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Childhood soft tissue sarcomas incidence and survival in European children (1978–1997): Report from the Automated Childhood Cancer Information System project

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ABSTRACT

This population-based study is based on 5802 cases of soft tissue sarcomas (STS) in children aged 0–14 years extracted from the database of the Automated Childhood Cancer Information System (ACCIS) and registered in population-based cancer registries in Europe for the period 1978–1997. STS represent almost 8% of neoplasms in children, almost half of whom are less than 5 years at diagnosis. Rhabdomyosarcoma is the most frequent childhood STS (50%). During 1988–1997 the age-standardised incidence of STS in Europe was 9.1 per million children, lowest in the West and East and highest in the North. The incidence of STS increased almost 2% per year over the period 1978–1997, attributable mostly to increase in genito-urinary rhabdomyosarcoma. Prognosis of children with STS was related to age and site of tumour. Five-year survival of children with STS increased from 46% in 1978–1977 to 66% in 1993–1997, reaching 74% in the North for those diagnosed in 1993–1997. This improvement is ascribed to therapy advances.

1. Introduction

Soft tissue sarcomas (STS) are a heterogeneous group of neoplasms developing from mesenchymal cell at any site of the body. STS comprise about 8% of all childhood cancers. Almost half of the patients with STS are less than 5 years of age at diagnosis. These neoplasms are categorised in two broad groups: rhabdomyosarcoma (RMS) and non-rhabdomyosarcoma STS (NRSTS). RMS is the single most frequent childhood STS, accounting for more than 50% of cases, and fibrosarcoma is the most common NRSTS, accounting for 10–20% of STS cases. The primary site is related to age at diagnosis and histological subtype.[1]

STS rarely occurs as part of congenital malformation syndromes. Patients with Li-Fraumeni syndrome, neurofibromatosis type 1 and other rare familial syndromes are at increased risk of developing STS. However, these genetic susceptibility conditions explain only a small proportion of child-

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hood cases.[2,3] Characteristic somatic changes are associated with specific types of STS.[4] Radiation therapy is the best-known environmental risk factor for STS.[2,5] HIV-infected patients are at a high risk of developing a specific STS, Kaposi's sarcoma (KS). KS is a complex multifactorial virally driven process: the HIV infection is necessary, but not sufficient for its development. However, the risk is lower among HIV-infected children in Europe and in North America than in Africa: this pattern is presumably related to a different prevalence of cofactors.[6]

Previous EUROCARE studies evaluated population-based survival of children diagnosed with STS in European Countries before 1994.[8,11] The prognosis of RMS is related to age, tumour site and size, histology and extent of disease at diagnosis. The findings of a large clinical series[7] are consistent with the results of the population-based study EUROCARE-2[8] and suggest poor prognosis for infants and adolescents with RMS, compared with children aged 1–9 years.

Over the last 40 years, the prognosis of children with RMS has improved from 25% in 1970s to 70% in 1990s due to use of multimodal therapy, as well as to development of an armamentarium of effective cytotoxic drugs.[4,7] The improvement in treatment strategies for RMS illustrates the value of multi-institutional co-operative groups to study large series of rare childhood tumours with clinical and biological heterogeneity.[7]

Until recently, the clinical relevance of histological classification of NRSTS was limited. Most of the clinical knowledge and experience gathered in the management of children with RMS has been applied also in the treatment of children with NRSTS, even though these are different biological entities with variable chemosensitivity.[4,9,10]

The aim of this report is to describe incidence and survival of STS in children in Europe and their geographical and temporal variations and suggest the direction for further studies. The present study benefits from a large population-based series of data, collected in the framework of the Automated Childhood Cancer Information System (ACCIS) from 80 European cancer registries for the period 1978–1997.[12]

2. Material and methods

This study is based on the data from 59 cancer registries in 19 European countries (Table 1) retrieved from the ACCIS database, and evaluated as comparable by the ACCIS Scientific Committee [Steliarova-Foucher, Kaatsch, Lacour and colleagues, this issue]. All malignant STS, as defined by the group IX of the International Classification of Childhood Cancer (ICCC), were included in the analyses.[13]

In total 5802 cases of STS in children, aged 0–14 years of age, living in the geographical areas covered by the participating registries with newly diagnosed STS during 1978–1997 were included in various analyses. Patterns of incidence and survival by gender, age and region were examined using a data-set of cases incident in the 10-year period 1988–1997, including data from all contributing registries, to ensure a reasonable stability of the estimates. Countries were grouped into five geographical regions: British Isles, East, North, South and West (Table 1). Thirty-two registries contributed to the analyses of time trends for the overall time period 1978–1997 (Table 1). Table 2 shows the distribution of cases in four 5-year periods and the five regions, together with selected quality indicators.

The results are presented for STS overall, and for the ICCC[13] diagnostic subgroups: IXa, RMS and embryonal sarcoma; IXb, fibrosarcoma, neurofibrosarcoma and other neurofibromatous neoplasms (including fibromatous neoplasms with exclusion of periosteal fibrosarcoma, and nerve sheath tumours); IXc, Kaposi's sarcoma; IXd, other specified STS (comprising myxomatous and lipomatous neoplasms, malignant myoepithelioma, mesenchymoma, and synovial-like neoplasms, myomatous neoplasms excluding rhabdomyosarcomas, blood vessel and lymphatic vessel tumours excluding Kaposi's sarcoma, Ewing's sarcoma of soft tissues and rhabdoid sarcoma in sites other than kidney, myxoid sarcoma, mesenchymal chondrosarcoma, melanotic and peripheral neuroectodermal tumour of soft tissues); IXe, unspecified STS. Throughout this paper the NRSTS included the diagnostic groups IXb, IXd and IXe. For RMS, selected data are also presented for the main histological subtypes: embryonal (M-8910/3, M-8991/3), alveolar (M-8920/3) and other and NOS histologies (M-8900/3, M-8901/3, M-8902/3) and the anatomic sites of clinical interest (Table 3).[14] Incidence rates are expressed as the average annual number of cases per million person-years and world standard population was used to standardise the incidence rates by age (ASR). Standardised rate ratio was used to compare sex-specific age-standardised rates. Differences in incidence rates for geographical areas and trends were evaluated using Poisson regression models with the British Isles as the region of reference.[15]

Survival analyses were carried out using actuarial life-table methods. The cases with zero follow-up time were excluded from analyses (Tables 1 and 2). Differences in survival between various patient groups were evaluated from comparison of entire survival curves and tested with the log-rank χ^2 tests.[16] Based on previous findings,[7,8] survival rates for RMS were reported for the age group 1–9 years, in addition to the 'standard' age groups 0, 1–4, 5–9 and 10–14 years. Most of the statistical analyses were conducted using STATA software. Further general details on the database and the methods of its exploration are presented elsewhere [Steliarova-Foucher, Kaatsch, Lacour and colleagues, this issue].

3. Results

3.1. *Incidence*

For the period 1988–1997 there were 3571 cases of newly diagnosed STS in children younger than 15 years of age included in the analysis (Table 4). They represented 6.6% of all childhood cancers in this data-set [Stiller, Marcos-Gragera, Ardanaz and colleagues, this issue]. The diagnosis of great majority of cases (99%) was microscopically verified (MV), and very few were based on death certificate only (DCO) (0.3%) in the registries with access to such information. There were 6% of cases allocated to the unspecified STS category. The differences in quality indicators between diagnostic sub-groups and regions were small (Table 4).

