

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. The current data pool consists of over 52,000 cancer cases. 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 (GBA)". 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.

Incidence of childhood cancers

About 1,800 cases of childhood 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 16.0 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.

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 (33.8 %), CNS tumours (24.0 %) and lymphomas (11.1 %). 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, eleven months. Boys are diagnosed with cancer 1.2 times more frequently than girls.

Leukaemias

Leukaemias make up more than a third of all cancers among the under-15-year-olds. The most common single diagnosis overall (26.3 %) is acute lym-

Figure 4.1
Cancer in children (determined for the period 2003 – 2012)

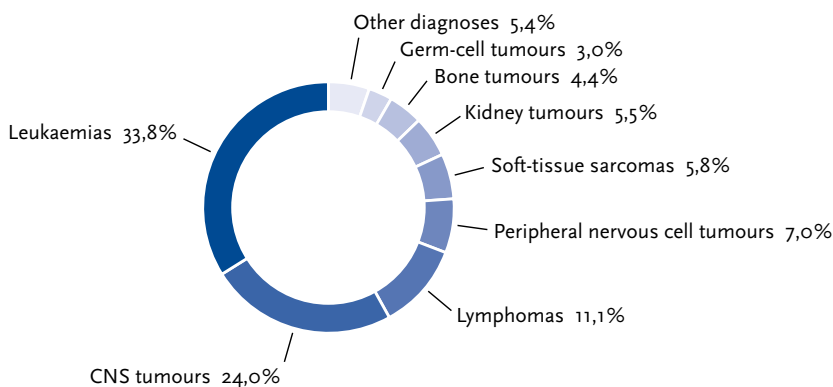
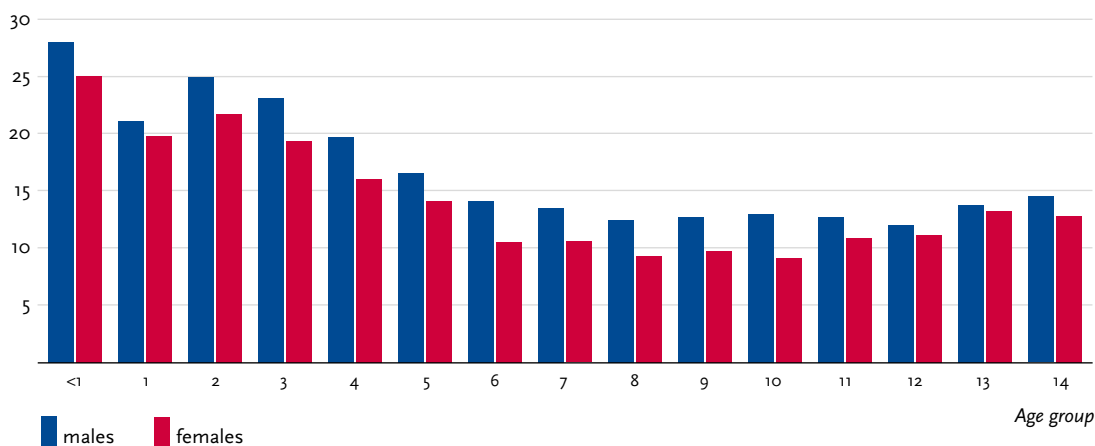


Figure 4.2
Incident cases by age and sex, all childhood malignancies
 Number of cases per 100,000 by age group, determined for the period 2003 – 2012



phatic leukaemia (ALL). 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 ALL. 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 in the

development of childhood leukaemias. Especially children with an insufficiently modulated immune system in infancy can have a higher risk of developing leukaemia.

CNS tumours

The most common single diagnoses among CNS tumours are astrocytomas (total: 11.1%), intracranial and intraspinal embryonal tumours (4.6%) and ependymomas (2.4%). The increase in the incidence of CNS tumours observed in a number of western countries over the past decades may be connected 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.

