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Geographical comparison of cancer survival in European children (1988–1997): Report from the Automated Childhood Cancer Information System project

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ABSTRACT

The aim of this study was to assess regional survival differences among childhood cancer patients in Europe. For this exercise, the Automated Childhood Cancer Information System (ACCIS) database was utilised. Survival data from 54 population-based cancer registries on 49,651 childhood cancer patients aged 0–14 years and diagnosed in 1988–1997 were analysed using life-table method. Overall, the 5-year survival was 72% among all patients, varying from 62% to 77% between the five geographical regions. The East region generally had lower survival rates than the rest of Europe. The geographical differences indicate the need for more co-ordination, systematisation and standardisation in diagnosis, referral and the treatment of childhood cancers in Europe. Increase of resources is necessary to improve the lower survival in the East region. Continuing data collection on a European level will facilitate monitoring of population-based survival of childhood cancer patients.

1. Introduction

Survival of children with cancer has improved considerably over the last decades in the developed countries worldwide. However, large differences were observed within Europe for children diagnosed over the period 1978–1992, which are also reflected in differences in mortality statistics.[1,2] In 1985–1989, 5-year survival for all childhood cancers combined varied from 55% to 77% between regions in Europe.[1]

The Automated Childhood Cancer Information System (ACCIS) is a collaborative project of the European cancer registries, aiming at collection, presentation and interpretation of data on cancer incidence and survival of children and adolescents in Europe.[3]

The ACCIS database contains data from 78 population-based cancer registries that cover about 50% of the population aged 0–14 years and about 25% of the population aged 15–19 years living in the 35 participating countries. It covers 1.3 billion person-years, giving rise to over 160,000 cases of childhood and adolescent cancer diagnosed during the period 1968–2001.

Using the ACCIS database, we aim to extend the general information on survival of children with cancer in Europe,

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describe the geographical differences, estimate their extent and discuss their possible reasons.

2. Patients and methods

All malignant neoplasms, together with non-malignant tumours of the central nervous system (CNS), registered between 1988 and 1997 in patients aged less than 15 years in the participating registries listed in Table 1 were extracted from the ACCIS database.

A standard set of variables included basic demographic data (age, sex, country or region of residence), information on the tumour (date of incidence, site, morphology and basis of diagnosis) and on follow-up (date of last contact and vital status). The tumours were grouped according to the International Classification of Childhood Cancer (ICCC), for presentation of the results.[4] For each case, the duration of survival was calculated as the time elapsed between the date of diagnosis and the date of death (if the patient died) or closing date of the study of the given cancer registry, shown in Table 1. Failure or withdrawal of each case was thus accounted for in the appropriate 1-year follow-up interval in the survival table. In the registries where the follow-up interval was longer than 1 year, the survival time of the patients withdrawn before the closing date of the study (lost to follow-up) was calculated as the time interval between the date of diagnosis and date last seen, plus a half of the usual follow-up interval for that registry. These censored observations thus contributed person-years up to those annual follow-up intervals, in which they were, on average, lost to follow-up.

The 54 population-based registries listed in Table 1 were qualified as 'comparable' for the purposes of this analysis [Steliarova-Foucher, Kaatsch, Lacour and colleagues, this issue]. Countries were then grouped into five geographical regions (Table 1).

Life-table method was used for survival analyses.[5] Only cases with non-zero survival time were included in the analyses. Their number and the percentage they represented of all registrations for the given period are shown in Table 1. Most of the excluded cases were those registered from death certificate only (DCO). The reported 5-year observed survival is the cumulative probability of surviving to the 5th anniversary of the date of incidence. In the graphs, the cumulative survival probability is plotted as a continuous line, joining the cumulative probabilities of survival for each year following the diagnosis. The 95% confidence intervals (95% CIs) of the cumulative survival were calculated according to Kalbfleisch and Prentice,[6] using Stata.

Observed survival was used instead of relative survival[7] as competing causes of death were rare among childhood cancer patients in developed countries. To verify this, the World Health Organization (WHO) core health indicator 'child mortality' (i.e. probability of dying before the age of 5 years) was checked.[8] In year 2000 among the countries included in the survival analysis, child mortality was highest in Belarus (17/1000 for boys and 12/1000 for girls) and lowest in Norway (5/1000 for boys and 4/1000 for girls). Thus, the lowest expected probability of survival was 983/1000, i.e. there was less than 2% mortality during the first 5 years of life (in boys in Belarus). In the countries included, the all causes mortality was, in general, less than 1%. Therefore, relative survival was only very slightly higher than observed survival (61% instead of 60% in the most extreme case of boys in Belarus), and it was practically the same in most of the other countries in this analysis.

