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Cancer survival in European adolescents and young adults

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Abstract

Survival of patients aged 15–24 years, diagnosed with cancer during the period of 1990–1994, is described within Europe. Data on 15 101 patients, extracted from the files of the 56 adult cancer registries included in the EUROCARE-3 database, representing 20 European countries, were analysed and compared. Five-year survival for 'all cancers combined' was 75% in males (ranging from 59% in Estonia to 89% in Iceland), and 78% in females (ranging from 59% in Estonia to 89% in Norway). The Northern European countries (except Denmark) and Austria had the highest survival figures, while survival in the Eastern European countries was lower than the European average. Denmark, UK, and the pool of the central European countries, had intermediate survival figures. Haemopoietic tumours were the most common malignancies: 5-year survival was high for Hodgkin's disease (89%), intermediate for non-Hodgkin's lymphoma (68%) and lower for acute lymphoblastic leukaemia (ALL) (47%) and acute myeloblastic leukaemia (AML) (39%). Five-year survival for gonadal germ cell cancers, the second most common malignancy in young adults, was 90%. Five-year survival for the other cancers under consideration was as follows: 89% for skin melanoma, 66% for all Central Nervous System (CNS) tumours, 57% for bone tumours, 58% for osteosarcoma, 42% for Ewing's sarcoma, 57% for soft-tissue sarcomas, 99% for thyroid carcinoma, 82% for uterine cervical carcinoma, and 83% for ovarian carcinoma. For more 'adult-specific tumours', 5-year survival was good for colon (77%) and lung (60%) cancers, and less favourable, compared with adults, for breast cancer (68%). Adolescents (15–19 years) had significantly worse survival than young adults (20–24 years) for all malignancies combined. Survival for Hodgkin's lymphoma, CNS tumours, melanoma and colon cancer showed marked regional variability. Since many of the tumours occurring in young adults are curable, these results should encourage, without delay, efforts to identify obstacles to improving outcome and reducing geographical inequalities in survival for this group of patients.

Keywords: Adolescents; Young adults; Europe; Population-based cancer registry; Cancer survival

1. Introduction

Cancer is uncommon in adolescents and young adults, with incidence rates at age 15–24 years of about 200 per million [1,2]. The types of cancers that occur in people of this age differ markedly from those that develop in younger children and in older adults [3]. Adolescents/young adults are rarely the subject of specific survival analyses, although two large-scale studies have been published recently: the Surveillance, Epidemiology and End-Results (SEER) paediatric monograph [3] considered adolescents aged 15–19 years in the United States, and a report from the Northern Region Young Person's Malignant Disease Registry in England provided results for patients in the age range of 15–24 years [4].

The recent EUROCARE-3 study [5] analysed cancer survival across Europe, considering 'young' people in the 10–14 and 15–44 year age classes. The EUROCARE database contains information on about 6.5 million European cancer patients, archived according to a uniform data collection policy, with data-checking and analytical procedures agreed in advance by all the cancer registries involved. This database therefore provides

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a unique opportunity to analyse cancer survival among 15–24 year-olds—an age class that is difficult to study at the population level because of the low incidence of cancer. In this paper, we present survival data for the major types of cancers and for all malignancies combined in teenagers and young adults, highlighting and analysing gender, age and regional differences in survival.

2. Patients and methods

Data on 15 101 patients aged 15–24 years and diagnosed with cancer in 1990–1994 were analysed. All malignancies except non-melanoma skin cancers were considered. The data were extracted from the files of the 56 adult cancer registries included in the EUROCARE-3 database [6], representing 20 European countries: Denmark, Finland, Iceland, Norway, Sweden, the Czech Republic, Estonia, Poland, Slovakia, Slovenia, Austria, France, Germany, Italy, Malta, The Netherlands, Portugal, Spain, Switzerland and the United Kingdom (UK).

The main characteristics of the dataset are summarised in Table 1. The data are grouped by country and European region: Northern Europe (Denmark, Finland, Iceland, Norway, Sweden), Eastern Europe (Czech Republic, Estonia, Poland, Slovakia, Slovenia), Central (Austria, France, Germany, The Netherlands, Switzerland) and Southern Europe (Italy, Malta, Portugal, Spain) and the UK. The French registry of Isère is not included in Table 1 as it registered only a single case of young adult breast cancer over the study period and this patient was lost to follow-up 1 year after diagnosis. Unlike the EUROCARE-3 adult cancer survival analysis, the Munich registry was included in this study because its survival rate was not significantly different from that of the Saarland cancer registry. Table 1 shows the proportions of male patients (55% overall), the proportions of younger (15–19 years) patients (37% overall), and data quality indicators. Overall, 92% of cases were histologically-verified, with 95% or more histologically-verified in most countries. The UK (85%) and Poland (81%) had the lowest proportions of histologically-verified cases. Overall, 0.7% of cases were lost to follow-up, although Warsaw (7.4%), Munich (20.8%), and Geneva (11.8%) had high proportions lost.

At least 4 years of follow-up from diagnosis were required by the study protocol. However, a few registries present a small proportion of cases not followed for 4 years from diagnosis (censored as 'alive'). In only three registries (Calvados, Côte d'Or and East Anglia) were greater than 10% of cases followed for 4 years. Note that the proportion of patients censored 'alive' is not available for registries who perform only passive follow-up, as in UK registries other than East Anglia.

