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Non-Hodgkin's lymphoma incidence and survival in European children and adolescents (1978–1997): Report from the Automated Childhood Cancer Information System project

M. Isabel Izarzugaza[a,*], *Eva Steliarova-Foucher*[b], *M. Carmen Martos*[c], *Snezana Zivkovic*[d]

[a]*Basque Country Health Department, Registro de Cáncer, Donostia-San Sebastian, 1. 01010 Vitoria-Gasteiz, Spain*
[b]*International Agency for Research on Cancer, 150 Cours Albert Thomas, Lyon, Cedex 08, France*
[c]*Aragon Government Health Department, Public Health Department, Paseo M[a] Agustín, No. 36 50004 Zaragoza, Spain*
[d]*Institute of Public Health of Serbia, Center for Prevention and Control of Non-Communicable Diseases, Childhood Cancer Registry for Central Serbia, 5, Dr Subotica Street, 11000 Belgrade, Serbia & Montenegro*

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ABSTRACT

Non-Hodgkin's lymphomas (NHLs) constitute a large and heterogeneous group of malignant tumours. This paper describes and interprets geographical patterns (1988–1997) and time trends (1978–1997) of NHL incidence and survival in European children and adolescents. All 7702 lymphomas that were not Hodgkin's, were extracted from the Automated Childhood Cancer Information System (ACCIS) database and included in different analyses. In children under 15 years of age and for the period 1988–1997, the overall NHL age-adjusted incidence rate was 9.4 per million and has been increasing over 20 years by 0.9% per year on average ($P = 0.002$). In adolescents aged 15–19 years, the age-specific incidence rate was 15.9 per million, increasing annually by 1.7% ($P = 0.007$). Five-year survival of children diagnosed in 1988–1997 was 77%, ranging from 58% in the East to 83% in the West. A substantial increase in survival was observed in all European regions. Systematic monitoring and evaluation of childhood and adolescent data on NHL will contribute to further improvement in public health policy for the young population of Europe.

1. Introduction

Non-Hodgkin's lymphomas (NHLs) constitute a heterogeneous group of malignant tumours, representing 6% of cancers both in children and in adolescents in populations of European descent.[1,2] Mature B-cell neoplasia comprise over 85% of NHL worldwide, of these only Burkitt's lymphoma (BL) and large B-cell lymphomas occur with any significant frequency in children.[3]

Classification of lymphomas, based on morphological features is not simple,[4] as documented by the constant search for best classification.[5–7] The increasingly widespread use of molecular and genetic markers in diagnostics is likely to influence further the classification,[8] prognostic stratification and tailored therapeutic strategies for lymphomas. The aetiology of these tumours is largely unknown. The major known risk factor for mature B-cell neoplasia appears to be an abnormality of the immune system, notably infection with the

* *Corresponding author:* Tel.: +34 945 019235; fax: +34 945 019280.
E-mail address: info5-san@ej-gv.es (M.I. Izarzugaza).
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human immunodeficiency virus (HIV),[3] which is partly responsible for the high rates of some forms of lymphomas in countries heavily affected by HIV, such as Uganda.[2] Another infectious agent is the Epstein Barr virus (EBV), found in about 30% of cases of the endemic variant of Burkitt's lymphoma in industrialised countries.[9] Genetic pathways cannot be excluded, notably translocation of Myc in cases of BL, although this is not entirely specific and has been reported in other tumours.[10]

The project Automated Childhood Cancer Information System (ACCIS) constitutes a large database of childhood and adolescent cancer cases registered in some 80 European regions since 1970.[11] The aim of this study is to describe in detail geographical and temporal pattern of incidence of NHL and survival of affected children and adolescents in Europe and interpret the observed results.

2. Materials and methods

All lymphomas that were not classified as Hodgkin's lymphoma were included in this study, namely the following diagnostic subgroups of the International Classification of Childhood Cancer (ICCC):[12] Non-Hodgkin's lymphoma (IIb), Burkitt's lymphoma (IIc), Miscellaneous lymphoreticular neoplasms (IId) and Unspecified lymphomas (IIe). The remaining lymphoma subgroup, Hodgkin's disease (IIa) is the subject of another study [Clavel and colleagues, this issue]. The classification rules are reprinted in this issue [Steliarova-Foucher, Kaatsch, Lacour and colleagues, this issue]. Due to heterogeneous coding practices across the participating registries, the four ICCC subgroups were pooled in order to avoid artefacts in the geographical and temporal comparison of the subgroups. For completeness, we also provide results for the individual lymphoma subgroups. To avoid confusion between the pooled NHL group and the ICCC NHL subgroup, the relevant code (IIb) is used whenever we refer to the single subgroup.

Altogether, 7702 NHL cases were extracted from the ACCIS database, according to registry-related selection criteria, such as quality of data, temporal and geographical coverage, type of registry (paediatric versus general), and availability of follow-up data. Only the data from registries considered comparable [Steliarova-Foucher, Kaatsch, Lacour and colleagues, this issue] were included in the analyses (Table 1). Overall, 62 population-based cancer registries (13 national, 49 regional) in 19 European countries contributed to this study. The results for adolescents are derived from general cancer registries only.

Basic quality indicators, such as the proportion of microscopically verified diagnoses (%MV), the proportion of cases known as Death Certificates Only (%DCO) and the proportion of unspecified cases, as well as indicators of follow-up, are shown in Table 1.

The pattern of occurrence and geographical differences are based on the cases diagnosed in the most recent and complete decade, 1988–1997. Five geographical regions were defined to compare differences in incidence and survival: British Isles, East, North, South and West (Table 1). Time trends are derived from the database of cases diagnosed between 1978 and 1997 in the areas covered by cancer registration for at least three of the four successive 5-year periods of diagnosis: 1978–1982, 1983–1987, 1988–1992 and 1993–1997. Table 2 shows the distribution of cases, and selected quality indicators, over the periods and regions.

Population at risk for the period of registration was provided by each registry [Steliarova-Foucher, Kaatsch, Lacour and colleagues, this issue]. Age-specific incidence rates were calculated for standard age-groups 0, 1–4, 5–9, 10–14 years in children, and 15–19 years in adolescents. For the age-range 0–14 years, the incidence rates were standardised (ASR) using the world standard population. All rates are expressed per million person-years at risk. The incidence rates and their 95% confidence intervals (95% CIs) were calculated according to standard methods.[13] The rate of change over time is expressed as average annual percent change (AAPC), calculated from a Poisson regression of number of cases on year, adjusted for age, sex and region, as necessary.

Changes in classification of NHLs and possible inconsistencies of coding the same tumour as NHL, HD or leukaemia in different registries and time periods might have influenced the incidence time trends of NHL observed in this study. We have therefore compared the incidence time trends for the three groups of neoplasms, selected according to the same criteria as NHL cases. Leukaemias included in this comparison were those classified into group I of ICCC [12] and the cases of Hodgkin disease were those classified into the subgroup IIa and respectively described in detail elsewhere [Clavel and colleagues; Coebergh, Reedijk, de Vries and colleagues; Stiller, Desandes, Danon and colleagues, this issue].