Differences in survival of two or more groups of patients were compared for the entire survival curves using the log-rank χ^2 test.[9]

Potentially, regional cancer registries may experience more difficulties in complete follow-up of cases than do nationwide registries. Furthermore, the region of cancer registration may not be representative of the whole country, particularly with respect to the timeliness and quality of diagnosis and treatment, which influence survival results. National mortality data, collected through an independent mechanism, provide an independent estimate of the prognosis of childhood cancer patients on a national level. To examine the possible bias in survival statistics in regional cancer registries, compared with those with national coverage, we used the equivalence formula:

$$\text{mortality} = \text{incidence} * (1 - \text{survival}),$$

derived from fatality ratio (deaths:cases) that is an indicator of survival.[10] The left side of the above formula refers to national mortality statistics, while the right side refers to the incidence and survival data from the ACCIS database; pooled regional data were used for the countries with several regional registries. The 'mortality' is the average of sex-specific standardised rate (World Standard population) per million in the age range 0–14 years for the period 1988–1997 (for Slovakia, only period 1992–1997 was available), weighted by the proportion of the two sexes in childhood population.[8] The 'incidence' is age-standardised (World Standard population) incidence rate for the age-group 0–14 years per million for the period 1988–1997. The 'survival' is the 5-year observed cumulative survival probability for the cases diagnosed during the period 1988–1997 at ages under 15 years. Spearman's correlation coefficient was calculated.

3. Results

In the period 1988–1997, the overall observed 5-year survival among the 49,651 childhood cancer patients across Europe was 72% (Table 2). It varied between 77% in the North and 62% in the East. It was 71% in the British Isles, 72% in the South and 75% in the West (Table 2, Fig. 1). The survival curves tested by log-rank test were significantly different between the pairs of regions with neighbouring ranks, with the exception of the survival curves for the British Isles and the South ($\chi^2 = 1.6$, $P = 0.30$). Survival for the East was markedly lower than the pooled survival of the other regions ($\chi^2 = 568.62$, $P < 0.0001$).

For all tumours combined, survival was lower during the first follow-up year among patients diagnosed in infancy (at less than 1 year of age) than in other age groups and the two survival curves (age 0 and age 1–14 years) differed significantly ($\chi^2 = 35.34$, $P < 0.0001$). There was no significant difference between the overlapping survival curves for the other three age groups ($\chi^2 = 3.81$, $P = 0.15$). In all age groups, the survival among patients diagnosed in the East was lower than those observed in the other regions (Fig. 2(a–d)).

Table 1 – Datasets contributed by the European cancer registries for the analyses of survival of children (age 0–14 years) with cancer diagnosed in 1988–1997, with indicators of coverage, data quality and follow-up (Source: ACCIS)

