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ANTI-TUMOUR TREATMENT

International patterns of cancer incidence in adolescents

Charles A Stiller *

Childhood Cancer Research Group, Department of Paediatrics, University of Oxford, 57 Woodstock Road, Oxford OX2 6HJ, UK

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Summary International patterns of childhood cancer incidence are well documented but equivalent information relating to adolescence is scarce. This article synthesises international data on cancer in adolescents from population based cancer registries. Total incidence ranged from 95 to 255 per million person years in the series studied. The highest rates were in Australia and among Jews in Israel and the lowest in India and Japan. Lymphomas were the most frequent cancers in western industrialised countries of the northern hemisphere and in the Middle East, and occurred in substantial numbers in all other regions. Hodgkin lymphoma outnumbered non-Hodgkin in western industrialised countries but was relatively rare in most developing countries and in Japan. Leukaemias were the most frequent diagnostic group in India, East Asia and Latin America. Melanoma was the commonest cancer of adolescents in Australia and New Zealand and moderately frequent in many other predominantly white populations but rarely seen elsewhere. Kaposi sarcoma was the most frequent cancer in both sub-Saharan African series studied. The highest rates for nasopharyngeal carcinoma were in Algeria and Hong Kong and for liver carcinoma in Hong Kong and sub-Saharan Africa. Testicular germ cell tumours were relatively frequent in predominantly white populations. Central nervous system tumours and thyroid carcinoma were most often registered in countries with higher standard of living. Osteosarcoma was moderately frequent almost everywhere. Characteristic embryonal tumours of childhood and the most common carcinomas of adulthood were rarely seen. Only osteosarcoma, ovarian germ cell tumours and, in some populations, nasopharyngeal carcinoma have their highest incidence at age 15—19 years. Total cancer incidence was higher in adolescent males than females, but there was often a female excess in melanoma and thyroid carcinoma, and Hodgkin lymphoma was at least as frequent among females as males in several countries with relatively high incidence. More complete delineation of worldwide patterns of cancer in adolescence would be facilitated by availability of more data classified in a standard way to take account of morphology.

* Tel.: +44 1865 315925; fax: +44 1865 315940.
E-mail address: charles.stiller@ccrg.ox.ac.uk

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Introduction

International patterns of childhood cancer incidence are well documented and have been studied extensively.[1–6] There have been several reports on cancer incidence among adolescents within single countries.[7–16] International comparative studies, however, are relatively scarce.[5,17,18] The aims of this article are to present and compare recent international, population-based data on cancer incidence in the 15–19 year age group, and to document and comment on time trends over past decades.

Materials and methods

Sources of incidence data

Incidence data were derived from population-based cancer registries and were taken from published sources. For Europe, the results are from the Automated Childhood Cancer Information System (ACCIS). The data for geographical patterns relate to the period 1988–1997, and those for time trends to the period 1978–1997.[18] In ACCIS, Europe was divided into five regions, namely British Isles, East, North, South and West. The results for 1988–1997 in the British Isles were from Scotland, Northern Ireland and the Republic of Ireland representing less than 15% of the total population at risk in this region, while the analysis of time trends referred to Scotland alone.[18] For the United States, use has been made of a recent report giving incidence rates for 1999–2003 among the three principal ethnic groups.[19] The data were compiled from 38 cancer registries participating in the Surveillance, Epidemiology and End Results (SEER) Program and the National Program of Cancer Registries (NPCR), which together cover 82% of the national population. Results on time trends in the United States are taken from the recent SEER monograph on cancer in adolescents and young adults, which includes data on all cancers combined and selected cancer sites among about 10% of the national population during 1975–2000.[16] For the rest of the Americas, Asia and Oceania, data are taken from the most recent volume of Cancer Incidence in Five Continents[20] and relate predominantly to the period 1993–1997. Data for African registries have been taken from the monograph on Cancer in Africa[21] since the coverage is geographically wider than in Cancer Incidence in Five Continents and some registries provided data for a longer calendar period.

Classification of diagnoses, and diagnostic categories included

The data from ACCIS were classified according to the International Classification of Childhood Cancer (ICCC),[22] but with subgroup XIf, 'Other and unspecified carcinomas', subdivided by primary site, broadly along the lines of the third edition of ICCC (ICCC-3).[23] The study followed ICCC in including all diagnoses classed as malignant in ICD-O-2 together with certain non-malignant intracranial and intraspinal neoplasms, but these tumours were not systematically registered by all contributing cancer registries. Intracranial and intraspinal germ cell tumours were grouped with germ cell tumours of other sites. Skin carcinomas were included, but were not systematically registered by a few registries (see Table 1).

The United States data in the SEER/NPCR study were classified according to ICCC-3. Malignant neoplasms as defined by ICD-O-3 were included except for myelodysplastic disorders, which were not regarded as malignant in earlier editions of ICD-O, but with the addition of pilocytic astrocytoma which had been classed as malignant in ICD-O-2 and ICCC.[19] Borderline malignant epithelial tumours of the ovary, which had been classed as malignant only in ICD-O-2, were excluded. In the SEER monograph, diagnoses were grouped according to a slightly modified version of ICCC and the standard SEER site recode.[16] Only malignant neoplasms as defined by ICD-O-2 were included. In both studies, intracranial and intraspinal germ cell tumours were grouped with germ cell tumours of other sites. Skin carcinomas were included but not analysed separately (see Table 2).

The data from Cancer Incidence in Five Continents[20] were classified mainly by site according to ICD-10 but additionally broken down by morphology for certain sites, notably bone, gonadal and CNS. Only malignant neoplasms were included. Germ cell tumours of the CNS were listed separately under that site, but all tumours of the pituitary and pineal were grouped under the heading 'Other endocrine' and not subdivided by morphology. Reporting practice for skin carcinoma and other non-melanoma skin cancers varied widely between registries (see Tables 3–6). Data from Cancer in Africa[21] were classified according to ICD-10. Non-melanoma skin cancers were routinely registered by all registries reported here (see Table 7).

Results

Geographical patterns

Total cancer incidence ranged from 105 to 264 per million in males and from 85 to 228 per million in females. The lowest rates were found in India and Japan for both sexes, while Algeria and mainland China also had incidence below 100 per million in females. The highest rates for both sexes were in Australia. In the United States, the incidence rates for both sexes were highest in non-Hispanic Whites, intermediate in Hispanics, and lowest in non-Hispanic Blacks. Incidence was higher in males than in females in all the data sets except for Uganda.

Incidence of leukaemia ranged from under 10 per million in Algeria and Uganda to over 35 per million in Hispanic populations of the Americas. In the United States, incidence among non-Hispanic Whites was higher than among non-Hispanic Blacks. In Europe, incidence was highest in the British Isles and the South and lowest in the East. Most of the variation between populations was accounted for by lymphoid leukaemia, which in this age group is virtually synonymous with acute lymphoblastic leukaemia (ALL). Lymphoid leukaemia was the most frequent subgroup in most populations but the excess was greatest among Hispanic populations and in Oman. In Japan, mainland China and Zimbabwe, ALL was less frequent than acute myeloid leukaemia (AML). AML had relatively constant incidence worldwide and was the only other subtype to have incidence consistently above 5 per million. Leukaemia was more frequent among males than

Table 1 Cancer incidence per million person-years at age 15–19 years in Europe, 1988–1997