The registries with acceptable quality of follow-up data were included in the analysis of survival. The individual cases with no follow-up time (DCO cases or losses to follow-up) were excluded from survival analyses. Table 2 shows the proportion of cases included in the survival analyses as an indicator of completeness of the follow-up. Survival was calculated using an actuarial life-table method and differences between entire survival curves were tested by log-rank tests.[13] The asymptotic 95% CIs were calculated.[14]

One, 3, 5 and 10-year observed survival and their 95% CIs were estimated. Time-trend in survival for the successive 5-year periods were tested by a log-rank test [15] and reported for the combined NHL and the ICCC subgroups of lymphomas for both boys and girls. Further general details on material and methods used can be found elsewhere [Steliarova-Foucher, Kaatsch, Lacour and colleagues, this issue].

3. Results

For the decade 1988–1997, 3850 children and 708 adolescents were included in the analyses (Table 3). The combined group of NHL constituted a variable proportion of neoplasm in children and adolescents: 1.7% in infants, 4.5% in children aged 1–4 years, 10% in age group 5–9 years, 9.6% in age-group 10–14 years and 8% in adolescents. Overall proportion in the age-range 0–14 years was 7.2%. Male to female ratio was 2.4, varying between 1 and 3 over the age units. The proportion of microscopically verified diagnoses (histology and/or cytology) was 98.2% (ranging between 95% and 99% by region) and the percentage of cases from DCO was 0.3% (ranging between 0% and 1.5% by region).

Table 1 – Datasets contributed by the European cancer registries for the analyses of non-Hodgkin's lymphoma incidence and survival in children (age 0–14 years) and adolescents (age 15–19 years), with indicators of coverage and data quality (Source: ACCIS)

Region	Registry	Coverage				NOS (IIe)%	Basis of diagnosis			Survival analysis				Notes
		Period	Time-trend	Number of cases by age-range			MV %	DCO %	unknown %	Included		Closing date	FU 5+y %	
				0–14	15–19					*n*	%			
British Isles	IRELAND, National	1994–1997		27	22	35	100	0	0	49	100	31.12.1998	0	
	UNITED KINGDOM, England & Wales	1978–1995	+	1,226	–	3	97	<1	2	1,195	97	31.1.2001	99	P
	UNITED KINGDOM, Northern Ireland	1993–1996		11	9	60	90	0	0	20	100	31.12.1999	12	
	UNITED KINGDOM, Scotland	1978–1997	+	162	95	20	98	0	0	253	98	31.12.1999	77	
East	BELARUS, National	1989–1997		210	–	<1	100	0	0	205	98	1.9.2000	68	P
	ESTONIA, National	1978–1997	+	55	28	18	96	0	0	76	92	31.12.1998	77	
	HUNGARY, National	1978–1997	+	330	–	2	100	–	0	327	99	1.1.2000	87	P
	SLOVAKIA, National	1978–1997	+	277	89	11	98	2	0	334	91	31.12.1997	71	
	GERMANY, NCR (only former East)	1978–1989	+	325	153	4	100	0	0	376	94	31.12.1987	68	S
North	DENMARK, National	1978–1997	+	173	116	17	98	<1	1	275	95	31.12.1997	69	
	FINLAND, National	1978–1997	+	199	89	66	100	0	<1	284	99	31.12.1998	68	
	ICELAND, National	1978–1997	+	4	5	–	100	0	0	9	100	31.12.2000	50	
	NORWAY, National	1978–1997	+	135	86	25	99	0	<1	221	100	1.1.2000	80	
South	ITALY, Piedmont paediatric	1978–1997	+	155	–	5	99	0	0	155	100	31.12.1999	88	P o2
	ITALY, Marche	1990–1997		21	–	10	95	–	0	21	100	30.9.2000	53	P o3
	ITALY, Ferrara	1991–1995		4	2	–	100	0	0	6	100	31.12.1998	100	
	ITALY, Latina	1983–1997	+	12	11	30	100	0	0	23	100	31.12.1998	81	
	ITALY, Liguria	1988–1995		6	3	–	89	0	0	9	100	15.4.2000	100	
	ITALY, Lombardy	1978–1997	+	32	17	4	98	0	0	49	100	23.9.1999	64	
	ITALY, Macerata	1991–1997		4	6	–	90	–	0	10	100	30.9.2000	78	o3
	ITALY, Parma	1978–1995	+	11	6	12	94	0	0	17	100	1.4.1999	89	
	ITALY, Piedmont general	1988–1997		13	11	8	100	0	0	23	96	31.5.2001	75	o2
	ITALY, Ragusa	1983–1997	+	9	7	13	100	0	0	16	100	30.3.2000	67	
	ITALY, Sassari	1992–1995		3	–	–	100	0	0	3	100	30.12.1999	67	
	ITALY, Tuscany	1988–1997		28	19	23	77	2	0	45	96	31.12.1998	43	
	ITALY, Umbria	1994–1996		5	4	11	100	0	0	9	100	31.12.1999	11	
	ITALY, Veneto	1990–1996		30	23	28	96	2	0	52	98	31.12.1998	38	
	MALTA, National	1991–1997		4	4	–	100	0	0	7	88	31.12.1999	100	
	SLOVENIA, National	1978–1997	+	88	37	9	99	0	0	122	98	31.12.1999	78	
	SPAIN, National	1990–1995		140	–	4	97	0	2	139	99	31.12.2000		Z
	SPAIN, Albacete	1991–1997		1	4	–	100	0	0	5	100	15.9.2000	50	
	SPAIN, Asturias	1983–1997	+	43	21	5	97	3	0	60	94	31.12.1997	68	

	SPAIN, Basque Country	1988–1994		37	24	11	100	0	0	61	100	31.12.2000	100	o4
	SPAIN, Canary Islands	1993–1996		13	7	–	95	0	0	–	–	–	–	
	SPAIN, Girona	1994–1997		3	2	–	100	0	0	5	100	31.12.1997	0	o4
	SPAIN, Granada	1988–1997		18	–	–	100	0	0	18	100	31.12.1999	64	G
	SPAIN, Mallorca	1988–1995		5	9	7	100	0	0	13	93	31.12.1998	88	o4
	SPAIN, Navarra	1978–1996	+	31	17	8	94	6	0	45	94	31.12.1997	77	o4
	SPAIN, Tarragona	1983–1997	+	16	8	4	100	0	0	24	100	31.12.1998	61	o4
	SPAIN, Zaragoza	1978–1996	+	50	17	6	94	6	0	64	96	31.12.1996	63	o4
	TURKEY, Izmir	1993–1996		34	22	4	100	–	0	–	–	–	–	
West	FRANCE, Brittany	1991–1997		37	–	3	92	–	8	37	100	1.1.2000	68	P
	FRANCE, Lorraine	1983–1997	+	78	–	–	99	–	0	78	100	1.1.1999	65	P
	FRANCE, PACA & Corsica	1984–1996	+	105	–	–	100	–	0	96	91	31.3.1998	58	P
	FRANCE, Rhone Alpes	1988–1997		104	–	9	99	–	0	97	93	1.6.2000	51	P o1
	FRANCE, Doubs	1978–1996	+	27	11	26	24	–	3	35	92	1.6.2001	29	
	FRANCE, Herault	1988–1997		20	13	3	97	–	0	–	–	–	–	
	FRANCE, Isere	1979–1997	+	65	22	8	99	–	0	–	–	–	–	o1
	FRANCE, Manche	1994–1996		3	2	–	100	–	0	2	100	31.5.2000	0	S
	FRANCE, Bas-Rhin	1978–1996	+	53	22	23	100	–	0	75	100	31.12.1997	67	
	FRANCE, Haut-Rhin	1988–1997		20	3	17	96	–	4	4	100	31.12.1995	100	S
	FRANCE, Somme	1983–1996	+	13	11	8	100	–	0	24	100	15.8.2000	55	
	FRANCE, Tarn	1983–1997	+	10	1	27	100	–	0	–	–	–	–	
	GERMANY, GCCR (East and West)	1991–1997	+	938	–	1	100	–	0	731	78	31.12.1998	46	P
	GERMANY, GCCR (only former West)	1983–1990	+	637	–	2	100	–	0	622	98	31.12.1998	91	P
	NETHERLANDS, National	1989–1995		234	109	3	99	–	0	228	97	31.12.1998	66	S o5
	NETHERLANDS, Eindhoven	1978–1997	+	39	22	10	97	–	0	60	98	1.7.1999	56	o5
	SWITZERLAND, Basel	1983–1997	+	15	6	29	100	–	0	21	100	30.6.2000	100	
	SWITZERLAND, Geneva	1978–1997	+	11	8	11	100	0	0	19	100	31.12.1999	81	
	SWITZERLAND, Graubunden & Glarus	1989–1997		2	2	25	100	0	0	4	100	25.5.2000	33	
	SWITZERLAND, St. Gallen Appenzell	1983–1997	+	19	9	18	96	0	0	27	96	1.2.2001	69	
	SWITZERLAND, Valais	1989–1997		6	2	–	100	0	0	4	100	1.12.1998	100	S

