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Skin cancer incidence and survival in European children and adolescents (1978–1997). Report from the Automated Childhood Cancer Information System project

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ABSTRACT

Patterns and trends of melanoma and skin carcinoma incidence and survival of European children (age 0–14 years) and adolescents (age 15–19 years) were investigated. Between 1978 and 1997, a total of 1419 melanoma and 485 skin carcinoma cases were recorded in the cancer registries contributing to the Automated Childhood Cancer Information System (ACCIS) study. During 1988–1997, the incidence of melanoma was 0.7 per million children and 12.9 per million adolescents; corresponding rates for skin carcinomas were 0.3 and 3.7 per million, respectively. The British Isles had the highest incidence of skin cancers in children and adolescents. For Europe, in adolescents melanomas were more common in the North and West, skin carcinomas in the South and East. Between 1978 and 1997 incidence increased annually in adolescents, by 4.1% for melanoma and 2.5% for skin carcinoma. Differences in aetiology between childhood and adolescent skin cancers cannot be excluded. Survival was relatively high and the geographical variations in incidence and survival seem to be associated.

1. Introduction

Skin carcinomas and malignant melanomas are rare in children, but increasingly common in adolescents. In white populations, reported age-standardised incidence rates vary between 0.7 (UK) and 8 (Queensland, Australia) per million person-years for melanoma and 0.6 (UK) per million person-years for skin carcinoma in children younger than 15 years (out of which basal cell carcinoma (BCC) 0.1 and squamous cell carcinoma (SCC) 0.1, other skin carcinomas 0.4 per million person-years).[1,2] Incidence rates in adolescents (age 15–19 years) are higher and increasing since the 1950s for both melanoma (above 10 cases per million person-years)[2–7] and non-melanoma skin cancer (2.4 cases per million person-years for UK, ages 15–19 years (BCC 1.7, SCC 0.2, others 0.5 cases per million person-years).[2]

The main inherent established and/or suspected risk factors for malignant melanoma in children are: a family history of melanoma, *Xeroderma Pigmentosum* and immunosuppression.[4] Congenital cutaneous melanomas are extremely rare;

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most melanomas in children are acquired after birth.[4] The risk of developing melanoma in young patients may be the result of an interaction between genetic and environmental factors in individuals with 'susceptible' pigmentary traits or a family history of melanoma.[8,9]

Children with an increased number of naevi, irrespective of their size, may be at increased risk of developing melanomas.[8–10] Some of the acquired melanomas arise from giant congenital naevi (GCN), occurring with incidence of less than 1 GCN in 20,000 newborns.[8] Individuals with small congenital naevi (SCN) also have an elevated risk of melanoma. SCN occur in 1% of newborns, but rarely develop into melanoma during childhood.[4,10] Melanomas may arise more often in dysplastic naevi than in SCN, also in children.[9,10] Sun exposure in young children, whether acute or chronic, has so far not been directly associated with an increased risk of melanoma in childhood and young adolescence.[4]

Diagnosing a childhood cutaneous melanoma is difficult, up to 40% of lesions initially diagnosed as cutaneous melanoma could be reclassified as naevi[11] and vice versa: some Spitz naevus diagnoses were later proved to be melanomas. The misclassification of melanoma in children implies that routinely published incidence rates should be interpreted with caution. In Europe, survival of children[2,12] and adolescents[2,13] with melanomas is relatively high.

Skin carcinoma incidence rates have been increasing rapidly in the past decades in all white populations worldwide. Rates in North-western Europe increased markedly in the second half of the 20th century, but are starting to level off or even decrease, mainly in young adults, whereas rates in South-eastern Europe, where increases in rates started later and have been more modest, continue to increase.[14,15]

The large database of the Automated Childhood Cancer Information System (ACCIS) makes it possible to study skin cancers and melanomas in children (aged 0–14 years) and adolescents (aged 15–19 years), in European regions.[16]

The aim of this study is to interpret incidence patterns and trends of both cutaneous malignant melanoma and skin carcinoma in children and adolescents and compare them with those in adults. In addition, survival rates for melanoma were studied and compared with incidence rates of melanoma in view of possible misdiagnosis and selective registration. Survival of children and adolescents with skin carcinoma is reported on briefly.

2. Data and methods

All 1419 cases of melanoma and 485 cases of skin carcinomas were extracted from the ACCIS database, according to predefined criteria. The cases were registered in 61 population-based general cancer registries of 20 countries, during the period 1978–1997 and diagnosed before the age of 20 years. The contributing cancer registries had satisfied quality criteria [Steliarova-Foucher, this issue] and were included in various analyses according to the availability of data (Table 1). Basic quality indicators are also shown in Table 1. The selected cases were all those classified into the subgroup XId (melanomas) or XIe (skin carcinomas) of the International Classification of Childhood Cancer.[17]

The geographical patterns of incidence and survival were assessed within the data-set of incident cases in all contributing registries over the decade 1988–1997, to achieve satisfactory stability of the estimated rates. Five geographical regions were defined in order to compare differences in incidence and survival: British Isles, East, North, South and West (Table 1). Time trends were studied for the period 1978 and 1997, in the 32 registries with sufficiently long registration period (Table 1). Table 2 shows the distribution of cases, and selected quality indicators (proportion of microscopically verified cases and those known from death certificate only), over the four successive time periods (1978–1982, 1983–1987, 1988–1992 and 1993–1997) and the five geographical regions.

The results for children (age 0–14 years) are based on the database including both paediatric and general cancer registries, while those for adolescents (age 15–19 years) are based on the data provided only by general cancer registries, the latter collecting information on all cancer cases in the defined population, irrespective of age at diagnosis. This approach guaranteed using the largest possible database for every type of analysis in this study.