Overall, 6.5% of cases had unspecified morphology; the highest proportions were from two Italian registries (Ragusa and Sassari) and three UK registries (South West, West Midlands and Wales).

Only first tumours were analysed; 382 cases were excluded from the analysis as they were (a) second primary tumours, (b) notified by death certificate only (DCO) or (c) only discovered at autopsy. The survival analysis was therefore carried out on 14 719 cases.

The survival data are presented for all cancers combined, and for 19 selected cancers. In view of the distinctive spectrum of cancers found in this age group, some are defined according to the International Classification of Childhood Cancers (ICCC) [7] and others according to the International Classification of Diseases (ICD)-9 [8]. The cancers considered separately are: acute lymphoblastic leukaemia (ALL) (ICCC Ia), acute myeloblastic leukaemia (AML) (ICD-9 205.0), Hodgkin's disease (ICCC IIa), non-Hodgkin's lymphoma (ICCC IIb), Central Nervous System (CNS) malignant tumours (ICCC III), astrocytoma (ICCC IIIb), cervix carcinoma (ICD-9 180), ovary germ cell tumours (ICCC Xc), testis germ cell tumours (ICCC Xc), ovary carcinoma (ICCC Xd), thyroid carcinoma (ICD-9 193), soft-tissue sarcoma (ICCC IX), Ewing's sarcoma (ICCC VIIIc), osteosarcoma (ICCC VIIIa), skin melanoma (ICD-9 172), and colon (ICD-9 153), lung (ICD-9 162), bone (ICD-9 170) and female breast (ICD-9 174) tumours.

Both observed and relative survival were calculated, but only observed survival is presented [9]. The difference between relative and observed survival never reached 1%, and, in most cases, was less than 0.5%. Observed survival was calculated by the actuarial method; 95% Confidence Intervals (CIs) were calculated after transformation to the log-hazard scale, so that upper and lower limits are constrained within the interval 0–100.

Survival for all cancers combined, adjusted by incidence case mix, was calculated, thereby enabling between-country survival comparisons unbiased by differing incidence patterns. To adjust by incidence case mix, cancer type-specific survival rates for each country were multiplied by the number of these cases formed from the European pool, summed and divided by the total number of cases. When there were no cases for a given cancer site in a country, survival was not calculated; in these cases the 'average' European survival for that site was used in the calculation. If survival data for two or more cancers were missing for a country, the adjusted survival was not calculated for that country. Astrocytomas, which were combined with 'brain tumours', and osteosarcoma and Ewing's sarcoma, combined with bone tumours, were not considered separately in this procedure. The cancer types considered in this study were all used to calculate the incidence-adjusted survival and constituted 88% of all cancers diagnosed in the study.

Table 1
Cancers recorded in young adults in European countries with indicators of data quality

