

4 Cancer in children

The German Childhood Cancer Registry (GCCR) has been based at the Institute of Medical Biostatistics, Epidemiology and Informatics at the University Medical Centre of the Johannes Gutenberg University Mainz, since beginning its work in 1980. Close cooperation with the Society for Paediatric Oncology and Haematology (GPOH) and its associated hospitals was part of the GCCR's original conception. This is a characteristic feature of the registry which cannot be easily applied to adult oncology. This nationwide, population based childhood cancer registry with a high level of data quality and a degree of completeness of over 95 % (since about 1987) has been built up covering the whole of Germany. The GCCR thus meets international standards for population based cancer registries. A further characteristic of the GCCR is that it has implemented an active, open-end, long-term follow-up observation system which continues long into adulthood. In this way, the registry also provides the basis for research into long-term effects and secondary tumours and for studies with long-term survivors in general. The registry population comprises children who are diagnosed with a malignant disease or a histologically benign brain tumour before their 15th birthday and are part of the resident population of the Federal Republic of Germany when diagnosed. Cancer cases in eastern Germany have also been registered since 1991. Since 1 January 2009, the GCCR has been registering all children and adolescents up to the age of 18 years (i. e. who are diagnosed before their 18th birthday) on the basis of the »Agreement of the Joint Federal Committee on Quality-Assurance Measures for the In-Patient Care of Children and Adolescents with Haemato-Oncological Diseases«. This will make it possible to better consider the needs of the collaborating hospitals which have been combining paediatric and adolescent medicine for several years now and thus also treat cancer patients aged 15 years and over.

The current data pool consists of over 55,000 cancer cases.

Incidence of childhood cancers

About 1,800 cases of childhood (under the age of 15 years) cancer are newly diagnosed every year in Germany. With an overall population of approx. 11 million children under the age of 15 years, this means an annual incidence of about 16.6 per 100,000 children in this age group. The likelihood that a newborn child will develop a malignant disease within the first 15 years of his/her life is 0.2 %. In other words, a malignant cancer is diagnosed in approx. one in 420 children up to their 15th birthday. Since 2009, the beginning of registration of all children and adolescents up to age 18, on average an additional 300 cases aged between 15 and 17 years were registered annually. Within the first 25 years since diagnosis, another cancer (subsequent cancer) was registered for 1,061 patients, which applies to 4.4 % of patients (cumulative incidence).

Range of diagnoses

The pattern of cancer diagnoses in children is completely different from that of adults. For example, children are mostly affected by embryonal tumours (neuroblastomas, retinoblastomas, nephroblastomas, medulloblastomas, embryonic rhabdomyosarcomas or germ-cell tumours); carcinomas, by contrast, are very rare in childhood (making up about 2 % of all malignant diseases). The largest diagnostic groups are leukaemias (33.4 %), CNS tumours (24.4 %) and lymphomas (10.9 %). Overall cancer incidence among children under the age of five is about twice as high as in the 5- to 14-year-old age group. The median age at onset among the under-15-year-olds is five years, ten months. Boys are diagnosed with cancer 1.2 times more frequently than girls.

Figure 4.1
Cancer in children (determined for the period 2004–2013)

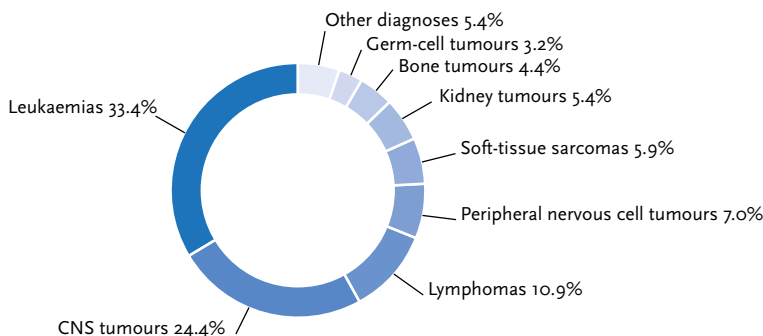
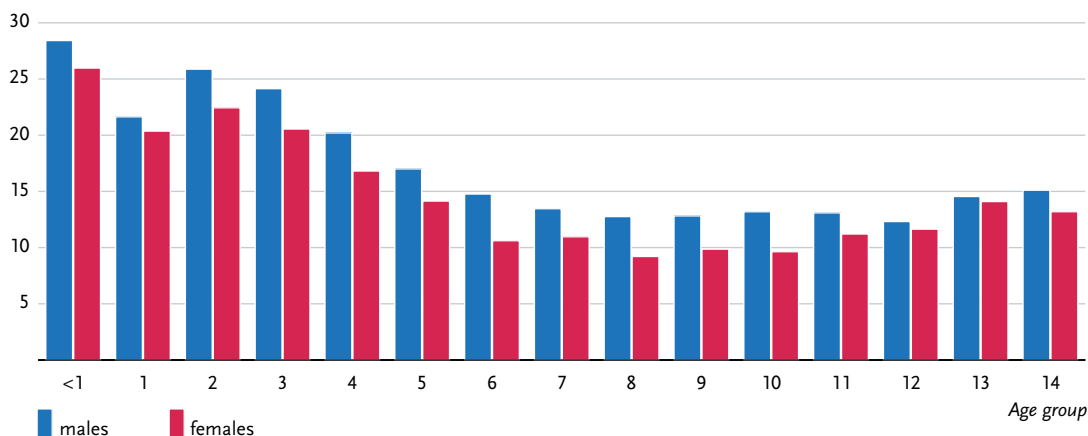