Region	British Isles	East	North	South	West	Europe	
Person-years	5,240,123	5,544,811	9,809,611	11,536,094	12,348,912	44,479,551	
Number of cases	968	935	2057	2153	2159	8272	
	Rate	Rate	Rate	Rate	Rate	Rate	M/F
Total	184.7	168.6	209.7	186.6	174.8	186.0	1.2
Total (excluding skin carcinoma)	176.7	165.6	207.0	182.5	172.2	182.3	1.2
Leukaemia	27.9	18.9	20.6	26.9	19.7	22.6	1.7
Lymphoid	15.3	8.8	11.5	15.0	11.9	12.6	2.0
AML	9.2	6.5	6.8	7.5	6.0	7.0	1.3
CML	1.7	1.6	1.7	1.8	1.1	1.6	1.7
Other/unspecified	1.7	2.0	0.5	2.5	0.6	1.4	1.2
Lymphomas	41.0	38.4	48.1	52.4	42.4	45.6	1.2
Hodgkin	26.1	28.0	31.7	32.3	27.8	29.7	1.0
Non-Hodgkin	14.9	10.5	16.4	20.0	14.6	15.9	2.0
CNS	24.4	27.4	33.0	21.1	17.0	23.8	1.3
Astrocytoma	12.0	13.2	8.5	10.3	9.8	10.3	1.2
PNET	2.1	1.8	2.5	2.1	1.3	1.9	2.2
Other gliomas	4.4	3.4	9.5	2.0	2.2	4.2	1.3
Other/unspecified	5.9	9.0	12.5	6.7	3.7	7.4	1.2
Sympathetic	1.5	2.3	1.3	1.2	1.7	1.6	0.8
Renal tumours	0.4	1.6	1.0	1.5	1.2	1.2	0.8
Hepatic tumours	1.0	1.4	1.0	1.2	0.9	1.1	1.8
Bone tumours	14.7	13.3	12.6	16.1	17.1	15.1	1.9
Osteosarcoma	7.3	5.8	8.8	8.3	9.7	8.4	1.9
Ewing's	5.2	5.4	2.2	5.0	3.9	4.2	2.0
Other/unspecified	2.3	2.2	1.6	2.8	3.5	2.6	1.6
Soft tissue sarcomas	11.5	9.4	14.6	12.9	13.9	13.0	1.2
Rhabdomyosarcoma	2.1	2.2	2.8	3.7	3.1	2.9	1.8
Fibrosarcoma, etc.	3.1	3.8	6.3	4.3	5.1	4.8	1.0
Kaposi	0.0	0.0	0.0	0.2	0.2	0.1	1.0
Other/unspecified	6.3	3.4	5.5	4.7	5.6	5.1	1.1
Germ cell/gonadal	17.7	26.9	32.0	19.6	20.9	23.4	2.7
CNS germ cell	1.7	1.1	2.1	0.6	1.5	1.4	5.9
Other non-gonadal germ cell	0.8	2.9	0.9	1.1	0.8	1.2	2.3
Gonadal germ cell	12.2	19.3	24.4	14.4	16.0	17.4	5.1
Gonadal carcinomas	2.5	2.5	2.9	3.0	2.2	2.6	0.0
Other gonadal	0.6	1.1	1.7	0.4	0.4	0.8	1.4
Other epithelial and melanoma	40.6	27.6	43.6	30.9	39.7	36.9	0.6
Adrenocortical carcinoma	0.2	0.7	0.2	0.5	0.3	0.4	0.3
Thyroid carcinoma	4.4	6.0	10.1	11.0	7.0	8.3	0.3
Nasopharynx carcinoma	0.4	2.7	0.4	1.5	1.4	1.2	1.2
Melanoma	18.7	6.3	17.3	6.7	15.5	12.8	0.6
Skin carcinoma	8.0	3.1	2.7	4.2	2.6	3.7	0.8
Salivary gland carcinoma	1.0	0.5	1.1	0.7	0.6	0.8	0.8
Other head/neck carcinoma	0.2	0.2	1.7	0.3	0.3	0.6	1.2
Stomach carcinoma	0.2	0.5	0.3	0.6	0.2	0.4	1.4
Appendix carcinoma	1.1	1.4	4.6	0.7	7.8	3.7	0.6
Other colorectal carcinoma	1.5	2.2	1.4	1.0	0.9	1.3	1.0
Lung carcinoma	1.1	1.4	1.4	0.5	0.6	0.9	0.8
Bladder carcinoma	0.8	0.7	0.2	0.5	0.6	0.5	1.6
All other carcinoma	3.1	1.8	2.1	2.7	2.0	2.3	0.7
Other and unspecified	4.0	1.3	1.7	2.9	0.4	1.9	1.4

The regions were represented by countries as follows: British Isles – Ireland and UK (Northern Ireland and Scotland); East – Estonia and Slovakia; North – Denmark, Finland, Iceland and Norway; South – Italy (12 registries), Malta, Slovenia, Spain (9 registries) and Turkey (Izmir); West – France (8 registries), the Netherlands and Switzerland (5 registries).
Source: ACCIS.[18]
Note: Skin carcinoma was not systematically registered in registries representing 20% of person-years in the South, 6% in the West and 7% in Europe as a whole.[24]

Table 2 Cancer incidence per million person-years at age 15—19 years in the United States, 1999—2003

Race/ethnicity	Hispanic		Non-Hispanic White		Non-Hispanic Black	
	M	F	M	F	M	F
Total	209.5	163.7	234.1	216.5	147.8	135.8
Leukaemia	45.9	28.3	32.5	21.7	24.5	17.7
Lymphoid	29.3	15.8	19.8	10.3	11.8	6.8
Myeloid	11.1	8.4	9.3	8.7	9.1	8.7
Lymphoma	44.0	32.6	57.7	52.5	39.1	33.6
Hodgkin	24.5	21.5	34.9	40.3	20.2	21.0
Non-Hodgkin (except Burkitt)	15.7	8.3	17.9	10.7	15.9	11.6
CNS	20.1	13.5	25.5	20.9	14.6	12.8
Astrocytoma	9.1	7.0	14.0	12.1	9.1	6.7
Embryonal	5.9	?	4.1	2.7	?	?
Renal	?	?	1.1	1.1	?	?
Hepatic	?	?	1.2	1.2	?	?
Bone	18.2	10.5	20.1	11.8	15.9	7.7
Osteosarcoma	11.4	6.5	11.7	5.9	12.4	5.5
Ewing sarcoma family	5.0	?	6.4	4.2	?	?
Soft-tissue sarcoma	14.7	14.4	15.9	14.1	20.2	13.7
Rhabdomyosarcoma	3.2	3.1	4.9	2.5	5.3	?
Germ cell and gonadal	46.0	19.7	42.0	13.6	9.5	16.6
Other epithelial and melanoma	16.7	41.4	36.5	77.0	16.8	28.0
Thyroid carcinoma	4.3	24.7	6.4	35.1	?	8.9

Source: SEER and NPCR registries in 38 states.[19]

females, and the male excess was most pronounced for lymphoid leukaemia.

The highest incidence of lymphomas, above 70 per million in both males and females, was found among Jews in Israel. The lowest rates were in mainland China, Japan and Zimbabwe. In North America, Europe and Oceania, and also in Costa Rica and among both Jews and non-Jews in Israel, Hodgkin lymphomas were more numerous than non-Hodgkin (NHL). In the United States, non-Hispanic Whites had higher rates of Hodgkin lymphoma than Hispanics or Blacks, whereas incidence of NHL was fairly similar in all three ethnic groups. Australia had markedly higher incidence than New Zealand for both types of lymphoma. Elsewhere in the world, NHL generally predominated, with Hodgkin lymphoma being especially rare in other parts of Asia and in Uganda. In North America, females had a higher incidence of Hodgkin lymphoma than males. In the United States, a female excess of Hodgkin lymphoma was observed only among non-Hispanic Whites. In most other populations, incidence was at least as high among males as among females. NHL occurred more frequently among males than females almost everywhere, the only exceptions being in Uganda and among Jews in Israel.