Country—Registry	Cases		Males (%)	Aged 15–19 years (%)	MV (%)	Lost (%)	DCO and autopsy (%)	Alive <4 years (%)	Cases from the unspecified diagnostic group[a] (%)
	Number	%							
NORTHERN EUROPE									
DENMARK	924	6.1	57	36	99	0.5	0.5	0.0	4.7
FINLAND	702	4.6	51	42	99	1.1	0.7	0.0	4.3
ICELAND	44	0.3	43	59	100	0.0	0.0	0.0	0.0
NORWAY	836	5.5	53	36	99	1.3	0.5	0.5	4.7
SWEDEN	1353	9.0	53	38	99	1.3	0.2	0.0	9.5
EASTERN EUROPE									
CZECH REPUBLIC—West Bohemia	163	1.1	57	45	94	0.0	3.1	0.0	4.9
ESTONIA	197	1.3	55	52	99	1.0	1.5	0.0	6.6
Cracow	65	0.4	58	45	86	1.5	0.0	0.0	9.2
Warsaw	175	1.2	58	45	79	7.4	0.6	0.0	9.1
POLISH REGISTRIES	240	1.6	58	45	81	5.8	0.4	0.0	9.2
SLOVAKIA	845	5.6	58	41	96	0.0	5.7	0.0	1.4
SLOVENIA	287	1.9	57	39	99	0.7	0.0	0.0	4.2
CENTRAL-SOUTHERN EUROPE									
AUSTRIA—Tyrol	140	0.9	58	36	98	0.0	2.1	0.0	2.1
Bas Rhin	172	1.1	58	30	100	1.2	0.0	5.5	6.4
Calvados	94	0.6	56	41	97	0.0	0.0	16.0	4.3
Côte D'or	28	0.2	61	43	100	0.0	0.0	12.5	3.6
FRENCH REGISTRIES	294	1.9	58	35	99	0.7	0.0	9.5	5.4
Munich	48	0.3	63	29	98	20.8	0.0	0.0	2.1
Saarland	139	0.9	55	36	100	0.0	0.0	0.0	3.6
GERMANY REGISTRIES	187	1.2	57	34	99	5.3	0.0	0.0	3.2
Ferrara	58	0.9	62	41	79	3.4	5.2	0.0	3.4
Genoa	107	0.7	56	37	93	0.0	0.0	0.0	2.8
Latina	56	0.4	50	48	93	0.0	3.6	0.0	8.9
Macerata	32	0.2	47	44	84	0.0	0.0	0.0	9.4
Modena	104	0.7	59	42	94	2.9	1.0	0.0	1.9
Parma	53	0.4	58	45	98	0.0	1.9	0.0	1.9
Ragusa	45	0.3	44	47	96	0.0	2.2	0.0	11.1
Romagna	63	0.4	49	51	89	0.0	0.0	0.0	1.6
Sassari	51	0.3	55	39	84	0.0	0.0	0.0	17.6
Turin	143	0.9	66	38	96	3.5	0.0	0.0	2.8
Tuscany	203	1.3	53	39	76	1.0	0.0	0.0	5.4
Varese	146	1.0	51	40	97	0.7	0.7	0.0	2.7
Veneto	357	2.4	50	43	96	2.0	2.0	0.0	6.2
ITALIAN REGISTRIES	1418	9.4	54	42	91	1.4	1.1	0.0	5.1
MALTA	20	0.1	65	40	100	0.0	0.0	0.0	0.0
Amsterdam	444	2.9	57	34	100	0.0	0.0	2.3	0.5
Eindhoven	168	1.1	49	35	100	0.0	0.0	2.6	2.4
DUTCH REGISTRIES	612	4.1	55	34	100	0.0	0.0	2.4	1.0
PORTUGAL—South Portugal	24	0.2	71	63	100	0.0	0.0	0.0	0.0
Basque Country	363	2.4	59	43	97	0.0	2.8	0.0	5.0
Granada	40	0.3	63	33	100	2.5	0.0	0.0	5.0
Mallorca	96	0.6	61	43	99	0.0	0.0	0.0	3.1
Murcia	3	0.0	33	33	100	0.0	0.0	0.0	33.3
Navarra	88	0.6	58	41	97	0.0	2.3	0.0	3.4
Tarragona	94	0.6	59	48	96	0.0	1.1	0.0	4.3
SPANISH REGISTRIES	684	4.5	59	43	97	0.1	1.9	0.0	4.5
Basel	37	0.2	68	19	100	8.1	0.0	0.0	2.7
Geneva	76	0.5	57	37	99	11.8	0.0	0.0	5.3
SWISS REGISTRIES	113	0.7	60	31	99	10.6	0.0	0.0	4.4
UNITED KINGDOM									
East Anglia	247	1.6	54	36	83	1.2	0.0	20.9	2.4
Mersey	320	2.1	58	33	91	n.a.	1.3	n.a	3.1
Oxford	461	3.1	57	34	97	n.a.	0.2	n.a	6.1
South West	1004	6.6	53	34	91	n.a.	0.0	n.a	11.0

(*continued on next page*)

Table 1 (*continued*)

Country—Registry	Cases		Males (%)	Aged 15–19 years (%)	MV (%)	Lost (%)	DCO and autopsy (%)	Alive <4 years (%)	Cases from the unspecified diagnostic group[a] (%)
	Number	%							
South Thames	822	5.4	55	31	86	n.a.	4.7	n.a	2.3
Trent	604	4.0	52	37	90	n.a.	0.8	n.a	3.6
West Midlands	815	5.4	50	37	49	n.a.	0.5	n.a	26.7
Yorkshire	485	3.2	49	34	98	n.a.	0.2	n.a	3.3
Wales	450	3.0	56	34	81	n.a.	0.0	n.a	15.6
Scotland	810	5.4	56	36	96	n.a.	0.1	n.a	3.8
UNITED KINGDOM	6018	39.9	54	35	85	0.1	0.9	0.9	8.8
Totals	15 101	100.0	55	37	92	0.7	1.1	0.6	6.5

Registry with national coverage in upper case. MV, microscopically-verified; n.a., not available; lost,, lost of follow-up; DCO, death certification only; ICCC, International Classification of Childhood Cancers. Source of data: EUROCARE 3.

[a] Unspecified diagnostic group (ICCC 01E, 02E, 03F,06C, 07C, 08E, 09E, 12B).

3. Results

Five-year survival for all cancers combined is shown in Table 2, by region, country and gender. Survival was slightly lower in males (75%) than females (78%). Survival variation between countries and regions was greater among males, ranging from 40% in Estonia to 89% in Iceland. There was less variation in females: from 59% in Estonia to 89% in Norway. Five-year survival in several Eastern European countries (Czech Republic, Poland and Slovakia) was lower than the European average (62% in males and 71% in females). The Northern European countries (except Denmark) and Austria had the highest survival figures (80% or more). The highest national survival was in Iceland for males (89%) and Iceland and Norway for females (88–89%). Denmark (78% in males and 76% in females) and the UK (73% in males and 78% in females) had less favourable survival than the other Northern European countries, although this was very close to the European average, as was the pool of Central European countries. In Southern Europe, Italy had the highest survival figures, close to the European average. Survival proportions were somewhat lower in Spain, while in Malta and Portugal they were similar to the average for Eastern Europe, although based on small numbers of cases.

The incidence-adjusted survival is presented on the right side of Table 2. Survival differences between countries reduced slightly when this adjustment was made for males only. However, the regional pattern of survival did not substantially change from that obtained without adjustment.

