4 Cancer in children

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) has been built up covering the whole of Germany. The GCCR thus meets the international standards for an epidemiological 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 also registers cancer cases in eastern Germany since 1991. Since 1 January 2009, the GCCR has been registering all children and adolescents up to the age of 18 years (i.e. those, who receive their diagnosis before their 18th birthday) on the basis of the 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 data pool contains the data of around 57,000 patients.

Childhood cancer incidence

Germany registers around 1,750 cases of cancer in children aged under the age of 15 every year. With around 11 million children under 15, this translates into an incidence rate of about 6.8 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/her life is 0.2%. Roughly, one in 410 children is diagnosed with a malignant cancer before their 15th birthday. Since 2009, when registration of all children and adolescents up to the age of 18 began, an additional 360 cases aged between 15 and 17 years have been registered on average each year. 1,253 patients were diagnosed with a further cancer (subsequent cancer) within the first 30 years after their initial diagnosis, a rate of 6.6% of patients (cumulative incidence).

Survival probability

Less than 1% of all cancer patients are children aged under 15. 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. Whereas in the early 1980s, the five-year relative survival rate of children with cancer was 67%; this figure has now risen to 85%. Regarding the total number of patients included in the registry and diagnosed with cancer and subsequently followed up between 2004 and 2013, the five-year rate was 85%, the ten-year rate 83% and the fifteen-year rate 82%.

Gradually, the encouraging rise in the number of long-term survivors has shifted the focus on the long-
A 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, already today, statements on long-term survival (for example after 15 years or more), as well as estimates regarding the risk of developing a second neoplasia after suffering cancer in childhood, are now possible. Further potential research fields include the incidence of other long-term impacts, such as the possible consequences of therapy on fertility, or studies that examine the health risks of descendants or cardiovascular implications of therapy at later stages of life. About 35,000 of the more than 46,000 patients currently known to be alive have been registered for at least five years. The majority of these former patients are now aged 18 or over.

**Range of diagnoses**

Compared to adults, children present a very different range of cancers. Most 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 3% of all malignant cancers). Diagnostically, the most important groups of cancer in children are leukaemias (32.9%), CNS tumours (24.6%) and lymphomas (10.7%). Cancer incidence rates for children aged under five are about twice as high as in the 5 to 14 age group. The median age at onset for children aged under fifteen is five years, ten months. Boys are diagnosed with cancer 1.2 times more frequently than girls.
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
Leukaemias
Among under 15 year olds, leukaemia accounts for about one third of all cancer cases. The most common single diagnosis overall (25.8 %) is lymphatic leukaemia (LL). It occurs more than twice as frequently among children under the age of five as in all other age groups. 4.3 % 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 as playing a role in the development of leukaemia at childhood age. In the meantime, it has however 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 loose association of these factors with 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 neoplasia.

Lymphomas
The most common lymphomas are non-Hodgkin lymphomas (NHL), including Burkitt’s lymphoma (6.3 %) and Hodgkin’s lymphomas (4.5 %). The chances of survival for patients with Hodgkin’s lymphoma are among the best in paediatric oncology. Unfortunately, with more than 13 % the frequency of subsequent cancer (within 30 years after diagnosis) following a 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.

CNS tumours
The most commonly diagnosed CNS tumours are astrocytomas (11.5 %), intracranial and intraspinal embryonal tumours (4.4 %) and ependymomas (1.9 %). 23 % of subsequent neoplasms are CNS tumours. Potentially, the increase in the incidence rates of CNS tumours observed in a number of western countries over the past few decades are related to better registration and also with general changes in environmental factors and related exposures. For example, a number of epidemiological studies is 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 (nerve-cell tumours), nephroblastomas (kidney tumours), germ-cell tumours, bone tumours and rhabdomyosarcomas (tumours of the skeletal muscle). The prognosis for children with nephroblastoma or germ-cell tumour is much more favourable than for the other tumours. Skin tumours and thyroid cancer and breast cancer among young women are other frequent subsequent cancers.

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

<table>
<thead>
<tr>
<th>Cancer cites</th>
<th>Incidence1 after 5 years</th>
<th>Survival rate in %2 after 5 years</th>
<th>after 10 years</th>
<th>after 15 years</th>
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<tbody>
<tr>
<td>Hodgkin’s lymphomas</td>
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<td>99</td>
<td>98</td>
<td>97</td>
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<tr>
<td>Retinoblastomas</td>
<td>0.4</td>
<td>97</td>
<td>97</td>
<td>97</td>
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<tr>
<td>Germ-cell tumours</td>
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<td>94</td>
<td>93</td>
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<td>Nephroblastomas</td>
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<tr>
<td>Lymphoid leukaemias</td>
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<td>91</td>
<td>90</td>
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<tr>
<td>Non-Hodgkin lymphomas</td>
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<td>89</td>
<td>88</td>
<td>86</td>
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<tr>
<td>Astrocytomas</td>
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<td>79</td>
<td>78</td>
</tr>
<tr>
<td>Neuroblastomas and ganglioneuroblastomas</td>
<td>1.4</td>
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<tr>
<td>Rhabdomyosarcomas</td>
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<tr>
<td>Acute myeloid leukaemias</td>
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<tr>
<td>Intracranial and intraspinal embryonal tumours</td>
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<tr>
<td>All malignancies</td>
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<td>85</td>
<td>83</td>
<td>82</td>
</tr>
</tbody>
</table>

1 Related to 100,000 children under the age of 15, age standardised (standard: Segi world population), children diagnosed 2006 – 2015
Br. Cancer 89, 1260 – 1265, 2003
Literature on cancer in children