Region	Registry	Coverage				Basis of diagnosis			Non-malignant	NOS	Follow-up				Notes
		Period	Person-years	Registrations included in analyses		MV	DCO	Unknown			Closing date	Median	< 5 years	Lost	
				n	%[a]	%	%	%	%	%		Years	%	%	
British Isles	IRELAND, National	1994–1997	3,417,728	427	98	95	0	<1	2	7	31.12.1998	3.1	100	–	
	UNITED KINGDOM, England & Wales	1988–1995	77,923,641	9773	98	91	<1	4	4	3	31.1.2001	8.7	1	<1	P
	UNITED KINGDOM, Northern Ireland	1993–1996	1,568,121	223	100	73	0	0	8	26	31.12.1999	1.2	94	–	
	UNITED KINGDOM, Scotland	1988–1997	9,631,411	1238	100	95	0	0	–	4	31.12.1999	6.5	33	–	
East	BELARUS, National	1989–1997	20,710,420	3168	99	96	0	0	2	7	1.9.2000	6.6	28	3	P
	ESTONIA, National	1988–1997	3,248,135	411	96	94	<1	0	–	11	31.12.1998	4.8	51	1	
	HUNGARY, National	1988–1997	20,017,358	2459	99	97	–	0	4	2	1.1.2000	6.7	35	10	P
	SLOVAKIA, National	1988–1997	12,638,341	1513	94	97	0	0	3	5	31.12.1997	4.9	52	–	
North	DENMARK, National	1988–1997	8,949,077	1366	97	91	0	2	9	10	31.12.1997	5.6	44	<1	
	FINLAND, National	1988–1997	9,667,700	1582	98	98	0	<1	2	11	31.12.1998	5.6	43	<1	
	ICELAND, National	1988–1997	644,792	84	100	99	0	0	2	5	31.12.2000	7.6	28	–	
	NORWAY, National	1988–1997	8,247,807	1186	100	97	<1	<1	2	11	1.1.2000	6.3	35	1	
South	ITALY, Ferrara	1991–1995	174,945	28	100	82	0	0	–	18	31.12.1998	5.6	36	–	
	ITALY, Latina	1988–1997	893,595	101	98	90	0	3	–	17	31.12.1998	6.5	23	–	
	ITALY, Liguria	1988–1995	565,441	89	99	78	0	0	2	7	15.4.2000	8.4	14	1	
	ITALY, Lombardy	1988–1997	1,135,353	190	99	94	0	0	–	4	23.9.1999	3.3	63	–	
	ITALY, Marche	1990–1997	1,559,718	243	100	88	–	9	–	12	30.9.2000	6.2	38	4	P
	ITALY, Parma	1988–1995	351,725	47	100	96	0	0	2	4	1.4.1999	7	16	2	
	ITALY, Piedmont paediatric	1988–1997	5,413,167	925	100	96	0	0	4	4	31.12.1999	6.7	24	<1	P
	ITALY, Ragusa	1988–1997	565,558	72	100	96	0	0	–	7	30.3.2000	7.2	25	3	
	ITALY, Sassari	1992–1995	304,735	41	100	93	0	5	–	5	30.12.1999	5.4	19	–	
	ITALY, Tuscany	1988–1997	1,376,966	219	98	62	0	0	5	11	31.12.1998	5.2	49	–	
	ITALY, Umbria	1994–1996	315,902	59	100	85	0	0	–	12	31.12.1999	4.4	74	–	
	ITALY, Veneto	1990–1996	1,730,175	286	99	94	0	0	–	8	31.12.1998	5	50	–	
	MALTA, National	1991–1997	570,071	76	97	96	0	1	7	5	31.12.1999	6	31	–	
	SLOVENIA, National	1988–1997	3,878,057	479	99	98	0	0	1	4	31.12.1999	6.5	37	< 1	
	SPAIN, Albacete	1991–1997	473,835	56	98	91	0	0	–	9	15.9.2000	7.2	33	–	
	SPAIN, Asturias	1988–1997	1,643,051	222	97	96	0	0	2	14	31.12.1997	8.3	0	–	
	SPAIN, Basque Country	1988–1989	814,226	118	99	97	0	0	–	10	31.12.2000	12.1	0	–	o1
	SPAIN, Girona	1996–1997	160,249	20	100	95	0	0	–	5	31.12.1997	0.9	100	–	o1

	SPAIN, Granada	1988–1997	1,695,848	204	98	99	0	<1	–	3	31.12.1999	6.7	32	–	G
	SPAIN, Mallorca	1988–1989	237,183	32	97	94	0	0	–	6	31.12.1998	10.7	12	3	o1
	SPAIN, National	1990–1995	10,377,774	1343	98	93	0	2	2	4	31.12.2000	6.1	9	<1	P o1 Z
	SPAIN, Navarra	1988–1996	270,972	33	97	97	0	0	–	6	31.12.1997	9.9	27	–	o1
	SPAIN, Tarragona	1988–1997	395,922	51	100	96	0	0	–	8	31.12.1998	2.7	56	–	o1
	SPAIN, Zaragoza	1988–1996	412,477	55	100	98	0	0	0	2	31.12.1996	7.6	29	–	o1
West	FRANCE, Bas-Rhin	1988–1996	1,731,876	252	100	98	–	0	–	8	31.12.1997	5.5	43	2	
	FRANCE, Brittany	1991–1997	3,809,039	522	99	98	–	2	5	3	1.1.2000	4.6	56	4	P
	FRANCE, Doubs	1988–1996	930,939	105	89	64	–	2	–	10	1.6.2001	1.4	91	–	
	FRANCE, Haut-Rhin	1988–1991	555,015	80	99	91	–	0	–	8	31.12.1995	7.3	15	4	S
	FRANCE, Lorraine	1988–1997	4,762,031	640	100	92	–	<1	3	3	1.1.1999	4.7	54	–	P
	FRANCE, Manche	1994–1995	196,312	23	96	91	–	0	–	0	31.5.2000	4.2	71	–	S
	FRANCE, PACA	1988–1996	7,623,567	943	89	98	–	0	3	3	31.3.1998	2.8	66	13	P
	FRANCE, Rhone Alpes	1988–1997	11,178,532	1278	93	97	–	<1	4	2	1.6.2000	5.2	48	–	P
	FRANCE, Somme	1988–1996	1,041,618	125	98	94	–	2	–	4	15.8.2000	2.9	68	16	
	GERMANY, GCCR (East and West)	1991–1997	93,284,500	10702	88	100	–	0	2	2	31.12.1998	3.9	67	–	P
	GERMANY, GCCR (only former West)	1988–1990	28,822,000	3543	96	100	–	0	3	3	31.12.1998	7.8	17	–	P
	NETHERLANDS, DCOG	1988–1997	2,709,561	2199	99	99	–	0	–	0	1.1.2000	8.8	19	1	P o2
	NETHERLANDS, Eindhoven	1988–1997	1,767,158	245	99	96	–	<1	–	6	1.7.1999	5.6	45	4	o2
	NETHERLANDS, National	1989–1995	19,372,876	2622	98	95	–	0	–	7	31.12.1998	5.9	36	8	S o2
	SWITZERLAND, Basel	1988–1997	628,241	99	100	98	–	0	–	5	30.6.2000	6.4	26	–	
	SWITZERLAND, Geneva	1988–1997	608,299	87	99	97	0	0	–	5	31.12.1999	5.6	40	5	
	SWITZERLAND, Graubunden & Glarus	1989–1997	367,257	48	100	90	0	4	–	8	25.5.2000	5	50	27	
	SWITZERLAND, St. Gallen Appenzell	1988–1997	987,860	132	99	97	0	0	2	6	1.2.2001	5.1	40	27	
	SWITZERLAND, Valais	1989–1993	245,170	31	97	100	0	0	–	6	1.12.1998	8.5	0	3	S