Five-year survival (with 95% CIs) for the entire European pool and for the main cancer types is shown in Table 3. Haemopoietic tumours were the most common malignancies in this age group: survival was high for Hodgkin's disease (89%), intermediate for non-Hodgkin's lymphoma (68%) and relatively low for ALL (47%) and AML (39%). Gonadal germ cell cancers were the second most common malignancy in young adults, and five-year survival was relatively high: 92% in males and 90% in females. Survival for skin melanoma (89%) was also good. Overall survival for CNS tumours was 66%, the same proportion as for astrocytomas, which formed about half of all CNS tumours.

Five-year survival for bone tumours was 57%, close to that for osteosarcoma (58%), but higher than survival for Ewing's sarcoma (42%). Overall 5-year survival for soft-tissue sarcomas was, at 57%, similar to that for bone tumours. Patients with thyroid carcinoma had the most favourable survival of all (99%).

Survival for cancer of the uterine cervix and carcinoma of the ovary was good, with 82 and 83% of patients, respectively, alive 5 years after diagnosis. Survival was also good for colon cancer (77%). For breast and lung cancer, 5-year outcomes were distinctly less favourable at 68 and 60%, respectively.

Between-country survival ranges are shown on the right-hand side of Table 3. The greatest differences were for Ewing's sarcoma, all bone cancers, astrocytomas, all CNS cancers and testicular germ cell tumours ($\geqslant$45 percentage points). Estonia had the lowest survival for NHL, testicular germ cell tumours, bone sarcomas and soft-tissue sarcomas. The Czech Republic had the lowest survival for astrocytoma and CNS tumours. Denmark ranked the lowest for osteosarcoma, whilst Sweden, Norway and Finland had the highest survival for Hodgkin's disease, CNS tumours, osteosarcoma and soft-tissue sarcomas. Austria, Switzerland and France had highest survival for AML, testicular germ cell tumours, astrocytoma, bone sarcoma and Ewing's sarcoma; and the Czech Republic for cervical cancer (based on only 5 cases). For cancer sites with less than 300 cases (ovary, colon, breast and lung), the between-country survival comparisons were not presented.

Five-year survival differed for the age classes 15–19 and 20–24 years, as shown in Fig. 1. Adolescents (15–19 years) had significantly poorer survival than young

Table 2
Five-year survival for young adult cancer in European populations, period of diagnosis from 1990–1994

	Crude						Cancer type adjusted			
	Males			Females			Males		Females	
	No of cases	5-year survival	2* S.E.	No of cases	5-year survival	2* S.E.	5-year survival	2* S.E.	5-year survival	2* S.E.
Northern Europe	2013	78.7	1.8	1763	83.7	1.8	78.0	1.8	83.4	1.8
ICELAND	18	88.9	14.8	25	88.0	13.0	–	–	–	–
SWEDEN	702	79.3	3.1	629	84.4	2.9	80.3	2.9	81.6	3.2
NORWAY	420	78.7	4.0	384	88.6	3.3	73.5	4.2	87.3	3.8
DENMARK	525	78.4	3.6	386	76.0	4.4	–	–	–	–
FINLAND	348	77.4	4.5	339	85.4	3.9	77.3	4.5	85.5	4.2
United Kingdom	3129	72.9	1.6	2725	77.6	1.6	73.9	1.5	78.5	1.6
Central Europe	747	75.6	3.2	580	80.5	3.3	73.3	3.0	81.7	3.0
The Netherlands	333	72.8	4.9	274	80.8	4.8	71.3	4.7	82.5	4.4
Germany	104	83.2	7.5	80	71.9	10.2	–	–	–	–
Austria	78	80.6	9.0	58	87.9	8.6	–	–	–	–
Switzerland	66	78.0	10.4	45	79.4	12.3	–	–	–	–
France	166	73.1	7.1	123	82.6	6.9	–	–	–	–
SOUTHERN EUROPE	1181	71.5	2.6	925	77.9	2.8	74.3	2.4	77.8	2.9
Italy	751	74.3	3.2	642	79.2	3.2	76.9	2.9	79.5	3.4
Spain	400	67.0	4.7	269	74.5	5.3	70.9	4.5	74.0	5.5
MALTA	13	61.5	27.0	7	71.4	34.2	–	–	–	–
Portugal	17	58.8	23.9	7	85.7	26.5	–	–	–	–
EASTERN EUROPE	946	61.9	3.2	710	70.8	3.4	63.6	3.1	70.6	3.5
SLOVENIA	163	70.5	7.2	123	73.7	8.0	–	–	–	–
SLOVAKIA	449	65.7	4.5	333	71.5	5.0	64.6	4.6	72.2	4.9
Poland	137	60.0	8.5	99	70.6	9.2	–	–	–	–
Czech Republic	90	56.7	10.5	68	77.8	10.1	–	–	–	–
ESTONIA	107	39.6	9.6	87	58.5	10.6	–	–	–	–
EUROPEAN POOL	8016	73.1	1.0	6703	78.8	1.0	74.0	1.0	79.5	1.0
WEIGHTED EUROPE	8016	75.0	2.2	6703	77.8	2.8	–	–	–	

Countries with national coverage in upper case. 2* S.E., double standard error. Source of data: EUROCARE 3.

adults (20–24 years) for all malignancies combined. In particular, adolescents had lower survival than young adults for osteosarcoma, ovary (carcinoma), lung, skin melanoma, and testicular germ cell tumours, but the survival differences between age groups were not significant for any individual tumour type. Adolescents had better survival than young adults for the following malignancies: cervix, breast, colon, astrocytoma, CNS, soft tissue, lymphoma, leukaemia and female germ cell; although none of the differences were statistically significant.

