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Survival of childhood lymphomas in Europe, 1978–1992: a report from the EUROCARE study

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Abstract

In most developed countries, malignant lymphomas account for 10–15% of all cancers occurring among children aged 0–14 years. The present study estimates survival after a diagnosis of lymphoma in childhood, based on the EUROCARE II database which includes 34 population-based cancer registries from 17 European countries. The survival pattern of children with malignant lymphoma diagnosed in 1985–1989 is reported, as well as the time trends since 1978. The analyses focus on Hodgkin's disease (HD, 1696 cases) and on non-Hodgkin's lymphoma (NHL, 2255 cases including Burkitt's lymphoma and unspecified lymphomas). For HD, the European weighted average 5-year survival rate was 93% (95% confidence interval (CI) 82–98) in 1985–1989. The survival rates were not affected by either age or gender. 5-year survival rates ranged from 68% (95% CI 34–90) in Estonia to 96% (95% CI 92–98) in Germany and 100% (95% CI 57–100) in Slovenia. Multivariate analyses for the time period 1978–1989 gave little suggestion of an improvement in survival over the later time periods of diagnosis. For NHL, the European weighted average 5-year survival rate was 74% (95% CI 67–80) in 1985–1989. Gender did not influence the survival rate. Children in the age group 0–4 years had a poorer prognosis compared with older cases (5-year rate: 66% versus 77% in the pool). 5-year survival rates ranged from 53% (95% CI 30–76) (Estonia) to 83% (95% CI 62–94) in France and 83% (95% CI 66–92) in Scotland. Multivariate analysis show a decreasing HR for the more recent periods of diagnosis from 1 in 1978–1981 to 0.67 (95% CI 0.56–0.79) in 1982–1985 to 0.48 (95% CI 0.40–0.57) in 1986–1989. Exploratory analysis, conducted including the cancer registries which provided cases diagnosed until 1992, show a positive trend over time for both types of lymphoma.

Keywords: Childhood lymphomas; Population-based survival; Cancer registries; EUROCARE study

1. Introduction

In most European countries, malignant lymphomas account for 10–15% of all cancers occurring among children aged 0–14 years. The main histological types are Hodgkin's disease (HD) and non-Hodgkin's lymphoma (NHL) — including Burkitt's lymphoma (BL) — accounting respectively for 35–40 and 55–65% of all cases. The remaining 5–10% are miscellaneous lymphoreticular neoplasms and unspecified cell type lymphomas. The male:female (M:F) ratio for the whole lymphoma group is 2–2.5:1. The M:F ratio is age-dependent for HD, being highest in boys aged 0–9 years, while the male predominance for NHL is marked in all age groups. The incidence rate for HD increases with age: the disease is very rare in the age group 0–4 years, while more than half the childhood cases are diagnosed at age 10–14 years. The childhood NHL are a heterogeneous group: more than half of the cases are diagnosed before the age of 10 years and the incidence rate peaks at 5–9 years; a similar trend is observed for BL, while diffuse large cell lymphomas are more common in adolescents [1,2].

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Clinical and population-based data indicate that more than 90% of all children and adolescents with newly diagnosed HD are curable with modern therapy. Since the selection of treatment is influenced by disease stage, histological subtype, gender and sexual maturity and the potential long-term effects of treatment related to them, careful clinical and/or pathological evaluation is essential [3–5].

NHL in children is generally considered to be widely disseminated from the outset, even when apparently localised. More than 70% of children and adolescents with NHL will survive at least 5 years with modern chemotherapy, although outcome is variable depending on a number of factors. The most important prognostic determinant, given optimal therapy, is the extent of disease at diagnosis as determined by pretreatment staging [5–8].