–, Not applicable; +, Included in time trend analyses; FU 5+ y, 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 1978–1987contributed only to analyses of time trends for Europe as a whole. Data on children for 1988–1989 were pooled with GCCR and included in West. For explanation, see Steliarova-Foucher, Kaatsch, Lacour et al. (this issue); NOS, Cases with unspecified histology, including the ICCC category IIe; o1-o5, 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 years; PACA, Provence, Alps, Côte d'Azur; S, Survival analyses were possible only for a restricted dataset (see Steliarova-Foucher, Kaatsch, Lacour et al., this issue); Unknown, Registrations with unknown basis of diagnosis; Z Covers only selected areas, see Steliarova-Foucher, Kaatsch, Lacour, et al. (this issue).

Table 2 – Numbers of cases and indicators of data quality and follow-up by region and age group for time trend analyses of non-Hodgkin's lymphoma incidence and survival in children (age 0–14 years) and adolescents (age 15–19 years) in Europe, 1978–1997 (Source: ACCIS)

Region	Period	Children (age 0–14)							Adolescents (age 15–19)						
		Cases	NOS	Basis of diagnosis			Follow-up		Cases	NOS	Basis of diagnosis			Follow-up	
		n a	% b	MV % c	DCO % d	Unknown % e	0+ days % f	5+ years % g	*n* a	% b	MV % c	DCO % d	Unknown % e	0+ days % f	5+ years % g
Europe[a]	1978–1982	981	10	97	<1	<1	96	98	228	21	97	<1	0	96	0
	1983–1987	1.418	6	99	<1	<1	97	91	247	16	99	<1	0	98	57
	1988–1992	1.508	7	98	<1	<1	98	90	210	30	97	<1	<1	97	88
	1993–1997	1.436	7	99	<1	<1	85	32	205	20	99	0	0	99	73
British Isles	1978–1982	381	4	99	0	<1	96	98	21	38	100	0	0	95	0
	1983–1987	351	5	97	<1	2	97	100	27	26	100	0	0	100	63
	1988–1992	404	4	95	<1	3	99	99	19	26	100	0	0	100	123
	1993–1997	252	6	95	2	2	98	86	28	29	96	0	0	100	59
East	1978–1982	166	7	97	2	0	92	100	34	29	97	0	0	97	0
	1983–1987	185	5	100	0	0	94	97	25	8	100	0	0	96	133
	1988–1992	178	4	99	<1	0	96	99	29	10	97	0	0	93	129
	1993–1997	133	8	98	2	0	97	31	29	14	100	0	0	93	54
North	1978–1982	127	39	98	<1	2	100	98	58	34	100	0	0	100	0
	1983–1987	122	31	100	0	0	100	100	77	31	100	0	0	100	44
	1988–1992	112	42	98	0	<1	100	100	77	48	99	0	1	100	77
	1993–1997	150	34	99	0	<1	100	24	84	31	99	0	0	100	69
South	1978–1982	115	9	97	2	0	98	98	18	17	94	6	0	94	0
	1983–1987	128	5	99	0	0	98	100	32	9	94	3	0	94	24
	1988–1992	109	6	97	2	0	97	96	50	14	96	4	0	96	52
	1993–1997	95	6	99	1	0	99	30	41	5	100	0	0	100	91
West	1978–1982	48	19	81	0	2	100	86	26	12	81	0	0	100	0
	1983–1987	504	4	98	0	0	98	91	28	4	96	0	0	100	38
	1988–1992	652	4	99	0	0	97	81	35	34	91	0	0	93	67
	1993–1997	806	1	100	0	0	74	18	23	4	100	0	0	100	92

0+ 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. *n*: Number of cases. NOS: Cases with unspecified histology or site, includes ICCC subgroup IIe.

a Europe includes East Germany, not included in any of the regions.

Table 3 – Incidence rates of non-Hodgkin lymphomas (Combined Group: IIb + IIc + IId + IId) per million in 1988–1997 (Source: ACCIS)