Five-year survival for the 17 major malignancies, according to the four European regions (Central and Southern Europe combined, UK, Eastern and Northern Europe), are shown in Table 4. For many of these cancers, Northern Europe had the highest survival. This was the case for Hodgkin's lymphoma, non-Hodgkin's lymphoma, ALL, germ-cell tumours in females, melanoma, CNS tumours, soft-tissue sarcomas, and cervical, colon and breast cancers. Eastern Europe had the lowest survival for all tumours considered, except those affecting the breast and lung.

Survival for Hodgkin's lymphoma, CNS tumours, melanoma and colon cancer showed marked regional variability with Northern European countries ranking the highest followed by South-Central Europe, the UK, and Eastern Europe. Survival for non-Hodgkin's lymphoma, ALL, and gonadal germ cell tumours was characterised by less variation between the UK, Northern and South-Central Europe, while Eastern Europe had much worse survival than the other European regions. For AML, the UK had the highest survival, closely followed by Northern Europe with substantially lower survival in Southern and Central Europe and even lower survival in Eastern Europe.

4. Discussion

Population-based studies of cancer survival can indicate whether cancers are being successfully treated at the population level, and, in particular, can reveal whether new treatment guidelines are being implemented on a large-scale. The population-based study reported here

Table 3
Five-year survival (%) for European young adults (aged 15–24 years) diagnosed with cancer during 1990–1994

			Number of cases	Survival (%)	95% CI		Between-country 5-year survival range[a]	
					Lower	Higher		
		Haemopoietic tumours						
ICCC	IIa	Hodgkin's disease	2482	89.0	87.7	90.2	78–95	ICE, S
	IIb	Non-Hodgkin's lymphoma	1062	67.8	64.8	70.5	23–83	EST, A[b]
	Ia	Acute lymphoblastic leukaemia	638	46.8	42.8	50.7	19–58	SK, S[b]
ICD-9	205.0	Acute myeloblastic leukaemia	477	38.6	34.2	43.1	18–57	NL, A[b]
		Germ cell tumours	2074	90.0	89.8	93.0		
ICCC	Xc	Testis	1896	91.7	90.3	92.9	55–100	EST, CH[b]
	Xc	Ovary	178	89.8	84.1	93.5	–	–
ICD-9	172	Skin melanoma	1493	89.4	87.7	90.9	67–100	SLO, A[b]
		CNS	1407	66.1	63.5	68.6	35–80	CZH, FIN[b]
	IIIb	Astrocytoma[c]	738	66.0	62.4	69.4	33–88	CZH, F[b]
		Bone	754	56.7	53.0	60.2	27–87	EST, F[b]
	VIIIa	Osteosarcoma	370	58.4	53.1	63.4	37–72	DK, SWE[b]
	VIIIc	Ewing's sarcoma	217	41.8	35.0	48.4	20–100	SK, F[b]
	XIb	Thyroid	710	98.7	97.5	99.3	75–100	CH, many countries[b]
	IX	Soft-tissue sarcomas	693	56.7	52.8	60.4	31–72	EST, N[b]
ICD-9	180	Cervix	335	82.0	77.4	85.8	60–100	FIN, CZH
ICCC	Xd	Ovary carcinoma	278	83.0	77.9	87.1	–	–
ICD-9	153	Colon	235	76.9	70.8	81.9	–	–
	174	Breast	176	67.5	59.7	74.1	–	–
	162	Lung	92	59.6	48.6	69.0	–	–

A: Austria, CH: Switzerland; CZH: Czech Republic, DK: Denmark, EST: Estonia, F: France, ICE: Iceland, I: Italy, MLT: Malta, N: Norway, NL: The Netherlands, P: Poland, SK: Slovakia, SLO: Slovenia, SCO: Scotland, S: Sweden, FIN: Finland. CNS, Central Nervous System; 95% CI, 95% Confidence Interval.

[a] Range: includes only countries with at least 5 cases.

[b] Registry CIs do not overlap.

[c] Finland excluded from astrocytoma survival analysis.

Source of data: EUROCARE 3.

concerns about 15 000 cancer cases diagnosed between 1990–1994 and is one of largest estimating survival in adolescents (15–19 years of age) and young adults (20–24 years of age) - age groups that are not often specifically described in the literature. As expected, several tumours that occur commonly among children (retinoblastoma, neuroblastoma, Wilms' tumour, ependymoma, rhabdomyosarcoma, primitive neuroectodermal tumour (PNET) and hepatoblastoma) were hardly even seen in young adults. To be precise, these solid tumours also known as 'late' paediatric-type cancers [4], accounted for only 2.6% of cases in our population.