MV, microscopically verified cases; DCO, registrations from death certificate only; NOS, cases with unspecified histology; <5 years, cases followed-up for less than 5 years, as a percentage of all those not decreased by the closing date; P, paediatric cancer registry, age-range of the patients is 0–14 years; G, general cancer registry, which has only contributed data for age-range 0–14 years; o1–o2, overlapping registration areas; S, survival analyses were possible only for a restricted dataset [see Steliarova-Foucher, Kaatsch, Lacour and colleagues, this issue]; Z, covers only selected areas [see Steliarova-Foucher, Kaatsch, Lacour and colleagues, this issue]; DCOG, Dutch Childhood Oncology Group; PACA, Provence, Alps, Cote d'Azur; NCR, National Cancer Registry of the former German Democratic Republic; GCCR, National German Childhood Cancer Registry (until 1990 only for the West, since 1991 for reunified Germany).

a Percentage of registrations included in analyses refers to the total number of cases registered for the period shown, including those with zero follow-up. Percentages for basis of diagnosis, non-malignant and NOS refer to the number of cases included in the survival analyses shown in the column under *n*, unless specified otherwise.

Table 2 – Observed 5-year survival (OS%) of childhood cancer patients in Europe, by region and by ICCG group (age-range 0–14 years, both sexes, patients diagnosed in 1988–1997) (Source: ACCIS)

ICCG group	Region																	SEER[a]
	Europe			British Isles			East			North			South			West			RS
	n	OS	CI	*n*	OS	CI	*n*	OS	CI	*n*	OS	CI	*n*	OS	CI	*n*	OS	CI	
I. Leukaemia	16,166	73	72–74	3781	74	73–76	2041	58	56–60	1234	78	75–80	1507	70	68–73	7603	77	76–78	74
II. Lymphomas ...	5824	84	83–85	1105	85	82–87	1005	74	71–76	394	81	77–85	714	82	79–85	2606	88	86–89	83
III. CNS tumours ...	10,532	64	63–65	2720	63	61–65	1696	53	51–56	1167	72	69–74	1022	66	63–69	3927	65	64–67	66
IV. Sympathetic NS tumours	3669	59	58–61	797	50	46–53	469	47	42–52	237	57	50–64	369	61	56–66	1797	67	65–69	66
V. Retinoblastoma	1201	93	91–94	368	96	93–97	151	83	75–88	128	97	92–99	106	93	86–97	448	92	88–95	95
VI. Renal tumours	2966	84	82–85	649	81	78–84	408	71	66–75	228	91	87–95	245	83	77–87	1436	87	85–89	90
VII. Hepatic tumours	411	57	52–62	102	56	46–65	79	44	32–54	47	83	69–91	43	62	45–75	140	54	44–63	56
VIII. Malignant bone tumours	2322	61	59–63	489	61	57–66	338	41	36–47	150	66	57–74	305	65	59–70	1040	66	63–69	68
IX. Soft tissue sarcomas	3342	65	63–66	862	63	60–66	449	50	45–55	295	74	68–79	326	74	68–78	1410	66	64–69	73
X. Germ-cell tumours ...	1627	84	82–86	357	87	83–90	194	62	55–69	147	90	84–94	159	81	74–86	770	87	84–89	87
XI. Carcinomas ...	1715	89	87–90	344	86	82–90	698	93	91–95	154	88	82–93	163	89	83–93	356	83	78–87	89
XII Other and unspecified tumours	202	74	67–80	87	89	80–94	23	32	15–52	37	78	61–88	30	76	56–88	25	56	33–73	–
All diagnostic groups	49,651	72	72–72	11,661	71	71–72	7551	62	61–63	4218	77	75–78	4989	72	71–73	21,232	75	74–76	75

