4 Cancer in children

The German Paediatric Cancer Registry (DKKR), Department of Childhood Epidemiology, has been based at the Institute of Medical Biometry, Epidemiology and Informatics at the University Medical Centre of the Johannes Gutenberg University Mainz since the beginning of its work in 1980. Close cooperation with the Society for Paediatric Oncology and Haematology (GPOH) and its member clinics was envisaged in the conception of the DKKR. As a result, the registry has a characteristic that is not readily transferable to adult oncology. A comprehensive epidemiological cancer registry was created, covering the whole of Germany with high data quality and a completeness rate of over 95% (since around 1987). The DKKR thus meets the international requirements for an epidemiological cancer registry. A further characteristic

Figure 4.1
Most frequent tumour sites as percent of all incident cancer cases in children under 18 years (determined for the period 2012 – 2021)

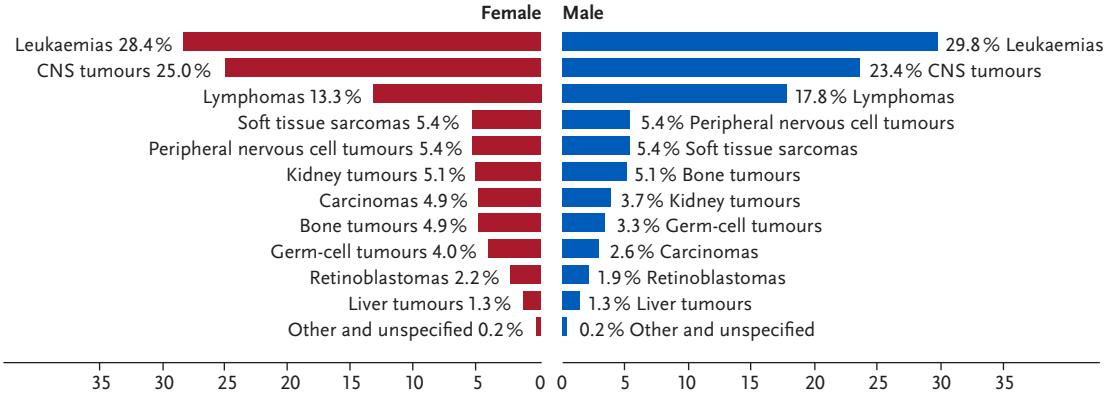


Table 4.1
Incidence* and survival rates for the most frequent diagnoses in childhood (under 18 years), by sex**

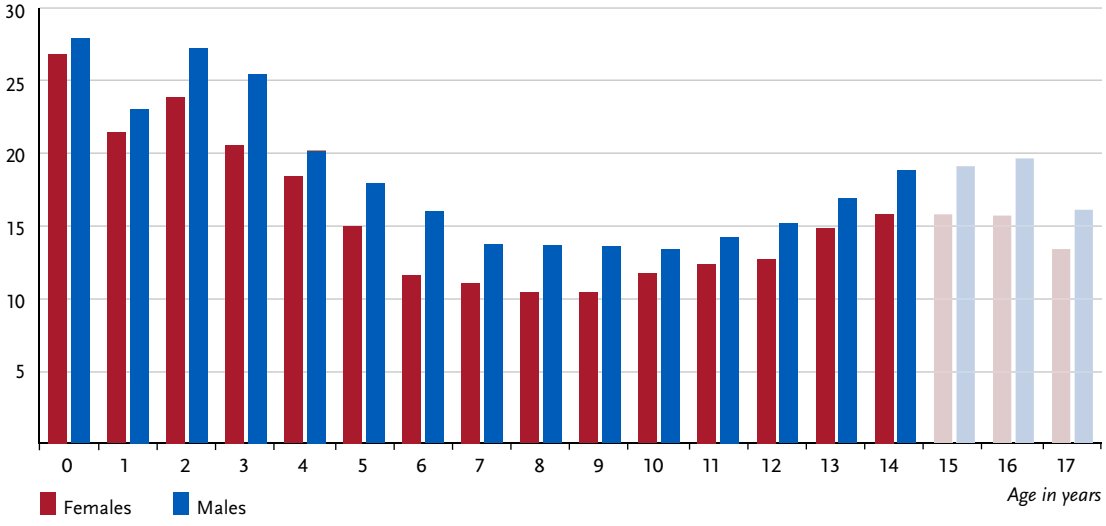
	Incidence*		Survival rate in %**					
			after 5 years		after 10 years		after 15 years	
Cancer sites	females	males	females	males	females	males	females	males
Lymphoid leukaemias	3.5	4.4	93	92	92	91	91	90
Acute myeloid leukaemias	0.7	0.8	78	77	77	77	76	76
Hodgkin lymphomas	1.1	1.2	98	99	97	98	97	97
Non-Hodgkin lymphomas	0.4	1.1	90	92	89	92	87	90
Astrocytomas	1.8	1.9	86	84	85	83	83	82
Intracranial and intraspinal embryonal tumours	0.6	0.9	68	68	63	62	61	59
Neuroblastomas and ganglioneuroblastomas	1.0	1.2	85	79	83	76	83	75
Retinoblastomas	0.4	0.4	98	99	98	99	98	99
Nephroblastomas	0.9	0.8	94	94	93	94	93	93
Osteosarcomas	0.4	0.4	78	74	76	66	74	66
Ewing sarcoma and related bone sarcomas	0.3	0.5	71	69	67	66	64	65
Rhabdomyosarcomas	0.4	0.6	74	74	73	72	72	72
Germ-cell tumours	0.6	0.6	97	93	96	93	95	92
All malignancies	16.1	18.9	88	87	86	85	85	84

