

# ALL case based learning resource

## Overview of the paediatric acute lymphoblastic leukaemia (ALL) case study: Ellie's story

This case study recounts the experience of Ellie, a 4-year-old female diagnosed with ALL.

The case study contains three sections:

1. Find the condition early.
2. Have the best treatment and support during active treatment.
3. Have the best treatment and support between and after active treatment.

It is recommended that you complete the sections and their related activities in order. This is because each section and each activity includes information that will help you complete the sections and activities that follow.

### Learning activities

At times, you will have learning activities to complete. Click on the learning activities button and a list of questions will pop up. The questions will relate to the content you've just read or the video you've just watched.

### Videos

There is a video component to this case study that is presented in seven parts. You can watch the video clips when prompted throughout this case study or at any time by clicking on the video icon in the right-side menu. Learning activities throughout the case study will discuss the video and ask questions about it.

### Resource Links

Resource links are included throughout the case study. These links lead to interesting articles or websites, and are designed to encourage you to explore other available resources.

### PDF of ALL module

You can download a PDF version of the ALL module.

This is version 2.1 of this resource.

Last modified:

Next review due:

### Suggested citation:

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[http://www.cancerlearning.gov.au/edcan\\_resources/#/xml/module\\_3/casestudies/paediatric\\_cancer](http://www.cancerlearning.gov.au/edcan_resources/#/xml/module_3/casestudies/paediatric_cancer)

## **Aim of the paediatric acute lymphoblastic leukaemia (ALL) case based learning resource**

This case study aims to facilitate the development of competencies that reflect the role of the Specialist Cancer Nurse (SCN) in managing disease and treatment related care for the child and family affected by ALL across the cancer journey.

### **Rationale**

Childhood cancer is highly curative, with 81% five-year relative survival among children aged zero-14 in the period 2004-2010. Despite this, cancer causes significant morbidity and mortality for children, and was a leading cause of death for those aged one–14 in 2008–2010.<sup>3</sup>

Acute lymphoblastic leukaemias are the most common cancer affecting children<sup>3</sup>, with a peak incidence in children aged zero to four.<sup>4</sup>

Children have unique developmental needs across all domains of health requiring responses of specialised health care professionals and services.

There are many points along the cancer journey when SCNs can improve outcomes for people at risk of, or affected by, childhood leukaemia. These include:

#### **Section 1: Find the condition early**

- Early diagnosis and treatment is important to achieve good survival outcomes and deliver treatment with the least intensity possible.<sup>5</sup>
- Increasing the awareness of clues to early diagnosis of cancer in the context of normal childhood development within the health care community may lead to earlier referrals to specialist cancer services.
- Specialist paediatric cancer services and multidisciplinary teams (MDTs) are considered to be more suited to providing evidence based, age-appropriate care and ensuring access to international clinical collaboration.

#### **Section 2: Have the best treatment and support during active treatment**

- The child and their family require the specialist support of an expert multidisciplinary paediatric cancer service involving paediatric oncologists, surgeons, radiotherapists, diagnostic services, allied health professionals and nurses with paediatric expertise throughout the cancer journey.
- The improved survival outcomes associated with childhood cancer can be attributed to advances in treatments, and delivery of individualised treatments based on the person's disease, presenting symptoms and risk factors.
- Families require information and support to make treatment decisions, which may involve enrolment in a clinical trial.
- Children require age appropriate supportive care to manage the effects of their disease and its treatment and procedural distress.

#### **Section 3: Have the best treatment and support between and after active treatment**

- Treatments used to cure childhood cancer can have long-term effects.
- 'Late effects' may impact all domains of health, and may persist or develop many years from the diagnosis of cancer.<sup>5</sup>
- People affected by childhood cancer need information and support about appropriate monitoring and health care following completion of treatment.
- The prognosis for children whose cancer relapses depends on a range of factors, requiring additional specialised treatment and supportive care interventions.

## Section 1: Find the condition early

### Objectives

On completion of this section, you should be able to:

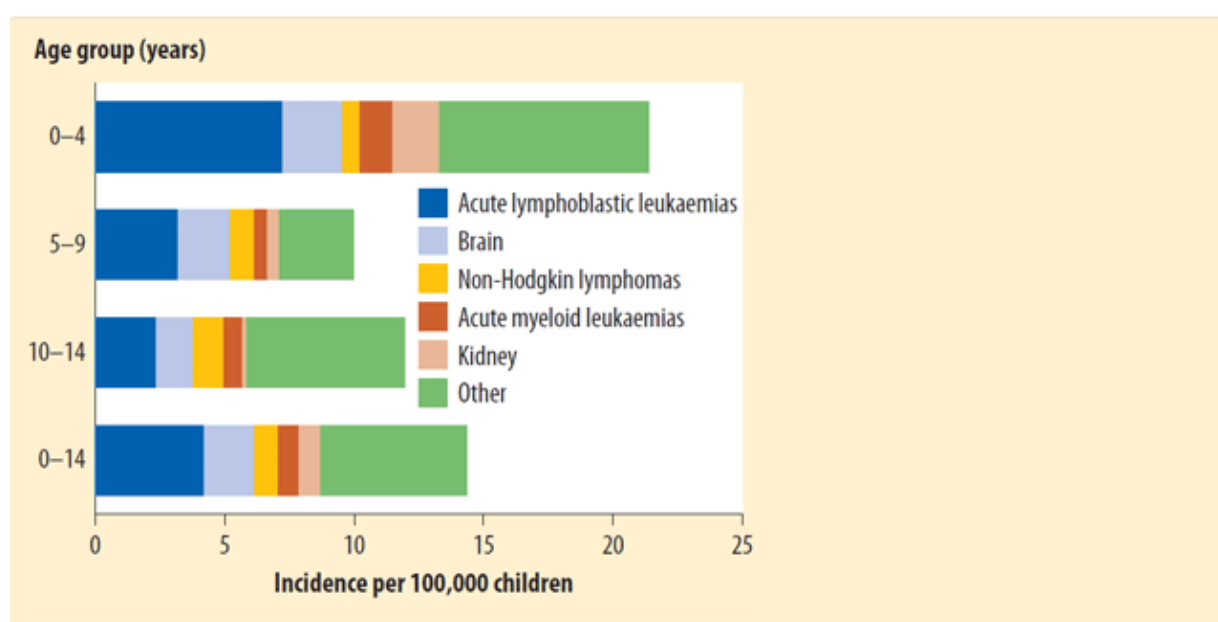
1. Interpret key epidemiological trends in cancer incidence, mortality and survival in children.
2. Discuss the unique characteristics of children and the impact of cancer on this population group.
3. Explain strategies the SCN may use to promote early detection of ALL in children.
4. Implement strategies to provide information, education and support to the child and their family when undergoing investigation of symptoms indicative of ALL.
5. Describe common responses and experiences of parents when their child is diagnosed with cancer.
6. Implement evidence based interventions to respond to supportive care needs of the child diagnosed with ALL and their family.

