Since taking up its work in 1980, 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. From the outset, the GCCR was conceived to enable close cooperation with the Society for Paediatric Oncology and Haematology (GPOH) and its associated hospitals. This feature of the registry distinguishes it from adult oncology and has allowed it to become a nationwide epidemiologic childhood cancer registry with a high level of data quality and over 95% coverage (since about 1987). The GCCR thus meets the international standards for an epidemiologic cancer registry. A further feature of the GCCR is its active, open-ended, long-term follow-up observation of patients into adulthood. The registry therefore also provides a basis for researching late effects and secondary tumours, as well as studies with long-term survivors in general.

The registry includes children who have been diagnosed with a malignant disease or a histologically benign brain tumour before their 15th birthday and are part of the German resident population at diagnosis. The GCCR began registering cancer cases in eastern Germany in 1991. On 1 January 2009, the GCCR began registering all children and adolescents through the age of 17 years (i.e., those who receive their diagnosis before their 18th birthday) on the basis of the Richtlinie des Gemeinsamen Bundesausschusses über Maßnahmen zur Qualitätssicherung für die stationäre Versorgung von Kindern und Jugendlichen mit hämato-onkologischen Krankheiten (Guideline 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.

Currently, the Registry contains data from around 61,000 patients.

**Childhood cancer incidence**

Germany registers around 1,800 cases of cancer in children under the age of 15 every year. With around 11 million children under 15, this translates into an incidence rate of about 16.9 per 100,000 children for this age group. For a child, the likelihood of developing a malignant cancer within the first 15 years of his or her life is 0.2%. Roughly one in 410 children is diagnosed with a malignant cancer before his or her 15th birthday. Since 2009, when registration of all children and adolescents up to the age of 18 began, an additional 360 cases between the ages of 15 and 17 years have been registered on average each year. 1,255 patients have been diagnosed with a subsequent cancer within the first 30 years after their initial diagnosis. This represents 7.3% of all childhood cancer patients (cumulative incidence).

**Survival**

Less than 1% of all cancer patients are children below the age of 15 years. Nonetheless, malignant neoplasms are the second most common cause of death for children. Luckily, survival prospects have improved over the past 30 years, in particular due to significantly more differentiated diagnoses and multimodal therapies. Of all children who were diagnosed with cancer and subsequently followed up between 2004 and 2013, 85% of patients were alive after five years, 83% after ten years and 82% after fifteen years. In the early 1980s, the five-year survival probability of children with cancer was still only 67%.

Gradually, the encouraging rise in the number of long-term survivors has shifted the focus towards the

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**Figure 4.1**

Cancer in children (determined for the period 2008–2017)

![Cancer Incidence Chart]

- Leukaemias 32.2%
- Lymphomas 10.8%
- Other and unspecified 0.2%
- Carcinomas 2.5%
- Germ-cell tumours 3.3%
- Bone tumours 4.2%
- Liver tumours 1.5%
- Retinoblastomas 2.3%
- Peripheral nervous cell tumours 6.7%
- CNS tumours 25.3%
- Kidney tumours 5.4%
- Soft-tissue sarcomas 5.6%
- Bone tumours 4.2%
- Liver tumours 1.5%
- Retinoblastomas 2.3%
- Peripheral nervous cell tumours 6.7%
- CNS tumours 25.3%
- Kidney tumours 5.4%
long-term observation of former paediatric cancer patients. The GCCR database is in this regard an ideal basis for studying long-term survivors. As the above figures reveal, analysis of long-term survival (for example after 15 years or more), as well as estimates regarding the risk of developing a second neoplasm after suffering cancer in childhood, are already possible. Further potential research fields include the incidence of other long-term impacts, such as the possible consequences of therapy for fertility, or studies that examine the health risks of descendants or cardiovascular implications of therapy at later stages of life. About 39,000 of the more than 50,000 patients currently known to be alive have been followed-up for at least five years. The majority of these former patients are now 18 years old or older.

**Range of diagnoses**

Compared to adults, children present a very different range of cancers. Most small children develop embryonal tumours (neuroblastomas, retinoblastomas, nephroblastomas, medulloblastomas, embryonic rhabdomyosarcomas or germ-cell tumours). Carcinomas, by contrast, are very rare in children (accounting for only about 2.5% of all malignant cancers). Diagnostically, the most important groups of cancer in children are leukaemias (32.2%), CNS tumours (25.3%) and lymphomas (10.8%). Cancer incidence rates for children under five years of age are about twice as high as in the 5- to 14-year age group. The median age at onset for children under fifteen years of age is five years, nine months. Boys are diagnosed with cancer 1.2 times more frequently than girls.