Comparison of incidence rates for intracranial and intraspinal tumours is complicated by the different ranges of diagnoses included under this heading in different publications, but some broad patterns can nevertheless be discerned. Overall incidence of CNS tumours was highest among mainly white populations in Europe, North America and Oceania, and also among Jews in Israel. In the USA, non-Hispanic whites had the highest incidence and non-Hispanic blacks the lowest. Recorded incidence was lower in Latin America and the rest of Asia, and lowest of all in some African populations. There was generally a male excess of CNS tumours. Astrocytomas were usually the most frequent well-defined subgroup, followed by other gliomas and PNET/embryonal tumours.

Tumours of the sympathetic nervous system had an incidence of under 2 per million in Europe. In data from other continents, most neuroblastomas would presumably be classified as tumours of the peripheral nerves or adrenal gland. By far the highest recorded incidence for cancer of peripheral nerves was 6.7 per million among Jews in Israel, but the morphology of these tumours was unknown and the moderately high rate was counterbalanced by a rather low rate for cancer of connective and soft tissue. Renal cancer was rare everywhere, with incidence nearly always below 2 per million.

Liver cancer was rare among adolescents in most world regions. The highest rates, 5—7 per million, were found in Hong Kong and the two sub-Saharan African registries. Incidence was somewhat lower, 2—3 per million, elsewhere in China and also in New Zealand, and below 1 per million in most other populations. Virtually all liver cancers of specified morphology were carcinomas.

Bone tumours are one of the more frequent groups of cancers among adolescents. In the Americas, Europe, Oceania, Africa and India, incidence was typically about 15 per million. The highest rate, 26 per million, was among Jews in Israel, while incidence seldom exceeded 10 per million in East Asia and the rest of West Asia. Males generally had higher incidence than females. The only two subgroups occurring in appreciable numbers were osteosarcoma and Ewing sarcoma. In many populations, osteosarcoma had about 1.5—2 times the incidence of Ewing sarcoma. Ewing sarcoma, however, was extremely rare in East Asia and among black populations in both Africa and the USA.

Table 3 Cancer incidence per million person-years at age 15–19 years in the Americas during the 1990s

Country	Canada		Costa Rica		Colombia	
Region(s)	National		National		Cali	
Years	1993–1997		1995–1996		1992–1996	
	M	F	M	F	M	F
Person-years	5,099,638	4,820,147	349,178	333,091	359,640	437,815
Number of cases	1020	890	83	53	61	55
Total	200.0	184.6	237.7	159.1	169.6	125.6
Total (excluding non-melanoma skin)	198.8	183.6	223.4	150.1	169.6	125.6
Leukaemia	28.4	19.5	80.2	15.0	55.6	29.7
ALL	18.2	10.0	63.0	12.0	27.8	9.1
AML	6.9	6.4	5.7	0.0	5.6	4.6
CML	1.6	1.7	5.7	0.0	5.6	6.9
Other/unspecified	1.8	1.5	5.7	3.0	16.7	9.1
Lymphomas	55.9	57.3	43.0	27.0	27.8	9.1
Hodgkin	34.9	47.9	28.6	18.0	13.9	4.6
Non-Hodgkin	21.0	9.3	14.3	9.0	13.9	4.6
CNS tumours	20.6	15.4	17.2	9.0	19.5	4.6
Ependymoma	0.8	1.0	0.0	3.0	0.0	0.0
Astrocytoma	9.6	7.9	11.5	6.0	13.9	2.3
PNET	3.5	1.5	2.9	0.0	0.0	0.0
Other gliomas	0.8	1.9	0.0	0.0	2.8	2.3
Germ-cell	1.8	0.2	0.0	0.0	0.0	0.0
Other/unspecified	4.1	2.9	2.9	0.0	2.8	0.0
Bone tumours	17.8	11.2	17.2	9.0	8.3	18.3
Osteosarcoma	9.2	6.2	14.3	9.0	2.8	13.7
Ewing's	4.9	2.5	2.9	0.0	2.8	2.3
Other/unspecified	3.8	2.5	0.0	0.0	2.8	2.3
Gonadal	31.4	18.5	14.3	30.0	13.9	13.7
Germ-cell	30.0	9.8	8.6	24.0	8.3	11.4
Carcinoma	0.0	7.9	0.0	3.0	0.0	2.3
Other/unspecified	1.4	0.8	5.7	3.0	5.6	0.0
Other reproductive	1.2	3.5	0.0	3.0	0.0	11.4
Melanoma	8.2	10.2	0.0	0.0	0.0	4.6
Skin	8.0	10.2	0.0	0.0	0.0	4.6
Eye	0.2	0.0	0.0	0.0	0.0	0.0
Non-melanoma skin	1.2	1.0	14.3	9.0	0.0	0.0
Adrenal	0.4	0.2	0.0	0.0	0.0	0.0
Thyroid	8.4	24.7	0.0	18.0	0.0	11.4
Other endocrine	2.9	1.2	0.0	0.0	2.8	0.0
Salivary glands	1.2	2.1	2.9	6.0	0.0	0.0
Nasopharynx	2.0	0.8	11.5	9.0	0.0	0.0
Other head/neck	2.4	1.5	2.9	0.0	5.6	0.0
Stomach	0.2	0.0	2.9	9.0	2.8	0.0
Colon/rectum	0.4	1.7	5.7	6.0	11.1	2.3
Liver	1.4	1.2	2.9	0.0	0.0	2.3
Other digestive	0.4	0.0	0.0	0.0	0.0	0.0
Trachea/bronchus/lung	1.0	1.5	0.0	0.0	0.0	0.0
Pleura/mediastinum (except mesothelioma)	1.8	0.2	8.6	0.0	2.8	0.0
Other resp/intrathoracic	0.2	0.2	2.9	0.0	0.0	0.0
Kaposi sarcoma	0.0	0.0	0.0	0.0	0.0	0.0
Peripheral nerves	0.0	0.2	2.9	3.0	0.0	2.3
Connective/soft tissue	9.6	7.3	5.7	0.0	13.9	11.4
Breast	0.0	1.5	0.0	0.0	0.0	0.0
Kidney	1.6	0.8	0.0	3.0	0.0	2.3
Bladder	1.0	1.2	0.0	0.0	2.8	0.0
Eye (except melanoma)	0.0	0.4	0.0	0.0	0.0	0.0
Other/unspecified	0.6	1.5	2.9	3.0	2.8	2.3

Source: Cancer Incidence in Five Continents, vol. VIII.[20]
Note: 'Non-melanoma skin' excludes squamous cell and basal cell carcinoma in Canada and Cali.