* cases per 100,000 children under age 18, age-standardised, standard: Segi world population, diagnosis years 2012 – 2021
** for children diagnosed between 2011 and 2020, predicted according to: 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

of the DKKR is the realisation of active, indefinite long-term follow-up, which continues well into adulthood. Thus, the registry also provides the basis for research into late effects, secondary tumours and generally for studies with long-term survivors.

Since 1980, the register population has included children who were diagnosed with a malignant disease or a histologically benign brain tumour before their 15th birthday and who belonged to the German resident population at the time of diagnosis. Since around 1987, it can be assumed that the survey has been largely complete. Since 1991, diseases in the new federal states have also been recorded. Since 2009, the DKKR has recorded all children and adolescents up to the age of 18 (= diagnosed before their 18th birthday) based on the "Directive of the Joint Federal Committee on Quality Assurance Measures for the Inpatient Care of Children and Adolescents

Figure 4.2
Incidence rate by age and sex, all childhood malignancies
Number of caces per 100,000 by age group, determined for the period 2012 – 2021



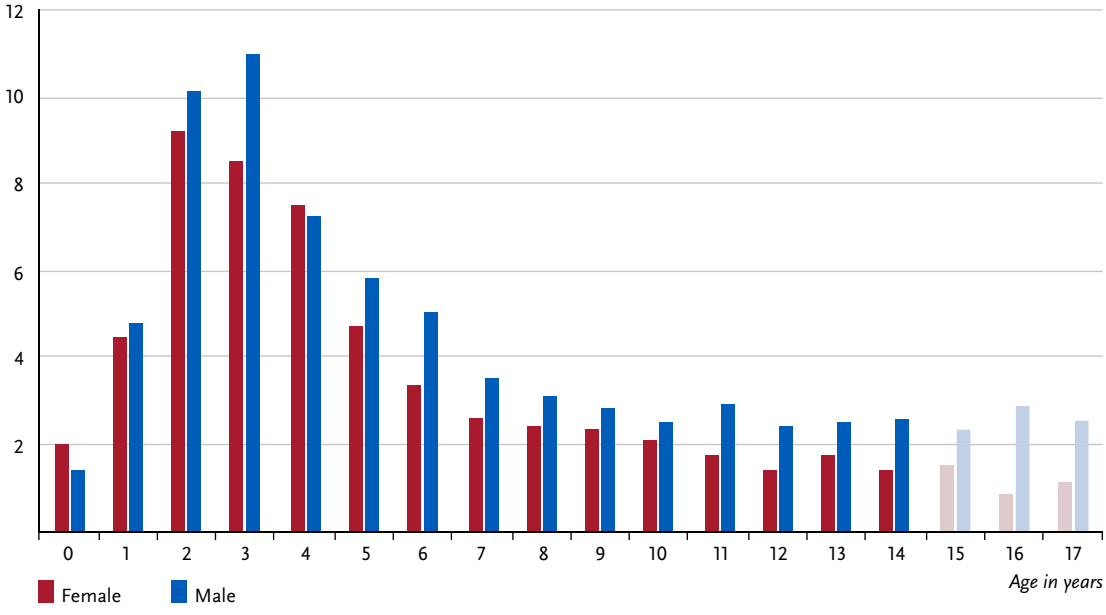
Suspected underreporting among adolescents 15 years and older.