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 2008 – 2017

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 2008 – 2017
Leukaemia
Among children under 15 years old, leukaemia accounts for about one third of all cancer cases. The most common single diagnosis overall (24.9%) is lymphoid leukaemia (LL). It occurs more than twice as frequently among children under the age of five as in all other age groups. 4.1% 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 significantly lower than for LL. About 11% of all subsequent neoplasms are AML.

The causes of childhood leukaemia still remain largely unclear today. For a long time, environmental factors were suspected of playing a role in the development of leukaemia among children. Recently, however, it has become quite clear that the number of cases related to environmental factors (such as low-dose ionising radiation, non-ionising radiation and pesticides) is quite small, even though a weak association between these factors and childhood leukaemia cannot be ruled out. A number of facts have given greater weight to hypotheses that assign a key role to infections and the immune system in childhood leukaemia. Increasingly, genetic causes continue to be researched and discussed for all childhood neoplasms.

Lymphomas
The most common lymphomas are Hodgkin lymphoma (4.7%) and non-Hodgkin lymphomas (NHL), including Burkitt’s lymphoma (6%). The chances of survival for patients with Hodgkin lymphoma are among the best in paediatric oncology. Unfortunately, at more than 9%, the frequency of subsequent cancers within 30 years after diagnosis of Hodgkin lymphoma is particularly high. Children with congenital or acquired immunodeficiency and those who have had immunosuppressive therapy are at increased risk of developing NHL.

CNS tumours
The most commonly diagnosed CNS tumours are astrocytomas (11.5%), intracranial and intraspinal embryonal tumours (4.3%) and ependymomas (1.9%). 23% of subsequent neoplasms are CNS tumours. The increase in the incidence rates of CNS tumours observed in a number of western countries over the past few decades is mostly related to better registration, but general changes in environmental factors and related exposures are also being discussed. For example, a number of epidemiological studies are investigating the influence of ionising radiation, electromagnetic fields, pesticides, the mother’s diet, as well as of genetic aspects.

Other common malignant diseases
Other common malignant cancers in childhood include neuroblastomas, nephroblastomas, germ-cell tumours, bone tumours and rhabdomyosarcomas (tumours of the skeletal muscle and connective tissue). The prognosis for children with nephroblastoma or germ-cell tumours is much more favourable than for the other tumours.

Table 4.1
Incidence* and survival rates for the most common diagnoses, determined for the period 2004 – 2013

<table>
<thead>
<tr>
<th>Cancer sites</th>
<th>Incidence*</th>
<th>Survival rate in %** after 5 years</th>
<th>after 10 years</th>
<th>after 15 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hodgkin lymphomas</td>
<td>0.7</td>
<td>99</td>
<td>98</td>
<td>97</td>
</tr>
<tr>
<td>Retinoblastomas</td>
<td>0.5</td>
<td>98</td>
<td>97</td>
<td>97</td>
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<tr>
<td>Nephroblastomas</td>
<td>1.0</td>
<td>93</td>
<td>93</td>
<td>93</td>
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<tr>
<td>Germ-cell tumours</td>
<td>0.5</td>
<td>94</td>
<td>93</td>
<td>93</td>
</tr>
<tr>
<td>Lymphoid leukaemias</td>
<td>4.3</td>
<td>92</td>
<td>91</td>
<td>90</td>
</tr>
<tr>
<td>Non-Hodgkin lymphomas</td>
<td>0.7</td>
<td>89</td>
<td>88</td>
<td>86</td>
</tr>
<tr>
<td>Astrocytomas</td>
<td>1.9</td>
<td>81</td>
<td>79</td>
<td>78</td>
</tr>
<tr>
<td>Neuroblastomas and ganglioneuroblastomas</td>
<td>1.3</td>
<td>80</td>
<td>77</td>
<td>77</td>
</tr>
<tr>
<td>Acute myeloid leukaemias</td>
<td>0.7</td>
<td>73</td>
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<tr>
<td>Rhabdomyosarcomas</td>
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<tr>
<td>Osteosarcomas</td>
<td>0.3</td>
<td>75</td>
<td>71</td>
<td>70</td>
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<tr>
<td>Intracranial and intraspinal embryonal tumours</td>
<td>0.8</td>
<td>66</td>
<td>58</td>
<td>56</td>
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<tr>
<td>All malignancies</td>
<td>16.9</td>
<td>85</td>
<td>83</td>
<td>82</td>
</tr>
</tbody>
</table>

* Cases per 100,000 children under the age of 15, age standardised, standard: Segi world population, children diagnosed 2008 – 2017
Figure 4.4
Trends of incidence of selected diagnosis 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

Skin tumours, thyroid cancer, breast cancer among young women and other carcinomas are very rare as primary diagnoses in children but are frequent subsequent cancers after childhood cancer, sometimes already occurring in childhood or adolescence.

Literature on childhood cancer


