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Childhood malignancies in the EUROCARE study: the database and the methods of survival analysis

C. Magnani [a,*], G. Gatta [c], I. Corazziari [b], E. Kramarova [d,e], G. Pastore [a], S. Viscomi [a], C. Stiller [f]

[a] *Childhood Cancer Registry of Piedmont — Cancer Epidemiology Unit of the Centre for Cancer Epidemiology and Prevention (CPO-Piemonte), ASO S. Giovanni, V. Santena 7, 10126 Turin, Italy*

[b] *Unit of Epidemiology Istituto Superiore di Sanità, Rome, Italy*

[c] *Epidemiology Unit, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Italy*

[d] *International Agency for Research on Cancer, Lyon, France*

[e] *Cancer Research Institute, Slovak Academy of Sciences, Bratislava, Slovakia*

[f] *Childhood Cancer Research Group, University of Oxford, Oxford, UK*

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Abstract

This paper describes the database of children with cancer in the EUROCARE study and the methodology used to analyse and report survival. This is the first systematic evaluation of survival after childhood cancer on a large scale in Europe: approximately 45 000 cases were included, diagnosed between 1978 and 1992 (34 814 cases diagnosed in 1978–1989 and an additional set of 9495 cases diagnosed in 1990–1992) and followed-up until 1995. Data were provided from 34 population-based registries (four specialised for childhood cancer registrations and one specialised registry for childhood leukaemia) in 17 countries of Europe (where there was national coverage in 10 countries). Quality of the data was fairly good, given the general differences among the countries and their health systems, thereby allowing for comparisons between them. Among cases diagnosed in 1978–1989, overall 2.0% were lost to follow-up, 91.8% were microscopically diagnosed and 93.4% of alive cases had at least 5 years of observation. Survival proportions (observed survival) were calculated for each of the countries involved, by age group (0, 1–4, 5–9, 10–14 years), gender, different time periods and selected diagnostic groups. Age-standardised cumulative survival rates and European averages (weighted and pooled) were also computed. Cox regression models were used to evaluate geographical and temporal differences. The EUROCARE database represents a unique source of information on survival of childhood cancer patients in Europe, intercountry differences and time trends in survival.

Keywords: Childhood neoplasm; Survival; Population-based cancer registry; Survival analysis methods; EUROCARE study; Europe

1. Introduction

The EUROCARE project started in 1990 with the main objective to describe population-based survival of cancer patients in Europe. The first publication of the results (EUROCARE I) described survival in 11 European countries for patients registered in 1978–1985 and unravelled relatively large differences in survival between the covered populations [1]. In that monograph, survival in children was evaluated only for eight major cancer sites, as defined by ICD-IX (nasopharynx, bone, ovary, testis, kidney, brain, Hodgkin's disease (HD) and leukaemia).

More recently, survival analyses were published for the period 1985–1989 (EUROCARE II), and the aim of these analyses was to provide a more detailed description of survival of the tumours in the adult European population [2,3]. Within the framework of the EUROCARE II study, separate analyses were conducted for the childhood cancer patients in the EUROCARE database and are presented in this special issue of the *European Journal of Cancer*. These analyses benefitted from the large number of registered cases and permitted geographical comparisons and evaluation of temporal trends even for rare groups of neoplasms.

* Corresponding author. Tel.: +39-011-633-6968; fax: +39-011-633-6960.

E-mail address: corrado.magnani@cpo.it (C. Magnani).

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In this special issue, we present survival of children with cancer according to typical groups of childhood neoplasms, using the International Classification of Childhood Cancer (ICCC) [4].

Over 30 general and four specialised population-based European cancer registries have contributed to this study, thus constituting a database of approximately 45 thousand cases. This paper describes the methods and procedures used for the collection, validation, classification and preparation of data for the analyses, as well as the statistical methods used for the survival analysis.

2. Patients and methods

2.1. The database

The analyses of childhood cancer survival reported in the articles of this special issue were based on 34 814 cases of malignant neoplasms diagnosed in children aged 0–14 years in the period 1978–1989 in Europe (Table 1). Data were provided by 34 population-based cancer registries in 17 countries [2]. The database included data from five specialised childhood cancer registries (England and Wales, Scotland, Germany, Piedmont and, limited to leukaemia, The Netherlands). Cases from England and Wales and from Scotland were provided by the National Registry of Childhood Tumours (NRCT). The NRCT ascertains cases from regional and national general cancer registries throughout Great Britain and from specialist regional childhood cancer registries, the UK Children's Cancer Study Group and clinical trial groups. Cases of leukaemia were provided from The Netherlands by the nationwide Dutch Leukaemia Registry. Ten of the registries included in this childhood EUROCARE study covered their respective countries completely (Denmark, England and Wales, Estonia, Finland, Iceland, Slovakia, Slovenia, Scotland, West Germany and, limited to leukaemia, The Netherlands). The list of registries contributing to the present study, the annual childhood population during the study period and the proportion of the national population in the area covered by the registry are provided in Table 1 which also includes the number of cases by quadriennial period of diagnosis and the date of the most recent follow-up. Details on the activity of the cancer registries included can be found elsewhere [1,2,5,6].