Table 4.2
Number of incident cancer cases, incidence rates* and survival rates among children under 18 years for each of the 4 most frequent diagnoses in childhood and adulthood according to ICD-10, by sex**

		Number of incident cases		Incidence rate*		Survival rate** in %					
						after 5 years		after 10 years		after 15 years	
Cancer sites	ICD-10	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂
Leukaemia	C91–C95	2,638	3,502	4.3	5.3	90.8	90.0	90.0	88.8	89.3	88.0
Central nervous system	C70–C72	1,453	1,818	2.3	2.7	70.6	69.5	66.9	64.5	64.8	62.2
Hodgkin lymphoma	C81	782	904	1.1	1.2	97.7	98.8	97.4	98.2	97.2	97.3
Soft tissue without mesothelioma	C46–C49	764	759	1.3	1.2	81.2	76.8	78.3	73.9	77.5	72.9
Lung	C33–C34	36	41	0.1	0.1	67.9	80.3	67.9	76.9	67.9	74.1
Prostate	C61	0	10	0.0	0.0						
Breast	C50	2	2	0.0	0.0						
Colon and rectum	C18–C21	202	117	0.3	0.2	99.3	88.3				

* cases per 100,000 persons under the age of 18, age-standardised according to the Segi world population, 2012 – 2021
** for children diagnosed between 2011 and 2020
♀ female, ♂ male

Figure 4.3
Incidence rate by age and sex, childhood lymphoid leukaemia (LL)
Number of cases per 100,000 by age group, determined for the period 2012 – 2021



Suspected underreporting among adolescents 15 years and older.

with Haemato-oncological Diseases". Some diagnostic groups in older adolescents are also treated outside the paediatric and adolescent oncology clinics; these are slightly under-recorded at the DKKR. The data currently available is based on a total of approximately 74,000 cases.

Incidence of childhood cancer

In Germany, there are about 2,250 newly diagnosed cases under the age of 18 every year. With a population of about 13 million under-18-year-olds, this results in annual incidence rates of 16.1 per 100,000 children for girls and 18.9 per 100,000 children in this age group for boys. The probability of a newborn child suffering a malignant disease within the first 18 years of life is 0.3%. Thus, about one in 330 children will be diagnosed with a malignant cancer by their 18th birthday. Within the first 30 years after initial diagnosis, at least one further cancer (secondary neoplasia) was reported in 1,739 patients.

In a European comparison, Germany's incidence rates are around mid-table. The most important reasons for differences in incidence rates are generally differences in data collection and random effects in countries with a very small database, e.g. where there is no nationwide coverage.

Diagnostic spectrum

In general, the diagnostic spectrum for children is completely different to that for adults. The most appropriate classification of entities for children therefore also focuses on morphology. The largest diagnostic groups are leukaemias (28 to 30%), tumours of the central nervous system (CNS; 23 to 25%) and lymphomas (13 to 18%), especially Hodgkin lymphomas. Embryonal tumours (neuroblastomas, retinoblastomas, nephroblastomas, medulloblastomas, embryonal rhabdomyosarcomas or germ cell tumours) are also common in childhood, but almost never observed in adulthood. Carcinomas, on the other hand, are extremely rare (about 3 to 5% of malignant diseases). The median age at diagnosis for children and adolescents under 18 years of age is seven years and seven months. Boys are 1.2 times more likely to develop the disease than girls.

Analogous to the usual recording and presentation in adulthood according to the ICD (predominantly localisation-based), the fourth most common diagnostic group after leukaemias, lymphomas and malignant CNS tumours is "tumours in soft tissue without mesotheliomas", which includes a range of different morphologies. By contrast, the organs most frequently affected in adulthood – lung, prostate, breast and colon – are extremely rarely affected in childhood and adolescence. Most childhood tumours in these locations are not carcinomas comparable to

the disease in adults; for example, the tumours in the colon reported in childhood are predominantly appendix carcinoids, while lung tumours are mostly lung carcinoids.

Probability of survival

The proportion of children under the age of 18 with cancer among all cancer patients is less than 1%. However, malignant neoplasms are the second most common cause of death in children. Fortunately, survival rates have improved considerably over the last 40 years thanks to significantly more sophisticated diagnostics and the use of multimodal therapy concepts. While the probability of still being alive five years after diagnosis was 67% for children diagnosed in the early 1980s, this figure is now 88% for girls and 87% for boys in the registry population diagnosed between 2011 and 2020. Survival probabilities vary relatively widely depending on the entity.