## Childhood cancer and leukaemia in Australia

Over the period 2009-2013, among children aged zero-14 in Australia:<sup>3, 50</sup>

- 922 new cases of Acute Lymphoblastic Leukaemia (ALL) were diagnosed<sup>50</sup>
- Incidence rates are unchanged from the previous period
- Higher incidence rates are present for those aged zero - four (21 per 100,000 children) compared with children aged five -nine (10 per 100,000) and 10-14 (12 per 100,000)
- The most common types of new cancer diagnosed were:
  - Acute lymphoblastic leukaemia (4.2 per 100,000 children)
  - Cancer of the brain (1.9 per 100,000 children)
  - Non-Hodgkin lymphomas (0.9 per 100,000 children)

### Most common types of new cancers among children aged 0-14, 2004-2008<sup>3</sup>



Note: Refer to *A picture of Australia's children 2012* Table B.2 for ICD-10-AM codes.

Source: AIHW Australian Cancer Database 2007.

<https://www.aihw.gov.au/reports/children-youth/a-picture-of-australia-s-children-2012/contents/table-of-contents>

Despite being relatively uncommon in children, cancer is a leading cause of death (19% of all deaths) in children aged one to 14 years in 2009-2011.<sup>6</sup>

The outlook for children diagnosed with cancer has improved. In the period 2004-2010, 5-year relative survival among children aged zero - 14 was 81% for all cancers compared with 68% in the period 1983-1989. Five-year relative survival for children aged zero - 14 years diagnosed with acute lymphoblastic leukaemia demonstrated significant improvement from 73% for diagnosis in 1983-1989 to 90% for diagnosis in 2004-2010.<sup>3</sup>

## Learning activity

Completed

Activity

- 1 Access the [AIHW Australian cancer incidence and mortality \(ACIM\) book](#)<sup>7</sup> to identify the following data relating to all lymphoid cancers, for male and female children aged zero – four, five – nine and 10-14, in 2010, 2000, and 1990:
  - incidence rate
  - mortality rate
  - summarise significant epidemiological findings.

## Early detection of childhood ALL

A timely diagnosis results in higher probability for improved outcomes and decreased requirements for intensive treatment.<sup>5</sup> For example, younger children with B-cell precursor ALL diagnosed prior to the development of high leukocyte counts can be treated with less intense regimens than those with high counts.<sup>5</sup>

ALL, a disease of unknown aetiology, is defined by an abnormal white blood cell proliferation primarily in the bone marrow but also in the peripheral blood, reticuloendothelial system and other body tissues.<sup>8</sup> Childhood ALL originates in the T- and B- lymphoblasts in the bone marrow. Most individuals with acute leukaemia present with greater than 25% blast cells in their bone marrow.<sup>9</sup>

Some factors associated with an increased risk of developing ALL include:<sup>9</sup>

- prenatal exposure to x-rays
- postnatal exposure to high doses of radiation
- Down syndrome and other genetic conditions
- Inherited genetic polymorphisms

Many presenting signs and symptoms of ALL in a child are manifestations of anaemia, thrombocytopenia, neutropaenia, and indicate a failure of normal haematopoiesis.<sup>5</sup> Signs and symptoms may include:<sup>5</sup>

- febrile illness
- pallor
- fatigue
- bleeding (petechiae, purpura)
- bone pain
- lymphadenopathy
- splenomegaly
- hepatosplenomegaly
- anorexia
- respiratory distress
- testicular enlargement
- central nervous system (CNS) manifestations (e.g. headaches, irritability).

Often, on presentation, the child may not appear acutely ill.<sup>10</sup> The duration of such symptoms varies with each child from days to months. Some children may present with conditions requiring emergent management, such as a mediastinal mass, or tumour lysis syndrome.<sup>11</sup>

The rarity of this disease, along with the fact many childhood cancers present with symptoms similar to those of common childhood diseases, can create delays and difficulties in diagnosis.