Twenty registries in 16 countries also provided information on cases incident in the 1990–1992 period, for a total of 9495 childhood cancer cases. Analyses for the period 1990–1992 were conducted and are presented separately, using the same methods of analyses described below. Although the German childhood cancer registry had covered the whole of Germany since 1991, the data analysed relates only to the former West Germany.

Variables collected from the registries as defined in the EUROCARE protocol [1] include: identification number, gender, dates of birth, diagnosis, follow-up or death, vital status, site (coded in ICD-IX) and morphology of the neoplasm (coded in ICD-O-I, [7]), behaviour code and microscopic verification of the diagnosis. The database included only anonymous data and dates were reported as months and years. Cases identified only on the basis of the death certificate (DCO cases) and cases diagnosed at autopsy were excluded from the analysis and do not contribute to the figures presented here. Benign tumours were also excluded, even if located intracranially as were second primary malignancies.

Evaluation of data quality was based on the proportion of cases without microscopical confirmation of the diagnosis, with unspecified morphology or lost to follow-up. All the records were checked for missing and invalid data [8] for the inclusion in the EUROCARE database. Individual records with invalid codes, or unlikely gender-age-site-morphology combinations were verified and corrected by the registries. Records still presenting clearly invalid fields were definitively excluded.

The childhood neoplasms were classified according to ICCC, based on both morphology and topography of tumour [4]. Since ICCC is designed for use on data coded to ICD-O-II classification [9] the procedure of allocation of tumours into ICCC categories was adapted to allow classification of the EUROCARE data-set coded to ICD-IX and ICD-O-I. 97% of cases were coded using the required standard international coding systems. Finnish and Swedish data, coded to non-standard systems could be classified to ICCC after consultation with the person in charge in each registry. With the exception of leukaemia, cases classified only on the basis of the site were always allocated to one of the unspecified ICCC subgroups. These tumours represented 1.8% in the database for 1978–1989.

2.2. Statistical methods

Cumulative survival was calculated by the actuarial method [10] using the program by Hakulinen [11] and was reported as percentages. Relative survival was not presented as in the young age groups covered by the study it corresponds closely to observed survival.

As survival is usually dependent on the age and gender of patients, and the age distribution of children may be different between countries, direct age- and gender-standardised survival rates were calculated, using the age distribution of the overall EUROCARE database as the standard. The standard population was broken down into three age classes: 0–4, 5–9 and 10–14 years. To allow for gender comparisons, the same standard was used for both girls and boys.

European survival was presented as both crude and weighted averages, always estimated including all coun-

Table 1
Descriptive statistics of the data set of childhood cancer cases incident in the period 1978–1989 and included in the EUROCARE study