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 2003 – 2012

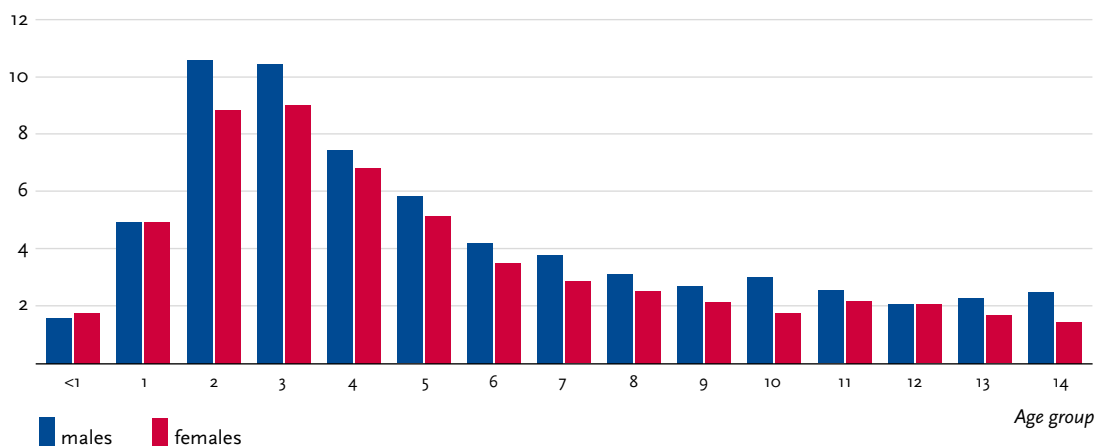


Figure 4.4
Trends of the incidence of selected diagnostic groups and for all childhood malignancies
Number of cases per 100,000 (age standardised), including eastern Germany since 1991