Population at risk for the period of registration was provided by each registry [Steliarova-Foucher, this issue]. Age-specific incidence rates were calculated for standard age-groups 0–4, 5–9, 10–14 years (children) and 15–19 years (adolescents). For the age-range 0–14 years, the incidence rates were standardised (ASR) using the World standard population. All rates are expressed per million person-years at risk. The incidence rates and their 95% confidence intervals (95% CI) were calculated according to standard methods.[18] The rate of change over time is expressed as average annual percent change (AAPC), calculated from a Poisson regression of number of cases on year, adjusted for age, sex and region, as necessary.

Incidence rates and survival proportions are also presented for three subgroups of melanomas, based on the topography of occurrence: skin, eye or 'other ($n = 10$) and unspecified ($n = 9$)'. Separate figures are also presented for specific histological types of skin carcinomas, namely basal cell carcinomas (BCC, histology codes M8090 to M8110), squamous cell carcinomas (SCC, histology codes M8050 to M8082) and 'other ($n = 13$) and unspecified ($n = 7$)' (histology code M8010), based on the International Classification of Diseases for Oncology.[19]

The registries with acceptable quality of follow-up data were included in the analysis of survival. The individual cases with no follow-up time (mostly DCO cases) were excluded from survival analyses. Tables 1 and 2 show the proportion of cases included in the survival analyses and indicators of completeness of the follow-up. Survival was calculated using actuarial life-table method and differences between entire survival curves were tested by log-rank tests.[18] Five-year observed survival and their asymptotic 95% CI were estimated.[20] Time-trends in survival for the successive 5-year periods were tested by a log-rank test.[21] Further general details on material and methods used can be found elsewhere [Steliarova-Foucher, this issue].

The ACCIS project was approved by the ethics committee of the International Agency on Research on Cancer (IARC).

Table 1 – Cancer registries included in various analyses with the indicators of coverage, data quality and patients follow-up (Source: ACCIS)

Region	Registry	Coverage					Basis of diagnosis			Survival analysis			Notes
		Period	Time-trend	Number of cases			MV	DCO	Unknown	*n*	Closing date	FU > 5y	
				Melanoma	Carcinoma	0–14 years	%	%	%	%		%	
British Isles	IRELAND, National	1994–1997		21	9	20	100	0	0	30	31.12.1998	0	
	UNITED KINGDOM, England & Wales	1978–1995	+	200	98	100	74	0	26	297	31.1.2001	99	P
	UNITED KINGDOM, Northern Ireland	1993–1996		9	3	8	100	0	0	12	31.12.1999	30	
	UNITED KINGDOM, Scotland	1978–1997	+	145	69	22	99	0	0	214	31.12.1999	74	
East	BELARUS, National	1989–1997		12	8	100	100	0	0	20	1.9.2000	72	P
	ESTONIA, National	1978–1997	+	25	8	21	100	0	0	33	31.12.1998	86	
	HUNGARY, National	1978–1997	+	3	3	100	100	0	0	6	1.1.2000	80	P
	SLOVAKIA, National	1978–1997	+	51	37	35	99	1	0	87	31.12.1997	62	
	GERMANY, NCR (only former East)	1978–1989	+	103	29	27	100	0	0	115	31.12.1987	75	
North	DENMARK, National	1978–1997	+	131	54	23	100	0	0	185	31.12.1997	74	
	FINLAND, National	1978–1997	+	78	5	25	98	0	0	83	31.12.1998	81	
	ICELAND, National	1978–1997	+	7	1	38	100	0	0	8	31.12.2000	67	
	NORWAY, National	1978–1997	+	176	4	19	100	0	0	180	1.1.2000	82	
South	ITALY, Piedmont paediatric	1978–1997	+	4	0	100	100	0	0	4	31.12.1999	67	P o2
	ITALY, Marche	1990–1997		2	1	100	100	0	0	3	30.9.2000	0	P o3
	ITALY, Ferrara	1991–1995		2	1	33	100	0	0	3	31.12.1998	50	
	ITALY, Latina	1983–1997	+	7	0	29	100	0	0	7	31.12.1998	83	
	ITALY, Liguria	1988–1995		1	1	0	100	0	0	2	15.4.2000	100	
	ITALY, Lombardy	1978–1997	+	7	11	39	100	0	0	18	23.9.1999	79	
	ITALY, Macerata	1991–1997		1	2	33	100	0	0	3	30.9.2000	67	o3
	ITALY, Parma	1978–1995	+	5	2	14	86	0	0	7	1.4.1999	67	
	ITALY, Piedmont general	1988–1997		3	9	25	100	0	0	12	31.5.2001	58	o2
	ITALY, Ragusa	1983–1997	+	0	3	33	100	0	0	3	30.3.2000	100	
	ITALY, Sassari	1992–1995		1	2	67	100	0	0	3	30.12.1999	100	
	ITALY, Tuscany	1988–1997		7	2	11	89	0	0	9	31.12.1998	44	
	ITALY, Umbria	1994–1996		0	1	100	100	0	0	1	31.12.1999	0	
	ITALY, Veneto	1990–1996		15	9	21	100	0	0	24	31.12.1998	59	
	MALTA, National	1991–1997		1	1	50	100	0	0	2	31.12.1999	100	
	SLOVENIA, National	1978–1997	+	21	4	24	100	0	0	25	31.12.1999	80	
	SPAIN, National	1990–1995		4	1	100	100	0	0	5	31.12.2000	100	P o4 Z
	SPAIN, Albacete	1991–1997		3	0	0	100	0	0	3	15.9.2000	33	e
	SPAIN, Asturias	1983–1997	+	10	7	53	100	0	0	17	31.12.1997	43	e
	SPAIN, Basque Country	1988–1994		10	0	40	100	0	0	10	31.12.2000	100	o4 e
	SPAIN, Canary Islands	1993–1996		2	0	0	100	0	0	–	–	–	
	SPAIN, Girona	1994–1997		3	1	25	100	0	0	4	31.12.1997	0	o4
	SPAIN, Granada	1988–1997		1	0	100	100	0	0	1	31.12.1999	100	P
	SPAIN, Mallorca	1988–1995		2	9	55	100	0	0	8	31.12.1998	50	o4
	SPAIN, Navarra	1978–1996	+	6	7	15	100	0	0	13	31.12.1997	73	o4