Country	Period contributed	Proportion of national coverage (%)	Size of childhood population (×1000)	1978–1984 *n* (%)	1985–1989 *n* (%)	Total 1978–1989 *n* (%)	Date of most recent follow-up (f.u.)	Proportion lost to f.u. (%)	Frequency of alive cases with f.u. < 5 years (%)
Austria (Tyrol)	1988–1989	7.8	121		28 (0.2)	28 (0.1)	12/95	0	0
Denmark	1978–1989	100	922	895 (5)	640 (4)	1535 (5)	12/94	0	0
The Netherlands (Eindhoven)	1978–1989	5.7	183	98 (0.5)	79 (0.5)	177 (0.5)	04/94	19.8	8.4
Dutch Childhood Leukemia Study Group[a]	1978–1989	100	2774	819 (4)	481 (3)	1300 (4)	12/96	2.2	0.4
England and Wales[a]	1978–1989	100	9602	7334 (39)	5357 (33)	12 691 (36)	02/98	0.8	0.4
Estonia	1978–1989	100	335	254 (1)	184 (1)	438 (1)	12/94	3.4	0
Finland	1978–1989	100	955	892 (5)	683 (4)	1575 (5)	12/95	0.2	0
French registries		3.9	482	268 (1)	225 (1)	493 (1)		1.6	25.7
Somme	1982–1989	1.0	117	39	54	93	12/92	0	26.2
Calvados	1978–1989	1.1	133	92	58	150	06/96	5.3	0
Cote d'Or[b]	1978–1989	0.9	110	34	40	74	12/95	0	2.2
Doubs	1978–1989	0.9	122	103	73	176	12/94	0	59.1
Germany (West)[a]	1980–1989	100	9185	4673 (25)	5372 (33)	10045 (29)	12/94	4.4	14.0
Iceland	1978–1989	100	64	60 (0.3)	36 (0.2)	96 (0.3)	05/96	0	0
Italian registries		15.4	1454	968 (5)	833 (5)	1801 (5)		1.6	0
Florence	1985–1989	2.0	156		112	112	12/94	0	0
Genoa	1986–1988	1.3	79		44	44	12/94	0	0
Latina	1983–1987	0.8	112	16	35	51	12/95	0	0
Modena	1988–1989	0.5	77		18	18	07/95	0	0
Parma	1978–1987	0.7	52	59	28	87	07/95	0	0
Piedmont[a]	1978–1989	7.5	701	706	432	1138	12/95	2.3	0
Ragusa	1981–1989	0.5	63	26	35	61	05/95	0	0
Romagna	1986–1988	0.7	73		33	33	12/93	0	0
Varese	1978–1989	1.4	141	161	96	257	05/97	1.2	0
Polish registries		6.2	457	88 (0.5)	126 (0.8)	214 (0.6)		2.3	1.0
Crakow	1978–1989	1.9	154	88	67	155	09/94	1.3	1.4
Warsaw	1988–1989	4.3	303		59	59	06/97	5.1	0
Scotland[a]	1978–1989	100	1005	836 (4)	541 (3)	1377 (4)	02/98	0.3	0.3
Slovakia	1978–1989	100	1346	1126 (6)	801 (5)	1927 (6)	12/92	0	21.8
Slovenia	1985–1989	100	430		229 (1)	229 (0.7)	12/94	1.7	0
Spanish registries		10.9	853		338 (2)	338 (1)		0.9	46.3
Basque Country	1986–1989	5.5	413		173	173	12/91	0	66.1
Girona[b]	1982–1986	1.3	98		2	2	11/93	50.0	0
Mallorca	1988–1989	1.5	114		32	32	12/93	0	70
Navarra	1985–1989	1.3	111		62	62	12/94	0	0
Tarragon	1985–1989	1.3	117		69	69	01/94	2.9	27.5
Sweden (South)	1978–1989	17.5	282	275 (1)	185 (1)	460 (1)	12/96	0	0
Switzerland (Geneva)	1978–1989	5.5	58	53 (0.3)	37 (0.2)	90 (0.3)	12/94	8.9	0
All participating registries				18 639 (100)	16 175 (100)	34 814 (100)		2.0	6.6

[a] Childhood cancer registry.
[b] Specialised registry (Cote d'Or, haemolymphopoietic, gynaecological, digestive; Girona, gynaecological).

tries. The crude average survival is the survival of patients in the pooled database. The European weighted-average was calculated as the weighted mean of the survival proportions calculated for each country. Weights (Table 2) were proportional to the contribution of the childhood population (0–14 years) of each country to the (EUROCARE) total, using population figures estimated by the statistical offices in the respective countries, collected in the World Health Organization (WHO) data bank and retrieved from EUCAN 4 software [12]. England and Wales and Scotland were considered as separate countries in the analyses. Weights for Germany are for the whole country. This method was based on the assumption that the survival of patients in the registries with regional coverage represented that of the overall childhood cancer survival in the whole country.

Confidence intervals (with bounds between 0 and 100) were estimated using a logistic transformation of the survival probabilities (s) and the corresponding standard errors, based on the binomial formula $[s(1-s)/(\text{number of cases})]^{1/2}$. When survival is based on a single or very few cases, its value is often either 0 or 100%. The above binomial formula then gives zero values that do not reflect the true sampling variability. In this case, we used the conservative expression $[(0.5\times0.5)/(\text{number of cases})]^{1/2}$. This correction was important to avoid underestimation of the sampling variability of the statistics.

For the comparisons of survival between each country and the European average we also computed the relative death rates (i.e. the ratios of logarithms of the corresponding survival values) [13]. It can be interpreted as a relative risk (RR) of death for subjects in a given category compared with the European average.

The Cox proportional hazard model [14] was used to compare hazard ratios (HR) between different periods of diagnosis taking into account the different distribution of age, gender and country. The 1978–1989 calendar period was divided into three sub-periods (1978–1981, 1982–1985, 1986–1989) and age at diagnosis was categorised into three 5-year age-groups. The proportionality assumption was tested inspecting the survival plots. The variability in the number of cases by registry and country is very large, which led to the decision to include in the multivariate analyses and the presentation of actuarial analyses only the countries with a minimum number of cases. For geographical comparison (targeted to the period 1986–1989), multivariate analyses were limited to countries with more than 10 cases in the period; while for the time trend of survival, we included only countries with 30 cases or more between 1978 and 1989 (after the exclusion of the registries that did not provide data in all three sub-periods). Lower limits were set for some rare cancer types.