Among haemopoietic malignancies, lymphomas were more common than leukaemias in this population—the reverse of the situation is in patients below 15 years of age. All haemopoietic malignancies, but particularly ALL, had a worse prognosis in 15–24 year-olds than in younger patients. Since the treatment of ALL in young adults has often been similar to that in children, this suggests that ALL in older patients differs biologically from ALL in childhood [10]. In more than 2000 patients aged 1 year or over, treated in the Medical Research Council Trials UKALL X (children) and UKALL XA (adults), survival declined steadily with age at diagnosis [11]. ALL blast cells in adolescents and young adults had a higher frequency of 'unfavourable' cytogenetic features (see Jeha S., this issue [12]) than in children, but age was still a highly significant adverse prognostic factor in a multivariate analysis which took cytogenetics into account. In the UKALL XA trial, high hyperdiploidy, which is associated with good prognosis, was more frequent among patients diagnosed at age 15–19 years than among those at 20–29 years, whereas the Philadelphia chromosome, which confers a poor prognosis, was less frequent [13]. In the United States, patients aged 16–20 years who were enrolled on adult trials of the Cancer and Leukaemia Group B (CALGB) had a 6-year event-free survival rate of only 38% compared with 64% for patients of the same age treated contemporarily in Children's Cancer Group (CCG) trials [14] and comparison of risk factors showed a higher incidence of adverse cytogenetics in the CALGB

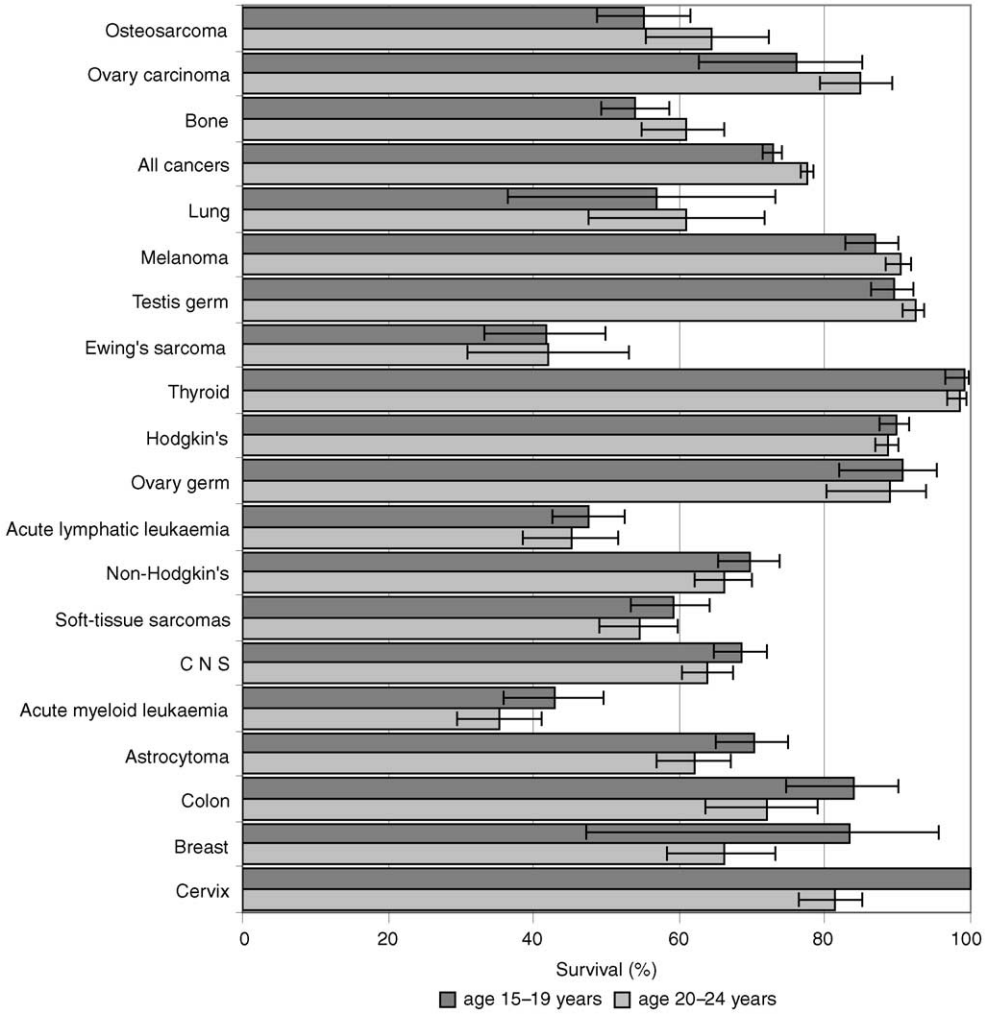

Fig. 1. Five-year survival in European adolescent (15–19 years) and young adults (20–24 years).

group. An Italian study [15] also identified a longer delay to the definitive diagnosis of leukaemia in young adults than in children.

For several solid tumours too, outcome for 15–24 year-olds was not as good as in younger patients reported in EUROCARE-3 [16]. For bone tumours—considered 'age-specific' cancers for adolescents and young adults (Table 3)—5-year survival was lower than for children aged 10–14 years [16]. For osteosarcoma, survival varied with age: 65% in 10–14 year-olds [16], 55% in 15–19 year-olds and 64% in 20–24 year-olds (Fig. 1). This age-trend was also observed in the major countries (Denmark, Finland and UK). In the two older categories, females had better survival than males; while survival of 10–14 year-olds was better in males [16].