n, numbers of patients; CI, 95% confidence interval; CNS, central nervous system; NS, nervous system.

a For comparison, United States data: 5-year relative survival rates (RS) for patients diagnosed in 1985–1999 in the nine SEER areas based on data from population-based registries in Connecticut, New Mexico, Utah, Iowa, Hawaii, Atlanta, Detroit, Seattle-Puget Sound and San Francisco-Oakland. Rates are based on follow-up of patients into 2000 in Ref. [11].

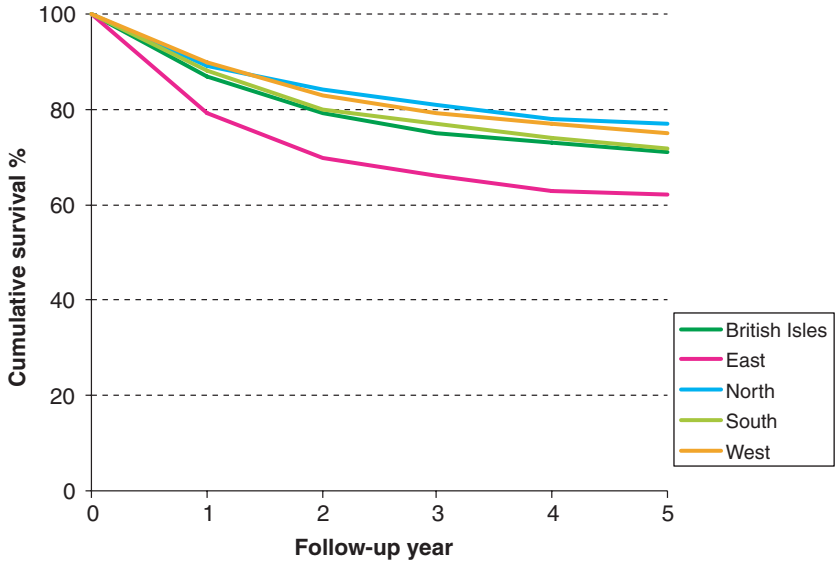

Fig. 1 – Cumulative survival of childhood cancer patients diagnosed in 1988–1997 in Europe, by region. All diagnostic groups, both sexes combined. Source: ACCIS.

Overall, 5-year survival was slightly lower in boys than in girls ($\chi^2 = 5.34$, $P = 0.021$), as shown in Table 3, but within the regions, a significant difference between boys and girls was seen only in the East where the 5-year survival among boys was 60% (95% CI 59–62%) and 63% (61–65%) among girls ($\chi^2 = 3.88$, $P = 0.049$). These differences were, however, entirely accounted for by the larger proportion of girls than boys among the thyroid cancer cases in Belarus (M/F ratio = 0.64). After excluding all thyroid cancer cases recorded in Belarus from the dataset, there were no differences in survival between boys and girls in the East ($\chi^2 = 0.1$, $P = 0.8$) or in the overall dataset ($\chi^2 = 2.5$, $P = 0.1$). By ICCC group, girls had significantly better survival in leukaemia ($\chi^2 = 23.35$, $P = 0.006$), neuroblastoma (group IV) ($\chi^2 = 7.29$, $P = 0.007$) and carcinomas (group XI) ($\chi^2 = 7.61$, $P = 0.006$) (Table 3). For carcinomas, the sex difference remained significant also after exclusion of