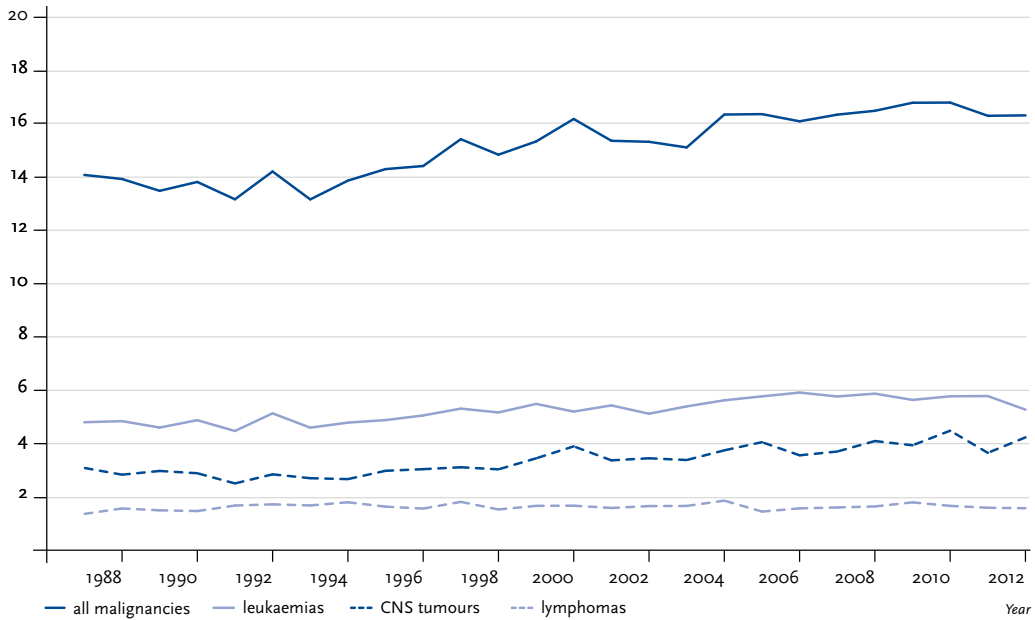
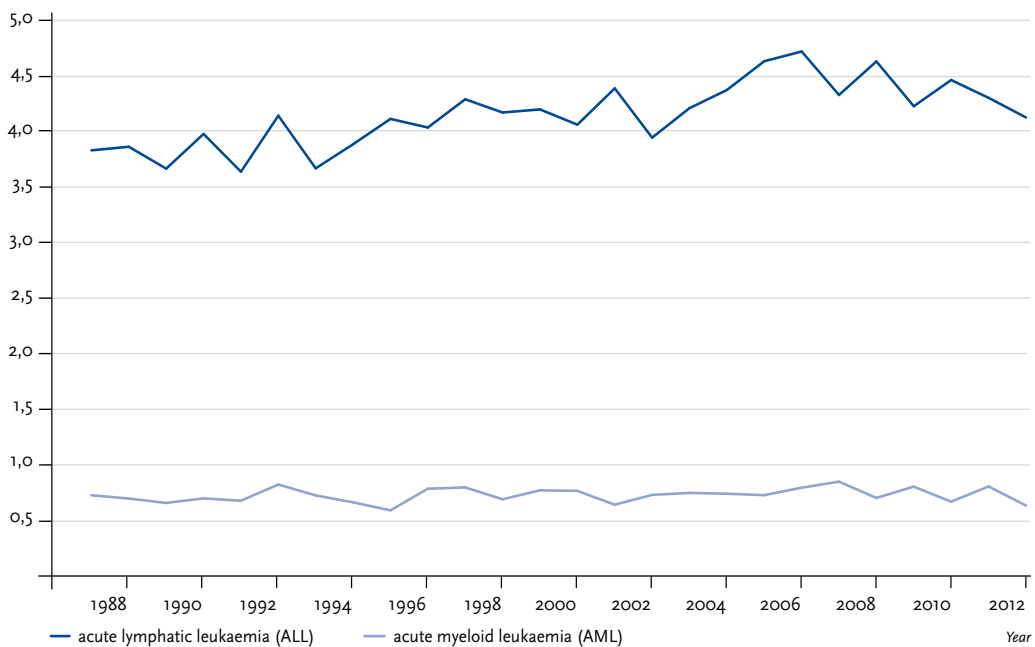


Figure 4.5
Trends of the incidence of childhood leukaemias, myeloproliferative and myelodysplastic disorders
Number of cases per 100,000 (age standardised), including eastern Germany since 1991



Lymphomas

The most common lymphomas are non-Hodgkin lymphomas (NHL), including Burkitt's lymphoma (total: 6.4 %) and Hodgkin's lymphoma (4.7 %). The chances of survival with Hodgkin's lymphoma are among the best in paediatric oncology. 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 others.

Survival

Children with cancer make up fewer 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 sig-

nificantly 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 2001 and 2010 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 malignancy 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 22,000 of the more than 37,000 patients currently known to be alive have been under observation by the registry for at least ten years. About three quarters 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 2001 – 2010

Cancer sites	Incidence*	Survival rate in %**		
		after 5 years	after 10 years	after 15 years
Hodgkin's lymphomas	0.6	98	98	97
Retinoblastomas	0.4	98	97	97
Germ-cell tumours	0.5	95	94	94
Nephroblastomas	1.0	93	92	92
Lymphoid leukaemias	4.4	91	89	88
Non-Hodgkin lymphomas	0.6	89	88	86
Astrocytomas	1.7	81	79	77
Neuroblastomas and ganglioneuroblastomas	1.4	79	76	75
Osteosarcomas	0.3	76	72	71
Rhabdomyosarcomas	0.5	72	71	69
Acute myeloid leukaemias	0.7	72	70	69
Ewing's tumours and related bone sarcomas	0.3	70	66	65
Intracranial and intraspinal embryonal tumours	0.8	67	60	56
All malignancies	16.4	84	82	81