Reliable population-based data on the survival of childhood lymphoma patients are available only for a few countries, where a large enough population is covered by a childhood or general cancer registry and where survival studies have been carried out [5,9–12]. Furthermore, comparability of these estimates is limited due to several factors, i.e. the quality of the data, the statistical method used, the disease definition, the coding and classification, etc. The EUROCARE centralised database which for childhood tumours includes 34 population-based cancer registries from 17 countries, provides a unique basis to study the survival of children with malignant lymphomas. The contributing registries correspond to those which provided data for the EUROCARE II analyses on adult cancer [13] plus five childhood cancer specialised registries (one limited to leukaemia). Cases from England and Wales and Scotland were provided by the respective National Childhood Cancer Registries, to which the Regional Cancer Registries contribute. The present study covered nine countries completely (Denmark, Estonia, England and Wales, Finland, Iceland, Slovakia, Slovenia, Scotland and West Germany). The list of registries contributing to the present study, the size of the childhood population covered during the study period and the proportion of the national population covered by the registry are provided elsewhere, as well as the details and references on the activity of each registry [14].

Knowledge of the survival profile on an international population base could lead to more effective health-care planning and improvement of the quality of medical care and research in Europe. The present paper, based on the EUROCARE data base, focuses on the population based survival analysis of childhood lymphomas in Europe. It reports the survival pattern of children with malignant lymphoma diagnosed in 1985–1989, as well as the time trends in survival since 1978. Survival was analysed also for period the 1978–1992 limited to the cancer registries which provided data for the period 1990–1992. In the framework of the EUROCARE I (1978–1985), analyses for lymphoma were limited to HD [15].

2. Patients and methods

The present study included the malignant lymphomas (4084 cases, International Classification of Childhood Cancer (ICCC) group 2) [16] diagnosed during 1978–1989 identified in the EUROCARE childhood cancer database. Both cases with and without histological confirmation of diagnosis were included, cases documented only by death certificate or diagnosed at autopsy were excluded. Description of methods used by the Cancer Registries participating to EUROCARE, as well as procedures used for follow-up and to ensure data comparability were reported in the EUROCARE monographs [15,17]. A description of the specialised Childhood Cancer Registries was previously published [1].

In order to focus on the diagnostic categories with numbers large enough to provide stable estimates, the analyses were limited to the HD (ICCC: IIa) and NHL (ICCC: IIb, IIc and IIe groups). Miscellaneous lymphoreticular neoplasms (ICCC: IId; 133 cases, 3% of total lymphomas), were excluded from both the descriptive and survival analyses on the basis of their limited numbers and because they were not a homogeneous category. Only four countries recruited more than 10 cases in this category and the proportion of miscellaneous lymphoreticular neoplasms in the total lymphoma group was in the range 0–2%, the highest figure being observed in Sweden.

As HD and NHL are separate entities from the point of view of aetiology, treatment and outcome, they were addressed separately throughout the paper. Table 1 shows the distribution by country, age and gender of the HD and NHL cases and the indicators of data quality. The HD and NHL accounted respectively for 42 and 55% of the total lymphoma cases in the database. Among NHL, BL and unspecified lymphomas were respectively 12 and 8%. The percentage of HD cases lost to follow-up in the different registries was in the range 0–8% with a single outlier value of 22% for The Netherlands and the percentage of microscopical confirmation of diagnosis was in the range 92–100%. Boys represented 66% of the HD cases (58–89% in the larger series; $n \geqslant 12$) overall. The boys:girls ratio was higher in the age groups 0–4 and 5–9 years (3:1) than at age 10–14 years (1.6:1). The corresponding figures for NHL were 0–5% lost to follow-up (one outlier value of 11% for The Netherlands); 73% boys (range 53–83%; $n \geqslant 5$) with the largest boys:girls ratio observed in the 5–9 year age group and 93–100% of microscopical confirmation. These figures corresponded to what has been reported in

Table 1
Number of cases and data quality for childhood malignant lymphoma cases in the EUROCARE database, 1978–1989