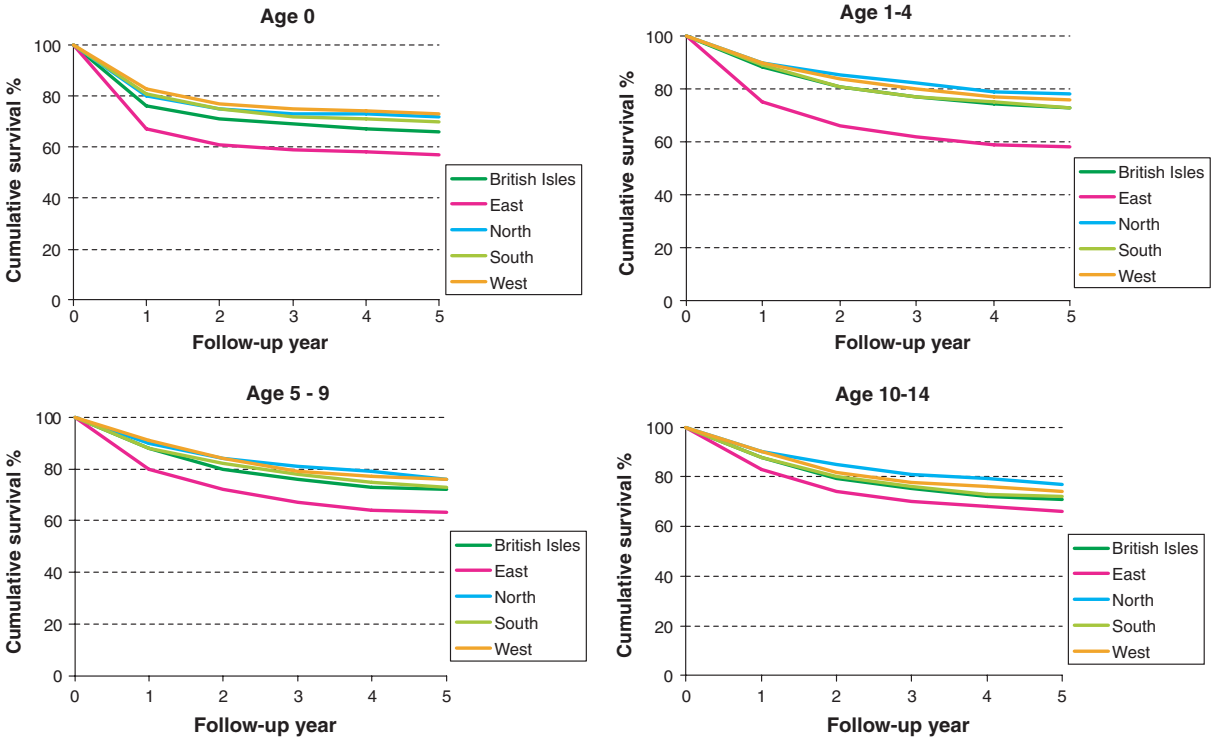

Fig. 2 – Cumulative survival of childhood cancer patients diagnosed in 1988–1997 in Europe, by age at diagnosis and region. All diagnostic groups, both sexes combined. Source: ACCIS.

Table 3 – Observed 5-year survival (OS%) of childhood cancer patients in Europe, by sex and ICCC group (age-range 0–14 years, patients diagnosed in 1988–1997) (Source: ACCIS)

ICCC group	Boys			Girls		
	n	OS	95% CI	*n*	OS	95% CI
I. Leukaemia	9075	72	71–73	7091	75	74–76
II. Lymphomas ...	3947	84	83–85	1877	82	80–84
III. CNS tumours	5745	63	62–65	4787	64	63–66
IV. Sympathetic NS	1972	57	55–59	1697	62	60–64
V. Retinoblastoma	614	93	90–95	587	93	90–95
VI. Renal tumours	1431	84	82–86	1535	83	81–85
VII. Hepatic tumours	249	56	49–62	162	59	50–66
VIII. Malignant bone tumours	1200	62	59–65	1122	60	57–63
IX. Soft tissue sarcomas	1869	66	63–68	1473	63	60–66
X. Germ-cell tumours ...	730	85	82–88	897	83	80–85
XI. Carcinomas etc.	738	87	84–89	977	91	89–93
XII. Other and unspecified	87	72	61–80	115	76	66–83
All diagnostic groups	27,479	72	71–72	22,172	73	72–73

n, numbers of patients; CI, 95% confidence interval; CNS, central nervous system; NS, nervous system.

thyroid cancer cases from Belarus ($P = 0.01$). Boys had significantly better survival in soft tissue sarcomas ($\chi^2 = 5.69$, $P = 0.017$) and, marginally, in bone tumours ($\chi^2 = 3.24$, $P = 0.072$).