Table 4 Cancer incidence per million person-years at age 15–19 years in West Asia, 1993–1997

Country	Israel		Israel		Oman	
Population	Jews		Non-Jews		Omani	
	M	F	M	F	M	F
Person-years	999,300	947,900	296,200	282,600	505,650	479,350
Number of cases	246	249	48	33	56	55
Total (excluding non-melanoma skin)	246.2	262.7	162.1	116.8	110.6	114.7
Leukaemia	29.0	21.1	23.6	14.2	29.6	20.9
ALL	13.0	6.3	10.1	3.5	25.7	12.5
AML	6.0	10.5	6.8	3.5	0.0	4.2
CML	2.0	1.1	0.0	3.5	0.0	4.2
Other/unspecified	8.0	3.2	6.8	3.5	3.9	0.0
Lymphomas	73.1	85.5	81.0	42.5	41.5	18.8
Hodgkin	45.0	54.9	54.0	35.4	9.9	6.3
Non-Hodgkin	28.0	30.6	27.0	7.1	31.6	12.5
CNS tumours	24.0	17.9	10.1	7.1	7.9	10.4
Ependymoma	1.0	1.1	0.0	0.0	0.0	0.0
Astrocytoma	11.0	12.7	0.0	3.5	5.9	4.2
PNET	2.0	3.2	0.0	0.0	0.0	0.0
Other glioma	3.0	0.0	0.0	3.5	2.0	4.2
Germ-cell	4.0	0.0	0.0	0.0	0.0	0.0
Other/unspecified	3.0	1.1	10.1	0.0	0.0	2.1
Bone tumours	34.0	17.9	6.8	7.1	7.9	10.4
Osteosarcoma	12.0	7.4	3.4	3.5	2.0	4.2
Ewing's	17.0	6.3	3.4	3.5	2.0	2.1
Other/unspecified	5.0	4.2	0.0	0.0	3.9	4.2
Gonadal	18.0	19.0	3.4	14.2	0.0	12.5
Germ-cell	16.0	5.3	3.4	3.5	0.0	4.2
Carcinoma	0.0	12.7	0.0	10.6	0.0	4.2
Other/unspecified	2.0	1.1	0.0	0.0	0.0	4.2
Other reproductive	1.0	6.3	0.0	0.0	0.0	6.3
Melanoma	12.0	22.2	0.0	0.0	0.0	0.0
Skin	12.0	22.2	0.0	0.0	0.0	0.0
Eye	0.0	0.0	0.0	0.0	0.0	0.0
Adrenal	0.0	2.1	0.0	0.0	0.0	0.0
Thyroid	14.0	33.8	3.4	14.2	0.0	8.3
Other endocrine	0.0	0.0	3.4	0.0	0.0	0.0
Salivary glands	1.0	0.0	0.0	0.0	0.0	2.1
Nasopharynx	4.0	1.1	10.1	3.5	0.0	0.0
Other head/neck	0.0	2.1	0.0	0.0	2.0	2.1
Stomach	2.0	2.1	0.0	0.0	2.0	2.1
Colon/rectum	2.0	2.1	0.0	0.0	2.0	0.0
Liver	1.0	0.0	0.0	0.0	0.0	0.0
Other digestive	0.0	3.2	0.0	0.0	0.0	0.0
Trachea/bronchus/lung	1.0	2.1	0.0	0.0	0.0	0.0
Pleura/mediastinum (except mesothelioma)	3.0	0.0	0.0	0.0	0.0	0.0
Other resp/intrathoracic	1.0	0.0	0.0	3.5	0.0	0.0
Kaposi sarcoma	0.0	1.1	0.0	0.0	3.9	0.0
Peripheral nerves	8.0	5.3	3.4	0.0	0.0	4.2
Connective/soft tissue	2.0	3.1	3.4	0.0	9.9	6.3
Breast	0.0	1.1	0.0	3.5	0.0	0.0
Kidney	4.0	3.1	3.4	0.0	2.0	0.0
Bladder	5.0	2.2	3.4	0.0	0.0	0.0
Eye (except melanoma)	1.0	1.1	0.0	0.0	0.0	0.0
Other/unspecified	6.0	7.4	6.8	3.5	2.0	10.4

Source: Cancer Incidence in Five Continents, vol. VIII.[20]
Note: Results not reported for non-melanoma skin.

Table 5 Cancer incidence per million person-years at age 15–19 years in South and East Asia, 1993–1997

Country	India		China		China		Japan	
Region(s)	Chennai (Madras), Mumbai (Bombay)		Hong Kong		Shanghai, Tianjin		Miyagi, Nagasaki, Osaka, Yamagata	
	M	F	M	F	M	F	M	F
Person-years	3,845,760	3,284,740	1,107,900	1,033,400	1,302,053	1,539,179	2,437,515	2,353,672
Number of cases	414	281	204	160	167	140	261	205
Total	107.7	85.5	184.1	154.8	128.3	91.0	107.1	87.1
Total (excluding non-melanoma skin)	106.6	85.5	180.5	152.9	128.3	90.3	105.0	85.4
Leukaemia	32.0	20.1	31.6	14.5	41.5	17.5	29.5	14.9
ALL	17.9	9.7	10.8	6.8	9.2	4.5	11.5	5.9
ML	8.1	6.4	7.2	5.8	13.1	5.2	12.3	6.4
CML	2.1	0.6	7.2	0.0	4.6	2.6	1.6	1.3
Other/unspecified	3.9	3.3	6.3	1.9	14.6	5.2	4.1	1.3
Lymphomas	19.0	6.7	31.6	13.5	10.8	8.5	16.0	10.2
Hodgkin	4.4	1.8	4.5	3.9	2.3	1.9	3.3	2.1
Non-Hodgkin	14.6	4.9	27.1	9.7	8.4	6.5	12.7	8.1
CNS tumours	8.6	9.4	26.2	12.6	21.5	10.4	11.9	6.8
Ependymoma	0.8	1.2	1.8	1.9	0.0	0.6	0.4	0.4
Astrocytoma	3.6	4.6	12.6	3.9	0.8	1.3	4.5	2.5
PNET	1.6	0.0	2.7	1.0	0.0	0.0	0.8	1.3
Other glioma	1.0	1.5	0.0	1.9	3.1	0.6	0.0	0.4
Germ-cell	0.0	0.0	6.3	1.0	0.8	0.0	1.6	0.8
Other/unspecified	1.6	2.1	2.7	2.9	16.9	7.8	4.5	1.3
Bone tumours	20.8	8.2	9.9	5.8	9.2	6.5	12.3	8.1
Osteosarcoma	12.2	3.3	7.2	4.8	3.1	0.6	8.2	4.2
Ewing's	5.5	3.3	0.9	0.0	0.0	0.0	1.6	2.5
Other/unspecified	3.1	1.5	1.8	1.0	6.1	5.8	2.5	1.3
Gonadal	4.2	12.5	9.0	0.0	0.8	11.7	4.1	14.4
Germ-cell	3.4	7.6	9.0	0.0	0.8	0.0	4.1	4.7
Carcinoma	0.0	2.4	0.0	0.0	0.0	0.6	0.0	4.7
Other/unspecified	0.8	2.4	0.0	0.0	0.0	11.0	0.0	5.1
Other reproductive	0.0	0.9	0.0	25.2	1.5	2.6	0.0	1.7
Melanoma	0.0	0.0	0.9	1.9	0.0	0.0	0.4	0.4
Skin	0.0	0.0	0.9	1.9	0.0	0.0	0.4	0.4
Eye	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Non-melanoma skin	1.0	0.0	3.6	1.9	0.0	0.6	2.1	1.7
Adrenal	0.0	0.9	0.0	0.0	0.0	0.0	0.0	1.3
Thyroid	0.5	4.0	3.6	34.8	4.6	10.4	2.1	10.6
Other endocrine	0.3	0.0	7.2	0.0	3.8	8.5	6.6	0.8
Salivary glands	1.3	1.8	3.6	1.0	0.8	0.0	0.4	0.8
Nasopharynx	3.1	1.8	13.5	8.7	3.8	0.6	2.9	0.4
Other head/neck	2.9	2.4	2.7	4.8	1.5	0.6	1.2	0.0
Stomach	0.8	1.5	0.9	0.0	4.6	1.3	1.6	1.7
Colon/rectum	1.8	1.5	0.9	1.0	0.8	1.9	2.1	2.5
Liver	0.5	0.9	9.0	4.8	3.1	1.3	0.4	0.4
Other digestive	0.8	1.2	0.9	0.0	0.8	0.0	0.4	0.8
Trachea/bronchus/lung	1.0	0.6	1.8	1.9	1.5	1.3	2.5	0.4
Pleura/mediastinum (except mesothelioma)	0.0	0.3	4.5	0.0	6.1	1.3	1.2	0.4
Other resp/intrathoracic	0.3	0.3	2.7	1.0	0.0	0.0	0.0	0.0
Kaposi sarcoma	0.0	0.0	0.9	0.0	0.0	0.0	0.0	0.0
Peripheral nerves	0.3	0.3	2.7	1.9	0.0	0.0	0.8	0.8
Connective/soft tissue	4.2	4.6	9.0	10.6	6.1	1.3	3.7	5.9
Breast	0.0	1.5	0.0	3.9	0.0	0.6	0.0	0.4
Kidney	1.0	0.9	0.9	1.0	0.0	0.6	0.4	0.0
Bladder	0.0	0.0	1.8	0.0	0.0	0.0	0.4	0.0
Eye (except melanoma)	0.0	0.0	0.0	0.0	0.8	0.0	0.4	0.0
Other/unspecified	3.4	3.0	5.4	3.9	4.6	3.2	3.7	1.3