Figure 4.2
Incident cases by age and sex, all childhood malignancies
Number of cases per 100,000 by age group, determined for the period 2004–2013



Leukaemias

Leukaemias make up more than a third of all cancers among the under-15-year-olds. The most common single diagnosis overall (26.5 %) is lymphatic leukaemia (LL). It occurs more than twice as frequently among children under the age of five as in the other age groups. 4.4 % of all childhood malignancies are acute myeloid leukaemias (AML). AML is most common among children under the age of two. The survival prospects for AML are markedly lower than for LL. About 13 % of all subsequent cancers are AML.

The causes of leukaemias in childhood remain largely uncertain, even today. For a long time, environmental influences were suspected of causing childhood leukaemias. Since then it has been shown that the number of cases caused by most environmental factors (low-dose ionising radiation, non-ionising

radiation and pesticides) is quite small after all, even if a weak association with leukaemias in childhood cannot be ruled out. A number of clues have meanwhile strengthened hypotheses that assign a key role to infectious pathogens and the immune system in the development of childhood leukaemias. Genetic causes are still researched and discussed for all neoplasia in childhood.

CNS tumours

The most common single diagnoses among CNS tumours are astrocytomas (total: 11.7 %), intracranial and intraspinal embryonal tumours (4.6 %) and ependymomas (1.9 %). Twenty-two percent of all subsequent cancers are CNS tumours. The increase in the incidence of CNS tumours observed in a number of western countries over the past decades may be connected

Figure 4.3
Incident cases by age and sex, childhood acute lymphatic leukaemia (ALL)
Number of cases per 100,000 by age group, determined for the period 2004–2013

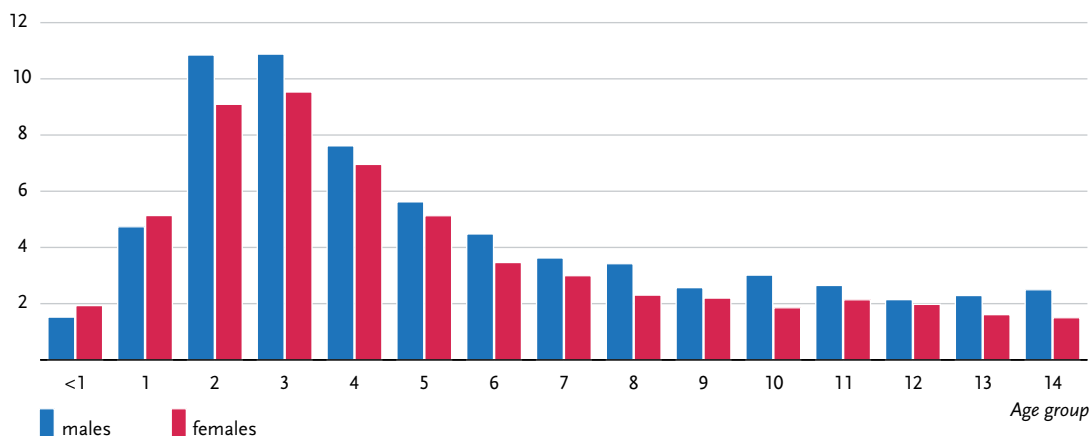


Figure 4.4
Trends of incidence of selected diagnostic groups and for all childhood malignancies
Number of cases per 100,000 (age standardised), including eastern Germany since 1991