	Children (age 0–14)					Adolescents (age 15–19)				
	Cases	% lymphomas	Male/ Female	ASR 0–14	(95% CI)	Cases	% lymphomas	Male/ Female	Age-specific rate	(95% CI)
EUROPE										
NHL Combined Group	3,850	60.3	2.4	9.4	(9.1–9.7)	708	34.9	2.0	15.9	(14.7–17.1)
IIb. NHL	2,709	42.4	2.3	6.5	(6.3–6.8)	489	24.1	2.0	11.0	(10.0–12.0)
IIc. Burkitt	785	12.3	3.8	1.9	(1.8–2.1)	68	3.3	6.5	1.5	(1.2–1.9)
IId. Miscellaneous	104	1.6	1.2	0.3	(0.2–0.3)	9	0.4	3.5	0.2	(0.0–0.4)
IIe. Unspecified	252	3.9	2.0	0.6	(0.5–0.7)	142	7.0	1.2	3.2	(2.7–3.7)
BRITISH ISLES										
NHL Combined Group	694	62.3	2.2	7.4	(6.8–7.9)	78	36.3	2.5	14.9	(11.6–18.2)
IIb. NHL	563	50.5	2.1	6.0	(5.5–6.5)	47	21.9	3.3	9.0	(6.4–11.5)
IIc. Burkitt	69	6.2	3.3	0.7	(0.6–0.9)	5	2.3	4.0	0.9	(0.3–2.2)
IId. Miscellaneous	10	0.9	1.5	0.1	(0.0–0.2)	2	0.9	1.0	0.4	(0.0–1.4)
IIe. Unspecified	52	4.7	2.5	0.5	(0.4–0.7)	24	11.2	1.6	4.6	(2.9–6.8)
EAST										
NHL Combined Group	521	42.5	2.4	9.1	(2.3–9.9)	58	27.2	2.0	10.5	(7.8–13.1)
IIb. NHL	366	35.8	2.3	6.3	(5.7–7.0)	43	20.2	1.9	7.7	(5.4–10.1)
IIc. Burkitt	122	3.5	3.5	2.2	(1.8–2.6)	7	3.3	6.0	1.3	(0.5–2.6)
IId. Miscellaneous	13	1.3	0.9	0.3	(0.1–0.4)	1	0.5	NA	0.2	(0.0–1.0)
IIe. Unspecified	20	1.9	2.0	0.3	(0.2–0.5)	7	3.3	1.3	1.3	(0.5–2.6)
NORTH										
NHL Combined Group	262	66.1	2.4	9.4	(8.2–10.5)	161	34.1	2.0	16.4	(13.9–18.9)
IIb. NHL	134	33.8	2.7	4.8	(4.0–5.6)	91	19.3	2.6	9.3	(7.4–11.2)
IIc. Burkitt	25	6.3	4.0	0.9	(0.5–1.2)	5	1.1	4.0	0.5	(0.2–1.2)
IId. Miscellaneous	5	1.3	4.0	0.2	(0.0–0.4)	2	0.4	NA	0.2	(0.0–0.7)
IIe. Unspecified	98	24.7	1.9	3.5	(2.8–4.2)	63	13.3	1.3	6.4	(4.8–8.0)
SOUTH										
NHL Combined Group	496	61.2	2.5	12.5	(11.4–13.7)	231	38.2	1.9	20.0	(17.4–22.6)
IIb. NHL	261	32.2	2.4	6.3	(5.5–7.1)	172	28.5	1.9	14.9	(12.7–17.1)
IIc. Burkitt	184	22.7	3.3	4.8	(4.1–5.5)	26	4.3	12.0	2.2	(1.5–3.3)
IId. Miscellaneous	24	3.0	1.2	0.8	(0.4–1.1)	2	0.3	NA	0.2	(0.0–0.6)
IIe. Unspecified	27	3.3	1.7	0.7	(0.4–1.0)	31	5.1	0.6	2.7	(1.7–3.6)
WEST										
NHL Combined Group	1,877	61.7	2.5	9.8	(9.4–10.3)	180	34.4	1.8	14.6	(12.4–16.7)
IIb. NHL	1,385	45.5	2.2	7.2	(6.8–7.6)	136	26.0	1.6	11.0	(9.2–12.9)
IIc. Burkitt	385	12.7	4.3	2.0	(1.8–2.2)	25	4.8	7.0	2.0	(1.3–3.0)
IId. Miscellaneous	52	1.7	1.1	0.3	(0.2–0.4)	2	0.4	1.0	0.2	(0.0–0.6)
IIe. Unspecified	55	1.8	1.9	0.3	(0.2–0.4)	17	3.2	1.8	1.4	(0.8–2.2)

ASR, age-standardized incidence rates per million world standard population.
% lymphomas: Percentage of lymphomas and reticuloendothelial neoplasms.
NA: Not available.

In Fig. 1, two patterns can be observed in age-specific incidence: a steady increase with age-group in children in the British Isles and the North, and two peaks, in the age-groups 5–9 years and 15–19 years, for the East, South and West. Burkitt's lymphoma (IIc), is most common in the age group 5–9 years and the Miscellaneous lymphoid neoplasms (IId) peak in infants under 1 year of age.

During 1988–1997, the overall incidence rate was 9.4 in children and 15.9 in adolescents (Table 3). The following regional patterns are observed: the highest incidence rates are observed in the South, both in children and in adolescents. Apart from few exceptions, the South also has the highest incidence rates for the individual diagnostic subgroups. NHL constituted a larger proportion of lymphomas in childhood (60%) than in adolescence (35%) in all regions. The true NHL subgroup (IIb) represents about 70% of the pooled NHL group and thus greatly influences the observed geographical and temporal patterns. In all regions, the overall incidence rate in adolescents was higher than that in children: this difference is largest in the South and lowest in the East. However, Burkitt's lymphoma was more common in children than in adolescents, in all regions Burkitt's lymphoma was less common in the British Isles and the North (under 1 per million) than in the other three regions. NHLs were about 2.4 times more common in boys than in girls and the sex ratio was even higher for Burkitt's lymphoma. Miscellaneous lymphoreticular neoplasms represented a small proportion of the total lymphomas, varying between 0.3% and 3%. The North had a substantially higher incidence of Unspecified lymphomas (IIe) in comparison with other regions, both in children and in adolescents.

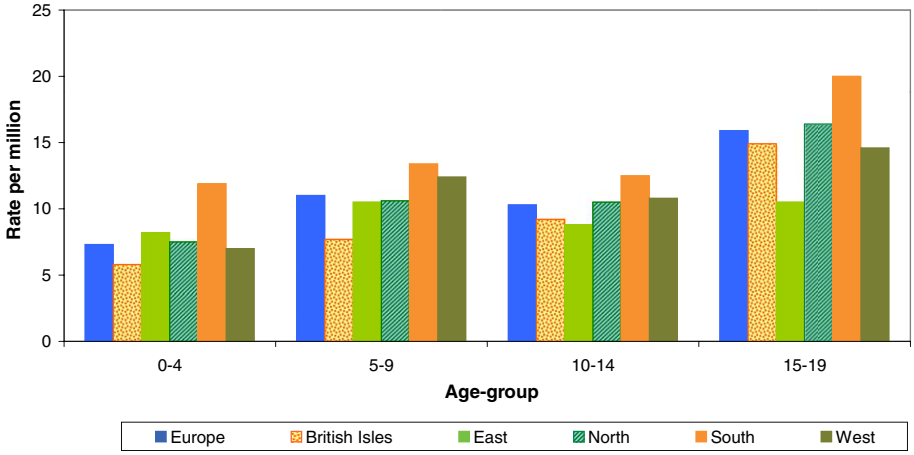

Fig. 1 – Non-Hodgkin's lymphomas (Combined Group: IIb + IIc + IId + IIe) age-specific incidence rate in children (*n* = 3850) and adolescents (*N* = 708) by region, both sexes, 1988-1997. Source: ACCIS.

Table 4 – Incidence rates of non-Hodgkin's lymphomas (Combined Group: IIb + IIc + IId + IIe) per million (Source: ACCIS)