More details on the design and general methodology of EUROCARE study can be found elsewhere [1–3].

Table 2
Weight of each country, based on the proportion contributed by each of the countries listed to the pool of general childhood population (ages 0–14 years) of these countries in 1990 (WHO data bank, retrieved from EUCAN 4 software [12])[a]

	Weight
Austria	1.9
Denmark	1.3
England and Wales	14.2
Estonia	0.5
Finland	1.3
France	15.3
Germany	17.6
Iceland	0.1
Italy	15.5
Poland	12.2
Scotland	1.0
Slovakia	1.4
Slovenia	0.6
Spain	11.7
Sweden	2.1
Switzerland	1.6
The Netherlands	3.9

[a] These proportions correspond to the weights used for computing European weighted survival in the EUROCARE study.

3. Results

The study base included 34 814 cases (Table 1) diagnosed in 1978–1989, 16 175 of which were diagnosed in the period 1985–1989 (corresponding to the recruitment for the EUROCARE II study). Additionally 9495 cases were diagnosed in 1990–1992. The largest contribution came from the nationwide registries of England and Wales (12 691 cases in 1978–1989) and West Germany (10 045 cases in 1980–1989). Overall quality of data appeared to be reasonably high, with little variation among registries (Table 1). Average percentage of losses to follow-up were 2.0%, with the highest values of 8.9% in Geneva and 19.80% in Eindhoven registries. A relatively large proportion of cases lost to follow-up was observed for Germany (4.4%). This was likely to be the consequence of most of the follow-up being an extension of the clinical follow-up. A relatively high proportion of those have since been followed up through administrative sources and personal contact successfully [15]. Most registries included all cases with at least 5 years of follow-up, although there were some exceptions (Table 1).

Table 3 presents the number of cases diagnosed in 1978–1989 for each major diagnostic category, by country, age and gender. The distribution by type of neoplasm and demographic variables reflect the expectation from the descriptive epidemiological studies.

Table 4 presents the frequency of cases in the 'unspecified' categories within selected major diagnostic

Table 3
Number of cases of childhood neoplasm incident in 1978–1989 and included in the EUROCARE database, by major diagnostic category and country and demographic variables[a]