Gonadal germ cell tumours are also considered to be relatively 'specific' for people of adolescent and young adult age [4]. In this study, patients with these tumours had good survival (90% overall), but not as good as in children up to 14 years of age (98% in boys and 94% in girls) [16].

Soft-tissue sarcomas constituted 6% of all the cancers analysed in this study. Five-year survival figures for these cancers were 76% in 15–19 year-old females, 69% in 15–19 year-old males and 57% in both male and female 20–24 year-olds. The difference in survival between children and young adults may be due, in part at least, to the case-mix, as rhabdomyosarcoma is by far the most common soft-tissue sarcoma of childhood, whereas in adolescence and early adulthood, fibrosarcoma and other types are commoner [17].

Participation in clinical trials is much lower among 15–19 year-olds than amongst younger children. Bleyer and colleagues [18] estimated that the two paediatric cooperative groups (Children's Cancer Group and Pediatric Oncology Group) registered $>94\%$ of the children <15 years of age diagnosed with cancer, but only 21% of the cancer patients in the 15–19-year-old age group. However, age is a major prognostic factor for several of these cancers, and differences in the biological behaviour of cancers in young adults, compared with children, may also explain the lower survival rates in young adults.

Table 4
Five-year survival for European young adults with cancer diagnosed during 1990–1994, by European grouping or country

	No. cases	5-year survival with 95% CI		
Hodgkin's disease	2482			
NordEU	522	92.1	89.3	94.2
SudCentralEU	599	90.4	87.6	92.5
UK	1036	87.8	85.5	89.7
EstEU	325	85.6	81.2	89.1
Non-Hodgkin's lymphoma	1062			
NordEU	218	71.5	64.8	77.1
UK	420	70.8	66.1	75.0
SudCentralEU	316	66.3	60.7	71.4
EstEU	108	52.8	42.8	61.8
Acute lymphoblastic leukaemia	638			
NordEU	138	52.7	43.8	60.8
UK	269	47.5	41.3	53.4
SudCentralEU	166	45.9	38.0	53.5
EstEU	65	33.3	21.9	45.1
Acute myeloblastic leukaemia	477			
UK	229	44.9	38.3	51.4
NordEU	103	41.7	31.9	51.1
SudCentralEU	96	30.6	21.5	40.2
EstEU	49	18.4	8.9	30.5
Testis, germ cell	1896			
UK	669	92.9	90.6	94.7
NordEU	587	92.7	90.2	94.6
SudCentralEU	397	92.6	89.4	94.8
EstEU	243	84.4	79.0	88.4
Melanoma	1493			
NordEU	489	94.5	92.0	96.3
SudCentralEU	330	89.7	85.8	92.6
UK	584	87.0	83.9	89.5
EstEU	90	76.4	65.9	84.1
Central nervous system	1407			
NordEU	427	75.6	71.1	79.5
SudCentralEU	285	65.1	59.0	70.5
UK	526	62.4	58.0	66.5
EstEU	169	55.5	47.4	62.8
Thyroid	710			
UK	221	99.1	96.3	99.8
SudCentralEU	215	99.1	96.2	99.8
NordEU	211	98.5	95.3	99.5
EstEU	63	96.8	87.6	99.2
Soft-tissue sarcomas	693			
NordEU	170	60.4	52.5	67.5
SudCentralEU	179	57.9	50.1	65.0
UK	266	56.7	50.4	62.6
EstEU	78	45.9	34.3	56.7
Osteosarcoma	370			
SudCentralEU	90	63.3	52.3	72.5
NordEU	98	62.8	52.1	71.8
UK	148	54.5	45.9	62.3
EstEU	34	50.0	32.1	65.5
Ewing's sarcoma	217			
UK	91	46.0	35.3	56.1
SudCentralEU	61	44.1	31.2	56.3
NordEU	38	42.1	26.1	57.3
EstEU	27	21.6	8.3	39.0
Ovary, carcinoma	278			
SudCentralEU	64	87.5	76.2	93.6
NordEU	61	82.4	69.3	90.3
UK	115	82.2	73.6	88.2
EstEU	38	79.0	61.9	89.0
Ovary, germ cell	178			
NordEU	30	100.0	100.0	100.0
SudCentralEU	38	97.4	82.1	99.6
UK	71	94.3	85.3	97.9
EstEU	39	66.4	48.8	79.1
Cervical carcinoma	335			
NordEU	85	85.8	76.2	91.8
UK	183	82.5	76.0	87.3
SudCentralEU	30	79.9	60.2	90.6
EstEU	37	73.0	55.2	84.6
Colon tumours	235			
NordEU	69	86.8	75.9	93.0
SudCentralEU	66	86.2	74.8	92.7
UK	81	65.2	53.5	74.7
EstEU	19	57.9	32.7	76.6
Breast carcinoma	176			
NordEU	32	73.6	53.4	86.1
EstEU	10	70.0	32.0	89.4
SudCentralEU	38	67.5	49.5	80.3
UK	96	65.2	54.4	74.0
Lung tumours	92			
SudCentralEU	24	70.7	47.7	85.0
NordEU	19	63.2	37.3	80.7
EstEU	15	53.3	25.8	74.7
UK	34	52.9	34.7	68.2

NordEU: Denmark, Finland, Iceland, Norway, Sweden. SudCentralEU: Austria, France, Germany, Italy, Malta, Portugal, The Netherlands, Spain, Switzerland. UK: England and Scotland. EstEU: Czech Republic, Estonia, Poland, Slovakia, Slovenia. Source of data: EUROCARE 3.