The age-standardised incidence rate (ASR) for STS was 9.1 per million children of 0–14 years of age: the corresponding figure for RMS (58% of all STS) and for NRSTS is reported in

Table 1 – Data-sets contributed by the European cancer registries in the analyses of soft tissue sarcomas incidence and survival in children (age 0–14 years), with indicators of coverage, data quality and follow-up (Source: ACCIS)

Region	Registry	Period	Time trend	Cases	Basis of diagnosis				Survival analyses		Follow-up			Note
					NOS	MV	DCO	Unknown			5+yrs	Median	Closing date	
				n	%	%	%	%	*n*	%	%	Years		
British Isles	IRELAND, National	1994–1997		24	0	100	0	0	24	100	0	3.5	31.12.1998	
	UNITED KINGDOM, England & Wales	1978–1995	+	1463	7	97	< 1	2	1448	99	99	12	31.1.2001	P
	UNITED KINGDOM, Northern Ireland	1993–1996		16	0	94	0	0	16	100	7	0.8	31.12.1999	
	UNITED KINGDOM, Scotland	1978–1997	+	170	14	99	0	0	169	99	70	8.4	31.12.1999	
East	BELARUS, National	1989–1997		171	4	100	0	0	171	100	79	7.1	1.9.2000	P
	ESTONIA, National	1978–1997	+	43	19	100	0	0	43	100	42	4.4	31.12.1998	
	HUNGARY, National	1978–1997	+	298	9	100	–	0	297	100	86	11.3	1.1.2000	P
	SLOVAKIA, National	1978–1997	+	203	10	100	0	0	189	93	71	8.5	31.12.1997	
	GERMANY, NCR (only former East)	1978–1989	+	340	6	100	0	0	279	82	70	6.8	31.12.1987	S
North	DENMARK, National	1978–1997	+	159	4	99	< 1	< 1	156	98	82	10.5	31.12.1997	
	FINLAND, National	1978–1997	+	213	6	100	0	< 1	207	97	69	8.3	31.12.1998	
	ICELAND, National	1978–1997	+	16	6	100	0	0	16	100	92	17	31.12.2000	
	NORWAY, National	1978–1997	+	148	12	100	0	0	148	100	78	10	1.1.2000	
South	ITALY, Piedmont paediatric	1978–1997	+	116	8	100	0	0	116	100	93	11.8	31.12.1999	P
	ITALY, Marche	1990–1997		14	0	93	–	0	14	100	80	7.7	30.9.2000	P
	ITALY, Ferrara	1991–1995		1	0	100	0	0	1	100	100	7.5	31.12.1998	
	ITALY, Latina	1983–1997	+	8	0	100	0	0	8	100	80	5.2	31.12.1998	
	ITALY, Liguria	1988–1995		6	0	100	0	0	6	100	100	8.6	15.4.2000	
	ITALY, Lombardy	1978–1997	+	29	0	97	0	0	29	100	62	7.9	23.9.1999	
	ITALY, Parma	1978–1995	+	9	0	100	0	0	9	100	88	14.3	1.4.1999	
	ITALY, Ragusa	1983–1997	+	3	0	100	0	0	3	100	0	3.3	30.3.2000	
	ITALY, Sassari	1992–1995		2	0	100	0	0	2	100	50	5.1	30.12.1999	
	ITALY, Tuscany	1988–1997		15	13	93	0	0	15	100	73	7.7	31.12.1998	
	ITALY, Umbria	1994–1996		3	0	100	0	0	3	100	0	3.8	31.12.1999	
	ITALY, Veneto	1990–1996		17	18	94	0	0	17	100	69	5.4	31.12.1998	
	MALTA, National	1991–1997		6	0	83	0	17	6	100	80	6	31.12.1999	
	SLOVENIA, National	1978–1997	+	71	7	100	0	0	71	100	81	11.2	31.12.1999	
	SPAIN, National	1990–1995		101	9	100	0	0	99	98	90	6.2	31.12.2000	PZ o1
	SPAIN, Albacete	1991–1997		4	50	100	0	0	4	100	0	4.4	15.9.2000	
	SPAIN, Asturias	1983–1997	+	26	4	100	0	0	26	100	67	7.8	31.12.1997	
	SPAIN, Basque Country	1988–1994		29	17	100	0	0	28	97	100	9.2	31.12.2000	o1
	SPAIN, Canary Islands	1993–1996		7	0	71	29	0	–	–	–	–	–	
	SPAIN, Girona	1994–1997		3	0	100	0	0	3	100	0	2.5	31.12.1997	o1
	SPAIN, Granata	1988–1997		14	0	100	0	0	14	100	78	5.2	31.12.1999	G

	SPAIN, Mallorca	1988–1995		8	0	100	0	0	8	100	100	5.8	31.12.1998	o1
	SPAIN, Navarra	1978–1996	+	19	0	100	0	0	19	100	43	4.1	31.12.1997	o1
	SPAIN, Tarragona	1983–1997	+	12	17	100	0	0	12	100	70	7.8	31.12.1998	o1
	SPAIN, Zaragoza	1978–1996	+	20	5	90	10	0	18	90	86	10.4	31.12.1996	o1
	TURKEY, Izmir	1993–1996		23	26	100	–	0	–	–	–	–	–	
West	FRANCE, Brittany	1991–1997		23	9	96	–	4	23	100	40	4.8	1.1.2000	P
	FRANCE, Lorraine	1983–1997	+	59	20	100	–	0	59	100	41	4.2	1.1.1999	P
	FRANCE, PACA	1984–1996	+	95	6	100	–	0	91	96	61	6.8	31.3.1998	P
	FRANCE, Rhone Alpes	1988–1997		56	7	100	–	0	54	96	63	5.4	1.6.2000	P o2
	FRANCE, Doubs	1978–1996	+	20	20	30	–	15	16	80	11	2.4	1.6.2001	
	FRANCE, Herault	1988–1997		11	18	100	–	0	–	–	–	–	–	
	FRANCE, Isere	1979–1997	+	32	9	100	–	0	–	–	–	–	–	o2
	FRANCE, Manche	1994–1996		1	0	100	–	0	1	100	–	–	31.5.2000	S
	FRANCE, Bas-Rhin	1978–1996	+	29	7	100	–	0	29	100	69	8.3	31.12.1997	
	FRANCE, Haut-Rhin	1988–1997		9	0	100	–	0	6	67	100	7.6	31.12.1995	S
	FRANCE, Somme	1983–1996	+	12	17	100	–	0	11	92	29	3.3	15.8.2000	
	FRANCE, Tarn	1983–1997	+	9	11	100	–	0	–	–	–	–	–	
	GERMANY, GCCR (East and West)	1991–1997	+	786	4	100	–	0	709	90	32	3.2	31.12.1998	P
	GERMANY, GCCR (only former West)	1983–1990	+	634	6	100	–	0	621	98	94	9.7	31.12.1998	P
	NETHERLANDS, National	1989–1995		197	3	100	–	0	195	99	61	6.2	31.12.1998	S o3
	NETHERLANDS, Eindhoven	1978–1997	+	33	15	97	–	0	33	100	68	9.9	1.7.1999	o3
	SWITZERLAND, Basel	1983–1997	+	9	0	100	–	0	9	100	80	9.8	30.6.2000	
	SWITZERLAND, Geneva	1978–1997	+	9	0	100	0	0	9	100	83	7.9	31.12.1999	
	SWITZERLAND, Graubunden & Glarus	1989–1997		3	0	100	0	0	3	100	50	5.1	25.5.2000	
	SWITZERLAND, St. Gallen Appenzell	1983–1997	+	18	6	100	0	0	18	100	53	5	1.2.2001	
	SWITZERLAND, Valais	1989–1997		6	17	100	0	0	4	67	100	7.2	1.12.1998	S