Country	IIa Hodgkin's disease					IIb, IIc, IIe Non-Hodgkin's lymphoma				
	No. of cases (%)	Boys (%)	Cases diagnosed in 1985–1989	LFUP (%)	MV (%)	No of cases (%)	Boys (%)	Cases diagnosed in 1985–1989	LFUP (%)	MV (%)
Northern Europe										
Denmark	55 (3)	66	17	0	100	90 (4)	76	32	0	100
Finland	47 (3)	60	16	0	100	106 (5)	72	41	1	100
Iceland	7 (0.4)	100	4	0	100	1 (0.04)	0	0	0	100
Sweden*	25 (1)	89	5	0	100	30 (1)	70	13	0	100
UK										
England and Wales	609 (36)	70	238	1	98	751 (33)	72	317	1	98
Scotland	59 (3)	59	23	0	100	88 (4)	74	36	1	99
Western and Central Europe										
Austria[a]	3 (0.2)	100	3	0	100	1 (0.04)	0	1	0	100
France[a]	21 (1)	48	10	0	95	47 (2)	72	27	2	100
Germany	537 (32)	63	234	2	100	718 (32)	73	397	5	100
Switzerland[a]	5 (0.3)	80	2	0	100	4 (0.2)	100	2	0	100
The Netherlands[a]	9 (0.5)	33	5	22	100	19 (0.8)	53	10	11	95
Southern Europe										
Italy[a]	93 (5)	69	43	2	98	135 (6)	74	65	1	96
Spain[a]	21 (1)	71	21	0	100	35 (2)	71	35	0	100
Eastern Europe										
Estonia	35 (2)	80	10	6	100	29 (1)	79	13	3	93
Poland[a]	12 (0.7)	58	7	8	92	18 (0.8)	83	10	0	100
Slovakia	147 (9)	64	49	0	100	160 (7)	71	74	0	99
Slovenia	21 (1)	62	21	0	100	23 (1)	83	23	0	100
Age (years)										
0–4	135 (8)	76	62	1	99	512 (23)	68	265	3	90
5–9	478 (28)	75	194	2	96	863 (38)	76	421	2	95
10–14	1083 (64)	61	450	1	96	880 (39)	72	409	2	95
Gender										
Boys	1122 (66)		450	2	96	1637 (73)		782	2	95
Girls	574 (34)		258	1	96	618 (27)		313	2	93
Total	1696 (100)	66	708	2	96	2255 (100)	73	1095	2	94

MV, morphologically verified; LFUP, lost to follow-up.
[a] < 20% of national population covered.

descriptive epidemiology studies in Western industrialised countries [1,5].

3. Statistical methods

Observed survival rates were calculated by the actuarial method [18] using the program prepared by Hakulinen [19]. Country- and gender-specific observed and relative survival rates were calculated for three age classes: 0–4, 5–9 and 10–14 years. Relative survival is not shown as it closely corresponds to the observed survival, given the low mortality in the relevant age classes.

As survival may be related to the age of patients, and the age distribution of children may be different between countries and gender, direct age-adjusted survival rates were calculated applying age-specific survival rates (age classes: 0–4, 5–9 and 10–14 years) to the standard population (the EUROCARE data base). The same weights were used for boys and girls, in order to allow for comparisons between gender. Age-standardised rates can be calculated only for those countries presenting cases in each of the three age classes.

Overall (European) survival was estimated in two ways. One was a weighted average of the survival of the individual countries, with weightings proportional to the childhood population (0–14 years) in each country [14]. For the five countries with partial coverage, the survival of patients, included in the study for each country, is assumed to be representative of the survival at the national level [20]. This weighted average may have the undesired effect of expanding the variability of survival estimates based on a very small number of cases, as occurs when small cancer registries represent large countries. Therefore, an average European survival

estimate was also calculated using pooled data from all cancer registries. Dealing with a rare disease such as childhood tumours, attention should be paid to ascertaining the reliability of the estimates. Comparing results from the two methods, to see whether they are consistent or not, can be useful to provide comment on reliability issues regarding the European average of childhood lymphoma survival probability. Actuarial survival analyses were conducted by entity, country, gender and age class on the entire EUROCARE data base (years of diagnosis 1978–1989) and on the subset gathered for the EUROCARE II study (years of diagnosis 1985–1989).