	SPAIN, Tarragona	1983–1997	+	9	10	37	100	0	0	19	31.12.1998	53	o4
	SPAIN, Zaragoza	1978–1996	+	11	4	40	100	0	0	15	31.12.1996	42	o4
	TURKEY, Izmir	1993–1996		4	4	0	100	0	0	–	–	–	
West	FRANCE, Brittany	1991–1997		1	2	100	100	0	0	3	1.1.2000	50	P
	FRANCE, Lorraine	1983–1997	+	10	7	100	100	0	0	17	1.1.1999	62	P
	FRANCE, PACA & Corsica	1984–1996	+	10	2	100	100	0	0	11	31.3.1998	82	P
	FRANCE, Rhone Alpes	1988–1997		1	2	100	100	0	0	3	1.6.2000	0	P o1
	FRANCE, Doubs	1978–1996	+	8	9	29	76	0	0	9	1.6.2001	38	
	FRANCE, Herault	1988–1997		13	1	36	100	0	0	–	–	–	
	FRANCE, Isere	1979–1997	+	22	2	42	100	0	0	–	–	–	o1 e
	FRANCE, Manche	1994–1996		2	0	50	100	0	0	2	31.5.2000	0	
	FRANCE, Bas-Rhin	1978–1996	+	14	0	21	100	0	0	14	31.12.1997	46	
	FRANCE, Haut-Rhin	1988–1997		15	4	42	95	0	0	5	31.12.1995	100	
	FRANCE, Somme	1983–1996	+	9	2	64	100	0	0	11	15.8.2000	60	
	FRANCE, Tarn	1983–1997	+	2	0	0	100	0	0	–	–	–	
	GERMANY, GCCR (East and West)	1991–1997	+	9	2	100	100	0	0	9	31.12.1998	0	P
	GERMANY, GCCR (only former West)	1983–1990	+	16	1	100	100	0	0	15	31.12.1998	82	P
	NETHERLANDS, National	1989–1995		145	21	18	99	0	0	30	31.12.1998	65	o5
	NETHERLANDS, Eindhoven	1978–1997	+	17	14	23	100	0	0	31	1.7.1999	69	o5
	SWITZERLAND, Basel	1983–1997	+	5	4	11	100	0	0	9	30.6.2000	100	
	SWITZERLAND, Geneva	1978–1997	+	21	7	32	100	0	0	28	31.12.1999	62	
	SWITZERLAND, Graubunden & Glarus	1989–1997		4	2	0	100	0	0	6	25.5.2000	50	
	SWITZERLAND, St. Gallen Appenzell	1983–1997	+	10	3	8	100	0	0	13	1.2.2001	46	
	SWITZERLAND, Valais	1989–1997		3	2	20	100	0	0	2	1.12.1998	100	

P, paediatric cancer registry (age-range 0–14 years); NCR, National Cancer Registry of the German Democratic Republic. Data for 1978–1987 contributed only to analyses of time trends for Europe as a whole. Data on children for 1988–1989 were pooled with GCCR and included in West for geographical analyses of the period 1988–1997. For explanation, see Steliarova-Foucher, Kaatsch, Lacour and colleagues [this issue]; GCCR, National German Childhood Cancer Registry (until 1990 only West, since 1991 for reunified Germany); +, included in time trends; % MV, percentage of microscopically verified cases; % DCO, percentage of registrations from death certificate only; % unknown, percentage of registrations with unknown basis of diagnosis; %FU > 5y, percentage of cases followed-up for at least 5 years among all those not deceased by the closing date; e, non-systematic registration of skin carcinomas; o1–o4, overlapping registration areas: for the overlapping years, data on children (age 0–14 years) are included only from the paediatric registry; o5, overlapping registration areas: for the overlapping years, data are included only from the national registry; Z, covers only selected areas, see Steliarova-Foucher, Kaatsch, Lacour and colleagues [this issue].

Table 2 – Numbers of cases and indicators of data quality by region and age group for time trend analyses (Source: ACCIS)