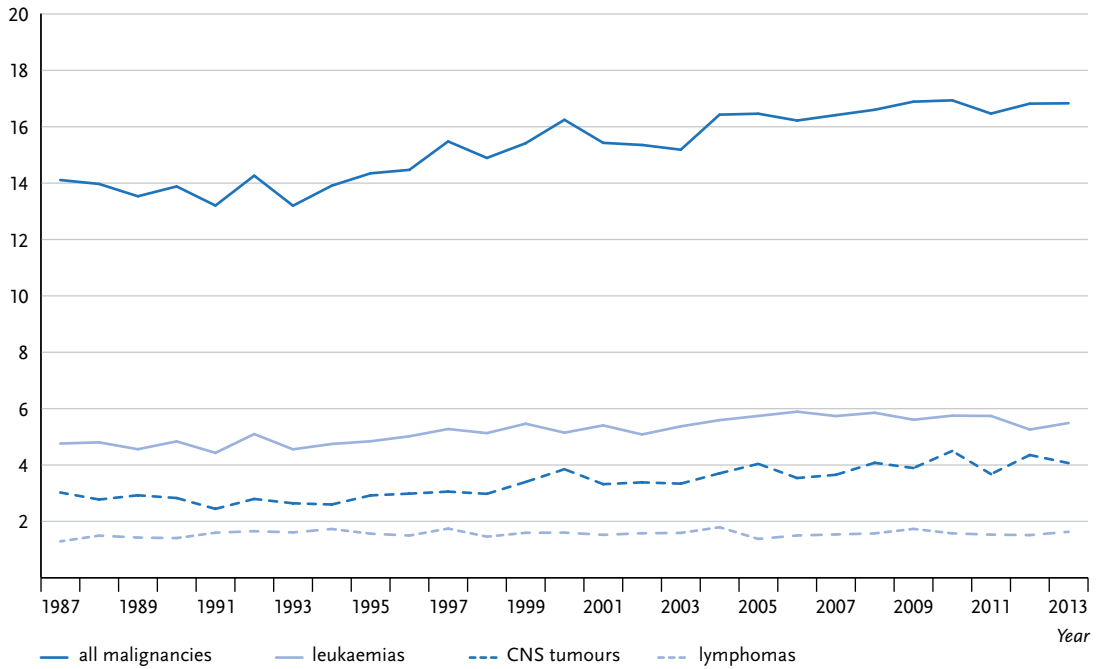
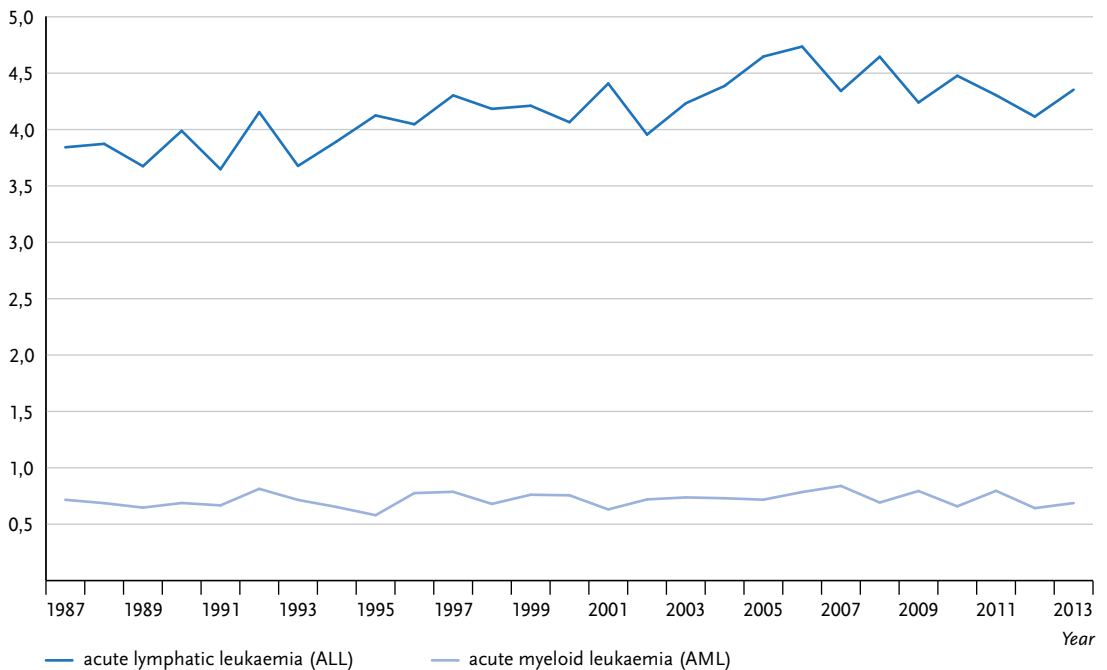