Cox proportional hazard models [21] were used to compare hazard ratios (HR) between different periods of diagnosis taking into account the different distribution of age, gender and country. The total calendar period was divided into three periods (1978–1981, 1982–1985, 1986–1989) and age at diagnosis in the three 5-year classes. Only countries with 30 cases or more between 1978 and 1989 are included, after excluding the registries that did not provided data in all three periods. Intercountry comparisons are computed for countries with more than 10 cases reported in 1986–1989. Analyses including 1990–1992 were conducted using the same methods and the registries were reported in Magnani and colleagues [14].

4. Results

Table 2 shows 5-year survival rates (age standardised) for the period of diagnosis 1985–1989 for HD. Since age-standardised figures were missing for some countries with no cases in some age classes, crude survival rates for the age class 10–14 years is also reported to provide a comparison. The European weighted average at 5 years was 93% (95% confidence interval (CI) 82–98) and the range was from 68% (95% CI 34–90) (Estonia) to 96% (95% CI 92–98) (Germany) and 100% (95% CI 57–100) (Slovenia). The countries with the poorer prognosis also showed lower survival rates 1 year after diagnosis (in 1985–1989 age-standardised: Denmark: 85% (95% CI: 56–96); Estonia 79% (95% CI: 39–96), data not shown in detail). For the entire period of 1978–1989, 5-year survival was in the range of 65% (95% CI: 48–79) (Estonia) to 95% (95% CI: 92–96) (Germany) (data not shown in detail).

Survival for NHL was poorer than for HD (Table 3): for cases diagnosed in 1985–1989, the European weighted average at 5 years was 74% (95% CI 67–80) and the survival rates for the countries ranged from 53% (95% CI 30–76) (Estonia) to 83% (95% CI 62–94) (France) and 83% (95% CI 66–92) (Scotland). From 1 to 5 years after diagnosis, survival in Europe (the pooled estimate) decreased from 83% (95% CI 80–85) to 74% (95% CI 74–77). This pattern was observed in all countries, with the exception of The Netherlands and Poland. In 1978–1989, the range of 5-year survival rates was 32% (95% CI: 17–52) (Estonia) to 76% (95% CI: 32–96) (Poland) (data not shown in detail). The survival rates did not vary by gender; children in age 0–4 years had a lower survival compared with the older children (5-year rate 65% versus 77%).

For both HD and NHL, weighted and pooled estimates of the European survival rates were very close to each other, even after stratification by age class and gender (data not shown), thereby confirming the reliability of these estimates.

Table 4 shows the results of the Cox proportional hazards analyses of survival by period and country for HD and NHL. The analyses generally confirmed the pattern already presented by the univariate analyses, with no evidence of gender-related differences in survival

Table 2
Age standardised and age-specific (10–14 years at diagnosis) 5-year survival rates (95% confidence limits) for childhood Hodgkin's disease in EUROCARE II database, 1985–1989

Country	IIa Hodgkin's disease	
	10–14 years	Age-standardised
Northern Europe		
Denmark	82 (52–95)	79 (51–93)
Finland	100 (72–100)	–
Sweden[a]	–	–
UK		
England and Wales	91 (85–94)	93 (89–96)
Scotland	75 (51–90)	84 (56–96)
Western and Central Europe		
France[a]	85 (46–97)	–
Germany	97 (93–99)	96 (92–98)
The Netherlands[a]	80 (38–96)	–
Southern Europe		
Italy[a]	89 (73–96)	91 (70–98)
Spain[a]	92 (67–99)	–
Eastern Europe		
Estonia	50 (19–81)	68 (34–90)
Poland[a]	100 (61–100)	–
Slovakia	87 (68–95)	84 (70–92)
Slovenia	100 (57–100)	100 (57–100)
Europe weighted	91 (78–97)	93 (82–98)
Europe pooled	92 (89–94)	92 (90–94)
Age, years (crude, pooled, age-specific)		
0–4		93 (84–97)
5–9		94 (89–96)
10–14		92 (89–94)
Gender		
Boys	93 (90–96)	93 (91–95)
Girls	89 (84–93)	91 (86–94)