Region	Period	Children (age 0–14 years)							Adolescents (age 15–19 years)						
		Melanomas (XId)	Skin carcinomas (XIe)	Basis of diagnosis			Follow-up		Melanomas (XId)	Skin carcinomas (XIe)	Basis of diagnosis			Follow-up	
				MV	DCO	Unknown	>0 days	5+ years			MV	DCO	Unknown	>0 days	5+ years
		n	*n*	%	%	%	%	%	*n*	*n*	%	%	%	%	%
Europe	1978–1982	101	52	92	0	7	99	99	130	49	99	0	< 1	99	100
	1983–1987	117	62	91	0	9	99	98	182	35	100	0	0	100	84
	1988–1992	133	53	80	0	20	98	94	179	42	98	0	0	99	93
	1993–1997	108	44	91	0	8	99	53	186	72	99	0	0	99	29
British Isles	1978–1982	52	22	82	0	15	99	98	12	15	100	0	0	100	100
	1983–1987	50	35	80	0	20	100	100	23	12	100	0	0	100	100
	1988–1992	73	29	64	0	36	100	99	39	10	100	0	0	100	100
	1993–1997	60	24	85	0	14	100	78	36	20	98	0	0	100	35
East	1978–1982	3	8	100	0	0	100	100	14	7	95	0	5	95	100
	1983–1987	5	9	100	0	0	100	100	9	1	100	0	0	100	100
	1988–1992	2	4	100	0	0	100	100	19	7	100	0	0	100	100
	1993–1997	11	2	100	0	0	100	8	16	10	100	0	0	100	0
North	1978–1982	25	7	100	0	0	100	100	56	11	100	0	0	100	100
	1983–1987	22	6	100	0	0	100	100	87	4	100	0	0	100	97
	1988–1992	20	5	100	0	0	100	100	88	6	99	0	0	100	94
	1993–1997	12	5	100	0	0	100	31	82	20	99	0	0	100	31
South	1978–1982	6	1	100	0	0	100	100	4	1	100	0	0	100	100
	1983–1987	6	2	100	0	0	100	100	16	8	96	0	0	100	100
	1988–1992	5	7	100	0	0	100	91	14	9	100	0	0	100	100
	1993–1997	10	8	100	0	0	100	20	19	12	100	0	0	100	17
West	1978–1982	4	1	100	0	0	100	100	12	3	93	0	0	91	100
	1983–1987	26	9	100	0	0	97	96	12	7	100	0	0	100	69
	1988–1992	30	8	100	0	0	88	70	19	10	90	0	0	88	60
	1993–1997	15	5	100	0	0	89	13	33	10	100	0	0	95	41

Data from the former GDR is only included in the data for Europe.
f, total number of cases in the registries with follow-up data; g, number of cases with follow-up > 0 day, who have not deceased by closing date; MV, microscopically verified cases; DCO, percentage of registrations from death certificate only.

3. Results

3.1. *Malignant melanoma*

For the period 1988–1997, a total of 871 cases of melanoma in the age group 0–19 years was included (346 boys, 525 girls). Of 723 cases registered in general cancer registries, 79% occurred in adolescents ($n = 571$), in whom the diagnosis of melanoma was made more frequently in girls ($n = 361$) than in boys ($n = 210$) (Table 3, Fig. 1).

Table 3 shows the number of cases by age and sex observed during 1988–1997. We noted that in children, the rates recorded exclusively in the general cancer registries (ASR = 1.2) were about double of those observed in the combined database of paediatric and general cancer registries (ASR = 0.7), the latter used elsewhere in this paper (Fig. 2).

Highest rates are seen in the British Isles in both children and adolescents. In adolescents, there is clear distinction between the regions with high and low incidence rates, whereas in children the geographical differences are more even.

The majority of the malignant melanomas involved skin. Eye melanomas constituted less than 4% (Table 3). The 'other and unspecified' sites included mouth (1 case), retroperitoneum ($n = 1$), central nervous system (CNS) ($n = 5$) and unspecified sites ($n = 3$) in children and retroperitoneum ($n = 1$), female genitals ($n = 1$), CNS ($n = 1$) and unspecified sites ($n = 6$) in adolescents. Overall, incidence rates of malignant melanoma remained rather stable in children (Table 4): the increase of number of new cases per year was not statistically significant ($P = 0.117$), based on a Poisson regression model adjusted for region and age group. In adolescents the incidence rate increased by 4.1% per year on average ($P < 0.0001$), adjusted for region and sex. Increases were slightly larger for adolescent girls than boys (Fig. 3). Most marked increases were observed in adolescents from the British Isles and Southern Europe (Table 4).

Overall 5-year survival for children with malignant melanoma was 86%, with no difference in overall survival between boys and girls ($\chi^2 = 0.23$, $P = 0.6$) or between age groups ($\chi^2 = 6.31$, $P = 0.1$). The outcome was similar in adolescents,

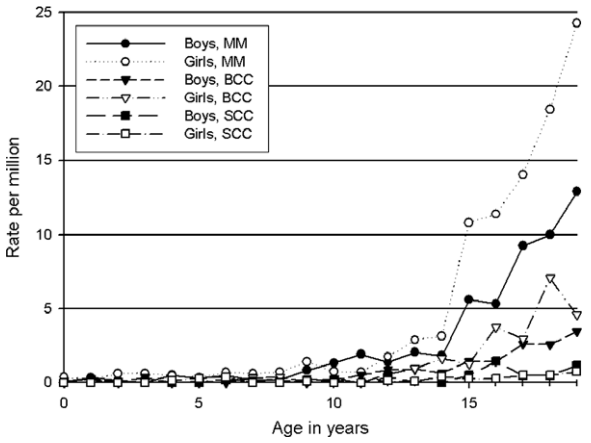

Fig. 1 – Age-specific incidence rates of melanoma and skin carcinoma in Europe, 1988–1997. Regions with non-systemic registration of skin carcinomas are excluded. MM, malignant melanoma; BCC, basal cell carcinoma; SCC, squamous cell carcinoma. The rates are weighted by the numbers of cases in the data-sets. Source: ACCIS.

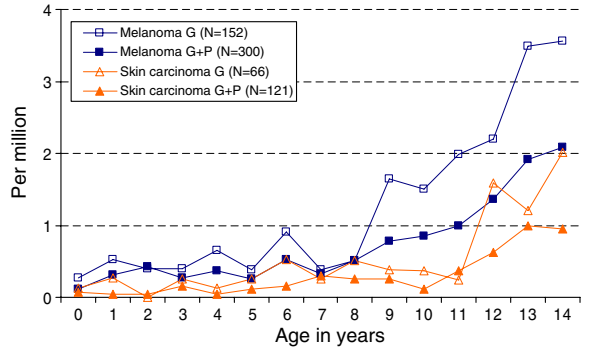

Fig. 2 – Age-specific incidence rates of melanoma and skin carcinoma in Europe, 1988–1997, based on data provided by the general cancer registries (G) or by both paediatric and general cancer registries (G+P). Total number of cases included is shown for each data-set. Source: ACCIS.