	Cases		Age specific rate					ASR	
	0–14	15–19	0	1–4	5–9	10–14	15–19	0–14	(95% CI)
EUROPE									
1978–1982	981	228	4.9	7.2	8.7	8.7	11.1	7.9	(7.4–8.4)
1983–1987	1,418	247	2.2	6.7	9.9	9.1	11.7	8.1	(7.7–8.5)
1988–1992	1,508	210	3.0	8.0	10.5	9.4	14.7	8.8	(8.4–9.3)
1993–1997	1,436	205	3.0	7.4	10.6	11.2	15.5	9.2	(8.7–9.7)
BRITISH ISLES									
1978–1982	381	21	4.1	5.4	7.0	7.6	9.3	6.4	(5.6–7.1)
1983–1987	351	27	1.1	5.1	7.6	8.1	12.4	6.5	(5.8–7.1)
1988–1992	404	19	1.3	7.4	8.6	8.3	10.6	7.6	(6.8–8.3)
1993–1997	252	28	0.9	5.7	6.9	10.3	17.8	7.0	(6.2–7.9)
EAST									
1978–1982	166	34	2.9	7.2	10.1	8.9	13.3	8.3	(7.1–9.6)
1983–1987	185	25	2.5	10.1	11.0	7.8	10.3	9.2	(7.8–10.5)
1988–1992	178	29	8.0	8.9	11.0	8.5	10.8	9.4	(8.0–10.8)
1993–1997	133	29	5.2	8.1	7.8	8.2	10.1	7.8	(6.4–9.1)
NORTH									
1978–1982	127	58	5.6	9.1	9.6	7.3	10.5	8.5	(7.0–10.0)
1983–1987	122	77	3.5	8.0	9.0	9.7	14.1	8.5	(7.0–10.0)
1988–1992	112	77	6.4	7.3	8.6	8.9	15.2	8.1	(6.6–9.7)
1993–1997	150	84	5.1	8.6	12.5	12.1	17.7	10.6	(8.9–12.3)
SOUTH									
1978–1982	115	18	12.1	10.5	14.9	12.6	10.5	12.5	(10.2–14.8)
1983–1987	128	32	1.8	12.2	16.0	10.2	12.2	12.0	(9.9–14.2)
1988–1992	109	50	8.1	13.5	11.5	12.0	19.1	12.0	(9.7–14.3)
1993–1997	95	41	11.1	10.2	11.8	14.2	17.4	11.9	(9.5–14.4)
WEST									
1978–1982	48	26	4.3	14.1	11.3	13.1	17.4	12.1	(8.6–15.6)
1983–1987	504	28	2.9	6.1	10.4	10.4	12.2	8.5	(7.7–9.2)
1988–1992	652	35	1.5	7.7	12.4	10.3	16.8	9.5	(8.7–10.2)
1993–1997	806	23	2.4	7.7	12.4	11.8	13.4	10.1	(9.3–10.7)

ASR, age-standarized incidence rate (world standard population). Europe includes East Germany, not included in any of the regions.

Overall, 5343 children and 890 adolescents were included in the analysis of time trends (Table 4). In children, the average annual percent change (AAPC) for the combined NHL group was 0.86% ($P = 0.002$), based on a model adjusted for region, sex and age group (Table 5). No time trend was observed for NHL incidence in age groups 0, 1–4 and 5–9 years. Adjusted for region and age group, the rate of increase was higher in girls (AAPC = 1.4%, $P = 0.008$) than in boys (AAPC = 0.7%, $P = 0.027$). The increase in the combined NHL group can be attributed exclusively to the increase in the subgroup IIb

Table 5 – Incidence time trends of Haemotopoietic neoplasms in Europe, 1978–1997 (Source: ACCIS)

	Children (age 0–14)			Adolescents (age 15–19)		
Group of neoplasms ICCC category (12)	Leukaemias I	Hodgkin lymphoma IIa	Other lymphomas IIb, IIc, IId, IIe	Leukaemias I	Hodgkin lymphoma IIa	Other lymphomas IIb, IIc, IId, IIe
Number of cases	26,690	3,628	5,343	1,491	1,911	890
AAPC	0.62%	0.72%	0.86%	0.62%	3.49%	1.73%
P-value	<0.0001	0.032	0.002	0.217	<0.0001	0.007

Average annual percent change (AAPC) is derived from Poisson regression model with year as explanatory variable, adjusted for sex, age group and region.

Fig. 2 – Incidence time-trends of non-Hodgkin's lymphomas (Combined Group: IIb + IIc + IId + IIe) in Europe, 1978–1997. Age standardized rates (world standard population) for children aged 0–14 (*n* = 5343) and age-specific rates for adolescents aged 15–19 (*n* = 890). Source: ACCIS.

(non-Hodgkin's lymphomas), since there was no trend observed for Burkitt's lymphoma (IIc) or Unspecified lymphomas (IIe), and the incidence of the Miscellaneous tumours (IId) was decreasing, AAPC = −2.8%, $P = 0.063$.

Overall incidence increased faster in adolescents than in children (Fig. 2, Table 5). The analyses for individual diagnostic subgroups did not show any specific pattern. Table 5 shows very similar concurrent temporal trends of leukaemias and

Hodgkin's disease in children, both increasing at only a slightly lower rate than the incidence of NHL. In adolescents the pattern was less homogeneous, with no increase in leukaemias, intermediate increase in NHL and twice as fast increase in Hodgkin's disease.

There were 3431 children diagnosed with NHL during the period 1988–1997 and included in the survival analysis. Overall survival of children with NHL was 84% at 1 year, 78% at 3 years and 77% at 5 years (Table 6). A marginally significant difference in survival ($\chi^2 = 3.89$, $P = 0.0486$) was observed between boys (78%, 95% CI (76, 80)) and girls (75%, 95% CI (72, 78)) (Fig. 3). However, the sex-specific survival differed significantly only in the West ($\chi^2 = 6.69$, $P = 0.0097$), where 5-year survival for boys was 85%, 95% CI (82, 87) and for girls it was 79%, 95% CI (75, 83). By regions, survival was lowest in the East and highest in the West (Table 6). The survival curves for the three other regions did not differ significantly and the pooled estimate of 5-year survival was 77%, 95% CI (75, 80).

Overall 5-year survival of children with Burkitt's lymphoma (IIc) was 81%, 95% CI (78, 84) higher than survival for the pooled NHL group, in all regions. The lowest 5-year survival was observed for the East 60%, 95% CI (50, 68). Survival curves do not differ significantly for the British Isles and the South ($P = 0.6$) and the pooled 5-year survival for these two regions is 80%, 95% CI (74, 85). The highest survival was observed in the West and the North, with the pooled 5-year survival of 89%, 95% CI (85, 92). No differences in survival between boys and girls or between the four age groups were observed.

Table 6 – Actuarial survival (%) and its 95% confidence intervals (95% CI) of children and adolescents with non-Hodgkin's lymphomas (Combined Group: IIb + IIc + IId + IIe) by histological type and region, both sexes, 1988–1997. (When cases <5, survival not shown) (Source: ACCIS)