## Learning activities

Completed	Activities
<input type="checkbox"/>	1 Outline proposed risk factors associated with development of childhood ALL.
<input type="checkbox"/>	2 Access the National Cancer Institute - <a href="#">Childhood Acute Lymphoblastic Leukaemia Treatment PDQ</a> <sup>9</sup> or an evidence based text. Explain the pathophysiology of common presenting symptoms of ALL in children.
<input type="checkbox"/>	3 Discuss the possible impact of a delayed diagnosis of ALL in a child from the parent's perspective.

## Diagnostic investigations

To achieve accurate diagnosis and sub classification, it is necessary to identify the immunophenotypic, cytogenetic and morphology features of ALL.<sup>5</sup>

Investigations used to confirm a diagnosis of ALL include:<sup>11</sup>

- full blood count - red cells, platelets, white cells and blast count
- bone marrow aspiration - histochemistry, immunophenotyping and cytogenetics
- chest x-ray
- blood chemistry - electrolytes, blood urea, uric acid, liver function tests, immunoglobulin levels
- cerebrospinal fluid examination - chemistry and cells
- coagulation profile
- cardiac function
- infectious diseases profile - varicella antibody titer, cytomegalovirus status, herpes simplex antibody and hepatitis antibody screening
- immunological screening - immunoglobulin levels.

In children presenting with lymphadenopathy, tissue specimens may be collected if a distinction between leukaemia and lymphoma is required.<sup>5</sup>

Learning activities	
Completed	Activities
<input type="checkbox"/>	1 List the diagnostic procedures and investigations commonly used to confirm a diagnosis of ALL, and discuss nursing interventions for a child undergoing these procedures.
<input type="checkbox"/>	2 Outline the immediate clinical and supportive care interventions required for a child who presents with: <ul style="list-style-type: none"><li>• pancytopenia</li><li>• indicators of tumour lysis syndrome.</li></ul>



## Meet Ellie

### Case study: meet Ellie

Ellie is a 4-year-old female diagnosed with ALL. This case study follows Ellie from diagnosis to recovery.

After watching the first video, work through the learning activities.

[Ellie's story 1: Ellie is diagnosed](#)



### Learning activities

Completed	Activities
<input type="checkbox"/>	1 Access relevant research on responses of parents to diagnosis of cancer in their child, and discuss how Renee's response may be explained by this evidence.
<input type="checkbox"/>	2 Explain how the SCN can support Renee and Sean in dealing with their emotional responses at the time of diagnosis.

## Experience of diagnosis

The family's needs for support are substantial at the time of diagnosis, as they cope with a serious physical illness and the fear that their child will not be cured.<sup>12</sup>

At diagnosis, parents must adjust to the emotional realisation that their child is living with a life-threatening disease, while simultaneously receiving a large amount of information on how to manage and care for their child during treatment. Parents are very vulnerable during this time, and have an intense need for support from partners, families, friends, employers, hospital staff, and other parents.<sup>13</sup>

How parents respond to their child's diagnosis can also have a profound effect on how the child develops and responds to his/her illness. Factors which may influence how parents react include:<sup>12</sup>

- reactions to previous crises
- reactions of the child
- child rearing practices and attitudes
- available support systems
- perception of the illness
- previous knowledge or experience with cancer
- cultural and religious beliefs
- beliefs about the cause of the disease
- effects of the disease on the family
- concurrent stresses in the family.

Characteristics which affect children's responses include:<sup>12</sup>

- age (most vulnerable - six months to four years)
- development level
- temperament
- social skills and self-concept
- pre-existing conditions and previous experiences
- intelligence level
- type of disease
- reactions of significant others.

Primary caregivers, who are important to the well-being of the child during treatment, need to understand the nature of the disease, treatment options and prognosis in order to participate in treatment decisions and to take on the care roles expected of them.<sup>10, 14</sup> Nurses working with children who have cancer have a significant supportive role in:<sup>12, 14</sup>

- providing information and supportive care
- helping the family understand the various therapies
- preventing or managing side effects or toxicities
- observing for early and late effects of treatment.

Learning Activities	
Completed	Activities
<input type="checkbox"/>	1 Access a paediatric oncology text and the following resource: <a href="#">Improving outcomes in children and young people with cancer</a> <sup>14</sup> <ul style="list-style-type: none"><li>• Summarise key principles in providing supportive care for people affected by childhood cancer during the diagnostic phase.</li><li>• Discuss the role of hope in the childhood cancer journey and the role of the SCN in maintaining hope.</li></ul>

## Case study

### Ellie's story 2: Experience of diagnosis



## Learning activities

Completed

Activities

2

Outline how you would respond to Sean's questions about what to say to Ellie about her illness.

3

Access the following resources:

- [Improving outcomes in children and young people with cancer](#)<sup>14</sup>
- [Clinical practice guidelines for the psychosocial care of adults with cancer](#)<sup>15</sup>

Utilising principles of age and development appropriate education, describe possible strategies to work with Ellie and her parents in the provision of information about her treatment and care requirements.

4

Identify sources of information and resources available from the major cancer organisations in your area that might be used to assist Sean, Renee and Ellie at this time. Discuss the quality, usefulness, and developmental appropriateness of this material.

5

Outline the key social and emotional issues Ellie's family may face over the next three months related to Ellie's diagnosis with ALL, and the role of the SCN within the multidisciplinary team (MDT) to respond to these issues.

## Paediatric care delivery

Successful treatment of leukaemia depends upon the effectiveness of the health-care system. Key areas include:<sup>16</sup>

- early detection,
- access to appropriate treatment services,
- collaboration between health-care professionals, and
- ongoing medical research and clinical trials.