Table 3 – Incidence rates of malignant melanoma (ICCC subgroup XId) in Europe, 1988–1997 (Source: ACCIS)

	Children (age 0–14 years)			Adolescents (age 15–19 years)		
	n	M/F	ASR (per million)	*n*	M/F	Rate (per million)
Europe	300	0.8	0.69	571	0.6	12.8
British Isles	140	0.8	1.44	98	0.5	18.7
East	25	1.8	0.39	35	1.2	6.31
North	32	0.6	1.08	170	0.4	17.3
South	25	0.4	0.56	77	0.7	6.68
West	78	1.1	0.39	191	0.6	15.5
Skin	279	0.8	0.64	542	0.6	12.2
Eye	11	4.5	0.025	20	1.2	0.45
Other and unspecified	10	1.5	0.024	9	0.3	0.20

M/F, sex ratio; ASR, age-standardised rate (World standard).

Table 4 – Trends in incidence rates of malignant melanoma in Europe, 1978–1997 (Source: ACCIS)

	Age group (years)	ASR in period			
		1978–1982	1983–1987	1988–1992	1993–1997
Boys	0–14	0.70	0.60	0.65	0.61
	15–19	4.65	6.65	8.52	10.0
Girls	0–14	0.87	0.68	0.84	0.71
	15–19	8.04	10.6	16.8	18.2
Europe	0–14	0.78	0.64	0.74	0.66
	15–19	6.30	8.60	12.6	14.0
British Isles	0–14	0.85	0.88	1.34	1.62
	15–19	5.31	10.6	21.8	22.9
East	0–14	0.15	0.28	0.09	0.59
	15–19	5.47	3.69	7.09	5.59
North	0–14	1.59	1.39	1.34	0.82
	15–19	10.1	15.9	17.4	17.2
South	0–14	0.65	0.56	0.41	1.12
	15–19	2.34	6.09	5.34	8.06
West	0–14	0.88	0.42	0.42	0.17
	15–19	8.02	5.22	9.14	19.3

ASR, age-standardised rate (World standard).

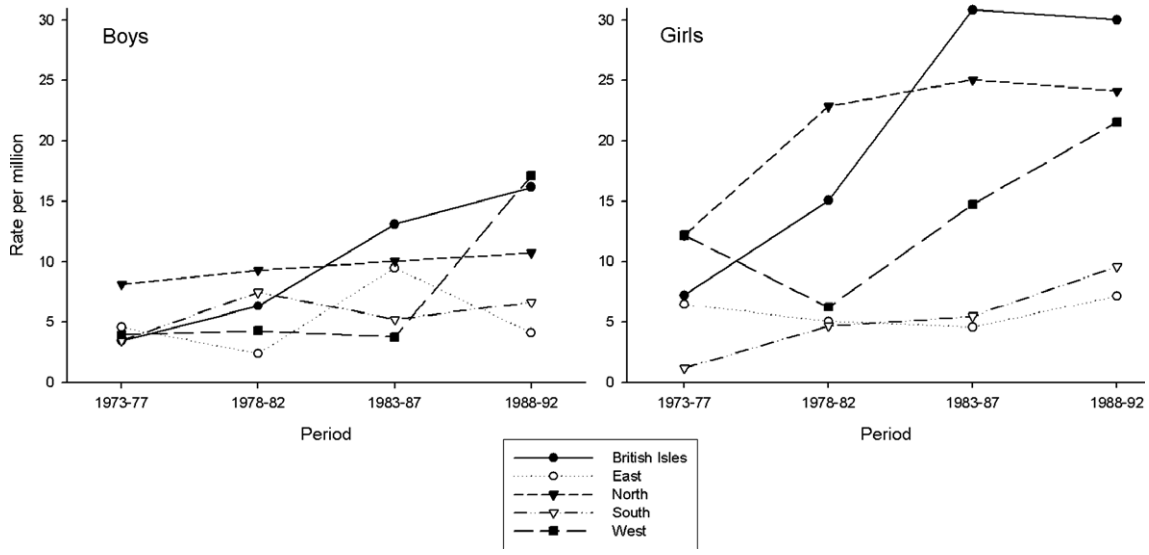

Fig. 3 – Incidence rates of melanoma in adolescents (aged 15–19 years) in Europe, 1978–1997. Source: ACCIS.

with similar survival in boys and girls ($\chi^2 = 2.44$, $P = 0.1$). We noted lower 5-year survival in the regions with the low incidence rates, i.e. Southern and Eastern Europe (Table 5, Fig. 4).

The survival outcome differed according to the site involved, with a lower survival for melanomas involving sites other than skin or eyes ($\chi^2 = 101.19$, $P < 0.0001$) (Table 5).

Survival of malignant melanoma improved during the period 1978–1997 from 76% to 88% in children and from 79% to 89% in adolescents (Table 6). Significant increases over time were observed in British and Eastern European children and in Western European adolescents.

