結果	SC-ST 1. 市町村別の検診体制 *2. 受診勧奨の有無* *3. 検診費用（年度別に）* 資料： 大阪府におけるがん検診 大阪府実施のアンケート調査 市町村対象チェックリスト結果 （大阪府より提供）	TR-ST 1. 施設別放射線治療医・がん薬物療法専門医の数 2. 病床数 3. 放射線治療設備 4. 外来化学療法室の有無 5. キャンサーボードの有無 資料： 厚生労働省がん診療連携拠点病院現況報告 大阪府がん診療連携拠点病院現況報告
Process (PR) プロセス指標	TC-PR 1. 喫煙者のステージ割合 2. 喫煙率*（市町村別）* 資料：おおさかQネット	HP-PR *1. 肝炎検査累積受診率* *2. 肝炎ウィルス陽性率* *3. 肝炎ウィルス陽性者の精検受診率* *4. 肝炎治療完遂率*	SC-PR 1. 受診率 2. 要精検率 3. 精検受診率 4. がん発見率 5. 初回受診割合 資料：大阪府におけるがん検診	TR-PR 1. 標準治療実施割合（部位別進行度別化学療法、放射線療法実施割合） 2. 部位別進行度分布 資料： 大阪府がん登録資料
Outcome (OC) アウトカム指標	TC-OC 1. 肺がん罹患率・死亡率 2. 喫煙関連がん罹患率・死亡率 3. がん以外の喫煙関連疾患の死亡率	HP-OC 1. 肝がん罹患率 2. 肝がん死亡率	SC-OC 検診実施の5部位のがん 1. 限局患者割合 2. 生存率 3. 罹患率 4. 死亡率	TR-OC 1. 各部位の進行度別5年相対生存率 2. 治癒割合・非治癒患者の生存時間

斜体文字は統計資料がないもの

３．がん対策進捗評価の可視化例：市町村別がん検診の精度管理指標

市町村が実施するがん検診のプロセス指標として、がん検診の精度管理指標（要精検率、精検受診率、がん発見率等）がある。大阪府では、これらの指標をがん検診の実施体制（集団方式／個別方式）別に市町村から収集し、毎年「大阪府におけるがん検診」という冊子（CD-ROM付）にて報告されている。しかしながら、大阪府の市町村の人口は数千人～数十万人とばらつきが大きく、点推定値で各精