	Children (age 0–14)				Adolescents (age 15–19)			
	Cases	Survival (95% CI)			Cases	Survival (95% CI)		
		1 year	3 years	5 years		1 year	3 years	5 years
EUROPE								
NHL Combined Group	3,431	84 (83–86)	78 (77–80)	77 (76–79)	541	82 (79–85)	69 (65–73)	66 (61–70)
IIb. NHL	2,410	85 (84–87)	78 (76–80)	77 (75–78)	353	82 (78–86)	68 (62–73)	64 (59–69)
IIc. Burkitt	705	83 (80–86)	82 (78–84)	81 (78–84)	46	56 (41–69)	48 (33–61)	48 (33–61)
IId. Miscellaneous	81	64 (52–73)	56 (44–67)	56 (44–67)	7	57 (17–84)	57 (17–84)	57 (17–84)
IIe. Unspecified	235	85 (80–89)	78 (71–83)	76 (69–81)	135	90 (84–94)	78 (70–84)	74 (65–81)
BRITISH ISLES								
NHL Combined Group	685	86 (83–88)	80(77–83)	79 (76–82)	78	79 (68–87)	73 (62–82)	67 (54–77)
IIb. NHL	558	86 (83–89)	79 (76–83)	78 (75–81)	47	79 (64–88)	71 (56–82)	67 (50–80)
IIc. Burkitt	69	83 (71–90)	83 (71–90)	83 (71–90)	5	40 (5–75)	40 (5–75)	40 (5–75)
IId. Miscellaneous	10	79 (39–94)	79 (39–94)	79 (39–94)	2	NA	NA	NA
IIe. Unspecified	48	89 (75–95)	83 (68–92)	83 (68–92)	24	87 (65–96)	82 (59–93)	70 (44–86)
EAST								
NHL Combined Group	505	69 (64–73)	60(56–64)	58 (54–63)	54	58 (44–70)	38 (25–52)	32 (19–46)
IIb. NHL	354	71 (66–75)	60 (55–65)	58 (52–63)	39	68 (51–80)	46 (29–62)	37 (20–54)
IIc. Burkitt	122	62 (52–70)	61 (51–69)	60 (50–68)	7	14 (1–14)	–	–
IId. Miscellaneous	12	67 (34–86)	50 (21–74)	50 (21–74)	1	NA	NA	NA
IIe. Unspecified	17	75 (46–90)	68 (40–85)	60 (31–80)	7	57 (17–84)	38 (6–72)	38 (6–72)
NORTH								
NHL Combined Group	260	85 (80–89)	79 (74–84)	77 (72–82)	160	91 (85–94)	72 (64–78)	71 (63–78)
IIb. NHL	134	83 (75–88)	78 (71–85)	78 (69–84)	90	91 (83–95)	71 (60–79)	71 (60–79)
IIc. Burkitt	25	96 (75–99)	92 (71–98)	92 (71–98)	5	60 (13–88)	60 (13–88)	60 (13–88)
IId. Miscelaneous	4	75 (13–96)	75 (13–96)	75 (13–96)	2	NA	NA	NA
IIe. Unspecified	97	87 (78–92)	77 (67–85)	74 (63–82)	63	94 (84–96)	75 (62–84)	73 (59–82)
SOUTH								
NHL Combined Group	441	82 (79–86)	76 (72–80)	75 (70–79)	198	82 (76–87)	73 (66–78)	69 (62–75)
IIb. NHL	235	85 (79–89)	76 (70–81)	74 (68–80)	144	82 (74–87)	72 (64–79)	68 (59–75)
IIc. Burkitt	160	83 (76–88)	79 (72–85)	79 (72–85)	24	67 (44–82)	54 (33–71)	54 (33–71)
IId. Miscellaneous	20	70 (45–85)	65 (40–82)	65 (40–82)	2	NA	NA	NA
IIe. Unspecified	26	69 (47–83)	60 (38–76)	60 (38–76)	28	100	92 (73–98)	88 (67–96)
WEST								
NHL Combined Group	1,540	89 (87–91)	84 (82–86)	83 (81–85)	51	81 (67–90)	64 (48–76)	64 (48–76)
IIb. NHL	1,129	90 (88–91)	84 (81–86)	82 (80–85)	33	83 (65–93)	55 (34–72)	55 (34–72)
IIc. Burkitt	329	90 (87–93)	90 (86–93)	89 (85–92)	5	80 (20–97)	80 (20–97)	80 (20–97)
IId. Miscellaneous	35	53 (35–68)	44 (25–61)	44 (25–61)	–	–	–	–
IIe. Unspecified	47	91 (78–97)	86 (72–93)	86 (72–93)	13	76 (43–92)	76 (43–92)	76 (43–92)

NA: Not available.

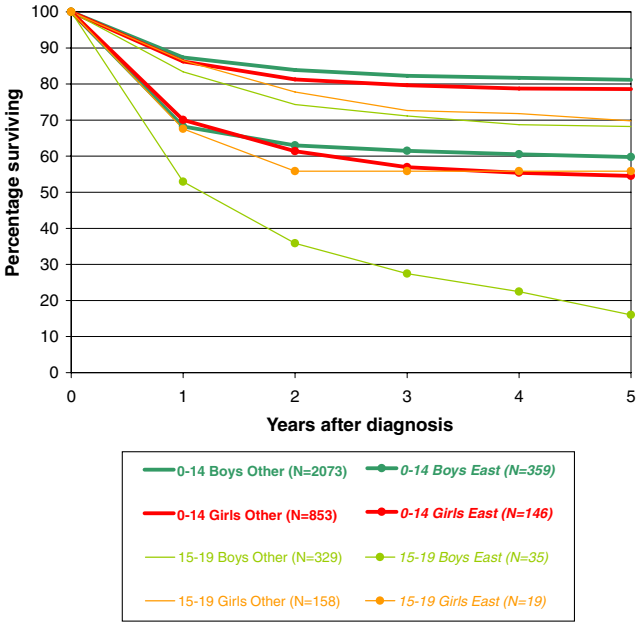

Fig. 3 – Survival (%) of children (age 0–14, thick lines) and adolescents (age 15–19, thin lines) (%) with non-Hodgkin's lymphomas (Combined Group: IIb + IIc + IId + IIe), in East and other regions of Europe, 1988–1997. Source: ACCIS.

Among 541 adolescents with NHL, 82% survived the first year, 69% the third year and 66% the fifth year after diagnosis. Five-year survival in adolescents was lower than that in children for all ICCC lymphoma subgroups with sufficient number of cases (Table 5). The lowest survival was observed in the East, the survival curves for the other four regions did not differ ($\chi^2 = 0.87$, $P = 0.8$), the pooled 5-year survival being 58% with 95% CI (54, 63). No difference in survival between boys and girls was observed ($\chi^2 = 1.14$, $P = 0.3$). Five-year survival of 46 adolescents with Burkitt's lymphoma was 48%, 95% CI (33, 61).

Analyses of survival time trends were based on 4874 children and 839 adolescents diagnosed during the period 1978–1997 (Table 7). A significant increase in survival of children with NHL was seen for combined dataset ($\chi^2 = 282$, $P < 0.0001$) and in each of the individual regions. Survival was increasing in all age groups and for both sexes. The increasing trend was not significant for some of the region-age-sex categories. However, no systematic pattern was discerned, except for the comparatively low survival in infants. The evolution of survival rates by region in children and adolescents is shown in Fig. 4. Five-year survival in children changed from 48% in the period 1978–1982, to 79% in the period 1993–1997, an increase was seen also in 10-year survival until the period 1988–1992 (Table 7). Five-year survival of children with Burkitt's lymphoma has increased from

Table 7 – Actuarial survival (%) and its 95% confidence intervals (95% CI) of children and adolescents with non-Hodgkin's lymphomas (Combined Group: IIb + IIc + IId + IIe). (When cases =<20, survival not shown) (Source: ACCIS)