–, not applicable; +, included in time trend analyses; 5+ years, cases followed-up for 5 or more years, as a percentage of all those not deceased by the closing date; DCO, registrations from death certificate only; G , general cancer registry, which has only contributed data for age-range 0–14 years; GCCR, National German Childhood Cancer Registry (until 1990 covering only West and since 1991 the reunified Germany); MV, microscopically verified cases; *n*, number of cases; NCR, National Cancer Registry of the former German Democratic Republic. Data for 1978–1987 contributed only to analyses of time trends for Europe as a whole. Data for 1988–1989 were pooled with GCCR and included in West. For explanation, see Steliarova-Foucher, Kaatsch, Lacour and colleagues (this issue); NOS, cases with unspecified histology, comprising the ICCC category IXe; o1–o3, overlapping registration areas: for the overlapping years, data from the registry with larger coverage are included in each analysis, according to availability (see text); P, paediatric cancer registry; age range for all registrations is 0–14; PACA, Provence, Alps, Côte d'Azur; S, survival analyses were possible only for a restricted data-set see Steliarova-Foucher, Kaatsch, Lacour, and colleagues (this issue); Unknown, registrations with unknown basis of diagnosis; Z, covers only selected areas, see Steliarova-Foucher, Kaatsch, Lacour, and colleagues (this issue).

Table 2 – Numbers of cases and indicators of data quality by region and period for time trend analyses of soft tissue sarcomas incidence and survival in children (age 0–14) in Europe, 1978–1997 (Source: ACCIS)

Region	Period	Cases	NOS	Basis of diagnosis			Follow-up	
				MV	DCO	Unknown	1+ days	5+ years
		n	%	%	%	%	%	%
Europe*	1978–1982	855	9	99	< 1	< 1	98	98
	1983–1987	1368	7	99	< 1	< 1	99	90
	1988–1992	1482	6	99	< 1	< 1	98	92
	1993–1997	1406	6	99	< 1	< 1	94	34
British Isles	1978–1982	387	8	99	< 1	0	99	99
	1983–1987	413	8	98	< 1	2	100	100
	1988–1992	472	6	97	< 1	2	99	99
	1993–1997	361	8	96	< 1	2	99	87
East	1978–1982	132	15	100	0	0	96	100
	1983–1987	126	10	99	0	0	98	98
	1988–1992	139	8	100	0	0	97	97
	1993–1997	147	7	100	0	0	97	30
North	1978–1982	101	9	99	0	< 1	98	98
	1983–1987	134	10	100	0	0	99	100
	1988–1992	148	7	100	0	0	97	99
	1993–1997	153	3	99	< 1	< 1	99	25
South	1978–1982	61	5	97	3	0	97	91
	1983–1987	97	5	99	0	0	100	100
	1988–1992	75	5	100	0	0	100	96
	1993–1997	80	8	100	0	0	100	36
West	1978–1982	34	12	85	0	0	96	86
	1983–1987	452	6	99	0	< 1	99	90
	1988–1992	594	6	99	0	< 1	97	83
	1993–1997	665	6	100	0	< 1	89	12

n, number of cases; NOS, cases with unspecified histology, comprising ICCC subgroup IXe.
* Europe includes the data of the former German Democratic Republic, which are not included in any of the regions; 1+ days, cases followed-up for 1 or more days, as a percentage of all cases in the registries with follow-up; 5+ years, cases followed-up for 5 or more years, as a percentage of all those not deceased by the closing date; DCO, cases registered from death certificate only; MV, microscopically verified diagnosis.

Table 3 – Definition of the topographic categories of rhabdomyosarcoma and the numbers of cases within each category in the complete data-sets composed of non-overlapping registries and periods (Source: ACCIS)

Site of tumour	ICD-O-2 topography code (14)	*n*
Head and neck	C00.0-C14.8, C30.0-C32.9, C41.0-C41.1, C44.0, C44.2-C44.4, C47.0, C49.0, C76.0	940
Orbit	C69.0-C699, C44.1	313
Pelvis	C41.4, C47.5, C49.5, C76.3	389
Genito-urinary	C51.0-C57.9, C60.0-C63.9, C64.9-C68.9	661
Limbs	C40.0-C40.9, C44.6, C44.7, C47.1, C47.2, C49.1, C49.2, C76.4, C76.5	432
Other	All codes not listed in another category	607
Not otherwise specified	C76.1, C76.2, C76.7, C76.8, C809	23
Total		3365

Europe, 1978–1997.

Table 4. Overall, the age-standardised rates were 3.5 cases per million children for embryonal RMS, 0.8 for alveolar type and 1.2 for the other RMS group. Only 6 cases of Kaposi's sarcoma were recorded, with the overall ASR of 0.015 per million per year.

For all STS combined, the highest incidence rates were found in the North and the lowest in the East and West. Among region-specific differences by ICCC subgroup, the most striking was the high risk of fibrosarcomas in the North, affecting especially age groups 0 and 10–14 years (Tables 4 and 5). The male:female ratio for all STS combined was 1.2 and for RMS 1.4. The overall excess of RMS in boys was observed in all the regions (Table 4).

The age-specific incidence curves for NRSTS were U-shaped; highest in the first year of life and after the age 10 years, when mainly the incidence of the other specified STS

Table 4 – Number of cases (n), incidence rates and data quality indicators in the data-sets included in the analysis of incidence of soft tissue sarcomas (STS) in children diagnosed in Europe in 1988–1997 (Source: ACCIS)