Due to the encouraging increase in long-term survivors, the long-term observation of former paediatric cancer patients is increasingly coming into focus. The DKKR represents an ideal database for conducting studies with long-term survivors. As can be seen from the above figures, it is already possible to make statements on the long-term probability of survival (after 15 years or more) or to estimate the risk of a second neoplasm occurring after childhood cancer. Questions about the occurrence of other late effects, such as possible effects of the therapy on fertility, offspring or cardiovascular late effects are examples of further research possibilities. Of the more than 60,000 patients currently known to the registry to be alive, about 47,000 have been under observation for at least five years. The majority of these former patients are now 18 years or older.

Leukaemias

Leukaemia accounts for almost a third of all cancers in patients under the age of 18. The most common single diagnosis overall is lymphocytic leukaemia (LL) at 21.9%. It is almost twice as common in the under-five-year-olds as in the other age groups. 4.1% of all childhood malignancies are acute myeloid leukaemia (AML). AML is most common in the under-two-year-olds. The probability of survival for AML is significantly lower than for LL.

In the case of leukaemia, a slight, steady upward trend was observed until the early 2000s, which was also observed in Europe as a whole. Since then, incidence rates have remained largely constant.

The causes of childhood leukaemia are still largely unclear today. Environmental factors have long been suspected of causing childhood leukaemia. In the meantime, it has been shown for most environmental factors (ionising radiation in the low-dose range as well as non-ionising radiation or pesticides) that the proportion of cases caused by them is rather low, even if a weak connection with the occurrence of childhood leukaemia cannot be ruled out. A number of indications have now increasingly led to hypotheses that attribute a central role to infectious agents and the immune system in the development of childhood leukaemias. Genetic causes are increasingly being investigated and discussed for all childhood neoplasms.

Lymphomas

The most common lymphomas are non-Hodgkin lymphoma (NHL) including Burkitt's lymphoma (6.2% overall) and Hodgkin's disease (7.4%). Survival rates for Hodgkin's disease are among the highest in paediatric oncology (97% after 15 years). Unfortunately, the risk of secondary neoplasia after Hodgkin's disease is also particularly high, with a particular risk of breast cancer in young women.

The incidence rate for lymphomas is largely constant, but since lymphomas occur much more frequently in older children and adolescents, significantly more cases have been recorded since the additional registration of 15- to 17-year-olds and a higher incidence rate has been observed than in those under 15 years of age.

There is an increased risk of developing NHL in children with congenital or acquired immunodeficiency and after immunosuppressive therapy.