ICCC Code	Leukaemia	Lymphoma	CNS neoplasm	Sympathetic nervous system	Retinoblastoma	Renal tumours	Hepatic tumours	Malignant bone tumours	Soft tissue sarcomas	Germ cell, throphoblastic, other gonadal	Carcinomas and other malignant epithelial	Other and unspecified neoplasms
	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII
	n (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Austria	8 (0.1)	4 (0.1)	3 (0.05)	1 (0.05)	3 (0.3)	2 (0.1)	0	0	4 (0.2)	3 (0.3)	0	0
Denmark	500 (4)	152 (4)	365 (6)	98 (4)	38 (4)	100 (5)	15 (4)	70 (4)	89 (4)	35 (4)	54 (7)	19 (12)
England and Wales	4371 (33)	1391 (34)	2615 (43)	783 (35)	360 (38)	718 (35)	112 (33)	680 (38)	843 (39)	402 (41)	380 (46)	36 (23)
Estonia	133 (1)	64 (2)	79 (1)	22 (1)	11 (1)	41 (2)	6 (2)	23 (1)	24 (1)	20 (2)	9 (1)	6 (4)
Finland	521 (4)	153 (4)	377 (6)	99 (4)	45 (5)	107 (5)	18 (5)	67 (4)	68 (3)	40 (4)	65 (8)	15 (9)
France	179 (1)	71 (2)	70 (1))	30 (1)	11 (1)	37 (2)	8 (2)	30 (2)	27 (1)	6 (0.6)	21 (3)	3 (2)
Germany (West)	3926 (30)	1305 (32)	1313 (21)	812 (36)	296 (31)	686 (33)	116 (34)	557 (31)	681 (31)	262 (27)	82 (10)	9 (6)
Iceland	35 (0.3)	8 (0.2)	19 (0.3)	4 (0.2)	3 (0.3)	4 (0.2)	0	8 (0.4)	11 (0.5)	3 (0.3)	1 (0.1)	0
Italy	620 (5)	245 (6)	330 (5)	135 (6)	30 (3)	90 (4)	22 (6)	123 (7)	113 (5)	36 (4)	49 (6)	8 (5)
Poland	78 (0.6)	30 (0.7)	35 (0.6)	10 (0.4)	1 (0.1)	19 (0.9)	2 (0.6)	8 (0.4)	11 (0.5)	14 (1)	4 (0.5)	2 (1)
Scotland	461 (4)	150 (4)	307 (5)	80 (4)	51 (5)	80 (4)	12 (4)	69 (4)	88 (4)	38 (4)	37 (4)	4 (3)
Slovakia	604 (5)	313 (0.9)	366 (6)	115 (5)	63 (7)	108 (5)	19 (6)	76 (4)	119 (6)	73 (8)	48 (6)	23 (15)
Slovenia	68 (0.5)	44 (1)	35 (0.6)	14 (0.6)	8 (0.8)	13 (0.6)	2 (0.6)	9 (0.5)	17 (0.8)	9 (0.9)	6 (0.7)	4 (3)
Spain	106 (0.8)	57 (1)	56 (0.9)	21 (0.9)	10 (1)	12 (0.6)	1 (0.3)	19 (1)	16 (0.7)	10 (1)	23 (3)	7 (4)
Sweden	138 (1)	57 (1)	104 (2)	19 (0.8)	14 (1)	26 (13)	4 (1)	22 (1)	26 (1)	13 (1)	20 (2)	17 (11)
Switzerland	29 (0.2)	9 (0.2)	14 (0.2)	11 (0.5)	3 (0.3)	3 (0.1)	0	6 (0.3)	7 (0.3)	0	8 (1)	0
The Netherlands	1300 (10)	31 (0.8)	42 (0.7)	15 (0.7)	7 (0.7)	14 (0.7)	4 (1)	18 (1)	19 (0.9)	6 (0.6)	16 (2)	5 (3)
Period												
1978–1981	3798 (29)	1206 (30)	1747 (28)	582 (26)	235 (25)	554 (27)	81 (24)	573 (32)	570 (26)	251 (26)	230 (28)	39 (25)
1982–1984	4554 (35)	1389 (34)	1985 (32)	766 (34)	314 (33)	710 (34)	108 (32)	612 (34)	756 (35)	327 (34)	276 (34)	54 (34)
1985–1989	4725 (36)	1489 (36)	2398 (39)	921 (41)	405 (42)	796 (39)	152 (45)	600 (34)	837 (39)	392 (40)	317 (39)	65 (41)
Age at diagnosis (years)												
0–4	6688 (51)	713 (17)	2229 (36)	1925 (85)	904 (95)	1551 (75)	241 (71)	103 (6)	903 (42)	474 (49)	83 (10)	58 (37)
5–9	3602 (28)	1360 (33)	2113 (34)	266 (12)	47 (5)	421 (20)	42 (12)	460 (26)	590 (27)	126 (13)	173 (21)	34 (22)
10–14	2787 (21)	2011 (49)	1788 (29)	78 (3)	3 (0.3)	88 (4)	58 (17)	1222 (68)	670 (31)	370 (38)	567 (69)	66 (42)
Boys	7185 (55)	2839 (70)	3396 (55)	1226 (54)	498 (52)	1025 (50)	193 (57)	913 (51)	1225 (57)	439 (45)	378 (46)	93 (59)
Girls	5892 (45)	1245 (30)	2734 (45)	1043 (46)	456 (48)	1035 (50)	148 (43)	872 (49)	938 (43)	531 (55)	445 (54)	65 (41)
All	130 77 (100)	4084 (100)	6130 (100)	2269 (100)	954 (100)	2060 (100)	341 (100)	1785 (100)	2163 (100)	970 (100)	823 (100)	158 (100)

[a] The list of registries contributing is given in Table 1.

Table 4
Quality indicators in the childhood cancer data base of the EUROCARE study by country and demographic variables: proportion of cases with microscopical confirmation of diagnosis and of cases with unspecified histology, classified in the 'other and unspecified' diagnostic subgroups of ICCC[a]