	n	Incidence rates per million					M/F	MV	DCO
		Age specific				ASR			
		0	1–4	5–9	10–14	0–14[a]		%	%
IX. Soft tissue sarcomas									
EUROPE	3571	14.5	11.0	7.1	8.0	9.1	1.2	*99	0.3
British Isles region	873	14.6	11.9	7.5	8.3	9.6	1.2	*97	0.7
East region	457	14.0	10.6	6.1	7.2	8.4	1.2	*100	0.0
North region	301	21.4	12.3	7.6	10.9	11.1	1.3	*99	0.3
South region	358	13.0	11.4	8.3	7.9	9.5	1.2	98	0.6
West region	1582	13.8	10.3	6.8	7.8	8.7	1.3	*99	0.0
IXa. Rhabdomyosarcoma									
EUROPE	2071	6.6	8.5	4.4	3.0	5.4	1.4	*99	0.2
British Isles region	496	6.0	9.3	4.6	2.7	5.6	1.3	*99	0.2
East region	246	6.2	7.8	3.8	2.2	4.8	1.5	*100	0.0
North region	160	10.4	9.9	3.6	3.7	6.1	1.7	*99	0.6
South region	214	7.6	9.7	5.1	2.8	6.1	1.4	*98	0.9
West region	955	6.1	7.8	4.5	3.4	5.4	1.4	*100	0.0
IXb. Fibrosarcomas									
EUROPE	459	3.0	0.6	0.8	1.6	1.1	1.0	97	0.4
British Isles region	99	2.0	0.6	0.8	1.6	1.1	0.9	92	2.0
ast region	75	3.1	1.0	0.6	1.9	1.3	1.2	100	0.0
North region	64	5.7	0.4	2.0	3.5	2.2	0.9	100	0.0
South region	47	3.6	0.5	1.3	1.1	1.2	0.9	98	0.0
West region	174	2.9	0.5	0.6	1.2	0.9	1.1	98	0.0
IXd. Other specified STS									
EUROPE	812	3.6	1.5	1.3	2.8	2.0	1.0	99	0.1
British Isles region	216	4.6	1.7	1.6	3.2	2.3	1.1	97	0.5
East region	108	3.1	1.4	1.2	2.8	1.9	0.8	100	0.0
North region	61	4.7	1.3	1.3	3.3	2.2	0.9	100	0.0
South region	63	0.9	0.7	1.1	2.7	1.4	0.9	98	0.0
West region	364	3.5	1.6	1.3	2.6	2.0	1.0	100	0.0
IXe. Unspecified STS									
EUROPE	223	1.4	0.5	0.4	0.6	0.6	1.2	97	0.4
British Isles region	60	2.0	0.4	0.4	0.8	0.7	0.9	92	1.7
East region	28	1.6	0.5	0.5	0.3	0.5	0.8	100	0.0
North region	16	0.5	0.7	0.7	0.4	0.6	1.7	100	0.0
South region	33	0.9	0.5	0.6	1.2	0.8	1.1	100	0.0
West region	86	1.2	0.4	0.3	0.5	0.5	1.6	*98	0.0

Age-standardised rate adjusted to world standard (ASR); M/F, ratio of the ASR in males (M) and females (F); microscopically verified diagnosis (MV); registrations from death certificate only (DCO). Both genders combined.

* The standardised rate ratio of the sex-specific age-adjusted rates was statistically significant at 5% level.

rose again (Fig. 1). This pattern was similar for both genders and for all the five regions (data not shown). As seen in Fig. 1, the incidence rates for RMS peaked at 2–3 years, decreasing thereafter. The shape of the age-specific curve for RMS was mainly influenced by that of embryonal subtype, while it was much flatter for the other RMS subtypes. Age-specific rates for alveolar RMS were about 1 per million and the curve was almost flat (Fig. 2). Figure 3 shows the distribution of RMS by histological subtypes and sites. Embryonal type represented close to 80% of genito-urinary or orbital rhabdomyosarcoma and only about 30% of tumours developing in limbs, where the alveolar type was the most common. For the other sites, the embryonal type comprised around 60% of tumours and the alveolar 10–20% (Fig. 3). For all sites combined the 'other and not otherwise specified (NOS) histologies' consisted largely of unspecified RMS (93%), the remainder being pleomorphic RMS (5%) and mixed type RMS (2%).

Table 6 shows the incidence rates of rhabdomyosarcoma at various body sites. The most common site of occurrence was head and neck, which, if orbit is included, was almost twice as common as any other group of sites. Unspecified sites were extremely rare. Each group of sites occurred more often in younger than older children; this pattern was least marked for limbs (Fig. 4). The predominance of boys was seen for several groups of sites (Fig. 4). The male to female ratio was highest for genito-urinary sites and for pelvis. The sex ratio was close to unity for limbs and 'other' (Table 6).

Incidence trends refer to 5111 cases of STS diagnosed during 1978–1997. Twenty-one cases were multiple primary

Table 5 – Geographical differences in incidence (IRR, incidence rate ratio) of childhood soft tissue sarcomas (STS) diagnosed in Europe in the period 1988–1997, as derived from Poisson regression model adjusted for gender and age-group (Source: ACCIS)

Region	*n*	IX Soft tissue sarcomas	IXa Rhabdomyosarcoma	IXb Fibrosarcoma	IXd Other specified STS	Ixe Unspecified STS
		IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)
British Isles	873	1	1	1	1	1
East	457	0.9 (0.78–0.98) *	0.8 (0.72–0.98)*	1.2 (0.91–1.66)	0.8 (0.64–1.01)	0.8 (0.49–1.21)
North	301	1.2 (1.01–1.32)*	1.1 (0.91–1.30)	2.2 (1.57–2.95) ***	0.9 (0.70–1.25)	1.0 (0.56–1.69)
South	358	1.0 (0.87–1.11)	1.1 (0.88–1.26)	1.1 (0.77–1.54)	0.7 (0.50–0.88)**	1.4 (0.91–2.14)
West	1582	0.9 (0.83–0.99)*	1.0 (0.87–1.08)	0.9 (0.68–1.12)	0.8 (0.71–0.99)*	0.7 (0.52–1.00)

n, number of cases included in the analyses.
* $P < 0.05$.
** $P < 0.01$.
*** $P < 0.001$.

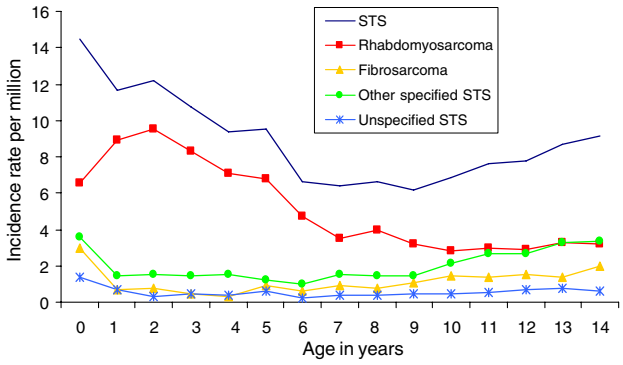

Fig. 1 – Age-specific incidence rates of soft tissue sarcomas (STS) by diagnostic subgroup in European children aged 0–14 years diagnosed during 1988–1997. Both genders combined (*n* = 3571). Source: ACCIS.

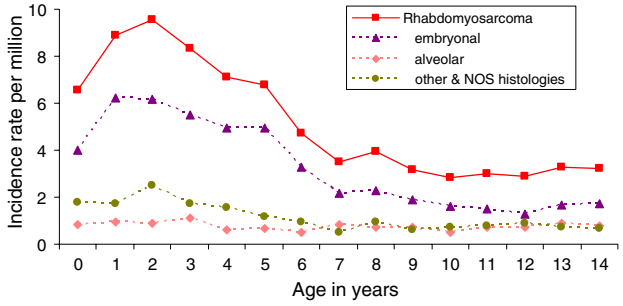

Fig. 2 – Age-specific incidence rates of rhabdomyosarcoma by histological subtypes in European children aged 0–14 years diagnosed during 1988–1997. Both genders combined (*n* = 2071). Source: ACCIS.