When a diagnosis of cancer is suspected or confirmed, referral to a paediatric cancer centre is required.<sup>5</sup> Guidelines for such centres have recently been published in the USA and UK.<sup>5, 14</sup> These specialist paediatric cancer services should have resources to:<sup>5</sup>

- enable accurate diagnosis and delivery of the most appropriate therapies, the provision of best supportive care and long-term follow up
- enable access to international cooperative group studies and international experts - this is important due to the small numbers of children with cancer and the need to pool expertise and access adequate numbers to ensure the validity of clinical trials
- provide access to an MDT including paediatric oncologists, specialist nursing and allied health staff and other paediatric sub-specialists, such as radiation oncologists, surgeons, and neurologists which are essential for ensuring the child's physical and psychosocial wellbeing.

A multidisciplinary approach to the management of childhood cancer has been recommended to provide the complex range of services required.<sup>14</sup> Anticipated benefits from such an approach include:<sup>14</sup>

- each person is considered from a range of viewpoints and expertise
- an MDT promotes shared learning between professionals
- a greater probability of timely, appropriate treatment and better continuity of care
- regular discussion in the context of an MDT is more likely to lead to improved clinical policies, more effective delivery of care and multidisciplinary participation in audit and research
- regular person-centred meetings, joint assessments and shared recording
- systems that enable teams to provide more comprehensive services.

Referral to specialist centres may involve relocation of the family from a rural or remote area, further increasing the burden.<sup>17</sup>

Learning activities	
Completed	Activities
<input type="checkbox"/>	1 Describe the characteristics of an MDT approach to working with a child and family affected by cancer. (access page 90 <a href="#">Improving outcomes in children and young people with cancer</a> <sup>14</sup> )
<input type="checkbox"/>	2 Identify the tertiary paediatric care services available in your local region, and outline the referral pathway to this service.

## Section 2: Have the best treatment and support during active treatment

### Objectives

On completion of this section, you should be able to:

1. Discuss the implications of classification of childhood ALL for the individual's cancer journey.
2. Discuss current treatment approaches for childhood ALL.
3. Use evidence based approaches to facilitate the ability of the person affected by childhood ALL to participate in decisions about treatment and care, according to their preferences.
4. Identify the implications of treatment approaches on childhood functioning across all domains of health during the treatment phase and in the longer term.
5. Explain the role and function of MDT members in ensuring optimal treatment and support for people affected by childhood ALL.
6. Implement evidence based interventions to respond to the supportive care needs of people affected by childhood ALL.
7. Tailor supportive care interventions to an individual's personal, developmental and social circumstances.
8. Explain methods for reducing procedural distress in children.

## Types of childhood ALL

Classification of ALL is based on the immunophenotypic and molecular genetic/cytogenetic features of the disease. The most clinically and biologically relevant classification schemes for ALL are those that incorporate molecular genetic or cytogenetic features, in conjunction with general immunophenotypic groups.<sup>5, 18, 19</sup>

Historically, the French American British (FAB) system was used to classify ALL. However, this system did not distinguish immunophenotypic disease groups. It has since been recognised that lymphoblast morphology is not helpful in sub-classifying ALL into clinically important prognostic groups.<sup>5, 8</sup>

The World Health Organization (WHO) classification of haematopoietic tumours classifies ALL based on immunophenotypic confirmation of immature lymphoid lineage.<sup>20</sup> This process is based primarily on classifying the disease using developmental features of normal maturing B and T lymphocytes. ALL is classified as precursor B-cell ALL or precursor T lymphoblastic leukaemia/lymphoma. Further sub-grouping of ALL is based on cytogenetic and molecular genetic abnormalities.<sup>5, 19</sup>

### Precursor B-cell ALL subgroups

All precursor B-cell neoplasms are placed in a single category under the WHO classification system. Precursor B-cell neoplasms are either bone marrow based (leukaemia) or lymph node or other organ based (lymphoma).

Precursor B-cell leukaemia is further divided into subgroups which include:<sup>5</sup>

- precursor B-cell ALL with MLL (HRX/ALL1) abnormalities
- acute lymphoblastic leukaemia with t (12;21) - TEL/AML1
- acute lymphoblastic leukaemia with t (1;19) - E2A/PBX1
- acute lymphoblastic leukaemia with t (9;22) - BCR/ABL (Philadelphia chromosome-positive ALL)
- hyperdiploid acute lymphoblastic leukaemia (greater than 50 chromosomes)
- diploid or near diploid acute lymphoblastic leukaemia (50 or fewer chromosomes) karyotype.

Children aged from one to five years old achieve the most favourable outcomes of those with precursor B-cell ALL, with children aged 10-14 doing the worst.<sup>21</sup>

### Precursor T lymphoblastic leukaemia/lymphoma

Precursor T lymphoblastic tumours constitute approximately 6-15% of paediatric lymphoblastic leukaemias<sup>22, 23</sup> and 85% to 90% of cases that present as lymphoblastic lymphoma.<sup>21</sup> Children who present with more than 25% blasts within their bone marrow are classified as having ALL, whereas those with less than 25% bone marrow involvement will be classified and treated as lymphoblastic lymphoma. Approximately 50% of children with T-cell ALL will present with a mediastinal mass, along with other organ site involvement.<sup>5</sup>

Immunophenotyping is required to distinguish precursor T-cell lymphoblasts from precursor B-cell lymphoblasts. While immunophenotypic classifications of T-cell ALL have been proposed, they are not universally used and do not correlate with recurring cytogenetic or molecular genetic abnormalities. Improved survival is, however, associated with abnormal karyotypes or with specific translocations, namely t (10;14)(p13;q11).<sup>5, 24</sup>