Figure 4.5
Trends of incidence of childhood leukaemias, myeloproliferative and myelodysplastic disorders
Number of cases per 100,000 (age standardised), including eastern Germany since 1991



with a better registration and also with general changes in environmental factors and related exposures. For example, a number of epidemiological studies is looking into the possible influence of ionising radiation, electromagnetic fields, pesticides, the mother's diet and genetic aspects.

Lymphomas

The most common lymphomas are non-Hodgkin lymphomas (NHL), including Burkitt's lymphoma (total: 6.5%) and Hodgkin's lymphoma (4.7%). The chances of survival with Hodgkin's lymphoma are among the best in paediatric oncology. Unfortunately, with more than 8% the frequency of subsequent cancer (within 25 years after diagnosis) after Hodgkin's lymphoma is particularly high. Children with congenital or acquired immunodeficiency and those who have had immunosuppressive therapy are at increased risk of developing NHL. An association is suspected between lymphomas and ionising radiation; this has not, however, been substantiated.

Other common malignant diseases

Other common malignant diseases in childhood include neuroblastomas (nerve-cell tumours), nephroblastomas (kidney tumours), germ-cell tumours, bone tumours and rhabdomyosarcomas (tumours of the skeletal musculature). Among these malignancies, the prognosis for children with nephroblastoma or a germ-cell tumour is much more favourable than for the other tumours. Skin tumours and thyroid cancer are other frequent subsequent cancers.

Survival

Children under 15 years of age with cancer make up less than 1% of all cancer patients. However, malignant neoplasms are the second most common cause of death among children. Fortunately, the survival rates have improved dramatically over the last 30 years thanks to significantly more differentiated diagnostics and the use of multimodal therapy concepts. In the early 1980s the chances of children with cancer being still alive five years after diagnosis were 67%; this figure has risen to 84% since then. Looking at all patients of the registry population who were diagnosed between 2002 and 2011 and followed up, the overall chance of survival is 84% after five years, 82% after ten years, and 81% after 15 years. The encouraging increase in the number of long-term survivors is increasingly focusing attention on the long-term observation of former paediatric cancer patients. The GCCR provides an ideal data basis for carrying out studies with long-term survivors. As the above figures show, it is already possible to provide information on long-term survival (for example after 15 years) and to estimate the risk of developing a second neoplasia after cancer in childhood. Examples of further research possibilities include the incidence of other long-term effects, such as the possible effects of therapy on fertility, and studies examining the health risks of the descendants of fathers and mothers who had childhood cancer. About 32,000 of the more than 42,000 patients currently known to be alive have been under observation by the registry for at least five years. The majority of these patients are at least 18 years old.

Table 4.1
Incidence and survival rates for the most common diagnoses, determined for the period 2002–2011

Cancer sites	Incidence*	Survival rate in %**		
		after 5 years	after 10 years	after 15 years
Hodgkin's lymphomas	0.6	99	98	97
Retinoblastomas	0.4	97	97	97
Germ-cell tumours	0.5	95	94	94
Nephroblastomas	1.0	93	92	92
Lymphoid leukaemias	4.4	92	90	89
Non-Hodgkin lymphomas	0.6	89	87	86
Astrocytomas	1.8	81	79	77
Neuroblastomas and ganglioneuroblastomas	1.4	79	77	76
Rhabdomyosarcomas	0.5	74	72	71
Acute myeloid leukaemias	0.7	73	72	71
Osteosarcomas	0.3	75	71	70
Intracranial and intraspinal embryonal tumours	0.8	67	59	56
All malignancies	16.6	84	82	81

* Related to 100,000 children under the age of 15, age standardised (standard: Segi world population), children diagnosed 2004–2013

** Brenner H, Spix C. Combining cohort and period methods for retrospective time trend analyses of long-term cancer patient survival rates. Br J Cancer 89, 1260–1265, 2003

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