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# Quality of haematological and oncological care in children<sup>1</sup>

## Executive Summary

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<sup>1</sup> Translation of the executive summary of the final report “Qualität der pädiatrisch-hämatologisch-onkologischen Versorgung” (Version 1.0; Status: 13.08.2009). Please note that this translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

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Institute for Quality and Efficiency in Health Care  
Dillenburger Str. 27  
51105 Cologne  
Germany

Tel.: +49 221 35685-0

Fax: +49 221 35685-1

[berichte@iqwig.de](mailto:berichte@iqwig.de)

[www.iqwig.de](http://www.iqwig.de)

# Quality of haematological and oncological care in children

## Executive summary

### Background

In Germany approximately 1800 children under 15 years of age are diagnosed with cancer every year. The most frequent paediatric tumour diseases are acute leukaemia (34%), followed by brain tumours (22%) and malignant lymphomas (12%). The children affected are treated in haemato-oncological paediatric centres. Based on cases reported to the German Childhood Cancer Registry, it is possible to make general statements on survival.

The G-BA's Quality Assurance Agreement (*Strukturvereinbarung*) applies to all children and adolescents under 18 years of age diagnosed with cancer, and has been in force since 1 January 2007.

### Research question

The aim of the investigation was to evaluate the quality of current medical care in Germany for children with haemato-oncological diseases.

A literature search, including the evaluation of publications located, and a search for clinical practice guidelines (CPGs) were conducted, and the results presented in appropriate form for the scientific investigation of existing infrastructures and quality in haemato-oncological paediatric care. Furthermore, epidemiological data were specifically used. The investigation of the quality of care in haemato-oncological paediatrics was conducted with regard to different disease phases or convalescent and palliative care plans.

The report focussed on the following aspects:

- presenting and analysing the aspects cited in the literature for Germany covering the quality of outcomes, procedures and infrastructure in haemato-oncological paediatric care
- international benchmarking of some aspects of quality of outcomes, procedures and infrastructure, where possible

The results were used to try to estimate the necessity of implementing quality-improvement measures.

### Methods

The target population in the report comprised children and adolescents under 18 years of age with acute leukaemia, malignant lymphomas and brain tumours.

In order to evaluate the quality of results, the following patient-relevant outcomes were investigated: survival, treatment-related death, health-related quality of life, pain, and long-term consequences of the disease and therapy. In order to evaluate the quality of procedures and infrastructure, the following outcomes were considered: information on standards and CPGs, particular features of quality indicators and organizational requirements for psychosocial support and rehabilitation.

As the research question covered a wide area, various types of study and publication were included in the report.

A systematic literature and CPG search was performed. A targeted search for relevant information was also performed in the databases and on the websites of DeStatis, the German Childhood Cancer Registry, the International Agency for Research on Cancer (IARC) and the German Pension Insurance Association (DRVVB).

After screening and evaluating the literature, the data were extracted and, as far as possible, synthesized. It was possible to benchmark 3 out of the 8 outcomes. The survival outcome was benchmarked at European level using German Childhood Cancer Registry data. For the pain outcome, a similar Swedish study could be compared to the German cross-sectional study. For information on standards and CPGs, a comparable British CPG was found and compared to the only German evidence-based S3 CPG.

The medical care situation was then assessed and evidence gaps noted. Basically, evidence gaps can indicate potential problems in care or poorly investigated areas. Based on a more detailed investigation of the evidence gaps and potential care problems, proposals can then be formulated for quality improvement measures.

## Results

Altogether, over 9000 abstracts and more than 1500 potentially relevant full texts were screened. The report included 245 publications (including multiple allocations).

(1) Survival: on an international comparison level, results for this important outcome are very good. During the last 2 to 3 decades, the overall survival has improved for all children with cancer in Germany. Within the diagnosis period 2000 to 2004, 80% of children with cancer survived 5 years. However, there were distinct differences between the diseases. Event-free (EFS) and progression-free survival (PFS) also improved over the course of time. In the ALL-BFM<sup>2</sup>-95 study, EFS based on the central neural system (CNS) result from the initial diagnosis was between 50% and 83% after 5 years. In the general analysis of the following studies stratified according to age groups, EFS was between 46% and 62% after 5 years

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<sup>2</sup> Acute Lymphoblast Leukaemia-Berlin-Frankfurt-Münster

depending on age at initial diagnosis: AML<sup>3</sup>-BFM-93, -98 (children and adolescents), AMLCG92/99, AMLSG HD93/98A (young adults). In the NHL<sup>4</sup>-BFM-95 study, EFS was 89% after 3 years. In the general analysis of GPOH<sup>5</sup>-HD-90 and -95 studies EFS was 86% after 10 years. For children with brain tumours, EFS after 5 years was between 0% and 87.6% depending on the tumour entity. PFS after 3 years was between 0% and 83.3% depending on the tumour entity and other factors.

(2) Treatment-related deaths: There were few publications on this outcome. Conclusions could be drawn concerning acute leukaemia and NHL. The evidence is incomplete on this outcome. For children with ALL, the proportion of treatment-related deaths was given as approximately 2%. For patients with AML, the proportion of premature deaths/treatment-related deaths was less than 10% during the current period. In patients with NHL, treatment-related deaths were investigated together with tumour lysis syndrome. Treatment-related deaths could be attributed to 11% for children having a tumour lysis syndrome.