In Europe, the 5-year survival among the 12 main ICCC groups ranged from 93% in retinoblastoma (Diagnostic group V) to 57% in hepatic tumours (group VII) (Table 2). In the East, the patients had lower survival in all ICCC groups except for carcinomas (group XI) (Table 2). The survival differences between the East and other European regions were generally 10 percentage points or more lower, but varied from 3 to 39 percentage points according to diagnostic group. Between the other European regions, the variability ranged from 4 to 27 percentage points according to diagnostic group (Table 2). In the carcinoma group (XI), the best survival was in the East. This was due to the exceptionally high proportion of thyroid carcinoma in the East region (83% of all carcinomas compared with, on average, 25% in other regions). The excess of thyroid tumours was limited to Belarus (92% of all carcinomas), while it was standard in the other countries of the East (26%). The excellent prognosis of thyroid cancer patients, therefore weighted the East to have the best survival in group XI.

In ICCC group-specific comparisons between the North, South, West and the British Isles, the highest survival figures were often observed in the North (Table 2). In all diagnostic groups combined, the survival figures ranged from 71% to 77%. Significant differences were seen between the regions with highest versus lowest 5-year survival; in CNS tumours (from 63% to 72%), in neuroblastoma (from 50% to 67%), in renal tumours (from 81% to 91%), in hepatic tumours (from 54% to 83%) as well as in germ cell etc. tumours (from 81% to 90%). Smaller differences were seen in leukaemia (from 70% to 78%) and in lymphomas (from 81% to 88%).

There was good correlation ($r = 0.75$) between the national mortality data in the age-group 0–14 years and the estimate of mortality defined as [incidence*(1–5-year survival)] derived from the ACCIS database (Fig. 3). The correlation pattern did not differ for the regional, compared with the national cancer registries.

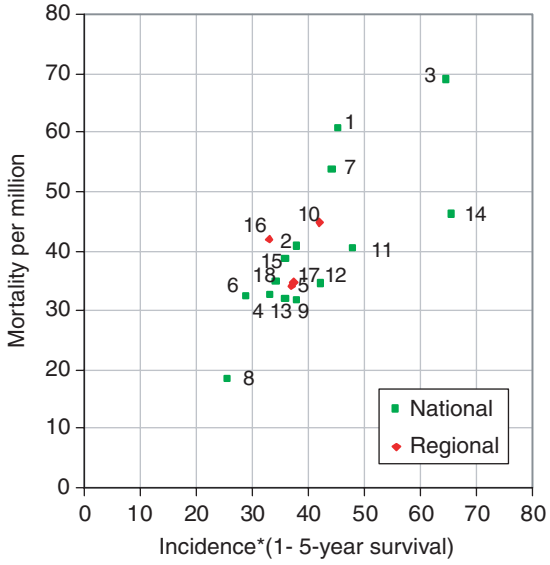

Fig. 3 – Comparison of official national mortality data with the mortality estimated from incidence and survival data collected by the national and regional cancer registries contributing to the ACCIS database, 1988–1997. (Numbers indicate countries: 1 Belarus, 2 Denmark, 3 Estonia, 4 Finland, 5 France, 6 Germany, 7 Hungary, 8 Iceland, 9 Ireland, 10 Italy, 11 Malta, 12 Netherlands, 13 Norway, 14 Slovakia, 15 Slovenia, 16 Spain, 17 Switzerland, 18 United Kingdom.) Source: ACCIS.

4. Discussion

This paper addresses the geographical differences in survival of childhood cancer patients in the different regions of Europe. The detailed description of the patient materials is given in a separate article in this Special Issue [Steliarova-Foucher, Kaatsch, Lacour and colleagues, this issue]. As pointed out in the Methods section, the use of observed survival rather than relative survival was justified, as we were able to

estimate the negligible error of the unadjusted survival proportions presented in this paper.

The 10-year calendar period from 1988 to 1997 was chosen to secure maximum power for the analyses by including the majority of the contributing registries and the most recent time period available in the ACCIS database, especially for the smaller tumour groups. Obviously, more recent survival figures (e.g. for 1993–1997) give slightly higher survival estimates, since survival has improved over the study decade [Magnani and colleagues, this issue]. However, for comparison between the regions the 10-year period is just as valid, especially because the 5-year follow-up period was less complete for the patients diagnosed in the final 5 years (Table 1).

The overall observed 5-year survival among all childhood cancer patients diagnosed across Europe in 1988–1997 was 72%, ranging from 62% in the East to 77% in the North. For comparison, the 5-year overall survival was 75% in the SEER results in the USA (Table 2) for patients diagnosed in 1985–1999.[11] Among the 12 main ICCC groups, the European average 5-year survival estimates were very close to those seen in the USA[11] with regional exceptions in neuroblastoma (group IV), renal tumours (group VI), bone tumours (group VIII) and soft tissue sarcomas (group IX) (Table 2).