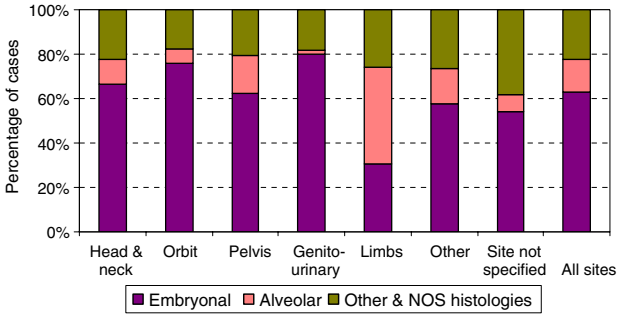

Fig. 3 – Distribution of rhabdomyosarcoma by histological subtype and primary site in European children aged 0–14 years diagnosed during 1988–1997, both genders combined (*n* = 2071). NOS, not otherwise specified. Other and NOS histologies include pleomorphic, mixed type and unspecified rhabdomyosarcoma. Source: ACCIS.

tumours. The percentage of microscopically verified diagnoses ranged from 97% to 100% between European regions and periods and the proportion of DCO was less than 1% in the registries with the access to this type of source of data (Table 2). Rates for all STS combined rose across the four periods (by about 1.8% per year), although the increase was limited to the subgroups of RMS (the embryonal type) and other specified STS (Table 7). Among the groups of sites, significant increase, was only seen for genito-urinary sites (Table 6), with the ASRs rising as follows: 0.9 in 1978–1982, 1.0 in 1983–1987, 1.2 in 1988–1992 and 1.1 in 1993–1997. A decrease, albeit non-significant, was observed in the rates for pelvis. The incidence of STS and RMS increased in all geographical regions except the West, while the increase in other specified STS was limited to two regions, the British Isles and the North (Fig. 5). There was no change in incidence for fibrosarcoma and unspecified STS (Table 7).

3.2. *Survival*

A total of 3342 children with STS diagnosed in 1988–1997 were included in the survival analyses. One hundred and twenty-three cases were excluded because the follow-up was shorter than 1 day from diagnosis, which explains the difference between the numbers given in Tables 4 and 8. The extent of the exclusion of cases from survival analyses may be evaluated from Tables 1 and 2. Survival data are presented for both genders combined, due to similar survival rates in boys and in girls.

For the pooled European data, the 5-year survival for children with STS was 65%, greatly influenced by the survival of children with RMS (63%), as seen in Table 8. There were differ-

Table 6 – Incidence and survival for children aged 0–14 years with rhabdomyosarcoma, according to site of tumour, Europe 1978–1997 (Source: ACCIS)

	Incidence							Survival								
	1988–1997							1978– 1997			1988–1997				1978–1997	
	n	Age-specific rates				ASR	M/F	5-year								
		0	1–4 years	5–9 years	10–14 years	0–14 years		*n*	AAPC	*P*	*n*	OS	95% CI		*n*	P(trend)
Head & neck	564	1.0	2.2	1.5	0.8	1.5	1.3	897	0.2	0.77	541	59	55	64	792	0.004
Orbit	190	0.5	0.6	0.6	0.3	0.5	1.5	311	0.1	0.96	181	83	76	88	270	0.17
Pelvis	248	0.9	1.0	0.5	0.4	0.7	1.8	355	−1.0	0.40	232	54	47	60	314	0.19
Genito-urinary	403	1.4	2.2	0.5	0.4	1.1	2.4	661	1.8	0.03	384	83	79	87	575	0.0001
Limbs	273	1.3	0.8	0.6	0.6	0.7	1.0	424	0.3	0.76	260	51	44	57	366	0.20
Other	380	1.4	1.6	0.7	0.6	1.0	1.0	574	0.4	0.67	354	50	44	55	494	0.0008
Unspecified	13	.	0.0	0.0	0.0	0.03	1.6	26	−1.1	0.85	10	68	29	88	17	0.002

n, number of cases included in the analyses; ASR, age-standardised rate adjusted to world standard; M/F, ratio of the ASR in males (M) and females (F); AAPC, average annual percent change derived from a Poisson regression model adjusted for gender, age group and region (with the corresponding *P*-value); 5-year OS, 5-year observed survival (with the corresponding 95% CI); *P* (for trend), test for trend in change of the survival curves for the fours successive periods: 1978–1982, 1983–1987, 1988–1992 and 1993–1997.

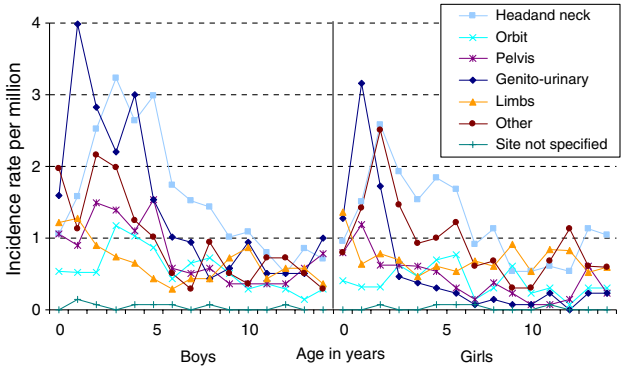

Fig. 4 – Age-specific incidence rates of rhabdomyosarcoma according to the site of tumour. Europe, 1988–1997 (*n* = 2071). Source: ACCIS.

ences in survival according to the site of occurrence (Table 6). The 5-year survival of children with either rhabdomyosarcoma of genito-urinary sites or orbit was 83% (95% CI 79–86), those with head and neck involved was about 60% and for the combined group of the other sites it was 51% (95% CI 48–55) and the difference between these three groups was significant ($P < 0.0001$). The children with fibrosarcomas had the highest 5-year survival (82%), while those with the other specified STS had 61% and those with unspecified, 59%. Survival data for children with Kaposi's sarcoma are not presented due to the small number of observations. The children with embryonal subtype of RMS fared better than those with alveolar or unspecified subtype ($\chi^2 = 55.5$, $P < 0.0001$). Children in the age group 1–9 years experienced higher survival rates compared with the other two age groups, and this was especially so for those with alveolar or unspecified type (Table 9). For children with embryonal RMS, orbit (84%) and genitourinary (83%) were the most favourable primary sites.

Children in the East experienced a lower survival: compared with the rest of Europe, the number of deaths observed (O) in the East region was twice that expected (E): O = 142 versus E = 73 for RMS ($P < 0.0001$) and O = 17 versus E = 8 for unspecified STS ($P = 0.0016$). Smaller significant differences

Table 7 – Age-standardised incidence rates (ASR) of soft tissue sarcomas (STS) diagnosed in children aged 0–14 years in Europe during 1978–1997 (Source: ACCIS)

	n	ASR				AAPC	*P*
		1978–1982	1983–1987	1988–1992	1993–1997		
IX Soft tissue sarcomas	5111	7.3	8.2	9.0	9.6	1.8	< 0.0001
IXa Rhabdomyosarcoma	2940	4.2	5.0	5.4	5.4	1.3	< 0.0001
– embryonal	1790	2.2	3.1	3.5	3.6	1.7	< 0.0001
– alveolar	419	0.46	0.65	0.77	0.83	0.6	0.605
– other	731	1.6	1.3	1.2	1.0	−0.03	0.964
IXb Fibrosarcoma	721	1.2	1.2	1.2	1.1	0.01	0.985
IXc Kaposi sarcoma	10	0.028	0.014	0.011	0.014	0.01	0.999
IXd Other specified STS	1084	1.3	1.4	1.8	2.5	2.8	< 0.0001
IXe Unspecified	356	0.63	0.58	0.55	0.60	0.04	0.971

n, number of cases included in the analyses.
Average annual percent change (AAPC) was derived from poisson regression model of rate on calendar year, adjusted for gender, age group and region.