–Too few cases for age standardisation.
[a] < 20% of national population covered.

for both diseases. For HD cases, multivariate analyses gave little suggestion for a trend in survival over time. Country differences were marked for HD: during the period 1978–1989 three countries (Denmark, Estonia and Slovakia) showed HRs higher than the reference and that were statistically significant. Germany, in contrast, showed a significant reduction in HR. The higher risk for Denmark and Slovakia was also observed when the analysis was restricted to the period of 1986–1989 (data not shown).

Prognosis after NHL showed a marked time trend, with a significant decrease of HR to 0.48 (95% CI 0.40–0.57) in 1986–1989 compared with 1978–1981 (the reference). Intercountry differences were less extreme, with only one country (Slovakia) showing a statistically significant increase in HR and one country (Germany) with a statistically significant reduced HR. Analyses of intercountry differences were also repeated when limited to patients diagnosed during 1986–1989 and results (data not shown) did not differ in general when compared with results observed for the 1978–1989 period. The greatest changes for HD were seen in Italy (HR = 1.29, 95% CI = 0.44–3.83), Finland (HR = 0, no deaths occurred) and Slovakia (HR = 3.17, 95% CI = 1.37–7.33). For NHL, the greatest difference was observed in the HR for Denmark (HR = 0.83, 95% CI = 0.59–1.15).

Exploratory analyses were conducted for cases diagnosed until the period 1990–1992, using a multivariate model including age, gender and country of diagnosis (Table 5). The countries providing data only until 1989 were excluded from this analysis. The analyses clearly showed a positive time trend for both HD and NHL. The average trend was estimated using the period as a

Table 3
Age-standardised 1- and 5-year survival rates (95% confidence limits) for childhood non-Hodgkin's lymphoma in EUROCARE II database, 1985–1989

Country	IIb, IIc, IIe non-Hodgkin's lymphoma	
	1-year rate	5-year rate
Northern Europe		
Denmark	82 (61–93)	71 (53–84)
Finland	84 (69–92)	76 (60–87)
Sweden[a]	93 (14–100)	81 (39–97)
UK		
England and Wales	82 (78–86)	74 (69–78)
Scotland	88 (72–95)	83 (66–92)
Western and Central Europe		
France[a]	91 (56–99)	83 (62–94)
Germany	87 (83–90)	79 (75–83)
The Netherlands[a]	74 (31–94)	74 (31–94)
Southern Europe		
Italy[a]	78 (66–87)	69 (57–79)
Spain[a]	92 (63–99)	75 (58–86)
Eastern Europe		
Estonia	77 (43–94)	53 (30–76)
Poland[a]	71 (24–95)	71 (24–95)
Slovakia	62 (49–72)	54 (42–65)
Slovenia	92 (58–99)	78 (56–91)
Europe weighted	85 (77–91)	74 (67–80)
Europe pooled crude	83 (80–85)	74 (72–77)
Age years (crude pooled)		
0–4	75 (69–80)	65 (59–71)
5–9	85 (81–88)	77 (73–81)
10–14	86 (82–89)	77 (73–81)
Gender		
Boys	83 (80–86)	75 (72–78)
Girls	82 (78–86)	73 (68–78)

[a] <20% of national population covered.