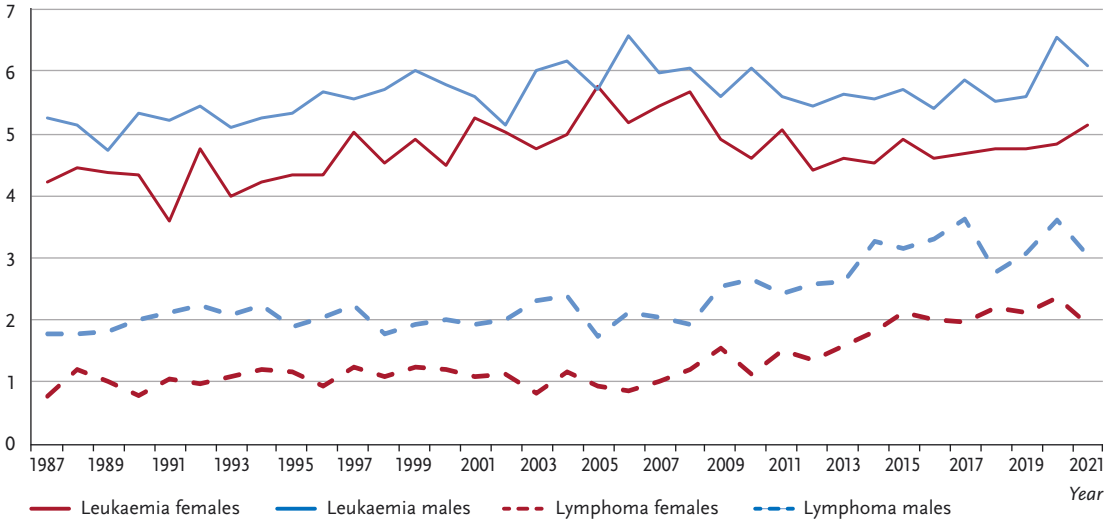
CNS tumours

The most common individual diagnoses of CNS tumours are astrocytomas (10.4% in total), intracranial and intraspinal embryonal tumours (3.9%) and ependymomas (1.5%). The increase in the incidence of CNS tumours observed in Germany in recent decades, but also in a number of western countries, is probably primarily related to better recording. General changes in environmental factors and the resulting exposures are also suspected. For example, a number of epidemiological studies have looked at the possible influence of ionising radiation, electromagnetic fields or pesticides as well as genetic aspects, but no consistent correlations have yet been found.

Other common malignant diseases

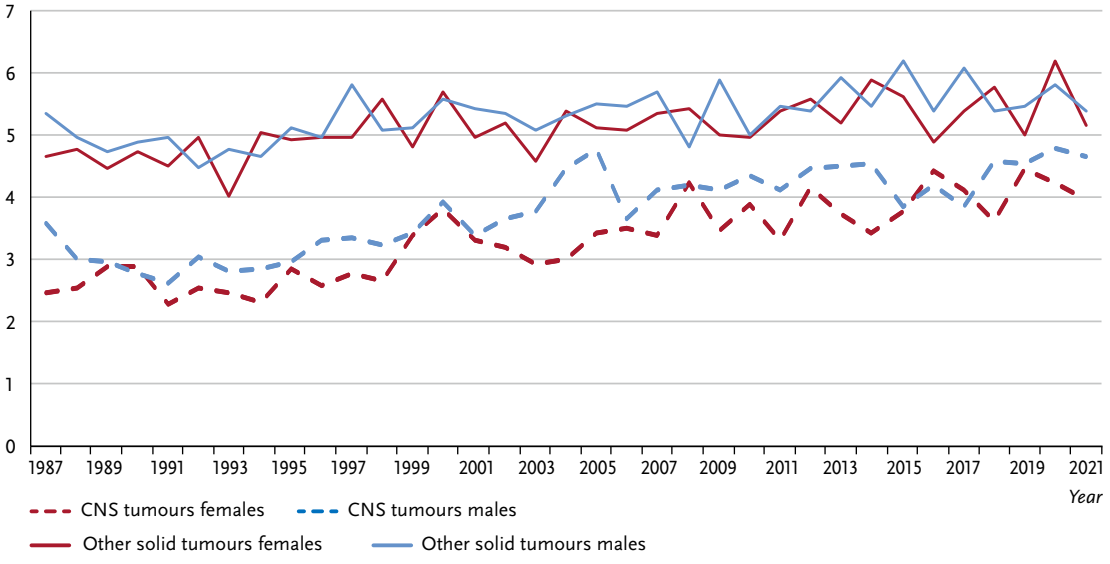
Other common malignant diseases in childhood are neuroblastoma (nerve cell tumour), nephroblastoma (kidney tumour), germ cell tumours, bone tumours and rhabdomyosarcoma (tumour of the skeletal muscles). The prognosis for children suffering from a nephroblastoma or germ cell tumour is significantly more favourable than for other tumours. Leukaemias and CNS tumours are particularly common secondary neoplasms after cancer in childhood and adolescence, as are skin tumours, thyroid carcinomas and breast cancer in young women.

Figure 4.4
Trends in incidence of childhood leukaemia and lymphoma (under 15 years until 2008, under 18 years from 2009), by sex, 1987 – 2021
Number of cases per 100,000 (age-standardised according to Segi), including eastern Germany since 1991



In the last decade, further neoplasms of the lymphatic system have been newly classified as malignant (Langerhans cell histiocytosis).

Figure 4.5
Trends in incidence of childhood CNS tumours and other solid tumours (under 15 years until 2008, under 18 years from 2009), by sex, 1987 – 2021
Number of cases per 100,000 (age-standardised according to Segi), including eastern Germany since 1991



There is no real trend in incidence rates for solid tumours outside the CNS. Over the years, individual additional diagnoses have been assessed as malignant and recorded. The recording of certain solid tumours in older children, some of which are not treated in paediatric and adolescent oncology, such as gynaecological and urological carcinomas and skin tumours, has been and continues to be slowly improved. Overall, this has led to a slight increase in the number of reported cases.

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