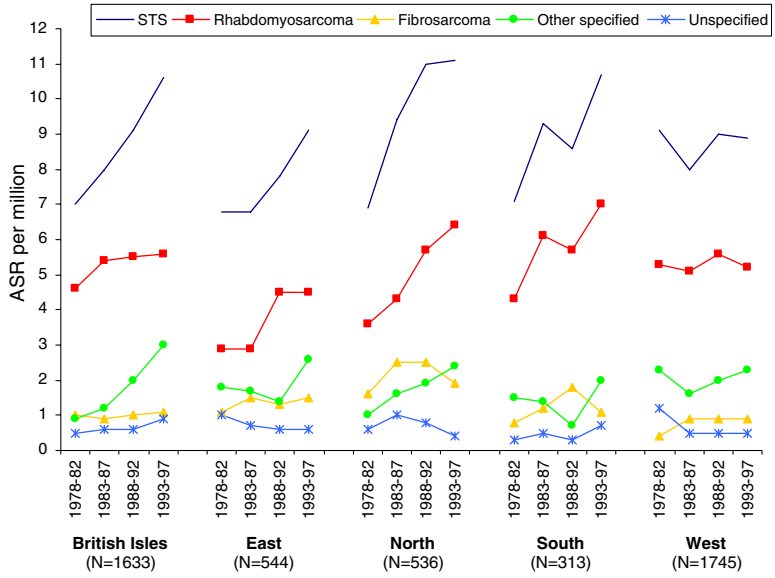

Fig. 5 – Trends of incidence of soft tissue sarcomas (STS) by geographical region and diagnostic group in children aged 0–14 years in Europe, 1978–1997. ASR, age-standardised rates (World standard). Source: ACCIS.

were also observed among the remaining four regions for STS group combined ($P = 0.0005$) and other specified ($\chi^2 = 10.62$, $P = 0.014$). In general, survival was higher in the North and South compared with the West and the British Isles (Table 8).

Among the age groups, children aged 5–9 years had most favourable outcome, infants the least favourable and the others intermediate. This pattern was consistent among different STS subgroups and regions, notably for the children with RMS in the age groups 0 and 10–14 years. In contrast, infants with fibrosarcomas have relatively good outcome compared with other age groups (Table 10).

Time trends in survival were evaluated from the record of 4868 children with STS diagnosed in the period 1978–1997 (further 148 cases with a follow-up less than 1 day were excluded from the analysis). Five-year survival of children with STS was increasing from 54% in 1978–1982 to 66% in 1993–1997 (Table 11). Over the four periods, the 5-year survival improved by 14 percentage points for both RMS and fibrosarcomas and 9 percentage points for other specified STS. Table 6 shows that the significant improvement in survival was seen for the groups of patients with rhabdomyosarcoma occurring in head and neck, genito-urinary system and the sites classified as 'other'. This is illustrated in Fig. 6. In the unspecified STS subgroup, the 5-year survival (95% CI) for the 4 successive periods was 46% (95% CI 34–57), 52% (42–62), 61% (50–71) and 53% (40–64); no improvement was observed in the last decade. In the most recent periods, the highest survival was observed in the North and South regions (Fig. 7). Survival of children with STS virtually did not change in the East region: no improvement was observed for RMS after the increase in survival between the two first periods and only a minimal improvement was seen for fibrosarcomas. As a result, children in East Europe show the lowest survival rates in every period and for each histological subtype. The 5-year cumulative survival of children with RMS increased in all age groups during the study period, except for infants under 1 year of age (Table 12). The NRMS have shown a more stable trend.

4. Discussion

The present study is the largest report on incidence and survival of childhood STS. The ACCIS database provided a uniquely large data-set of almost 6000 cases. The analyses were performed including only quality registries considered comparable. This does not preclude remaining differences in the diagnostic, registration and coding practices. Main indicators of data quality (proportions of microscopically verified cases, cases registered from death certificate only and those classified as unspecified STS) were comparable by period and by region.

STS arise from a variety of anatomical sites, classified within the ICCC according to histology type.[13] The incidence rates observed were comparable with those previously described among predominantly white populations in the international studies.[1,17,18] However, in the North, rates for STS all combined, as well as within subgroups of rhabdomyosarcoma, fibrosarcomas and other specified, were higher than elsewhere, although still within the rates observed in the Nordic countries previously.[1] It might be worth investigating whether these high rates, particularly in infants and for also fibrosarcomas in children aged 10–14 years may be due to the differences in diagnosis or classification of these tumours in the registries included within the North.

Advances in laboratory techniques have allowed better characterisation of the STS and their subtypes differentiate them from other tumours. Fibrosarcomas might have been diagnosed more frequently than RMS in some registries previously,[1] when immunochemistry and electromicroscopy techniques were not available.[6,10] For example, in the early 1990s a new variant of RMS, spindle cell RMS – was described, which might have been classified as fibrosarcoma in the absence of

Table 8 – Number (n) of children (0–14 years) with soft tissue sarcoma diagnosed in Europe in the period 1988–1997, 5-year survival rates (5-y%) and 95% confidence interval (95% CI), by diagnostic groups and geographical regions (Source: ACCIS)

	n	5-y%	95% CI
IX. SOFT-TISSUE SARCOMAS			
Europe	3342	65	63–66
British Isles	862	63	60–66
East region	449	50	45–55
North region	295	74	68–79
South region	326	74	68–78
West region	1410	66	64–69
Log-rank test			$P < 0.0001$
IXa. Rhabdomyosarcoma			
Europe	1962	63	60–65
British Isles	494	62	58–67
East region	244	40	34–47
North region	158	67	59–74
South region	197	71	64–77
West region	869	67	63–70
Log-rank test			$P < 0.0001$
IXb. Fibrosarcoma			
Europe	421	82	78–86
British Isles	97	82	73–88
East region	74	78	67–86
North region	63	89	78–94
South region	44	80	64–89
West region	143	81	73–87
Log-rank test			$P > 0.05$
IXc. Other specified soft tissue sarcomas			
Europe	761	61	58–65
British Isles	213	59	52–66
East region	107	56	46–65
North region	59	74	59–85
South region	58	76	62–85
West region	324	59	53–65
Log-rank test			$P < 0.01$
IXd. Unspecified soft tissue sarcomas			
Europe	194	59	51–65
British Isles	57	53	39–65
East region	24	33	16–52
North region	15	73	44–89
South region	27	77	56–89
West region	71	62	48–73
Log-rank test			$P < 0.01$

Both genders combined.

molecular techniques.[19] Also, cases of undifferentiated neuroblastoma or other small blue cell tumours might have been grouped with RMS or pPNET/Ewing's sarcoma of the soft-tissues before the molecular and genetic techniques became available.[20] The impact of modern diagnostic laboratory techniques on the classification criteria of STS has been examined in a hospital-based study of 281 STS cases diagnosed during 1972–1994 in Denmark.[10] The overall disagreement between original and reviewed diagnosis was 42%. Agreement was less than 20% for fibrosarcomas, which might have been either over-diagnosed, or misclassified as a benign tumour, mostly fibromatosis. Applying the results of the Danish study[10] to the ICCC categories[13] would result in a decrease of more than 50% in the subgroup of fibrosarcomas, and an increase of 40% in the subgroup of other specified STS; the changes possibly varying over time. Such changes would contribute to explaining the temporal trends of incidence observed within the diagnostic subgroups. Even nowadays, differential pathological diagnosis may be difficult between fibrosarcoma and fibromatosis in infants,[21] between neurofibrosarcoma and malignant peripheral nerve sheath tumours (MPNST) or between malignant and benign behaviour of neurofibromatosis. These difficulties may be reflected to a various extent in the observed regional differences of incidence rates by subgroup. We cannot exclude that the fibrosarcoma group may be over-represented in the North due to classification of benign lesions as malignant. However, despite a possible shift over time from the fibrosarcomas and neurofibrosarcomas group to other diagnostic subgroups in the North, this region remains the one with the largest proportion of fibrosarcoma and neurofibrosarcoma cases during the whole study period, and with relatively high rates in the other subgroups.