## Risk group classification of childhood ALL

### Risk group classification

In ALL prognostic factors such as age, white blood cell count and the presence of specific cytogenetic abnormalities at diagnosis are used for the initial stratification of children into risk groups. These factors are further subdivided based on clinical and laboratory features at diagnosis, leukemic cell characteristics, and response to initial treatment.<sup>8, 23</sup>

The National Cancer Institute risk group classification stratifies risk according to age and white blood count:<sup>25</sup>

- Standard risk – WBC count less than 50,000/ $\mu$ L and age 1 to younger than 10 years
- High risk – WBC count 50,000/ $\mu$ L and/or age 10 years or older

In Clinical Oncology Group (COG) trials, children with precursor B-cell ALL are initially assigned to a standard-risk or high-risk group based on age and initial WBC count. Children with T-cell phenotype are stratified as high risk regardless of age and initial WBC count. Early treatment response, assessed by day seven or day 14 marrow morphology and end-induction Minimal Residual Disease (MRD) studies, and cytogenetics are subsequently used to modify initial risk-group classification and determine the treatment pathway.<sup>8, 11</sup>

### Prognostic factors

Risk-based treatment assignment requires the availability of prognostic factors that reliably predict outcome. Individual characteristics affecting prognosis include:<sup>25</sup>

- Age at diagnosis
- WBC count at diagnosis
- Central nervous system (CNS) involvement at diagnosis
- Testicular involvement at diagnosis
- Down syndrome (trisomy 21)
- Gender
- Race

Leukaemic cell characteristics affecting prognosis include:<sup>25</sup>

- Morphology
- Immunophenotype
- Cytogenetics / genomic alterations

A summary of the implications of these prognostic characteristics can be found on the [National Cancer Institute website](#).<sup>25</sup>

Prognostic factors favourable for b-cell precursor ALL include:<sup>12, 23</sup>

- female
- Caucasian
- between two and 10 years old
- a white blood cell count less than 50,000/mm<sup>3</sup>
- absence of CNS disease
- common ALL antigen (CALLA) - positive, early pre B-cell
- FAB morphology (L1)
- hyperdiploid (50 chromosomes, DNA index greater than 1<sup>16</sup>; trisomies 4 and 10 and translocations t (12/21) (p21/q22)
- minimal leukaemia cell burden.

All childhood T cell ALL is generally considered to be at high or very high risk of poor prognosis, depending on the child's response to initial therapy.<sup>23</sup> For T cell ALL, age and leukocyte count have little

clinical significance, though a higher white cell count at diagnosis may warrant more intensive central nervous system- directed therapy for this group.<sup>23</sup>

Learning activities	
Completed	Activities
<input type="checkbox"/>	1 Describe the criteria used in classifying ALL, and the implications of these criteria for treatment planning and prognosis.
<input type="checkbox"/>	2 Describe what is meant by 'genetic translocation' and provide an example of its significance in childhood leukaemia.
<input type="checkbox"/>	3 Define 'early treatment response' and explain its significance in childhood leukaemia.
<input type="checkbox"/>	4 Identify resources which may assist people affected by childhood leukaemia to understand disease classifications.



## Treatment approaches for childhood ALL

Treatment for childhood ALL is based on the assigned risk group classification. Children who present with good prognostic indicators are treated on standard risk regimes which are less toxic than those required for children who are classified as high or very high risk.

The stratification of treatment is important to ensure the best chances of cure while limiting the significant potential long-term effects of treatment on normal growth and development. The duration of therapy for children with ALL ranges between two and three years.<sup>5</sup>

Successful treatment of children with ALL requires the control of systemic disease (e.g., marrow, liver and spleen, lymph nodes) as well as the prevention or treatment of extramedullary disease, particularly in the central nervous system (CNS).<sup>8</sup>

The aims of treatment for ALL are:<sup>11</sup>

- to induce a clinical and haematological remission
- to maintain remission by systemic antineoplastic agents and prophylactic CNS therapy
- to treat the complications of the disease and treatment.

Treatment protocols for childhood ALL are typically divided into:<sup>26</sup>

- Remission induction (at time of diagnosis)
- Post induction therapy (after achieving complete remission)
  - consolidation or intensification therapy (including CNS prophylactic therapy)
  - maintenance or continuation therapy

Learning activities	
Completed	Activities
<input type="checkbox"/>	1 Access <a href="#">Improving outcomes in children and young people with cancer</a> <sup>14</sup> , and summarise the evidence about the benefits of protocol-driven treatment.
<input type="checkbox"/>	2 Access the <a href="#">NCI Childhood Acute Lymphoblastic Leukaemia Treatment PDQ</a> <sup>9</sup> , and: <ul style="list-style-type: none"><li>• outline the role of central nervous system (CNS) therapy</li><li>• describe the nursing considerations associated with CNS therapy delivery</li><li>• outline the indications for haematopoietic stem cell transplantation.</li></ul>

## Cancer clinical trials and children

International clinical trials are used in the treatment of ALL. Many of these trials are conducted by COG and are designed to compare therapy that is currently accepted as standard for a particular risk group with a potentially better treatment approach that may improve survival outcome and/or diminish toxicities associated with the standard treatment regimen.<sup>27</sup>

The child with ALL has a high chance of being recommended for treatment within a clinical trial. Over 80% of children with cancer are enrolled in clinical trials, compared with less than 15% twenty years ago.<sup>28</sup>

A participant will be assigned to the control group, which receives the best standard treatment, or the experimental group which receives the new treatment being tested through a process of randomisation. Parents and carers need additional information and support to understand the aims of the trial and associated risks and benefits.<sup>27</sup>

There are likely to be benefits associated with being in a clinical trial and allocation to either the control group or the experimental group.<sup>27, 28</sup> This may be because individuals who take part in trials:<sup>27</sup>

- are fitter and better able to comply with treatment than people who aren't in trials
- get the best available treatment or treatment that may be better, as their treatments, tests and follow up abide by strict plans and guidelines
- receive extra personalised care and attention from their research nurses and treating doctors
- get extra information about their disease and treatment.