A third category of cancers occurring in young adults [4] are 'early onset' cancers, which can arise in a number of anatomical sites. Skin melanoma and thyroid carcinoma have the highest incidence, but rarer tumours (tumours of the colon, breast, lung, cervix and ovary) also occur. In this study, nearly all these cancers had better survival than in adults aged 15–44 years and 45–54 years [19]. The exception was breast cancer for which a young age at diagnosis is a well known poor prognostic factor [20,21]. The reasons for better survival for these 'early onset' tumours in young patients are largely unknown. It may be that better prognosis histotypes (particularly the colon malignant carcinoid, borderline or 'low malignancy' ovarian cancers, and lung sarcomas) predominate in young people. Alternatively, many of these cancers may arise because of inherited predisposition [4]. Such tumours may have a different prognosis than those that arise sporadically.

This study, like EUROCARE analyses of adult cancer survival [2], has revealed large survival variations across Europe for cancer patients in the age range of 15–24 years. Survival was generally best in Northern European countries (over 80% for all cancers combined, with only Denmark below this figure at 77%). In Central Europe, survival was around 75%, whilst in Southern Europe, it was more variable, ranging from approximately 75% (Italy) to 59% (Portugal). In Eastern Europe, survival was lower at 66%, with very low survival in Estonia (48%). In general, survival in the UK was lower than in the Northern European countries and similar to that in the pool of Central European countries. A notable exception was AML, for which the UK has the highest survival of all. This presumably reflects the high participation rate in the national Molecular Research Council (MRC) trial—'AML10′ —, which had better results than any previously reported large trial for this disease [22].

In this study, we observed particularly low survival rates for young adults in Estonia, a country which after 1991 underwent an abrupt transition from a Soviet Republic to an 'open-market' economy. Among the participants in the EUROCARE project, Estonia had the lowest Gross Domestic Product, least National Expenditure on health and shortest life expectancy in the early 1990s. Delayed introduction of modern diagnostic procedures and delayed adherence to effective treatments also likely contributed to the poor outcome for young patients in Estonia [23].

Survival for all cancers combined can be confounded by tumour distribution in the European population. This is why the case-mix was considered in the 'between-countries' comparisons and why survival figures were estimated only after adjustment for cancer type. The adjusted survival figures differed slightly from the non-adjusted figures in that regional variation was reduced and the survival of Eastern European countries increased, mainly because melanoma formed a smaller proportion of the total in Eastern Europe than Europe as whole (5% versus 10%). The adjusted survival figures are important indicators of the comparative performance of healthcare systems in treating cancer.

Before drawing conclusions from our results, it is important to consider possible sources of bias. Biases may arise due to differences in the quality and comparability of the data between one registry and another. The main indicators of data quality are the proportion of DCO cases, the proportion of microscopically-verified cases, and the proportion of cases lost to follow-up. In the EUROCARE young adult database, DCO cases were rare (approximately 1% overall) except in the Slovakian (5.7%) and South Thames (4.7%) registries (Table 1). Furthermore, a high proportion of cases (92% overall) were confirmed microscopically, although the Polish and English/Welsh registries had somewhat low figures for microscopic confirmation (81 and 83%, respectively, Table 1). Microscopic confirmation is a particularly important indicator of data quality for the tumours included in this study, since they are primarily classified by histological type. It is noteworthy that few cases (only 1.1% overall) were lost to follow-up. All countries, except Germany and France, provided follow-up of at least 4 years; in Germany and France, legislation makes difficult to collect life-status data [6]. These considerations on data quality indicate that the cancer survival differences we identified between these European populations are unlikely to be due to registration artefacts.

In conclusion, 5-year survival for all cancers combined was 76% in our study. However, for haemopoietic tumours, osteosarcoma, Ewing's sarcoma and astrocytoma, survival was not as good as that for the same cancers in childhood, even though defined protocols seemed to be available and tumours in young adults are considered to be potentially curable [4]. The reasons for these differences are not entirely clear, but may include: (a) a lower enrolment in clinical trials in the 15–24 year-old age group than in younger children [18], (b) that there is a shortage of units reserved for adolescents or young adults, even though several types of cancers require multimodal therapy [10] and (c) that tumours in young adult patients may differ biologically from those in childhood. Our study has also revealed large variations in cancer survival for 20–24 year-olds across Europe. Patients from Northern European countries enjoyed the highest survival, whereas survival in Eastern Europe was low. For non-Hodgkin's lymphoma, leukaemia and gonadal germ cell tumours, there was little variation between the UK, Northern Europe and South-Central Europe, but patients in Eastern Europe had much worse survival for these tumours. By contrast, for Hodgkin's disease, CNS tumours and melanoma, survival varied markedly from region to region. Since many of the tumours occurring in young adults are curable, each country or group of countries should try to identify the obstacles to achieving better survival. It is also important that both paediatric and 'adult' oncological associations take note of the large variations in survival across Europe and the peculiar characteristics of cancers in adolescents and young adults.

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