The slightly lower incidence rates of STS in the East might be the result of some misclassification, since 100% of cases were microscopically verified within STS, while this percentage was 96% for the total childhood cancers [Stiller, Marcos-Gragera, Ardanaz and colleagues, this issue]. Some STS cases without microscopic verification might therefore have been included in the group of unspecified neoplasms (XIIb) of the ICCC.[13] Under-ascertainment cannot be excluded as the explanation of the slightly lower incidence rates of STS in the East, if this is a problem for all tumours in general.

The Surveillance Epidemiology and End Results (SEER) program of the USA has reported time trends for STS,[18,22–24] which are consistent with those observed in this study: the increasing incidence for STS, RMS and the other specified STS. Any classification shifts between subgroups within STS would not explain the increase in the combined group of STS. Although neuroblastoma misdiagnosed as peripheral primitive neuroectodermal tumour (M-9364/3) might have been classified as STS in the past, this cannot explain the rise of STS incidence, because the incidence of neuroblastoma [Spix and colleagues, this issue], and all childhood cancers was also increasing [Kaatsch and colleagues, this issue]. Because of the dramatic improvements in survival, multiple primary tumours could have contributed to the rising of childhood cancer incidence, but our data-set only comprised 21 multiple primaries among 5111 cases of STS included in incidence time trends. HIV, the well-established risk factor for Kaposi's sarcoma did not affect the presented time trends, since only a few cases were present in the ACCIS data. Kaposi's sarcoma was shown to be rare among HIV-infected children in Europe and North America.[4]

The described variations in diagnostic, classification and registration criteria may explain the geographical differences in incidence observed within Europe. The increase in incidence over time is probably also affected, although to a lesser extent, since the rise is observed in the majority of the tumour groups concerned by misclassification. Further surveillance and aetiological studies may help to disentangle the contribution of the artefacts and the risk factors.

The improvement in survival of children with RMS in this and other studies has been ascribed to advances in therapeutic

Table 9 – Number (n) of children (0–14 years) with rhabdomyosarcoma diagnosed in Europe in the period 1988–1997, 5-year survival rates (5-y%) and 95% confidence interval (95% CI) by histological subtypes and age groups (Source: ACCIS)

	Alveolar			Embryonal			Other specified		
	n	5-y%	95% CI	*n*	5-y%	95% CI	*n*	5-y%	95% CI
Europe	292	44	38–50	1247	67	65–71	423	61	56–66
Age group (years)									
0	21	42	21–61	99	61	51–70	39	61	43–75
1–9	179	50	42–57	951	68	60–71	291	66	60–71
10–14	92	34	24–44	197	69	61–75	93	47	36–57

Both genders combined.

Table 10 – Number (n) of children (0–14 years) with soft tissue sarcoma (STS) diagnosed in Europe in the period 1988–1997, 5-year survival rates (5-y%) and 95% confidence interval (95% CI) by diagnostic groups according to ICCC, age groups and geographical regions (Source: ACCIS)

	Age 0			Age 1–4 years			Age 5–9 years			Age 10–14 years		
	n	5-y%	95% CI	*n*	5-y%	95% CI	*n*	5-y%	95% CI	*n*	5-y%	95% CI
IX. Soft-tissue sarcoma	336	57	52–63	1108	64	60–66	885	70	67–73	1013	63	60–66
IXa. Rhabdomyosarcoma	159	58	50–66	859	65	61–68	562	68	62–71	382	55	49–60
IXb. Fibrosarcoma	71	86	75–92	54	74	60–84	104	86	78–92	192	81	74–86
IXd. Other specified STS	79	41	30–52	151	53	44–61	165	72	64–79	366	65	59–69

Both genders combined.

Table 11 – Time trend survival rates. Number (*n*) of children (0–14 years) with soft tissue sarcomas (STS) diagnosed in the period 1978–1997, 5-year survival rates (5-y%) and 95% confidence interval (95% CI) by diagnostic groups according to ICCC and period of diagnosis. Both genders combined (Source: ACCIS)

Period of diagnosis	IX. Soft tissue sarcomas			IXa. Rhabdomyosarcoma			IXb. Fibrosarcoma			IXd. Other specified STS		
	n	5-y%	95% CI	*n*	5-y%	95% CI	*n*	5-y%	95% CI	*n*	5-y%	95% CI
1978–1982	831	54	51–58	466	51	46–55	143	67	59–74	148	55	46–62
1983–1987	1343	62	59–64	801	59	56–62	205	73	66–79	238	65	59–71
1988–1992	1384	65	62–67	829	64	61–68	186	82	76–87	286	57	51–62
1993–1997	1310	66	63–68	732	65	61–69	146	81	73–87	353	64	58–69
Log-rank test for trend		$P < 0.001$			$P < 0.0001$			$P < 0.0001$			$P < 0.05$	

options (adaptation of chemotherapy dose intensity, improvements in surgical approaches and changes in indication for radiation therapy techniques) and the development of prospective multi-centre randomised trials.[25–32] Today's objectives are to treat patients according to the well-defined risk factors which would combine the pre-treatment biological factors with the classical post-surgical ones (e.g. the new staging Intergroup Rhabdomyosarcoma Study Group System).[33] The proportions of children included in the trials in different European countries during the study varied from 30% to 60%.[27,28,31]

Large cooperative study groups focusing on treatment of childhood RMS were started in the early 1970s. The North American Intergroup Rhabdomyosarcoma Study Group (IRSG, now the Soft Tissue Sarcoma Committee of the Children's Oncology Group) played a pivotal role in designing clinical trials.[26] Three major study groups were activated in Europe: the International Society of Paediatric Oncology (SIOP),[27] the Italian and German co-operative groups.[28–30]

All the European groups shared the same treatment philosophy based on the use of intensive initial chemotherapy (to avoid radical mutilating surgery) and a local therapy tailored to the tumour response. However, several differences in the treatment have emerged related to the method and timing of local therapy. The German and Italian cooperative groups administer local therapy depending on tumour site, patient's age and response to primary chemotherapy.[29,31]

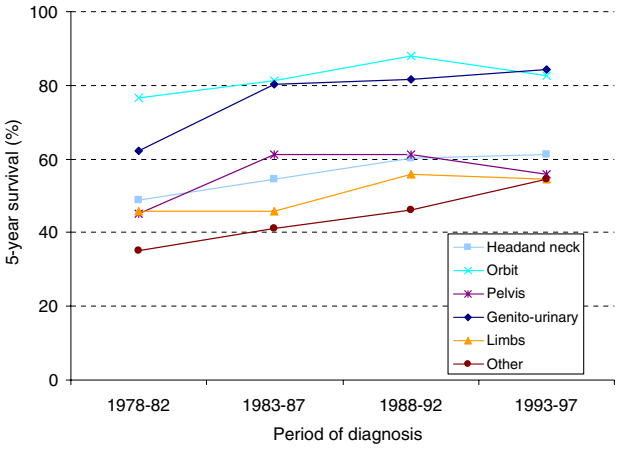

Fig. 6 – Time trends in 5-year survival of children diagnosed with rhabdomyosarcoma of various body sites at ages 0–14 years in the periods shown in Europe. Both genders combined. The total number of 2811 cases were included in the analysis, excluding a small group of 17 patients with site of tumour not specified. Source: ACCIS.