	Children (age 0–14)					Adolescents (age 15–19)				
	Cases	Survival (95% CI)				Cases	Survival (95% CI)			
		1 year	3 years	5 years	10 years		1 year	3 years	5 years	10 years
NHL Combined Group	4,874					839				
1978–1982	920	65 (62–68)	51 (48–54)	48 (45–51)	46 (43–49)	210	51 (44–58)	39 (33–46)	36 (30–42)	33 (27–40)
1983–1987	1,360	76 (74–78)	67 (65–70)	66 (63–68)	64 (61–66)	234	68 (61–74)	54 (47–60)	50 (43–56)	50 (43–56)
1988–1992	1,402	84 (82–86)	80 (77–82)	78 (76–80)	77 (75–79)	196	79 (73–84)	64 (56–70)	61 (54–68)	59 (52–66)
1993–1997	1,192	87 (85–89)	80 (78–83)	79 (77–82)	NA	199	85 (79–89)	73 (66–79)	72 (64–78)	NA
NHL (IIb)	3,599					576				
1978–1982	663	69 (65–73)	53 (50–57)	51(47–54)	48 (44–52)	148	51 (43–59)	42 (34–49)	41 (33–49)	37 (29–45)
1983–1987	1,010	79 (77–82)	70 (67–73)	68 (65–71)	66 (62–68)	174	69 (61–75)	54 (46–61)	48 (41–56)	48 (41–56)
1988–1992	1,039	86 (83–88)	80 (78–83)	79 (76–81)	77 (75–80)	112	81 (72–87)	62 (52–70)	59 (49–67)	57 (47–65)
1993–1997	887	88 (86–90)	80 (77–82)	79 (76–81)	NA	142	84 (77–89)	71 (62–78)	69 (60–77)	NA
Burkitt (IIc)	743					59				
1978–1982	105	45 (35–54)	35 (26–44)	34 (25–43)	34 (25–43)	10	40 (12–67)	20 (3–47)	20 (3–47)	20 (3–47)
1983–1987	207	65 (58–71)	62 (55–68)	62 (55–68)	61 (54–67)	18	61 (35–79)	50 (26–70)	50 (26–70)	50 (26–70)
1988–1992	236	82 (76–86)	80 (74–85)	80 (74–84)	80 (74–84)	16	38 (15–60)	31 (11–54)	31 (11–54)	31 (11–54)
1993–1997	195	86 (80–90)	85 (80–90)	85 (80–90)	NA	15	80 (50–93)	80 (50–93)	80 (50–93)	NA
Miscellaneous (IId)	171					15	–	–	–	–
1978–1982	59	53 (39–64)	44 (31–56)	41 (28–53)	37 (25–49)	6	–	–	–	–
1983–1987	60	61 (48–72)	46 (33–58)	46 (33–58)	44 (31–56)	3	–	–	–	–
1988–1992	29	61 (41–76)	58 (38–73)	58 (38–73)	58 (38–73)	5	–	–	–	–
1993–1997	23	69 (46–84)	52 (28–71)	52 (28–71)	NA	1	–	–	–	–
Unspecified (IIe)	361					189				
1978–1982	93	67 (56–75)	58 (47–67)	51 (41–61)	49 (39–59)	46	57 (41–69)	37(23–51)	24 (13–37)	24 (13–37)
1983–1987	83	73 (63–82)	69 (57–77)	66 (55–75)	65 (54–74)	39	64 (47–77)	51(35–66)	51(35–66)	51(35–66)
1988–1992	98	82 (73–88)	75 (65–83)	73 (63–81)	73 (63–81)	63	89 (78–95)	76 (63–85)	73 (60–82)	71(58–81)
1993–1997	87	89 (81–94)	83 (72–89)	81 (70–88)	NA	41	88 (73–95)	76 (53–87)	76 (58–87)	NA

NA: Not available.

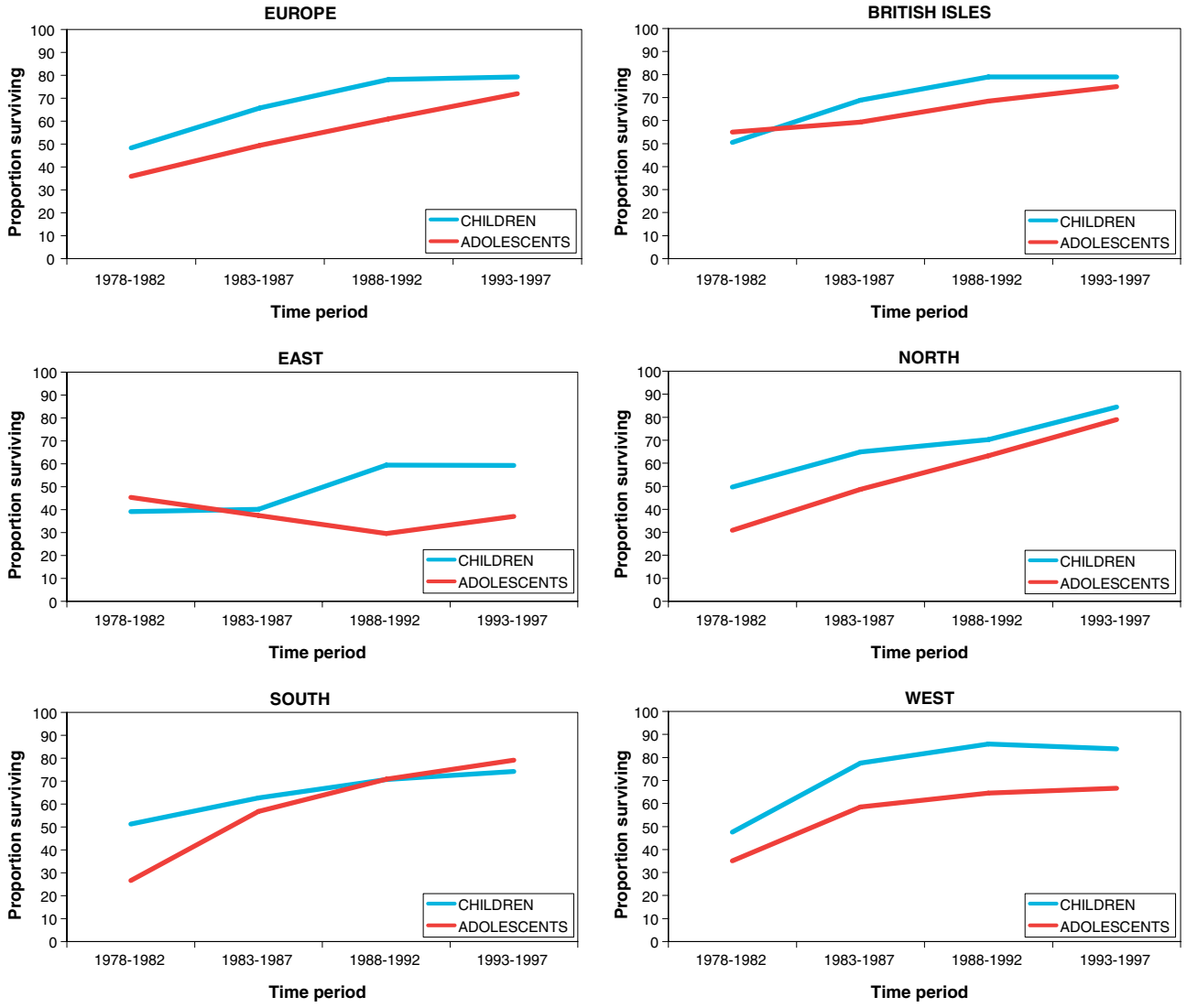

Fig. 4 – Time-trend in 5-year survival (%) of children (age 0–14, *n* = 4874) and adolescents (age15–19, *n* = 839) with non-Hodgkin's lymphomas (Combined Group: IIb + IIc + IId + IIe), both sexes. Source: ACCIS.