3.2. *Skin carcinoma*

For the period 1988–1997, there were 286 reported cases of skin carcinoma included in the analyses. In the general cancer registries covering the age-range 0–19 years, 71% of 231 skin carcinomas were detected in adolescents (72 boys, 93 girls). As with melanomas, the incidence rates recorded for children in the general cancer registries (ASR = 0.6) were approximately double those generated from the combined database constituted by both paediatric and general cancer registries (ASR = 0.3), as seen in Fig. 2. The combined database was used to report

Table 5 – Survival of patients with malignant melanoma, diagnosed in Europe in 1988–1997 (Source: ACCIS)

	Children (age 0–14 years)		Adolescents (age 15–19 years)	
	n	5 year survival (%) (95% CI)	*n*	5 year survival (%) (95% CI)
Europe	285	86 (82–90)	427	86 (82–89)
British Isles	140	92 (86–95)	98	84 (73–90)
East	25	91 (69–98)	35	75 (56–87)
North	32	87 (70–95)	170	92 (86–96)
South	25	75 (53–88)	71	73 (59–83)
West	63	74 (60–84)	53	96 (84–99)
Skin	265	89 (84–92)	402	88 (85–91)
Eye	10	89 (43–98)	19	94 (65–99)
Other and unspecified	10	18 (2–47)	6	33 (5–68)

n, number of cases included in survival analyses; CI, confidence interval.

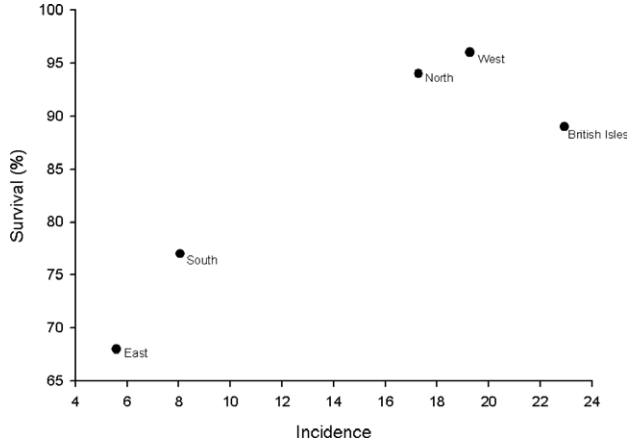

Fig. 4 – Incidence versus survival rates of melanoma in Europe, adolescents (aged 15–19 years), 1993–1997. Source: ACCIS.

the results below. Excluding the few registries without systematic registration of skin carcinomas (Table 1), 76% were basal cell carcinomas (BCC, $n = 212$), 17% squamous cell carcinomas (SCC, $n = 47$) and 7% other skin carcinomas ($n = 20$, out of which 7 not specified) (Table 7) of the total 279 cases.

Incidence rates of skin carcinomas were very low (less than 1 case per million) among children, rates in adolescents were considerably higher (varying from 2.6 to 8 per million) (Table 7). Generally, rates in males were lower than in females, except for the squamous cell carcinomas. The difference in age-specific incidence rates between the 10–14 and 15–19 year age groups was smaller than for melanoma.

No statistically significant increases in incidence rates were observed in the years 1978–1997 for children ($P = 0.233$) (age 0–14 years: 1.01 (95% CI 0.99–1.03). In adolescents, the increase was marginally significant; age 15–19 years: 1.02 (95% CI 0.99–1.05) with AAPC = 2.5, $P = 0.053$, adjusted for region). However, the rates in adolescents did rise in the latest 15-year period (Table 8), with an average of 4.4% ($P = 0.028$) per year.

Due to small numbers of incident cases in the period 1988–1997 and very low case-fatality rates, survival for the three histological subgroups are reported for Europe as a whole (Table 9). Five-year survival of basal cell carcinoma was 100% for children and 98% for adolescents. Survival rates were less favourable for squamous cell carcinomas: 80% for children and 76% for adolescents (Table 9).

Survival of skin carcinoma did not change over the period 1978–1997 (Table 10), neither did survival of any of the histological subgroups change over time (results not shown).

4. Discussion

This study observed regional differences in rates of melanoma. In adolescents, rates were highest in North-western Europe (regions North, West and British Isles), which coincided with the observed differences in melanoma incidence in adults.[14] Increases over time were seen in adolescents only and in the British Isles and Southern Europe. The incidence of melanomas in children younger than 14 years seems unchanged over time. This difference between trends in adolescents and children is in accordance with earlier studies and points to increases in a risk factor that probably becomes critical only in adolescence and beyond.[5,6,10] The most important risk factor for the development of adolescent and adult melanomas is believed to be intermittent sun exposure during childhood. In contrast, risk of developing a melanoma in childhood does not seem to be related to sun exposure. As exposure to ultraviolet radiation has increased over the past decades, and increases in incidence rates were only observed from puberty on, this gives indications of a latency time for the development of melanoma of at least 10 years,[22,23] but does not reveal much about the risk factors that would affect the occurrence of childhood melanoma, which does not seem to be increasing. The increase in incidence of melanoma amongst adolescents may also be a result of changes in diagnostic practices, reflecting better accessibility to sanitary services and development of the cult of body image in adolescents. The increasing trend of melanoma incidence observed in this study may therefore be part of a complex picture of increasing exposure to risk factors combined with improved surveillance. This may be shifting diagnosis to earlier ages. Such cohort-specific effect would also contribute to an improvement in survival, as was observed.