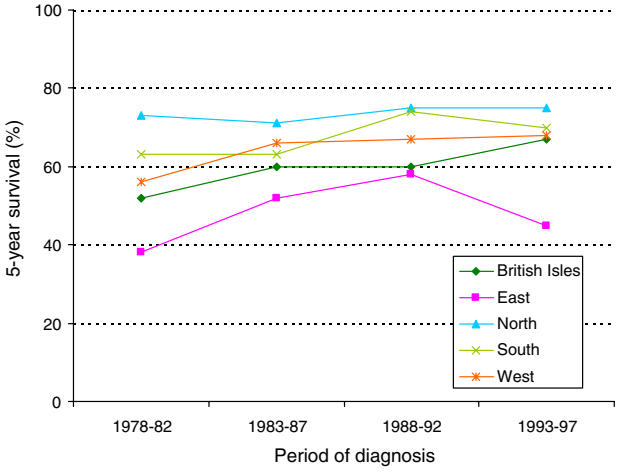

Fig. 7 – Five-year survival of children diagnosed with soft tissue sarcomas at ages 0–14 years in Europe in the periods and regions shown. Both genders combined (n = 4868). Source: ACCIS.

The SIOP Group continued chemotherapy as long as continuous regression was demonstrated, reserving surgery and/or radiation therapy for patients who did not achieve complete remission.[34] This approach was expected to produce fewer late complications, however local relapse rate was higher in the SIOP studies than in other groups.[29,30] In the SIOP trials, relapsed patients required very aggressive therapy, the toxicity of which is not yet documented.[34] Overall, the results obtained by the Intergroup Rhabdomyosarcoma Study Group trials have been superior to those reported in the SIOP trials.[26] However the population-based data for the period 1988–1997 in this study did not show a significant difference (P = 0.55) in survival between the RMS patients reported from Germany and Italy (n = 669, the 5-year survival for combined data was 69% (95% CI 65–72) and those reported from other registries grouped within the South or West (n = 397, 5-year survival 66% (95% CI 61–71). Our results show almost no improvement in survival in the East, whether for RMS or for NRSTS. The reasons for this are complex and are discussed in detail in the overview paper [Pritchard-Jones and colleagues, this issue]. Within RMS patients the major improvement has been observed in patients with localised embryonal tumours. Alveolar RMS was consistently associated with poor prognosis. In clinical trials, the tumour sites in the limbs, para-meningeal head-neck, bladder/prostate, trunk, pelvis were found to be unfavourable prognostic factors, together with the size of tumour larger than 5 cm; regional lymph node involvement and patient's age <1 and >10 years.[6,7,25,29,31,32] In our study the favourable sites were those of orbit and genito-urinary system, compared with the involvement of other sites and the conclusions were concurrent with clinical trials also regarding the age at diagnosis. While survival of patients with orbital RMS did not change significantly during the study period, that of genito-urinary system improved considerably. Unfortunately, our data do not permit evaluation of survival by stage at diagnosis, which data might be useful to collect in population-based series, in order to modulate comparison between regions. In hospital series, 5-year survival of patients with metastatic RMS, remains disappointing at 20–30% in spite of the use of high-dose chemotherapy.[30]

Children with NRSTS are usually staged according to the system adopted for RMS, although for these tumours with limited chemo-sensitivity, the extent of surgical resection is of overriding prognostic importance. Strategies for the management of NRSTS in children generally derive from experience with RMS. Complete surgical excision is the mainstay of treatment for 'adult type' NRSTS, but patients with unresectable tumours at diagnosis are often offered neoadjuvant chemotherapy with the aim of permitting subsequent radical excision, even if it is not clear whether this translates into a survival advantage.[35,36] The limited clinical information in the ACCIS data-base reduces the possibility of interpreting the causes of inter-regional differences in survival. Collection of additional information of prognostic value (such as extent of disease at diagnosis, treatment, place of treatment) should be considered in future interpretation within the ACCIS study.

In conclusion, we observed an increase in the incidence rates of STS over the study period and variations of incidence between regions. The changes in diagnostic and classification criteria may contribute partially to explanation of these patterns, although they probably do not explain completely the increase of almost 2% per year, mostly limited to the genito-urinary rhabdomyosarcoma, largely represented by the embryonal type. Detailed studies, focusing on a comparison on diagnostic and registration practices in the individual registries would help to quantify the extent of artificial versus risk-related variations in incidence. Investments and improved collaboration between the European countries may contribute to reduce the geographical differences in survival within Europe and help to achieve the most favourable outcome everywhere.

Table 12 – Time trend survival rates. Number (*n*) of children (0–14 years) with rhabdomyosarcoma, fibrosarcoma and other specified soft tissue sarcoma (STS) diagnosed in the period 1978–1997, 5-year survival rates (5-y%) and 95% confidence interval (95% CI) by period and age groups. Both genders combined (Source: ACCIS)

Period of diagnosis	Age 0			Age 1–4			Age 5–9			Age 10–14		
	n	5-y%	95% CI	*n*	5-y%	95% CI	*n*	5-y%	95% CI	*n*	5-y%	95% CI
IXa. Rhabdomyosarcoma												
1978–1982	47	44	29–57	182	51	44–58	148	56	47–63	89	47	37–55
1983–1987	73	56	44–67	318	63	57–68	231	59	53–65	179	53	46–60
1988–1992	65	66	53–76	362	67	62–72	248	66	60–72	154	53	45–61
1993–1997	63	56	41–68	318	69	63–74	206	70	62–76	145	56	47–65
Log-rank test for trend		$P > 0.05$			$P < 0.0000$			$P < 0.0000$			$P < 0.0000$	
IXb. Fibrosarcoma												
1978–1982	21	76	52–89	19	67	41–84	44	64	48–76	12	83	48–96
1983–1987	31	87	68–95	28	71	50–84	44	75	59–85	20	80	55–92
1988–1992	33	85	67–93	25	67	44–82	53	86	74–90	17	100	–
1993–1997	26	88	68–96	21	73	46–88	31	89	69–96	15	78	47–93
Log-rank test for trend		$P > 0.05$			$P > 0.05$			$P < 0.001$			$P > 0.05$	
IXd. Other specified STS												
1978–1982	19	74	48–88	29	45	27–62	41	58	42–69	59	51	37–63
1983–1987	26	68	47–83	43	56	39–69	51	67	52–78	118	68	58–75
1988–1992	36	36	21–51	66	49	37–61	52	67	53–78	132	62	53–70
1993–1997	37	43	26–59	67	55	41–67	82	74	61–83	167	66	57–74
Log-rank test for trend		$P > 0.05$			$P > 0.05$			$P > 0.05$			$P > 0.05$	

Conflict of interest statement

None declared.

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