Source: Cancer Incidence in Five Continents, vol. VIII.[20]

Soft tissue sarcomas had a combined incidence of 13 per million in Europe, slightly lower that that for bone tumours. Within Europe, incidence was lowest in the East and highest in the North and West. Incidence was slightly higher in the

Table 6 Cancer incidence per million person-years at age 15–19 years in Oceania, 1993–1997

Country	Australia		New Zealand	
	M	F	M	F
Person-years	3,275,772	3,118,044	683,840	663,370
Number of cases	865	710	150	119
Total	–	–	219.3	179.4
Total (excluding non-melanoma skin)	264.1	227.7	217.9	179.4
Leukaemia	36.6	21.5	35.1	16.6
ALL	21.7	9.0	26.3	6.0
AML	8.9	7.7	4.4	7.5
CML	3.4	1.3	4.4	1.5
Other/unspecified	2.7	3.5	0.0	1.5
Lymphomas	46.4	38.2	30.7	18.1
Hodgkin	25.6	25.3	17.5	15.1
Non-Hodgkin	20.8	12.8	13.2	3.0
CNS tumours	18.9	17.6	24.9	10.6
Ependymoma	1.5	1.3	1.5	0.0
Astrocytoma	9.8	10.9	13.2	7.5
PNET	1.8	1.3	–	3.0
Other glioma	1.5	1.9	4.4	0.0
Germ-cell	1.2	0.3	1.5	0.0
Other/unspecified	3.1	1.9	4.4	0.0
Bone tumours	19.5	11.2	17.5	18.1
Osteosarcoma	9.2	4.5	11.7	10.6
Ewing's	6.7	3.8	4.4	6.0
Other/unspecified	3.7	2.9	1.5	1.5
Gonadal	28.4	11.5	26.3	15.1
Germ-cell	25.3	7.1	21.9	9.0
Carcinoma	0.0	3.8	0.0	4.5
Other/unspecified	3.1	0.6	4.4	1.5
Other reproductive	0.3	4.5	0.0	7.5
Melanoma	70.8	78.3	33.6	64.8
Skin	69.9	77.9	33.6	64.8
Eye	0.9	0.3	0.0	0.0
Non-melanoma skin	–	–	1.5	0.0
Adrenal	0.3	0.3	0.0	3.0
Thyroid	4.6	15.4	2.9	4.5
Other endocrine	3.1	1.3	10.2	0.0
Salivary glands	1.8	1.3	0.0	0.0
Nasopharynx	2.4	1.0	2.9	1.5
Other head/neck	6.4	2.6	2.9	1.5
Stomach	0.0	0.3	4.4	0.0
Colon/rectum	2.4	3.2	1.5	0.0
Liver	0.3	0.6	4.4	1.5
Other digestive	0.6	1.9	0.0	0.0
Trachea/bronchus/lung	0.3	1.0	0.0	1.5
Pleura/mediastinum (except mesothelioma)	2.1	0.0	2.9	0.0
Other resp/intrathoracic	0.9	0.3	0.0	0.0
Kaposi sarcoma	0.0	0.0	1.5	0.0
Peripheral nerves	0.6	1.0	0.0	0.0
Connective/soft tissue	9.8	6.1	11.7	4.5
Breast	0.0	1.6	0.0	0.0
Kidney	1.8	1.9	1.5	4.5
Bladder	3.4	1.9	0.0	1.5
Eye (except melanoma)	0.3	1.0	1.5	0.0
Other/unspecified	1.8	1.9	1.5	4.5

Source: Cancer Incidence in Five Continents, vol. VIII.[20]
Note: Incidence for 'non-melanoma skin' not available for Australia; 'non-melanoma skin' excludes squamous cell and basal cell carcinoma in New Zealand.

USA, with non-Hispanic blacks having the highest rates. Elsewhere in the world, the rates for cancer of connective and soft tissue give minimum estimates of incidence, since this rubric does not include sarcomas of specific organs, nor those of unspecified tissue type of origin. If incidence in Canada and Oceania is assumed to be similar to that in Europe and the USA, this suggests that incidence is similar also in Japan, in Colombia and Hong Kong, and lower in India. In the two registries of sub-Saharan Africa, incidence of Kaposi sarcoma was very high; it was the single most frequent cancer in adolescents of both sexes in Uganda and of females in Zimbabwe. There were also moderate numbers of cases of other soft tissue sarcomas in both these registries.

Geographical patterns of incidence of germ cell and gonadal tumours varied markedly by primary site, and between the sexes for gonadal tumours. Testicular cancer had incidence of 25—30 per million in Europe, Canada and Oceania, 18 per million among Jews in Israel and less that 10 per million in all other populations. Incidence was not reported from the USA for 1999—2003 but in 1992—1997 the rate was 27.5 per million for all ethnic groups combined.[14] Since non-Hispanic blacks had a total incidence for all germ cell and gonadal tumours of only 9.5 per million in 1999—2003, their rate for testicular germ cell tumours must have been even lower. Ovarian germ cell tumours had incidence of 5—10 per million in most populations, though Costa Rica had an exceptionally high rate of 24 per million based on eight cases. Intracranial and intraspinal germ cell tumours had incidence of 1.4 per million in Europe. The highest incidence of these tumours almost certainly occurs in East Asia. For germ cell tumours with site specified as CNS, incidence was above 3 per million in Hong Kong and 1.2 per million in Japan. The incidence of germ cell tumours of intracranial endocrine sites was not recorded separately, but total incidence of cancers of endocrine glands other than thyroid and adrenal was over 3.5 per million in both these localities, compared with no more than 2 per million virtually everywhere else. Ovarian carcinomas generally had incidence similar to or lower than that of ovarian germ cell tumours.