* Related to 100,000 children under the age of 15, age standardised (standard: Segi world population), children diagnosed 2003 – 2012

** 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

Literature on childhood cancer

- Brenner H, Spix C. Combining cohort and period methods for retrospective time trend analyses of long-term cancer patient survival rates. *Br J Cancer*. 2003;89(7):1260-5.
- Dieluweit U, Debatin KM, Grabow D, Kaatsch P, Peter R, Seitz DC, et al. Educational and vocational achievement among long-term survivors of adolescent cancer in Germany. *Pediatr Blood Cancer*. 2011;56(3):432-8.
- Gatta G, Zigon G, Capocaccia R, Coebergh JW, Desandes E, Kaatsch P, et al. Survival of European children and young adults with cancer diagnosed 1995-2002. *Eur J Cancer*. 2009;45(6):992-1005.
- Grabow D, Spix C, P K. Langzeitüberlebende nach Krebs im Kindesalter: eine populationsbezogene Kohorte am Deutschen Kinderkrebsregister. *Ärzteblatt Rheinland-Pfalz*. 2012;6.
- Grabow D, Spix C, Blettner M, Kaatsch P. Strategy for long-term surveillance at the German Childhood Cancer Registry - an update. *Klin Padiatr*. 2011;223(3):159-64.
- Hammer GP, Seidenbusch MC, Regulla DF, Spix C, Zeeb H, Schneider K, et al. Childhood cancer risk from conventional radiographic examinations for selected referral criteria: results from a large cohort study. *AJR Am J Roentgenol*. 2011;197(1):217-23.
- Kaatsch P. Epidemiology of childhood cancer. *Cancer Treat Rev*. 2010;36(4):277-85.
- Kaatsch P, Reinisch I, Spix C, Berthold F, Janka-Schaub G, Mergenthaler A, et al. Case-control study on the therapy of childhood cancer and the occurrence of second malignant neoplasms in Germany. *Cancer Causes Control*. 2009;20(6):965-80.
- Kaatsch P, Scheidemann-Wesp U, Schuz J. Maternal use of antibiotics and cancer in the offspring: results of a case-control study in Germany. *Cancer Causes Control*. 2010;21(8):1335-45.
- Kaatsch P, Spix C. German Childhood Cancer Registry - Annual Report 2011 (1980-2010). Mainz: Institute of Medical Biostatistics, Epidemiology and Informatics (IMBEI) at the University Medical Center of the Johannes-Gutenberg University Mainz; 2012.
- Kaatsch PS, C.; Jung, I.; Blettner, M. Leukämien bei unter 5-jährigen Kindern in der Umgebung deutscher Kernkraftwerke - Schlusswort. *Dtsch Ärztebl*. 2009;106(23):394.
- Roman E, Lightfoot T, Smith AG, Forman MR, Linet MS, Robison L, et al. Childhood acute lymphoblastic leukaemia and birthweight: Insights from a pooled analysis of case-control data from Germany, the United Kingdom and the United States. *Eur J Cancer*. 2012.
- Schmiedel S, Blettner M, Kaatsch P, Schuz J. Spatial clustering and space-time clusters of leukemia among children in Germany, 1987-2007. *Eur J Epidemiol*. 2010;25(9):627-33.
- Schuz J, Grell K, Kinsey S, Linet MS, Link MP, Mezei G, et al. Extremely low-frequency magnetic fields and survival from childhood acute lymphoblastic leukemia: an international follow-up study. *Blood Cancer J*. 2012;2:e98.
- Spix C, Kaatsch P, Schüz J. Umweltfaktoren bei Leukämieerkrankungen im Kindesalter. *pädiat prax*. 2013;80:233-54.
- Spix C, Schulze-Rath R, Kaatsch P, Blettner M. Case-control study on risk factors for leukaemia and brain tumours in children under 5 years in Germany. *Klin Padiatr*. 2009;221(6):362-8.