Learning activity	
Completed	Activity
<input type="checkbox"/>	1 Identify the standard treatment recommendations and possible clinical trials currently available for children with Pre-B ALL. <b>Resource</b> <a href="#">Australian Children's Cancer Clinical Trials Registry</a> <sup>29</sup>

### Case study

#### [Ellie's story 3: Clinical trials](#)



Learning activities	
Completed	Activities
<input type="checkbox"/>	2 Discuss the possible issues Ellie's parents might struggle with when deciding whether or not to enrol Ellie on the clinical trial.
<input type="checkbox"/>	3 Describe the role of the clinical trials nurse and the SCN in supporting Renee and Sean as they face these issues.
<input type="checkbox"/>	4 Describe how an SCN might respond to the concerns raised by Sean and Renee.

## Supportive care needs of the child with ALL

Treatment side effects are a major cause of morbidity, sometimes involving lengthy hospital admissions and intensive nursing, medical and allied health support.

Outcomes in cancer are dependent on the timely and effective management of the acute and longer-term side effects. Increased survival has been associated with improvements in supportive care.<sup>17</sup>

Supportive care considerations for the child with cancer include:<sup>12, 30</sup>

- education of the child and family
- psychosocial support for the child and family
- preparation of the child for procedures
- management of pain
- prevention and management of infection
- management of fever and neutropaenia
- management of nausea and vomiting
- nutritional support
- blood and blood product support
- monitoring and management of drug toxicity
- management and monitoring of effects of treatments
- management of oncological emergencies
- management of central venous access devices (CVADs)
- health promotion (dental care, immunisation)
- monitoring of long-term effects of treatment.

The SCN has a role in the prevention and management of these effects, teaching parents and carers to recognise symptoms so that appropriate health care can be implemented as soon as possible.<sup>31</sup>

Effective supportive care can facilitate timely discharge for ongoing care in the home environment and promote the health and wellbeing of those affected by childhood cancer.<sup>14</sup>

### Resource link

The [Leukaemia Foundation](#)<sup>32</sup> offers a number of different support services to people affected by leukaemias, lymphomas and related blood disorders. This includes practical support (like help with transport to and from treatment appointments), counselling, accommodation, and education programs.

## Learning activities

Completed

Activities

1 Identify the cytotoxic chemotherapy agents within the [Acute Lymphoblastic Leukaemia BFM 2000 Treatment Overview](#) (You will need to open a free account with EviQ to view this protocol)<sup>33</sup>

For each drug, outline:

- the mechanism of action of the drug and how it works at the level of the cell cycle
- the method of administration and associated precautions
- the areas of education required for the child and family
- the immediate, short-term, and long-term effects of each drug
- other supportive care considerations.

2 Summarise the nursing assessment and management of the febrile neutropaenic child.

3 Outline the advice you would give parents to prevent and/or manage the following key issues that may arise at home post treatment:

- febrile episode/infection
- nausea and vomiting
- bleeding.

4 Outline the indications for the following in blood and blood product administration for children:

- leukodepletion
- irradiation
- CMV negative blood products.

5 Develop a teaching session for a beginning registered nurse on administration of blood and blood products for a child with a haematological malignancy.

## Case study

### Ellie's story 4: Supportive care needs



## Learning activities

Completed

Activities

6

Ellie's mother Renee phoned the ward out of hours to inform nursing staff that Ellie had a temperature of 38.9° Celsius. Outline the questions you would ask Renee about Ellie's condition and the advice you would give.

7

Develop a policy for telephone triage for handling this type of situation.

8

Describe the nursing priorities for Ellie during this admission.

9

Outline strategies you would use to support the management of Ellie's post treatment care in her own environment.

## Supportive care needs during procedures

Treatment for childhood leukaemia may involve invasive procedures such as:<sup>12</sup>

- intravenous cannulation
- frequent blood tests
- regular accessing of CVADs
- intramuscular injections
- subcutaneous injections
- lumbar punctures
- bone marrow aspirations
- insertion of naso-gastric tubes
- naso-pharyngeal aspirates
- multiple oral drug administration.

Placement of a long-term CVAD facilitates delivery of antineoplastic agents, medications, total parenteral nutrition, blood and blood products and blood sampling. CVAD options include external tunneled catheters and implanted subcutaneous ports. The following factors may be considered when choosing a CVAD:<sup>34</sup>

- age of the child
- intensity of the therapy
- frequency of blood sampling
- bathing/activity limitations
- family ability to care for the catheter
- treatment protocol.

Procedures such as bone marrow aspirations and lumbar punctures are often performed under sedation or a short general anaesthetic. In some instances local anaesthetic or topical anaesthetic creams are used to reduce pain associated with venipunctures and injections.<sup>12</sup>

Studies indicate more than one half of all children with cancer experience moderate to severe cancer related pain.<sup>35</sup> One of the most distressing events for children is pain resulting from diagnostic procedures and treatments.<sup>36</sup>

Fear of the unknown in regards to treatment and procedures can develop into the fear of the known for the child with cancer. Interventions can include pharmacological and non-pharmacological strategies for the child and their family to reduce procedural distress.<sup>12</sup> These strategies should take account of the child's age, developmental stage, understanding of their situation and previous responses to stressful situations.