			ICCC category							
	Total *n* cases	Microscopic confirmation	Unspecified leukaemia Ie	Unspecified lymphoma IIe	Unspecified CNS neoplasm IIIf	Unspecified malignant renal tumours VIc	Unspecified malignant hepatic tumours VIIc	Unspecified malignant bone tumours VIIIc	Unspecified soft tissue sarcomas IXe	Other and unspecified malignant gonadal tumours Xe
	n (%)	%	*n* (%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
Austria	28 (0.1)	96.4	0 (0)	0 (0)	1 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Denmark	1535 (4)	94.9	5 (1.0)	16 (10.5)	74 (20.3)	10 (10.0)	0 (0)	4 (5.7)	7 (7.9)	0 (0)
England and Wales	12691 (36)	93.4	50 (1.1)	21 (1.5)	136 (5.2)	0 (0)	0 (0)	9 (1.3)	63 (7.5)	7 (1.7)
Estonia	438 (1)	90.0	37 (27.8)	3 (4.7)	23 (29.1)	6 (14.6)	0 (0)	5 (21.7)	6 (25.0)	2 (10.0)
Finland	1575 (5)	99.8	11 (2.1)	60 (39.2)	34 (9.0)	1 (0.9)	1 (5.6)	4 (6.0)	7 (10.3)	0 (0)
France	493 (1)	94.3	5 (2.8)	25 (35.2)	9 (12.9)	1 (2.7)	2 (25.0)	0 (0)	6 (22.2)	0 (0)
Germany (West)	10045 (29)	99.7	34 (0.9)	15 (1.1)	4 (0.3)	0 (0)	0 (0)	5 (0.9)	45 (6.6)	1 (0.4)
Iceland	96 (0.3)	99.0	2 (5.7)	0 (0)	1 (5.3)	0 (0)	0 (0)	1 (12.5)	1 (9.1)	0 (0)
Italy	1801 (5)	91.4	23 (3.7)	11 (4.5)	40 (12.1)	1 (1.1)	2 (9.1)	4 (3.3)	6 (5.3)	0 (0)
Poland	214 (0.6)	93.0	0 (0)	6 (20.0)	10 (28.6)	0 (0)	0 (0)	1 (12.5)	0 (0)	1 (7.1)
Scotland	1377 (4)	95.7	6 (1.3)	4 (2.7)	12 (3.9)	0 (0)	0 (0)	2 (2.9)	12 (13.6)	1 (2.6)
Slovakia	1927 (6)	96.4	10 (1.7)	17 (5.4)	48 (13.1)	9 (8.3)	0 (0)	2 (2.6)	12 (10.1)	1 (1.4)
Slovenia	229 (0.7)	97.8	1 (1.5)	2 (4.5)	1 (2.9)	1 (7.7)	0 (0)	0 (0)	1 (5.9)	0 (0)
Spain	338 (1)	97.0	5 (4.7)	0 (0)	9 (16.1)	0 (0)	0 (0)	0 (0)	3 (18.8)	0 (0)
Sweden	460 (1)	98.7	5 (3.6)	0 (0)	5 (4.8)	0 (0)	0 (0)	1 (4.5)	2 (7.7)	1 (7.7)
Switzerland	90 (0.3)	100	0 (0)	0 (0)	1 (7.1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
The Netherlands	1477 (4)	98.4	38 (2.9)	0 (0)	8 (19.0)	0 (0)	1 (25.0)	0 (0)	2 (10.5)	0 (0)
Period										
1978–1981	9866 (28)	91.6	73 (1.9)	60 (5.0)	136 (7.8)	12 (2.2)	2 (2.5)	15 (2.6)	49 (8.6)	4 (1.6)
1982–1984	11851 (34)	92.4	88 (1.9)	58 (4.2)	138 (7.0)	9 (1.3)	1 (0.9)	11 (1.8)	50 (6.6)	6 (1.8)
1985–1989	13097 (38)	91.6	71 (1.5)	62 (4.2)	142 (5.9)	8 (1.0)	3 (2.0)	12 (2.0)	74 (8.8)	4 (1.0)
Age at diagnosis (years)										
0–4	15872 (46)	91.9	130 (1.9)	51 (7.2)	152 (6.8)	24 (1.5)	4 (1.7)	9 (8.7)	73 (8.1)	1 (0.2)
5–9	9234 (27)	91.4	40 (1.1)	56 (4.1)	133 (6.3)	4 (1.0)	2 (4.8)	11 (2.4)	40 (6.8)	5 (4.0)
10–14	9708 (28)	92.4	62 (2.2)	73 (3.6)	131 (7.3)	1 (1.1)	0 (0)	18 (1.5)	60 (9.0)	8 (2.2)
Boys	19410 (56)	92.2	132 (1.8)	119 (4.2)	229 (6.7)	15 (1.5)	4 (2.1)	19 (2.1)	92 (7.5)	1 (0.2)
Girls	15404 (44)	91.5	100 (1.7)	61 (4.9)	187 (6.8)	14 (1.4)	2 (1.4)	19 (2.2)	81 (8.6)	13 (2.4)
All	34814 (100)	91.8	232 (1.8)	180 (4.4)	416 (6.8)	29 (1.4)	6 (1.8)	38 (2.1)	173 (8.0)	14 (1.4)

[a] The latter is given as the proportion of number of cases in the corresponding major diagnostic category. The registries considered in each country are listed in Table 1.