34%, 95% CI (25, 43) for those diagnosed in 1978–1982 to 85%, 95% CI (80, 90), for those diagnosed in 1993–1997, and significant improvements were seen in all regions and both sexes.

Survival improved also in adolescents, although it did not reach the levels observed in children (Table 7). The improvement was statistically significant for the pooled NHL group ($\chi^2 = 95.10$, $P < 0.0001$) and for Burkitt's lymphoma ($\chi^2 = 3.77$, $P = 0.0523$), with even greater extent of change (Table 7).

4. Discussion

Incidence and survival data presented here are based on the ACCIS database, resulting from collaboration of European population-based cancer registries. A detailed review of each registry-specific dataset aims at ensuring highest possible quality and comparability [Steliarova-Foucher, Kaatsch, Lacour and colleagues, this issue]. Due to strict criteria, 2124 NHL cases contained in the ACCIS database were excluded from this study.

The high proportion of cases with microscopic verification observed in the contributing registries was particularly important for NHL, which has been subjected to changes in diagnosis and classification. Despite the high proportion of microscopically verified cases, large differences in incidence of different lymphoma subgroups were observed between the registries. This can be attributed partly to the differences in tumour coding and classification, notably in the Nordic countries, often using non-standard classification.[16,17] These differences motivated our approach of pooled analyses for all lymphomas, which are not Hodgkin's lymphoma. Our decision was based on the assumption that true cases of Hodgkin's lymphoma are less likely to be classified into unspecified or other lymphoma subgroups, while the separation of the other four lymphoma subgroups could be less clear-cut. Numerous changes in the classification of lymphomas and difficulties in establishing an accurate diagnosis influence the interpretation of geographical patterns and time trends.[5–7,18] In addition, it is recognised that lymphoid

leukaemia and NHL are different presentations of the same disease, which is now reflected in the ICD-O-3 classification.[19] In particular, precursor B or T lymphoblastic leukaemia and lymphoblastic lymphoma constitute, each one, a biological unity and the distinction between leukaemia and lymphoma is arbitrary.[20] Our comparison of incidence time trends in three groups of lymphoid neoplasms does not exclude exchanges between various histological types. However, the overall increases being very similar in children, such changes do not seem to contribute to the explanation of the overall temporal trends in agreement with the results obtained in the Netherlands.[21]

The low proportion of DCO cases, taking into account those registries with access to this source of data, and the minimal changes in this indicator over time indicates high completeness of incidence data, providing that the registries do have access to individual mortality data [Steliarova-Foucher, Kaatsch, Lacour and colleagues, this issue]. A relatively small proportion of cases lost to follow-up and excluded from the survival analysis is unlikely considerably to affect survival figures, although improved completeness of follow-up in many contributing registries would certainly result in more precise indicators of prognosis.

The geographical regions we have constituted are not homogeneous and the patterns observed for a region as a whole may differ between the constituent individual registries. However, analysis of large data-sets may reveal patterns that would remain hidden at the registry level.

A great effort has been made to ensure best quality and comparability of data, but some artificial variations could have persisted. Therefore, we interpret the results cautiously, taking into account the different periods of study covered by registries, the method of data collection and follow-up of patients, classification of tumours, and so on.

Previous childhood cancer studies have estimated incidence for the subgroup of NHL (IIb) in different European geographical areas,[2,22] while we present the results for the combined group composed of the four subgroups of ICCC (IIb, IIc, IId, IIe). We observed a relatively high incidence of NHL in children in the South region, constituted of several Mediterranean countries, where elevated incidence of the subgroups within NHL was reported previously.[22,23] In this study we show that the incidence of NHL in the South is also elevated in adolescents. NHL constitutes a larger proportion of lymphomas in childhood (60%) compared with adolescence (35%). These proportions are relatively stable across the regions, with the exception of the East, where NHLs are markedly less common within lymphomas in favour of Hodgkin's disease [Clavel and colleagues, this issue]. These diversities in the age-region-specific patterns of occurrence may point to slightly different external or host risk factors, which will be worth exploring in more detail.

We observed an increase in incidence rates, notably due to the true NHLs subgroup (IIb) and in the older age groups, although this increase was not universal across all regions. We cannot exclude a contribution of the improvement of registration to the rising incidence of NHL in Europe, although given the careful data selection for the analyses, this is unlikely to be the only factor responsible for the increase.

Few environmental risk factors for NHL lymphomas have been investigated in comparison with those for leukaemias. The pattern of increasing incidence rates in lymphomas seen in adults may resemble that seen in adolescents, but it is different from that for children, and the established major-risks factors, e.g. AIDS, immunosuppression, autoimmunity, which explain a small fraction of the 'adult' cases,[24] do not seem to affect the incidence in the young age-groups in Europe. Few other risks were studied in children: effect of breast-feeding, exposure to viral infection, and to pesticides.[23]

Survival of children with NHL declines mostly between the first and third year after diagnosis, although the increased fatality continues during the consecutive years. Our results are in agreement with the findings of the Eurocare study.[25] Since the most important prognostic determinants are therapy and extent of disease at diagnosis, regardless of histology,[26,27] the focus should be on early diagnosis, timely referral and the investment in treatment modalities,[28] especially in the East. Smaller differences observed between the other four 'western' regions point to the potential for improvement in those regions with lower survival. The differences in survival between the regions are further interpreted in the overview paper [Pritchard-Jones and colleagues, this issue].

The most positive finding in this study is the improvement in survival of young patients with NHL over the last 20 years observed in all European regions, and attributed to the improvement in treatment.[29] In this population-based study, however, the findings also reflect the overall health policy and its implementation on the national scale.

This large study gave us the opportunity to assess incidence and survival of Burkitt's lymphoma, which is rare in Europe. The high occurrence of this tumour in Southern countries has been reported previously.[30,31] The specific patterns of occurrence, notably the excess in the South, in males and in the age-group 5–9 years merit further study. This tumour is highly sensitive to polychemotherapy [10] and an early and adequate staging and treatment could result in improvement in survival, as seen in this study.

The results observed for adolescents are based on a smaller number of cases than for children, and it was therefore not possible or useful to provide survival data for patients with rare histological types. However, our results suggest that the management of adolescents with NHL is a challenge for clinical medicine in Europe, since the incidence rates are relatively high and increasing compared with other tumour types [Stiller, Desandes, Danon and colleagues, this issue], while survival is lower than in children, as also shown previously.[32] As is the case for incidence patterns, survival of adolescents with NHL resembles that seen in adults, which may indicate that different types of lymphomas affect children and adolescents, respectively, but also the fact that patients in this particular age-group participate less in clinical trials. In any case, this age group deserves further investment in terms of clinical care, as well as research.

NHLs represent an important group of tumours in the young population. The geographical differences observed in Europe may serve as ground for establishing aetiological hypotheses and studies. Further descriptive studies may attempt to delimit groups of lymphomas with common

patterns of occurrence and the possible reasons for the slight increase. Despite the undeniable progress in treatment in these neoplasms, there are still areas and patient groups with modest prognosis, notably infants and adolescents in the majority of regions and the majority of patients in the East region. Continuous monitoring of incidence and population-based survival is a prerequisite for successful public health policies.[33]

Conflict of interest statement

None declared.

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