By far the highest incidence of malignant melanoma was observed in Australia, where it was the most frequent type of cancer in both sexes and accounted for one third of all cancers in female adolescents and one quarter in males. Incidence varied considerably between Australian states and was highest of all, around 130 per million, in Queensland. Melanoma was equally frequent among males and females in Australia. The next highest incidence was in New Zealand, where it was also the most frequent cancer. In New Zealand, in contrast to Australia, females were affected almost twice as often as males. Incidence was somewhat lower again in Europe, especially the East and South, and in Canada. Incidence of melanoma in the USA was not reported for 1999—2003, but in 1992—1997 the rates of cutaneous melanoma in all ethnic groups combined were 9.3 per million for males and 14.2 per million for females.[14] Incidence among Jews in Israel was comparable with that in Northern and Western Europe. In the rest of Asia, and also in Latin America and Africa, malignant melanoma was seldom registered among adolescents. Skin carcinoma was generally less frequent than malignant melanoma in Europe; basal cell carcinoma had a higher rate, 3.1 per million, than squamous cell carcinoma, 0.6 per million.[24] Elsewhere in the world, registration of non-melanoma skin cancer, which also includes other tumour types, such as sarcomas, together with unspecified tumours, was variable, with some registries not reporting results for this diagnostic group at all and others explicitly excluding skin carcinomas. Incidence in the Americas and Asia was generally well below 5 per million. Much higher rates were reported from Costa Rica, but it should be noted that no cases of melanoma were registered there. Few cases were registered in the African countries represented in Table 7. In Tunisia, where skin carcinoma is exceptionally frequent in children,[1] there were high rates for non-melanoma skin cancer at age 15—19 of 7.8 per million in males and 16.5 per million in females.[21]

The most frequent site for carcinomas in much of Europe was the thyroid, with incidence of 3.7 per million in males and 13.1 per million in females.[25] Within Europe, the South had the highest rates for males (4.9 per million) and females (17.4 per million).[25] Incidence was considerably higher among non-Hispanic Whites in the United States, among Jews in Israel, and in Hong Kong. Australia, Japan and mainland China had similar rates to Europe. In most other populations, including United States Blacks, India and New Zealand, incidence was somewhat lower. No cases were recorded in the two series from sub-Saharan Africa.

The highest incidence of nasopharyngeal cancer, over 20 per million, was in Algeria, where it equalled lymphomas as the most frequent type of cancer in males, though it was outnumbered by lymphomas and bone tumours in females. Incidence was above 10 per million in Hong Kong and Costa Rica and there was also a moderately high rate, nearly 7 per million, among non-Jews in Israel. Everywhere else, incidence was below 5 per million. Cancers of the salivary glands were usually less frequent than those of the nasopharynx. The relatively high incidence in Costa Rica was based on only three cases. Cancers of other head and neck sites were very infrequent almost everywhere. The somewhat higher incidence among males in Australia was accounted for by a particularly high rate of 4.3 per million for cancer of the lip. Cancer of the eye had an incidence of 6.9 per million for both sexes combined in Uganda, the same as that of leukaemia.

In Europe, recorded incidence of carcinomas of the appendix was 3.7 per million overall, and varied from 0.7 per million in the South to 7.8 per million in the West. Other colorectal carcinomas had an incidence of 1.3 per million on average, with rather less inter-regional variation. In other world regions, data were not available separately for cancers of the appendix and other colo-rectal sites; the highest rates for all colo-rectal sites combined were in the two Latin American registries. No series contained more than a handful of registrations for stomach cancer in adolescents.

Bladder cancer appeared to have a relatively high incidence among Jews in Israel, but this was still well below 10 per million and based on only seven cases. Cancers of the lower respiratory tract, breast and non-testicular male reproductive sites including the prostate were rare everywhere. The same almost certainly applies to non-ovarian female reproductive tract cancers; the remarkably high rate for 'other reproductive' sites among females in Hong Kong appears to be an artefact resulting from failure to record ovary as a specific primary site.

Table 7 Cancer incidence per million person-years at age 15–19 years in Africa during the 1990s

Country	Algeria		Uganda		Zimbabwe	
Region(s)	Algiers, Constantine, Oran, Setif		Kyadondo County		Harare (African)	
Years	1993–1998		1993–1997		1990–1997	
	M	F	M	F	M	F
Person-years	1,364,667	1,343,262	302,970	417,895	503,145	636,630
Number of cases	189	124	41	67	80	70
Total	138.5	92.3	135.3	160.3	159.0	110.0
Total (excluding non-melanoma skin)	136.3	89.3	135.3	160.3	155.0	103.7
Leukaemia	6.7	6.0	9.9	4.8	27.8	4.7
Lymphoid	3.0	3.7	6.6	0.0	11.9	1.6
Myeloid	3.7	1.5	0.0	0.0	15.9	3.1
Other/unspecified	0.0	0.7	3.3	4.8	0.0	0.0
Lymphomas	33.0	23.1	23.0	28.7	15.9	6.3
Hodgkin	14.7	9.7	3.3	4.8	6.0	1.6
Non-Hodgkin	18.3	13.4	19.8	23.9	9.9	4.7
CNS tumours	5.1	4.5	0.0	2.4	11.9	3.1
Bone tumours	19.1	11.9	16.5	9.6	23.8	14.1
Gonadal	2.2	5.2	0.0	7.2	2.0	6.3
Other reproductive	0.0	1.5	6.6	12.0	0.0	4.7
Melanoma of skin	0.0	0.0	0.0	0.0	4.0	0.0
Non-melanoma skin	2.2	3.0	0.0	0.0	4.0	6.3
Adrenal	0.7	0.0	0.0	0.0	0.0	0.0
Thyroid	3.7	6.7	0.0	0.0	0.0	0.0
Other endocrine	2.2	0.0	0.0	0.0	0.0	0.0
Nasopharynx	33.0	9.7	3.3	4.8	2.0	4.7
Other oral/pharynx	1.5	0.0	0.0	0.0	0.0	1.6
Stomach	3.7	0.7	3.3	2.4	0.0	0.0
Colon/rectum	4.4	3.0	6.6	0.0	4.0	3.1
Liver	0.0	0.7	6.6	4.8	6.0	7.9
Other digestive	0.7	0.0	0.0	0.0	2.0	0.0
Trachea/bronchus/lung	1.5	0.7	0.0	0.0	0.0	4.7
Other respiratory	3.7	0.7	0.0	2.4	4.0	0.0
Kaposi sarcoma	0.0	0.0	29.7	55.0	17.9	25.1
Peripheral nerves	0.0	0.7	0.0	0.0	0.0	0.0
Connective/soft tissue	4.4	6.0	9.9	4.8	13.9	3.1
Breast	0.0	0.7	0.0	7.2	0.0	0.0
Kidney	0.7	0.0	0.0	4.8	4.0	3.1
Bladder	0.7	0.0	0.0	0.0	0.0	0.0
Eye	0.7	0.0	9.9	4.8	2.0	1.6
Other/unspecified	8.8	7.4	9.9	4.8	13.9	9.4

Source: Cancer in Africa.[21]

Time trends

Formal analyses of time trends in incidence of a wide range of cancers specifically for the 15–19 year age group were only available for Europe and the United States.[16,18,26] The results are summarised in Table 8. There was little consistency between the two studies either in the overall rate of increase or in the relative magnitude and direction of change for individual diagnostic groups.

Discussion

Adolescents have a distinctive distribution of types of cancer. In most populations, the great majority of cases are accounted for by leukaemias, lymphomas, CNS tumours, bone and soft tissue sarcomas, gonadal tumours, thyroid carcinoma and malignant melanoma. Most of the embryonal tumours of childhood, including neuroblastoma, retinoblastoma and nephroblastoma (Wilms tumour) are exceedingly uncommon. Some of the most frequent carcinomas of adults, such as carcinomas of lung, breast and prostate, are also rarely seen. Many cancers occurring in adolescence nevertheless represent the early part of the age-incidence distribution for diagnostic groups that are much more frequent in adulthood while some others are cases of typical childhood cancers diagnosed at a more advanced age. Only a few cancers are truly characteristic of adolescence in the sense that their peak incidence occurs at around this age. Two important examples are the principal types of bone

Table 8 Time trends in the incidence of cancer at age 15–19 years in Europe (1978–1997) and the United States (1975–2000)

	Europe		United States
All cancers	2.0		0.7
Leukaemia	0.6		1.5
Lymphoid/ALL	1.9		2.8
AML	0.4		8.5
Unspecified	−2.3		?
Hodgkin lymphoma	3.5		−0.4
NHL (except Burkitt)	1.1	1.7	2.3
Burkitt lymphoma	−2.0		1.6
Other and unspecified lymphoma	1.9		
CNS tumours	1.7		0.3
Bone tumours	0.6		1.0
Osteosarcoma	0.7		1.1
Ewing sarcoma family	0.3		?
Soft tissue sarcomas	0.9		−0.8
Gonadal germ cell tumours	2.5		?
Male genital tract tumours	?		1.5
Ovarian tumours	?		−0.1
Thyroid carcinoma	2.5		1.2
Malignant melanoma	4.1		0.9