(3) Health-related quality of life: There were few publications on this outcome. Only one of them could be included in the report. It concerned a report of the CRANIOPHARYNGEOMA-2000 study, which had tested the quality of life of craniopharyngeoma patients using a validated instrument. The evidence is incomplete.

(4) Pain: No clinical trials where children had self-reported pain could be included in the report. The evidence appears to be incomplete. However, a survey of doctors and nurses on pain management in children with cancer could be compared with a Swedish study. The WHO staging ladder was used in more than 90% cases in Germany and more than 60% in Sweden. Flaws in managing pain were also reported.

(5) Long-term consequences of the disease and therapy: A number of publications on different long-term consequences in different patient groups was identified. A synthesis of the publications did not produce a comprehensive picture. There was little data on frequencies. Gaps in evidence must be assumed here as well.

Growth abnormalities following cranial and/or spinal radiotherapy were investigated in children with brain tumours. This revealed growth retardation and an over-proportionate increase in body weight. However, the number of patients lost to follow-up was relatively high.

Intellectual problems were investigated in children and adolescents following treatment for acute leukaemia. No major reduction in intelligence was found, although problems in learning

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<sup>3</sup> Acute myeloid leukaemia

<sup>4</sup> non-Hodgkin lymphoma

<sup>5</sup> German Society for Paediatric Oncology and Haematology

and concentration were present. No neuropsychological tests were carried out on patients with brain tumours who frequently need far higher cranial radiation doses.

Infertility was only investigated in young men who had received treatment for Hodgkin's lymphoma. At most, there was a slight delay in pubertal development. However, there were indications of a lack of hormones, which was taken to be an indicator of potential infertility.

The cardiotoxicity of anthracyclines was investigated in children and adolescents with AML. The frequency of subclinical cardiomyopathy was given as approximately 4%. Clinically relevant cardiomyopathy was less frequent.

Recurrences were observed over a wide range, from 0% to over 30% depending on the disease and prognostic factors. The cumulative incidence of second tumours was maximum 1.6% after 10 years for patients with Hodgkin's lymphoma. In general, there is increased risk of cancer survivors having a second tumour.

(6) Information on standards and CPGs: The systematic CPG search only produced one evidence-based German CPG and numerous consensus-based CPGs and recommendations from medical societies and cancer centres.

In Germany the care standards for paediatric haemato-oncology are formulated in the protocols of therapy optimizing studies and converted into TOSs. 90% of all children and adolescents with cancer were treated in these studies.

(7 and 8) Particular features of quality infrastructure and procedures for psychosocial support and rehabilitation: There are no quality indicators for infrastructure or for procedures for paediatric haemato-oncology in Germany. The identified publications only indicated important aspects of the infrastructure. Conclusions on care nationwide were therefore not possible. One study described the infrastructure/staffing resources of the 46 largest paediatric-oncological centres. However, it is not possible to draw conclusions on the smaller facilities. Several publications gave indications concerning the situation of psychosocial services. Another cross-sectional study presented palliative care. It was frequently dependent on the personal input of staff at a centre. This report cannot judge the extent to which the recently announced G-BA directive on outpatient palliative care has altered the situation.

Family-oriented rehabilitation plays an important role in managing the disease. About 70% of all children with incidental disease undergo rehabilitation.

## **Conclusions**

In Germany the overall survival of children with cancer is very good when compared internationally. Paediatric oncological care in Germany is better than care for adults with cancer when measured against the mortality-incidence ratio across the population.

However, there are some gaps in the evidence: for instance, there are very few studies on the health-related quality of life in children with cancer. The situation is even worse for the patient-relevant outcome "pain". In addition, results on the outcomes "treatment-related deaths" and "long-term consequences of the disease and therapy" could not be presented for every clinical picture included in the report. It is practically impossible to systematically quantify the long-term consequences. Second tumours are the exception. Compared to the general population, second tumours are observed 10 to 20 times more frequently in those surviving cancer in childhood.

CPGs and recommendations are generally based on consensus. Efforts should be made to produce evidence-based CPGs and recommendations. 90% of all children with cancer are treated in therapy-optimizing studies, which can be viewed as indicative of a high standard of care. This is particularly clear in survival probability.

The quantitative data on quality infrastructure and procedures included in the report was sparse and, in part, no longer current. Other results relate solely to the large centres so that the baseline situation in the smaller centres prior to the introduction of the quality assurance agreement remains unclear. Quality indicators for infrastructure and procedures are urgently required in order to obtain information on care coverage and regional variations.

It is not possible to ascertain from the literature search to what extent the evidence gaps presented indicate actual deficits in care.

Further studies on the above-mentioned evidence gaps are urgently required. If problems in medical care are concealed by these evidence gaps, proposals for quality-improvement measures could be formulated, based on a more detailed investigation of the above-mentioned evidence gaps.

**Keywords:** Paediatric oncology, paediatric haemato-oncology, quality of care, acute lymphatic leukaemia (ALL), synonym: acute lymphoblastic leukaemia (ALL), acute myeloid leukaemia (AML), Hodgkin's lymphoma, non-Hodgkin lymphoma (NHL), brain tumour, mortality/survival, quality of life, long-term consequences, psychosocial care, benchmarking, systematic review

The full report (in German) is available on [www.iqwig.de/index.529.html](http://www.iqwig.de/index.529.html)