Table 6 – Survival of patients with malignant melanoma, diagnosed in Europe in 1978–1997 (Source: ACCIS)

Region / Period of diagnosis		Children (age 0–14 years)		Adolescents (age 15–19 years)	
		n	5-year survival (%) (95% CI)	*n*	5-year survival (%) (95% CI)
Europe	1978–1982	99	76 (66–83)	125	79 (71–85)
	1983–1987	113	88 (81–93)	181	85 (79–90)
	1988–1992	124	88 (81–92)	175	85 (78–89)
	1993–1997	106	88 (79–93)	180	89 (82–94)
Test for trend		χ^2(df = 1) = 5.45		χ^2(df = 1) = 3.75	
		Pr > χ^2 = 0.0195		Pr > χ^2 = 0.0527	
British Isles	1978–1982	51	70 (55; 81)	12	67 (34–86)
	1983–1987	50	94 (83–98)	23	87 (65–96)
	1988–1992	73	90 (81–95)	39	82 (66–91)
	1993–1997	60	93 (83–97)	36	89 (69–96)
Test for trend		χ^2(df = 1) = 11.75		χ^2(df = 1) = 0.92	
		Pr > χ^2 = 0.0005		Pr > χ^2 = 0.3386	
East	1978–1982	3	33 (1–77)	13	77 (44–92)
	1983–1987	5	60 (13–88)	9	100
	1988–1992	2	100	19	79 (53–92)
	1993–1997	11	90 (49–99)	16	68 (32–87)
Test for trend		χ^2(df = 1) = 4.26		χ^2(df = 1) = 0.34	
		Pr > χ^2 = 0.0389		Pr > χ^2 = 0.5571	
North	1978–1982	25	92 (72–98)	56	84 (71–91)
	1983–1987	22	86 (63–95)	87	91 (82–95)
	1988–1992	20	85 (60–95)	88	92 (83–96)
	1993–1997	12	91 (51–91)	82	94 (82–98)
Test for trend		χ^2(df = 1) = 0.01		χ^2(df = 1) = 2.22	
		Pr > χ^2 = 0.9173		Pr > χ^2 = 0.1366	
South	1978–1982	6	83 (27–97)	4	75 (13–96)
	1983–1987	6	83 (27–97)	16	56 (30–76)
	1988–1992	5	80 (20–97)	14	50 (23–72)
	1993–1997	10	66 (27–88)	19	77 (28–95)
Test for trend		χ^2(df = 1) = 0.42		χ^2(df = 1) = 1.35	
		Pr > χ^2 = 0.5183		Pr > χ^2 = 0.2445	
West	1978–1982	3	100	8	61 (21–86)
	1983–1987	22	81 (59–93)	11	39 (6–69)
	1988–1992	24	82 (59–93)	15	93 (60–99)
	1993–1997	13	74 (38–91)	27	96 (73–99)
Test for trend		χ^2(df = 1) = 1.40		χ^2(df = 1) = 5.28	
		Pr > χ^2 = 0.2360		Pr > χ^2 = 0.0216	

CI, confidence interval; Pr, probability; df, degrees of freedom.

Table 7 – Incidence rates of skin carcinoma (ICCC subgroup XIe) in Europe, 1988–1997 (Source: ACCIS)

	Children (age 0–14 years)			Adolescents (age 15–19 years)		
	n	M/F	ASR (per million)	*n*	M/F	Rate (per million)
Europe	121	0.8	0.27	165	0.8	3.71
British Isles	53	0.8	0.54	42	0.5	8.02
East	14	1.3	0.21	17	0.7	3.07
North	10	0.7	0.33	26	0.6	2.65
South	19	1.11	0.39	48	0.9	4.16
West	25	0.6	0.13	32	1.3	2.59
Basal cell carcinoma[a]	83	0.8	0.19	129	0.6	3.11
Squamous cell carcinoma[a]	21	0.6	0.05	26	1.9	0.63
Other (not specified)[a]	14(5)	0.8	0.03	6(2)	1.0	0.15

M/F, sex ratio. AAPC, average annual percent change.
a The registries with non-systematic registration of skin carcinomas (*n* = 4) are excluded from analyses by subtype.

Table 8 – Trends in incidence rates of skin carcinoma in Europe, 1978–1997 (Source ACCIS)

	Age group (years)	ASR in period			
		1978–1982	1983–1987	1988–1992	1993–1997
Boys	0–14	0.34	0.26	0.28	0.22
	15–19	1.99	1.48	2.20	4.72
Girls	0–14	0.43	0.36	0.31	0.30
	15–19	2.78	1.84	3.74	6.18
Europe	0–14	0.39	0.31	0.30	0.26
	15–19	2.38	1.65	2.95	5.44
British Isles	0–14	0.33	0.56	0.53	0.64
	15–19	6.63	5.53	5.58	12.7
East	0–14	0.39	0.40	0.19	0.11
	15–19	2.73	0.41	2.61	3.49
North	0–14	0.43	0.36	0.32	0.33
	15–19	1.99	0.73	1.19	4.21
South	0–14	0.10	0.14	0.72	0.83
	15–19	0.59	3.04	3.43	5.09
West	0–14	0.24	0.14	0.11	0.06
	15–19	2.01	3.05	4.81	5.84

ASR, age-standardised rate (World standard).

Table 9 – Survival of patients with skin carcinomas, diagnosed in Europe in 1988–1997 (Source: ACCIS)

	Children (age 0–14 years)		Adolescents (age 15–19 years)	
	n	5 year survival (%) (95% CI)	*n*	5 year survival (%) (95% CI)
Europe	113	96 (90–99)	144	96 (87–99)
British Isles	53	98 (87–100)	42	93 (73–98)
East	14	91 (52–99)	17	100
North	10	88 (41–98)	26	89 (43–98)
South	18	100	43	100
West	18	93 (59–99)	16	100
Basal cell carcinoma	79	100	127	98 (87–100)
Squamous cell carcinoma	17	80 (51–93)	10	76 (32–94)
Other histologies	14	93 (59–99)	4	100

n, number of cases included in survival analyses; CI, confidence interval.