Table 5
Description of childhood cancer cases diagnosed in the period 1985–1989 and included in the EUROCARE database[a]

Country (Registries)	Microscopical confirmation %	Proportion lost to follow-up %	Frequency of alive cases with a follow-up shorter than 5 years %
Austria (Tyrol)	96.4	0	0
Denmark	100	0	0
The Netherlands (Eindhoven)	81.0	15.2	18.9
Dutch Childhood Leukemia Study Group[b]	100	0.8	0.6
England and Wales[b]	91.8	0.6	0.4
Estonia	91.8	4.3	0
Finland	99.7	0	0
French registries (Somme, Calvados, Cote d'Or[c], Doubs)	95.6	0.4	41.5
Germany (West)[b]	100	3.4	18.7
Iceland	100	0	0
Italian registries (Florence, Genoa, Latina, Modena, Parma, Piedmont,[b] Ragusa, Romagna, Varese)	88.5	2.9	0
Polish registries (Crakow, Warsaw)	92.1	3.2	1.4
Scotland[b]	95.2	0	0.6
Slovakia	96.0	0	47.9
Slovenia	97.8	1.7	0
Spanish registries (Basque Country, Girona,[c] Mallorca, Navarra, Tarragon)	97.0	0.6	46.3
Sweden (South)	97.8	0	0
Switzerland (Geneva)	100	10.8	0
All participating registries	91.7	1.7	10.3

[a] The registries considered in each country and the number of cases in each are listed in Table 1.
[b] Childhood cancer registry.
[c] See Table 1.

groups. The proportion of cases allocated to these codes was greater than 5% only for CNS neoplasms (6.8%) and soft tissue sarcomas (8.0%). 37% of cases of carcinoma (ICCC group XI) were of the unspecified type (data not presented). Microscopic confirmation of the diagnosis was available for 91.8% of cases, the lowest proportion being observed for CNS neoplasms (87%).

Table 5 shows, for cases diagnosed in 1985–1989, the proportions with microscopic confirmation, lost to follow-up and of cases alive and with follow-up shorter than 5 years. These indicators, in general, did not differ from the values observed for the entire data set.

Table 6 presents survival at 1 month since diagnosis for the main diagnostic categories, by country for the

Table 6
One month survival (%) among childhood cancer cases diagnosed in the period 1985–1989 and included in the EUROCARE database[a]

Country	All cancers %	ALL Ia %	ANLL Ib %	NHL IIb %	Medulloblastoma IIIc %	Neuroblastoma IVa %	Wilms' VIa %	Osteosarcoma VIIIa %	Ewing's VIIIc %
Denmark	97	96	90	92	93	92	100	100	100
England and Wales	95	96	86	93	91	95	98	100	100
Estonia	90	94	83	85	75	90	100	100	100
Finland	96	96	86	98	96	95	100	100	100
France	96	100	91	89	100	100	100	100	100
Germany (West)	96	98	92	96	94	98	98	99	100
Italy	95	98	89	94	96	98	95	97	100
Poland	96	99	88	90	67	100	100	100	
Scotland	94	98	81	92	89	80	100	100	100
Slovakia	93	95	87	91	90	92	94	100	100
Slovenia	97	96	75	96	100	100	100	100	100
Spain	94	92	84	94	93	90	92	100	100
Sweden	97	100	80	100	100	83	100	100	100
The Netherlands	94	98	83	73	50	83	100	100	100

NHL, Non-Hodgkin's lymphoma; ALL, acute lymphoblastic leukaemia; ANLL, acute-non-lymphocytic leukaemia.
[a] See text for details.

Table 7
Description of childhood cancer cases diagnosed in the period 1990–1992 and included in the EUROCARE database[a]

Country (Registries)	Period contributed to the database	Total number of cases in 1990–1992	Microscopical confirmation	Proportion lost to follow-up	Frequency of alive cases with a follow-up shorter than 5 years:
		n (%)	%	%	%
Austria (Tyrol)	1990–1992	46 (0.5)	100	0	71.4
Denmark	1990–1992	403 (4)	100	0	100
The Netherlands (Eindhoven)	1990–1992	37 (0.4)	94.6	8.1	100
Dutch Childhood Leukemia Study Group[b]	1990–1992	320 (3)	100	0.6	3.9
England and Wales[b]	1990–1992	3421 (36)	91.1	0.1	30.0
Estonia	1990–1992	123 (1)	95.9	0.8	100
Finland	1990–1992	446 (5)	100	0	67.9
France (Calvados, Cote d'Or, Doubs)	1990–1992	60 (0.6)	98.3	0	97.8
Germany (West)[b]	1990–1992	3613 (38)	100	1.1	73.2
Iceland	1990–1992	26 (0.3)	96.2	0	37.5
Italy (Modena, Varese)	1990–1992	56 (0.6)	91.1	1.8	21.4
Poland (Crakow)	1990–1992	37 (0.4)	83.8	2.7	100
Scotland[b]	1990–1992	363 (4)	95.6	0.3	40.0
Slovakia	1990–1991	298 (3)	96.7	0	100
Slovenia	1990–1991	90 (0.9)	96.7	1.1	100
Spain (Mallorca, Tarragon)	1990–1992	62 (0.7)	100	0	100
Sweden (South)	1990–1992	94 (1)	100	0	39.8
All participating registries		9495 (100)	98.4	0.5	56.5