It is important to recognise that young children will often view non-invasive procedures such as imaging, radiological tests and radiation treatment as painful and may become distressed prior to and during these procedures. Issues such as lying still for prolonged periods, confined spaces and being separated from parents can also exacerbate this distress.<sup>12</sup>

## Learning Activities

Completed

Activities

Access the following documents:

- [Management of procedure-related pain in children and adolescents](#)<sup>37</sup>, The Royal Australasian College of Physicians (2006)
- [Psychological interventions for needle-related procedural pain and distress in children and adolescents](#)<sup>38</sup>, Uman, L.S. et al (2006)

1 Outline the key principles of pain management in children.

2 Identify pain assessment tools used within your care facility and compare them to tools within the NCCN guidelines.

3 Choose three commonly used analgesics in children and outline:

- indications
- dose range
- administration considerations
- adverse effects
- other nursing considerations.

4 Describe measures to prevent and manage the following effects of analgesics in children:

- constipation
- nausea
- sedation.

5 Outline the information and supportive care needs of the child and their family regarding pain management.

6 Identify the CVADs commonly used in your health care facility, and describe indications, advantages and disadvantages associated with their use in children.

## Case study

[Ellie's story 5: Support during procedures](#)



## Learning activities

Completed

Activities

7

Outline evidence based strategies to:

- prepare and support Ellie during the accessing of her CVAD
- support Ellie's parents during invasive procedures.



## Childhood development during the cancer journey

SCNs involved in caring for children receiving treatment for cancer need to be aware of normal developmental milestones, and how the child's experience of cancer can influence their well-being and development.

Unlike an adult, a child being treated for cancer is still growing, maturing and developing. Some developmental processes may be affected by anxiety, the disease, its treatment and subsequent side effects.

As treatment for many childhood cancers continues over a long period of time, it is important to ensure that the child's social and psychological development is supported. Families can be supported to promote development and assist their child to reach his or her developmental potential.<sup>39</sup>

Infants require sensory, motor and intellectual stimulation in order to promote cognitive, social and emotional development. As infants progress to toddlers they need support to develop independence and autonomy. Feeling secure, and adhering to routines and rituals, is important for the developing toddler.<sup>40</sup>

Preschool children are commonly described as magical thinkers and can have difficulty understanding abstract concepts such as illness. As children develop and enter school age they are more able to link concrete symptoms to bodily events, and are more likely to have a greater understanding of the impact of disease and treatment<sup>40</sup>

Learning activities	
Completed	Activities
<input type="checkbox"/>	1 Access a paediatric oncology text and describe the normal child development milestones that a diagnosis of cancer may impact.
<input type="checkbox"/>	2 Describe examples of how SCNs can help children reach their normal developmental milestones during treatment.
<input type="checkbox"/>	3 Outline recommendations you would make regarding attendance at a kindergarten or school for children during treatment.
<input type="checkbox"/>	4 Outline the advice you would provide to a carer asking about immunisation: <ul style="list-style-type: none"><li>• for the child receiving antineoplastic agents</li><li>• for the child's sibling.</li></ul>

## **Section 3: Have the best treatment and support between and after active treatment**

### **Objectives**

On completion of this section, you should be able to:

1. Explain the recommended follow up regimen post treatment for childhood ALL.
2. Identify long-term effects following treatment for childhood ALL.
3. Describe common health concerns of individuals after treatment for childhood ALL across all domains of health.
4. Implement evidence based interventions to promote optimal health across all domains for a person following treatment for childhood ALL.

## Follow up

Completion of treatment and transitioning to follow up care is a period of mixed emotion for many families. Families often establish relationships with other parents and members of the health care team during treatment, therefore finishing treatment may create a sense of significant loss. While most people affected by childhood cancer are happy that the treatment is over, they are also fearful of the future.

The early work on childhood survival by Koocher and O'Malley suggested that 'a metaphorical Sword of Damocles hangs by a single horsehair over the head of cancer survivors and shadows their lives ever after'.<sup>41</sup> This implied that the childhood cancer survivor's life is at all times overshadowed by the threat of cancer recurrence and ongoing negative consequences of the disease and its treatment.

Fear of relapse, secondary malignancy and the threat of the child's death are commonly reported fears by parents and, in some instances, the child. In addition, fears about the future such as returning to school, their ability to bear children, get married or get a job are other concerns for the child. Some children also worry about returning to the hospital for follow up tests and examinations.<sup>12</sup>

Common challenges experienced by the childhood cancer survivors include:<sup>42, 43</sup>

- Impact on growth, development and intellectual function
- Organ system impairment – cardiovascular disease, renal dysfunction, severe musculoskeletal problems and endocrinopathies
- The development of second cancers
- Psychosocial problems

Significantly, it has been found that the incidence of chronic health conditions increases over time and does not appear to plateau. This adds further evidence to support continued follow-up of survivors of childhood cancer and an emphasis on surveillance for chronic conditions.<sup>43</sup>

A summary of current studies in childhood survivorship proposes that:<sup>41</sup>

- some survivors of childhood cancer have managed to grow in positive ways as a result of their cancer experience
- most are relatively normal in psychosocial terms and on most psychosocial measures
- an important minority experiences on-going psychological and/or social adjustment problems
- all survivors, even those apparently doing quite well, continue to be concerned about the physical, psychological and social quality of their current and future lives.