Table 4
Results of Cox proportional hazards analyses for childhood malignant lymphoma in the EUROCARE database, 1978–1989[a]

	IIa Hodgkin's disease HR (95% CI)	IIb, IIc, IIe non-Hodgkin's lymphoma HR (95% CI)
Gender		
Boys	1 (reference)	1 (reference)
Girls	1.13 (0.85–1.50)	0.99 (0.84–1.17)
Age, years		
0–4	0.73 (0.42–1.28)	1.03 (0.85–1.24)
5–9	0.65 (0.46–0.91)	0.86 (0.73–1.02)
10–14	1 (reference)	1 (reference)
Period		
1978–1981	1 (reference)	1 (reference)
1982–1985	1.01 (0.74–1.39)	0.67 (0.56–0.79)
1986–1989	0.90 (0.63–1.29)	0.48 (0.40–0.57)
Country		
Denmark	2.30 (1.35–3.94)	1.27 (0.92–1.75)
England and Wales	1 (reference)	1 (reference)
Estonia	4.32 (2.49–7.49)	–
Finland	1.22 (0.59–2.51)	0.85 (0.60–1.20)
Germany	0.52 (0.35–0.76)	0.68 (0.57–0.83)
Italy[a]	0.59 (0.26–1.35)	1.12 (0.83–1.51)
Scotland	1.53 (0.86–2.74)	1.12 (0.79–1.57)
Slovakia	1.57 (1.01–2.44)	2.06 (1.63–2.60)

HR, hazard ratio; CI: 95%, confidence interval; – No deaths.
[a] Countries with fewer than 30 cases or not providing data for each of the three periods were excluded.

Table 5
Results of Cox proportional hazards analyses for childhood malignant lymphoma in EUROCARE database period 1978–1992, selected cancer registries[a]

Period	IIa Hodgkin's disease HR (95% CI)	IIb, IIc, IIe non-Hodgkin's lymphoma HR (95% CI)
1978–1981	1 (reference)	1 (reference)
1982–1985	0.98 (0.72–1.36)	0.66 (0.55–0.78)
1986–1989	0.85 (0.56–1.23)	0.47 (0.39–0.56)
1990–1992	0.53 (0.30–0.93)	0.38 (0.31–0.48)
Continuous	0.86 (0.75–0.99)	0.72 (0.67–0.76)

HR, hazard ratio; CI: 95%, confidence interval.
[a] Countries with fewer than 30 cases or not providing data for each of the four periods are excluded.

continuous variable: the result showed a statistically significant trend over the period of diagnosis for both HD and NHL.

5. Discussion

This study reports that survival rates for HD were high and stable during the study period and in the same range as that observed in other non-European countries (Table 6). HD is an example of childhood cancer which can be cured in over 90% of cases with a reasonable burden of late effects [3,4]. The improvement of staging and treatment protocols is the result of new diagnostic imaging techniques and of refinements in radiotherapy (RT) treatment. Treatment strategies have been tailored to individual risk factors and to reducing the burden of side-effects. Until the 1960s, children with HD received only palliative therapy. During the 1970s, the improved understanding of the natural history, the systematic use of RT and the development of cytotoxic drugs offered to children with localised HD (stages I–III) resulted in a high rate of long-term survival and cure. In the early 1980s, a variety of strategies with particular attention on the morbidity related to RT and chemotherapy (CT) were developed. In the late 1980s, the major objective became the reduction of treatment-related side-effects and a new focus on the quality of life. Changes in therapy to reduce late effects while maintaining high cure rates have been the goal of paediatric oncologists. Radiation therapy has been decreased in dose, duration and field sizes. Chemotherapy regimens have been developed which limit alkylating agents and anthracyclines to decrease the risk of second neoplasms, loss of fertility, and late cardiopulmonary toxicity. One of challenges of future treatment programmes will be the definition of the risk group in order to tailor therapy to stage, cell-subtype and individual risk [3,4,22].

Table 6
Comparison of EUROCARE results for children with malignant lymphoma with other series — 5-year actuarial survival rates (%) (age 0–14 years, see notes)

Project/Country	Period	5-year survival rate (%)	
		Hodgkin's disease	Non-Hodgkin's lymphoma
EUROCARE/Europe[a]	1978–1989	91	65
	1985–1989	92	74
SEER/USA [5][b]	1975–1984	87	56
	1985–1994	91	72
Australia [10]	1980–1989	92	69
Canada [12][b]	1985–1988	90	68
Giappone [9]	1980–1984	n.a.	56

n.a., not available.
[a] Data based on the present study.
[b] The rates are presented for the age group 0–19 years.