Table 10 – Survival of patients with skin carcinoma, diagnosed in Europe in 1978–1997 (Source: ACCIS)

Period of diagnosis	Children (age 0–14 years)		Adolescents (age 15–19 years)	
	n	5-year survival (%) (95% CI)	*n*	5-year survival (%) (95% CI)
1978–1982	51	96 (85–99)	48	100
1983–1987	62	97 (88–99)	35	97 (80–100)
1988–1992	51	98 (86–100)	38	97 (82–100)
1993–1997	43	98 (84–100)	70	91 (59–98)
Test for trend	χ^2(df = 1) = 0.05		χ^2(df =1) = 1.80	
	Pr > χ^2 = 0.8182		Pr > χ^2 = 0.1793	

CI, confidence interval; Pr, probability; df, degrees of freedom.

We observed higher survival in regions with high melanoma incidence compared with the other regions in Europe, in agreement with previous observations in adults.[14,15] This most likely reflects earlier detection of melanomas, which simply means a large proportion of cases with good prognosis within a patient group. Early detection may occur naturally in the populations with high incidence, with presumably high awareness, of melanoma. Over-diagnosis of melanoma is probably unlikely, since even if diagnosis of a melanoma may be missed due to complete regression, the tumour still

carries a metastatic potential and may resurface later. Other possible reasons contributing to the differences in survival between regions are discussed in detail elsewhere [Sankila and colleagues, this issue].

In the Southern and Eastern regions survival in adolescents was relatively poor compared with the other regions. In the regions with clearly increasing incidence rates, survival rates also improved further, albeit not always significantly. This pattern of good survival in regions with high and increasing incidence rates, and poor survival in regions with lower and more stable incidence rates has also been observed in adults.[14,15] For adults, early diagnosis has substantially improved stage at diagnosis of melanoma in regions with high incidence and has therefore also improved survival. Some authors have hypothesised a better survival of Spitz-like melanomas, a variety of melanoma most often observed in children and adolescents, than conventional melanomas even at a metastatic stage.[11]

In earlier studies it was proven that histological confirmation of melanoma is very difficult: between 30% and 95% of malignant melanoma cases in children were really Spitz naevus or another benign lesion.[10–12] Although in the ACCIS database almost all melanomas were histologically verified, their diagnosis was not reviewed for the current study and therefore we cannot exclude a misdiagnosed Spitz or spindle cell naevus or another type of benign lesion, which was found to be of concern particularly among patients aged under 12 years.[4] A Swedish study found the risk for histopathological overdiagnosis of melanoma to be much higher in children (95%), than in adults (4%).[24] However, Swedish data were not included in this study and we cannot imply the same results in other registries, notably the paediatric ones, which are known for more precision of recorded information per case [Steliarova-Foucher, this issue]. At later ages the accuracy of the diagnosis seems to improve; the large majority of the observed cases in our study (85% of cumulative incidence) were adolescents.

Small increases were observed for SCC in most regions, but we are not aware of exogenous factors that could explain the increases, other than sun exposure and immunosuppression, for example after organ transplants. Skin carcinomas or some histological subtypes are sometimes intentionally excluded from routine registration, although this applies to only a few registries in our data. Nevertheless, changes in registration practices will influence the reported rates and time-trends. Further, in the few patients affected by *Xeroderma Pigmentosum*, misdiagnoses may occur (for instance desmoplastic trichoepithelioma misdiagnosed as basal cell carcinoma.[25]) Finally, the superficial location of skin carcinomas and melanomas make out-patient treatment possible, which may lead to the possibility of missing some cases from registration. Specific concern may relate to the completeness of registration, especially in paediatric cancer registries, which may devote less attention to obtaining cases from dermatologists. Variation of registration practices over time and regions may thus also explain part of the variations in the incidence rates.

Although most cases of skin carcinomas are present with basal cell type and therefore survive, the small percentage of squamous cell type cases have lower survival outcome.

Our results also indicate that, in spite of rigorous quality checks, we were not able to exclude all artefacts possibly affecting results. Seemingly, the incidence rates of skin carcinoma depend more on registration techniques than on the geographical region. Incidence rates of melanoma seem to be affected to a similar extent by type of registration and the geographical area. Interestingly, in the British Isles, with a large proportion of cases coming from a paediatric cancer registry of England and Wales, the incidence of melanoma is highest among the regions. This may result from regular data linkage with the general cancer registries in the UK. Since the areas of the contributing registries did not overlap completely, we cannot exclude genuinely higher incidence rates of melanoma and skin carcinomas in the areas covered by the general cancer registries only, compared with those covered also by the paediatric ones. Furthermore, even if the inclusion of paediatric cancer registries halved the value of incidence rates reported from general cancer registries, it is difficult to argue which of the two figures is more reliable. On one hand, the paediatric cancer registries may have difficulties in ascertaining all cancer patients and, on the other hand, they may exclude more efficiently misdiagnosed cases, which is known to be a problem, especially for melanoma.[10–12] We have therefore based our estimates on the larger of the two possible datasets. The reasons for the differences caused by selection of registries deserves a detailed study and, as much as possible, harmonisation of the registration techniques.

5. Conclusion

Malignant melanoma and skin carcinomas are rare in children, but increase substantially with age, especially after the age of 15 years. Increases in incidence over time were observed only for adolescents, possibly reflecting a change in risk factors relevant to adolescents and adults, but not to children. Survival is good, although further improvement is necessary for patients with melanomas and squamous cell skin carcinomas.

The variation in incidence and survival of melanoma across Europe among adolescents is comparable to variation observed among adults, with high incidence and survival rates in the Northern and Western regions, including the British Isles, and lower incidence and survival rates in the South and East.

Study of comparability of data from various European sources is warranted in order correctly to interpret the possible associations with putative risk factors. ACCIS represents a perfect framework for such future studies.

Conflict of interest statement

None declared.

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