As reported previously, the survival estimates in the East region were lowest in almost all diagnostic groups and in all age groups.[12,13] The high survival rates observed in the East in the carcinoma group (XI) reflect the favourable prognosis for thyroid carcinoma with the exceptionally high incidence in Belarus due to the Chernobyl accident. Encouraging improvements in survival have been seen in the East [Magnani and colleagues, this issue], but no significant increase was observed for some tumours, e.g. soft tissue sarcomas [Pastore, Peris-Bonet, Carli and colleagues, this issue]. It should also be noted that the overall survival in countries grouped within the East is as heterogeneous as that between the geographical regions within Europe. Possible reasons for these differences and opportunities for continued improvement are discussed elsewhere [Pritchard-Jones and colleagues, this issue].

The survival figures in the North were often the highest. This is most likely largely due to the long-term achievements within the framework of the Nordic Society of Paediatric Haematology and Oncology (NOPHO) and the relatively high overall standard of healthcare systems and socio-economic status in these five countries. Over the last two decades, impressive efforts in Nordic co-operation and collaborative clinical trials have led to standardisation of treatment protocols in all the five countries (e.g. Ref. [14]).

However, organisation of specialist care cannot be the only contributing factor to high survival rates. In the British Isles, more than 75% of UK children in most ICCC groups have been treated in specialist paediatric oncology centres affiliated to the UK Children's Cancer Study Group (UKCCSG) since the mid 1980s, together with a high rate of recruitment to international and national trials.[15,16] Despite this, there was a moderately lower overall survival rate in the British Isles (71%) compared with the North (77%) and West (75%) regions though it was not significantly different from the South (72%). One potential confounding factor is the shorter period of coverage for England and Wales, ending in 1995 and which supplied 85% of cases for the British Isles. However, survival analysis restricted to the cases diagnosed up to year 1995 yielded similar results as unrestricted analysis and the rank of the regions (as shown in Table 2) did not change. Possible reasons for lower survival in the British Isles and the differences in region-specific survival in general are discussed in the overview paper [Pritchard-Jones and colleagues, this issue].

In Finland, astrocytomas (subgroup IIIb) cannot be separated from other gliomas (IIId) due to the old classification system. However, the overall results for CNS tumours (72% in the North versus 64% elsewhere) were not affected by this misclassification. Whether the diagnostic criteria are the same in all the countries may be questionable and should be investigated. The large differences in survival from hepatic tumours would require more in-depth studies involving a pathology review [Stiller, Pritchard-Jones and Steliarova-Foucher, this issue]. The high survival rates of neuroblastoma patients (in ICCC group IV) in the West may, partially, be explained by screening – organised or opportunistic – or by incidental findings [Spix and colleagues, this issue]. It is also possible that immigrants, accounting for variable percentage in the study populations, may be lost to follow-up in greater proportions than patients from the native population, but the effect of this phenomenon on overall survival rates could not be assessed using these data.

To evaluate any systematic differences between regional and national cancer registries in respect of provision of survival data, the official national mortality data were compared graphically with a mortality estimate based on incidence and survival provided by the cancer registries. The official mortality data and the mortality estimate derived from registry-based incidence and survival for the same period do not correspond exactly for several reasons: (i) the (age-standardised) mortality is annual mortality in the 0–14 years age group, but the survival reflects also deaths in the age group 15–19 years, if they were diagnosed at 10 years or more and then followed up for over 5 years. (ii) In our formula, we used 5-year survival, while there is still excess mortality among childhood cancer patients after the first five follow-up years, accounted for in official cancer mortality. (iii) The official mortality figures include survival experience of the patients diagnosed before the period 1988–1997, while survival estimates also include survival time after 1997. However, mortality estimates based on incidence and survival derived from the (pooled) regional registries correlate with the national mortality just as well as those from the national cancer registries. This provides evidence against a systematic difference in survival data provided by the regional as compared with national registries contributing to the ACCIS database.

Based on reports from clinical and epidemiological studies, it can be concluded that the immense work carried out in developing improved therapies for childhood cancer patients has borne fruit. However, after surviving for 5 years, childhood cancer patients still experience excess mortality that is mostly related to late relapses and recurrences.[17] The existing geographical differences in Europe are indicative of the potential for further improvement. It is encouraging to note continued increase in survival in the majority of the diagnostic groups over the study period even in the North, the region with most favourable results [Magnani and

colleagues, this issue]. Continuing data collection and follow-up of the patients and systematic analysis on a European level will facilitate monitoring of population-based survival of childhood cancer patients and evaluation of European public health policy in paediatric oncology.

Conflict of interest statement

None declared.

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