Results are expressed as average annual percentage change.
Sources: Europe, ACCIS[18,26]; United States, SEER.[16]

tumour that affect adolescents, namely osteosarcoma and Ewing sarcoma. The highest incidence of osteosarcoma, and often also of Ewing's sarcoma, is at 15–19 years of age in males, though the peak for both tumour types among females tends to occur earlier, within the range 10–14 years.[27] Among adolescent girls, ovarian germ cell tumours are most frequent at age 15–19 years, and this observation applies equally to dysgerminomas, malignant teratomas and mixed germ cell tumours.[28,29] In regions of intermediate risk for nasopharyngeal carcinoma, the age incidence graph is bimodal with the first peak occurring in adolescence.[30]

Worldwide patterns of childhood leukaemia occurrence are dominated by the early peak in ALL which is most marked in mainly white populations and most attenuated or even absent in sub-Saharan Africa.[2] In contrast, leukaemias were the most frequent diagnostic group among adolescents in India, East Africa and Latin America. They were only slightly outnumbered by lymphomas among Hispanics in the United States, for whom lymphomas were the most numerous group. Other variations between populations in the occurrence of leukaemias among adolescents were broadly similar to those among children, with highest rates of ALL in Hispanic populations of the Americas and relatively little variation for AML.[4,19,31]

Lymphomas collectively were the most frequent diagnostic group in Europe, North America and West Asia, and also in Algeria. In Australia and New Zealand they were the most frequent group after melanoma, and in Uganda they were outnumbered only by Kaposi sarcoma. There were marked, systematic differences between populations in the relative frequencies of Hodgkin lymphoma and NHL.

The different patterns of occurrence of Hodgkin lymphoma were recognised decades ago, a steep rise in incidence through late childhood into adolescence and early adulthood in the most affluent western populations contrasting with a childhood peak followed by declining incidence among adolescents in many developing countries.[32] These patterns are readily apparent in the present study in relation to the Americas, Europe, Oceania and India. Some of the lowest rates were found in East Asia where Hodgkin lymphoma is also rare among both children and adults.[4,20] The high incidence among both Jewish and non-Jewish adolescents in Israel indicates that Hodgkin lymphoma occurs according to the pattern characteristic of affluent societies in both population groups. This is in marked contrast to other Middle Eastern countries such as Oman and Egypt,[33] which have the low incidence typical of developing countries. Most cases of Hodgkin lymphoma in children and older adults are attributable to EBV infection.[34] EBV is unlikely to explain variations in occurrence of Hodgkin lymphoma among adolescents and young adults, however, since the proportion of EBV-positive cases is lowest in this age group and does not vary with levels of economic development.[35]

Incidence of NHL was moderately high among predominantly white populations of North America, Europe and Oceania that also have relatively high incidence among adults, and also the Mediterranean region and parts of tropical Africa that have high incidence among children.[4,20] In Uganda, Burkitt lymphoma accounts for much of the high incidence of childhood NHL but is rare in adolescence.[36]

Interpretation of variations in recorded incidence of CNS tumours is complicated by inconsistency in classification and inclusion of non-malignant neoplasms. The latter have been estimated to account for 36% of CNS tumours among adolescents in the United States,[37] but in the ACCIS study they represented only 14%.[18] Incidence in England was 15.6 per million during 1979–1997,[11] somewhat lower than the 24.4 per million in other parts of the British Isles during 1988–1997. These results are not necessarily inconsistent; however, since the English data refer to a calendar period on average 5–6 years earlier than ACCIS and do not include non-malignant tumours. The lower rates among less affluent populations, most notably in Africa, probably reflect scarcity of facilities for diagnosis and treatment rather than markedly lower underlying risk.[21]

Worldwide, an estimated 54% of cases of liver cancer are attributable to hepatitis B infection and a further 31% to hepatitis C.[34] The highest incidence rates at all ages combined are found throughout East Asia and parts of sub-Saharan Africa, corresponding mostly to high prevalence of hepatitis B virus infection.[38] In Japan, hepatitis B is relatively uncommon and most cases are attributable to hepatitis C.[38] Infection is rare among young people, however, consistent with the low incidence of liver cancer among Japanese adolescents.[39] New Zealand had higher incidence among adolescents than most western populations, though this was based on only four cases. Results were not available separately for the Maori and non-Maori populations, but high incidence of hepatocellular carcinoma at all ages combined among Maori and other non-European people in New

Zealand has previously been related to their higher prevalence of hepatitis B surface antigen carriers.[40]

The incidence peak for bone sarcomas in the teenage years is clearly linked to rates of bone growth, especially as it occurs at a younger age among girls than boys, corresponding to the earlier occurrence of the adolescent growth spurt among girls.[41] The absence of striking variations in incidence of osteosarcoma between populations provides few clues to its causes. By contrast, the very low incidence of Ewing sarcoma in populations of East Asian and sub-Saharan African origin is long established, suggesting a likely genetic component to the aetiology of this tumour.[42] Further support for this is given by genetic differences between Ewing sarcomas from Japanese and European patients.[43]

The most marked variations between populations in the occurrence of soft tissue sarcoma among adolescents relate to Kaposi sarcoma. Nearly everywhere in the world this tumour is extremely rare among young people but it had very high incidence and was the most frequent type of cancer in the two sub-Saharan African registries in this study. Uganda and Zimbabwe both lie in the region of Eastern and Central Africa where endemic Kaposi sarcoma occurs, caused principally by HHV-8 infection. Since the onset of the AIDS epidemic in the region, Kaposi sarcoma has taken an epidemic form with total incidence increased by a factor of around 20.[21] This is probably because immunosuppression resulting from HIV infection makes uncontrollable infection by HHV-8 more likely.[34] Although Kaposi sarcoma is more frequent in males than females overall, females had higher incidence than males during adolescence and early adulthood. This pattern was also found in Malawi,[21] consistent with the much higher rates of HIV infections among female compared with male adolescents throughout the region.[44] Little can be said about worldwide variations in the incidence of other soft tissue sarcomas, since morphology-based data were only available for Europe and the United States.

The pattern of high incidence of testicular germ cell tumours among mainly white populations in Europe, North America and Oceania and low rates in other world regions and ethnic groups is similar to that among adult men.[20] Cases occurring in adolescence represent the beginning of the age incidence curve for this cancer, which is very much more common in adulthood. By contrast, ovarian germ cell tumours varied little in incidence between populations. As noted earlier, they are one of the very few cancers to have their peak incidence in adolescence, presumably related to hormonal factors around puberty. The pattern of highest rates for intracranial germ cell tumours in East Asian populations have also been found in children.[4] Gonadal carcinomas hardly ever occur in adolescent males. The results for females showed little systematic variation, and interpretation is made more difficult by the likely inclusion of variable but substantial proportions of borderline malignant tumours in data coded by ICD-O-2 or ICD-10.[13]

The pattern of by far the highest incidence of melanoma in Australia and New Zealand, fairly high rates among mainly white populations in North America and Europe and also among Jews in Israel, and low incidence in virtually all other populations, is similar to that for adults[20] and presumably reflects the combination of levels of sun exposure and innate susceptibility. Adolescents in England had lower incidence of melanoma, 8.1 per million,[11] than the other parts of the British Isles represented in ACCIS, again consistent with the pattern for adults.[20] Variations in the occurrence of skin carcinomas are hard to assess because of inconsistency in registration practices. The exceptionally high rates in Tunisia, however, are likely to reflect increased risk associated, like the high rates in children, with unusually high prevalence of xeroderma pimentosum.[1]

The international variations in thyroid cancer incidence among adolescents were broadly similar to those for adults.[20] By far the highest rates among adolescents during the period under review, however, occurred in the areas of Eastern Europe most heavily contaminated by radioactive iodine from the Chernobyl nuclear power plant disaster in Ukraine.[45]

Most other carcinomas, including those of the most frequently affected sites in adults such as breast, lung and large bowel, were rare among adolescents everywhere.