For NHL, the most important conclusion from this study is that improvements in survival from NHL during the 1980s, already reported from individual countries and in clinical series, are confirmed as having taken place throughout much of Western Europe on a population basis. These results compare favourably with those observed in non-European countries (Table 6). The improvement in survival observed in European countries paralleled that observed for acute lymphoblastic leukaemia (ALL) [23]. The better understanding of the natural history and of the heterogeneity of this cancer type, as well as the referral of children to specialised centres and the refinement of treatment strategies improved the prognosis of children with ALL, as well as those with NHL. Before 1970, the vast majority of them would have died shortly after diagnosis, while in 1990, over 70% are alive 5 years after diagnosis, and probably cured [6–8]. The therapeutic refinements, as well as the attention to late effects and quality of life, are the future challenges for the paediatric oncologist involved in the care of children with NHL. Until now, many questions related to the biology and therapy of NHL are unanswered. In fact, the term NHL covers a range of disease subtypes. The need for reliable prognostic factors is a priority in all subtypes of NHL, as well as the solving of the problem of terminology and classification. The Revised European American classification of Lymphoid neoplasms (REAL) is aimed at addressing this latter problem. As in the acute leukaemias, several specific chromosomal abnormalities involving specific oncogenes have been described in NHL [24]. The differential diagnosis between ALL and NHL is not always straightforward. A study in The Netherlands in 1973–1985 did not suggest that changes in diagnostic classification had occurred: 20% of NHL overlapped with 5% of ALL [25].

CT is the key factor in the treatment programme for NHL, surgery is limited to resolving abdominal complications and RT is sparsely used due to long-term effects on the growing child. There is evidence that treatment must be tailored to the subtypes and the extension of the disease at diagnosis. Patients with a single extra-abdominal/extra-thoracic tumour and those with totally resected intra-abdominal tumour have an excellent prognosis (a 5-year survival rate of approximately 90%), regardless of histology. Patients with extensive intrathoracic or intra-abdominal disease and patients with bone marrow or central nervous system (CNS) involvement at diagnosis require intensified therapy. These therapies have improved the outcome for patients with advanced stage disease. B cell NHL is characterised by a fast proliferation rate and by early relapse, so effective treatment for this cell-type NHL has to be short, intensive and include CNS therapy. In Europe, the French and the German–Austrian Cooperative Groups have contributed largely to the

improvement in the survival rate. Successful treatment programmes for T-cell lymphoblastic lymphomas are derived from those used for high-risk ALL. Attempts have been made by several groups to improve outcome over 75%. At present, a large number of children affected with localised T-cell lymphoblastic lymphoma are being overtreated and therefore will have an increased risk of late effects (second malignant neoplasms, neurological, endocrinological and cardiac impairments) [6,7].

Differences in survival and mortality rates [26] between Western and Eastern Countries are more marked for NHL than for HD; in fact, for HD, effective treatment strategies have been available since the 1970s [3–7].

The limited clinical information in the EUROCARE data base precludes analyses using prognostic variables such as cell subtype, site, stage and therapy. The lack of this information limits our ability to interpret intercountry differences. Biases may arise also in the collection of clinical data with incomplete inclusion of cases in areas with a poor standard of care or cancer registration and in the follow-up. These aspects were however addressed in the EUROCARE database and the results among countries are more comparable than is usually the case for published figures.

Actual differences in survival rates, as well as in mortality rates [26], can be due to inequalities in the provision of care (accessibility, early diagnosis, proper therapy, access to specialised cancer centres, ability to deal with early and late complications), entry in a clinical trial and in the earlier diagnosis, as well as to differences in the cases. Future perspectives could include the collection of detailed information in order to address these issues in samples of patients [27].

6. The EUROCARE Working Group for this study

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