[a] For countries with no nationwide registration, the registries contributing are listed in brackets.
[b] Childhood cancer registry.

period 1985–1989. Since dates were recorded for the EUROCARE database as months and years, this table corresponds to survival in the month following the month of diagnosis and, more appropriately corresponds on average to survival at 45 days since diagnosis. In children, short-term survival is an indicator of acute toxicity from treatment rather than an indicator of cases with very advanced diseases. For total cancers, the range is from 90% (Estonia) to 97% (Denmark, Sweden and Slovenia). ALL, ANLL, NHL and neuroblastoma show higher mortality. For these diseases the pattern among the countries is not always consistent, although the Nordic countries and countries in Central Europe tend to show a better performance.

Table 7 describes the cases diagnosed in 1990–1992. Out of a total of 9495 cases, 5344 (56%) were boys and 4151 (44%) girls, 4773 (50%) were aged 0–4 years at diagnosis, 2473 (26%) were aged 5–9 years and 2249 (24%) were aged 10–14 years. The highest proportion of cases without microscopic confirmation was observed in the Polish (16.2%) and Italian registries (8.9%) and in England and Wales (8.9%). The proportion of cases lost to follow-up was lower, but the duration of follow-up was shorter than for cases diagnosed in 1978–1989 and in 1985–1989: overall 56.5% of alive cases were observed for less than 5 years.

4. Discussion

The EUROCARE database represents one of the largest data sets on cancer survival in the world and the largest in Europe. Its capability in underlining differences in cancer survival among European countries has already been demonstrated for adults [1,2], but to a lesser extent for children [1]. In analyses on the EUROCARE I database, the classification was limited to the cancer site, which does not represent well the histology types that are typical in childhood [16]. The classification of childhood cancers according to an internationally accepted system adapted to the typical patterns of childhood cancer occurrence (ICCC) allows analyses of survival according to relatively homogeneous groups of childhood tumours and comparisons with the results from other population-based studies [4]. Some of us had explored in a previous study the applicability and usefulness of such classification of data provided by non-specialised cancer registries and coded using ICD-IX [17].

The quality of data provided from the cancer registries for the present study is reasonable when evaluated on the basis of the available indicators (proportion of subjects with the microscopic confirmation of the diagnosis, proportion coded in unspecified categories, frequency of errors in the data, proportion lost to follow-up). The data quality was further strengthened by data checks performed in collaboration with contributing registries. The registries contributing to this study had also been verified during the selection process for contribution to IARC publications *International Incidence of Childhood Cancer* [6] and *Cancer Incidence in Five Continents* (5). Some minor differences in the number of cases might be observed however, since in the present data-set cases of benign intracranial neoplasms and DCO cases were not included.

Issues of comparability are nevertheless at stake when examining survival results by period and country. The proportion of cases with no microscopical confirmation ranged from 0 to 10%, with proportions higher than 5% in the registries in Estonia, Poland, Italy, France, England and Wales and Denmark. The very low proportion of cases without microscopical confirmation in the German registry was probably the consequence of the extension of clinical trials in that country, but may also reflect incompleteness [18,19].

93.4% of alive cases diagnosed in 1978–1989 had been followed for a period longer than 5 years, indicating that information in the database was adequate for describing actual survival curves.

The information on survival extended to 1992 is a useful indication of survival trends but requires a careful interpretation. Cases diagnosed in 1990–1992 compared with the period 1978–1989 presented the same or even better indicators of quality, but the geographical coverage in some countries was smaller and the follow-up shorter, leading to a less precise estimation of survival rates. Moreover, some registries contributed cases only up to 1989. Because of this caution should be used when comparing the results of the survival analyses extended to 1992 with the previous period.

The interpretation of the European average survival also requires some attention. Population coverage by a cancer registry was as low as 3.9% in some countries (Table 1). Therefore, simple pooling gives too little weight to the countries with low coverage, while a weighing procedure exaggerates the contribution of the registries which are not representative of their country. Moreover, a weighted average, providing wider confidence intervals is less precise. As both solutions are imperfect, both estimates were calculated and their appropriateness was evaluated individually in the light of other partial results for each tumour type. Overall European survival can thus be represented by either weighted or unweighted averages, or even by both if they diverge.

Childhood neoplasms are rare and represent approximately 1% of the total cancer occurrence. The EUROCARE study permitted the population-based survival to be described even for specific subgroups of tumours and over long time periods. Extension of this investigation in time and space will continue to monitor the progress or pinpoint weaknesses of all aspects of cancer care in Europe and support the fight against cancer in childhood.

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