The overall incidence of nasopharyngeal carcinoma is highest in South China, including Hong Kong, and moderately high rates are found in the rest of China and south-east Asia, indigenous peoples of the Arctic, and Arabs of the Middle East and North Africa.[30] In most parts of the world the incidence increases steadily with age, but Arab populations have a peak in adolescence. These patterns are consistent with the results reported here. By far the highest incidence of nasopharyngeal cancer was in Algeria, where lymphomas were the only more frequent type of cancer, and Hong Kong also had high rates. Virtually all nasopharyngeal carcinoma in high and medium risk regions is EBV-related,[34] but the reasons for the adolescent peak among Arab populations are not yet well understood.

While this study has shown clear differences in cancer occurrence among adolescents in different populations, few conclusions can be drawn from the available information on changes over time. No analyses were available for most continents and the differences in the results between Europe and the United States are hard to relate to variations in risk factors.

The two highest rates of increase in Europe were for Hodgkin lymphoma and malignant melanoma. For Hodgkin lymphoma this may indicate that Europe has been becoming increasingly like North America with respect to as yet undetermined risk factors for the disease, though the most recent incidence rates among adolescents in all parts of Europe were still appreciably lower than those in the United States and Canada. Incidence of melanoma among adolescents in parts of Europe has overtaken that in the United States but it is impossible to tell whether this is due to increased childhood sun exposure, improved detection or other factors. In New South Wales, Australia, incidence at age 15—34 years fell between 1983 and 1996, with the decrease being highly significant among females, but birth cohort analysis suggested that changes in the rates for adolescents were minimal.[46]

Moderate upward trends were found in both Europe and the United States for NHL and thyroid cancer. The increases in NHL are part of a pattern affecting most age groups but the causes are largely unknown. At least in the United States, increases in incidence of thyroid cancer have been partly attributed to increases in the intensity of diagnostic activity,[47] while in Scotland a rapid increase in papillary

carcinoma among teenage girls seems likely to have been due to earlier diagnosis.[48]

The most rapid increases in the United States were reported for the two main types of leukaemia affecting adolescents, namely ALL and AML. The rate of increase for both subgroups was lower than that for leukaemia as a whole, suggesting that a decrease in the recorded incidence of unspecified leukaemias, as seen in Europe, was a contributing factor.

In Europe, the rate of increase was greater among adolescents than children for all cancers combined,[18] whereas in the United States it was lower.[16] The rate of increase fluctuated between successive five-year age groups from birth to 44 years in the United States.[16] Therefore, it is probably unwise to make inferences about rates of change in incidence specifically among adolescents from those reported for broader age ranges such as 15–24 years,[10,11] at least when the magnitude of the changes is fairly moderate and their causes are largely unknown. It is safe to say, however, that the changes in incidence of any type of cancer among adolescents in North America and most of Europe are small in comparison with the spectacular increases in thyroid cancer in parts of Ukraine, Belarus and Russia[49] following the Chernobyl disaster or in Kaposi sarcoma in parts of Africa most severely affected by the AIDS epidemic.[50]

Past and current trends in cancer incidence are not necessarily of use for predicting future patterns. A few predictions may confidently be made, however, on the basis of currently available data. A return to pre-Chernobyl levels of thyroid cancer among children born since 1986 has already been observed in the area around Chernobyl[51] and a similar decrease will now probably be taking place in the rates for adolescents, all of whom will now have been born since the accident. Incidence of Kaposi sarcoma among adolescents in sub-Saharan Africa will presumably continue to reflect geographical variations in levels of HIV infection, at least in regions with a high prevalence of HHV8. The reduction in hepatocellular carcinoma first seen among children in Taiwan consequent on high levels of hepatitis B immunisation should also become apparent among adolescents there and elsewhere in East Asia as immunisation programmes become established.[52]

This is the first detailed study of cancer incidence among adolescents worldwide. Its main strength is that it relies on data from high quality, population-based cancer registries. For some regions, the results are based in very large numbers of cases.

The study does, however, suffer from several weaknesses. Variations in classification systems and also in registration practices between the different principal sources make accurate comparison of rates impossible for some of the more frequent types of cancer seen in adolescents, most notably intracranial tumours and soft tissue sarcomas. It is well recognised that, as with childhood cancers, cancer among adolescents is better described by means of a classification scheme largely based on morphology.[7] ICCC was criticised as a suitable scheme for classification of cancer among adolescents and young adults, however, since carcinomas of several numerically and epidemiologically important sites were buried in a single subgroup whereas several childhood tumours that hardly ever occur at older ages were felt to have undue prominence.[11] The first of these criticisms was largely answered in ICCC-3, in which the subgroup of miscellaneous carcinomas was subdivided to allow standardised presentation of data on all of the carcinomas that most frequently affect adolescents.[23] Meanwhile an alternative classification was proposed for cancers of teenagers and young adults[11,53] in which all carcinomas were assembled in a single diagnostic group, but with more subdivisions than in ICCC-3, and the embryonal tumours of childhood were combined into relatively few categories. At the same time, many different types of soft-tissue sarcoma, some of which are more frequent in adolescents than in children, were combined into a single subgroup whereas in ICCC-3 they have their own divisions. While such a scheme has advantages over ICCC and, to a lesser extent ICCC-3, for classifying cancers within the age range to which it refers, it is probably less useful for making comparisons with data relating to children. As it eliminated several of the subgroups of unspecified tumours of particular sites which exist in ICCC-3, its applicability to data sets containing relatively large numbers of cases on unknown morphology is also reduced. Maybe the best classification, applicable to the widest range of existing data, would combine the greater specificity of ICCC-3 for many non-epithelial tumours with the more detailed subdivision of carcinomas in the scheme of Birch and colleagues and an equivalent subdivision by site for tumours of unspecified type.

Another limitation of this study is the incomplete geographical coverage, which is most severe for assessment of time trends. Some world regions were represented by relatively small series from only one or two cancer registries and it is questionable how accurately they represent cancer incidence in neighbouring areas. In theory the problem of small numbers might be alleviated by aggregating the data of Cancer Incidence in Five Continents, vol. VIII with those of the previous volume but this would have involved combining results presented according to ICD-9 and ICD-10. A further, particular problem suggests that data from some subnational registries may be especially unrepresentative of the corresponding national pattern among adolescents. In most parts of the world, there is a small excess of males over females in the adolescent population. In this study, however, the registries representing Colombia, mainland China, Uganda and Zimbabwe all had a substantial excess of females in their population at risk. For the sub-Saharan African registries, this may be in part due to especially high mortality in the young male population. In Colombia and China, however, the female excess was in marked contrast to the more expected small male excess among both children and younger adults,[20] suggesting that the populations of adolescents at risk in these registries may be biased as regards, for example, educational level or eligibility for military service.

In conclusion, this study has highlighted distinctive variations in cancer incidence among adolescents of different world regions and ethnic groups. A more complete description should be possible if comparable data could be assembled from a wider range of registries and classified according to a single, standard scheme as has been done for childhood cancer worldwide[1,4] but so far for adolescents only within Europe.[18]

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