While research has looked at the experience of survivorship from the perspective of the child with cancer, it is suggested that further work is required to appreciate the impact on parents and siblings. The health and well-being of the childhood cancer survivor is viewed as inextricably linked to the health and well-being of their parents and siblings.<sup>41</sup> This has implications for long-term supportive care strategies for survivors.

The role of the SCN in preparing and reassuring families that the child will be closely monitored while they are off treatment, and encouraging parents to ring or visit if they feel the need, is extremely valuable for families. Encouraging families to maintain social networks throughout treatment or re-establish links before completing treatment can minimise the sense of loss of relationships developed during treatment.

Follow up regimens are determined by the child's treatment protocol. Many protocols have an ongoing reporting requirement that continues for many years after the child has completed treatment. In some

instances a health related quality of life assessment is incorporated into the study, and continues for up to two years post completion of treatment.<sup>33</sup>

The need to provide appropriate and comprehensive follow up evaluation for this population is of paramount importance. While many tertiary institutions have established late effect services, the service delivery model of care varies at each institution. Variations will occur if the service is based at an adult hospital, paediatric hospital or in the community.<sup>5</sup>

Health professionals, the survivor or carer of the survivor need to have sufficient information relating to their diagnosis and treatment history to facilitate appropriate follow up and survivorship care.

### Key resource

Cancer Learning Cancer Survivorship Modules

### Learning activities

Completed	Activities
<input type="checkbox"/>	1 Describe practice examples of responses of children and their carers to completion of treatment, and discuss the strategies that were used to provide supportive care in light of current evidence.
<input type="checkbox"/>	2 Access the editorial by <a href="#">Zebrack and Zeltzer</a> , <sup>41</sup> and discuss how you perceive the Sword of Damocles - as a sword of doom or a sword survivors may wield for their own personal growth? Reflect on practice examples in your response.
<input type="checkbox"/>	3 Outline issues people affected by childhood cancer may face transitioning to adult care systems.
<input type="checkbox"/>	4 Discuss factors to consider in determining post treatment follow up for a child with ALL.

### Case study

[Ellie's story 6: Follow up](#)



### Learning activities

Completed	Activities
<input type="checkbox"/>	5 Discuss how the SCN can support the transition for Ellie from active treatment into the community following completion of treatment.
<input type="checkbox"/>	6 Outline strategies which can enable Renee and Sean to regain confidence in their ability to respond to their child's health related needs.

## Late effects of treatment in children

With improved cure rates for childhood malignancies, there are more childhood cancer survivors than ever before. This has led to a growing population of individuals with specific needs related to late effects of treatment.<sup>5, 44</sup> It has been reported that the improvements in survival can only be justified if the physical, emotional and social quality of life are also protected. A life-long trajectory of survival has been associated with cancer.<sup>41</sup>

It has been reported that two out of every three survivors will experience at least one late effect, and about one of four will experience a late effect that is severe or life threatening.<sup>5, 44</sup> Late effects can be physical or psychological and be related to the disease or its management. All organ systems can be involved in late effect complications, but psychosocial problems in the survivors and members of the family are more common.<sup>5</sup> Specific functional effects include:<sup>10, 45</sup>

- neurological
- endocrine
- hypothalamic-pituitary and thyroid
- gonadal
- hearing and vision
- dental, head and neck
- cardiac
- respiratory
- gastrointestinal
- hepatic
- genitourinary
- musculoskeletal
- haematopoietic/immunologic
- psychosocial
- second malignancies.

Survivors treated for bone cancer, central nervous system tumours and Hodgkin Lymphoma are at highest risk for late effects<sup>44</sup>. Late effects may not be recognised until years later when the child matures.<sup>5</sup>

The extent of any late effect from treatment will depend on the:<sup>45</sup>

- primary disease
- type and intensity of treatment
- radiation therapy and dose
- child's age at diagnosis
- child's physiological and developmental status at the time of diagnosis and treatment.

In a study assessing the health of survivors of childhood cancer diagnosed between 1970 and 1986, significant health problems were identified in this cohort 30 years after diagnosis:<sup>43</sup>

- Almost three quarters of survivors had a chronic health condition
- More than 40% of survivors had a serious health problem
- One third of survivors had multiple conditions
- Groups at highest risk of health problems were survivors of bone tumours, central nervous system tumours, and Hodgkin's disease

This increased risk of chronic health conditions in childhood cancer survivors has implications for ongoing health surveillance and promotion of self-management strategies.

## Learning activities

Completed

Activities

Access the following document to answer these learning activities:

- [Establishing and enhancing services for childhood cancer survivors: long-term follow up program resource guide](#)<sup>44</sup>

- 1 Outline the key components of a long-term follow up service for survivors of childhood cancer.
- 2 Complete the questions on page 8, Choosing a Model: Considerations. Based on these responses, develop recommendations to meet the long-term supportive care needs of people affected by childhood cancer in your health care region.
- 3 Critique existing treatment summary documentation in your health care facility in light of recommendations and templates provided in the resource guide above.

## Case study

[Ellie's story 7: Renee discusses the end of treatment](#)



## Learning activities

Completed

Activities

- 4 Access the [NCI Late Effects of Treatment for childhood Cancer \(PDQ\)](#)<sup>46</sup> and [Late effects of childhood cancer and treatment](#)<sup>47</sup>  
Describe the risk factors and the pathophysiological basis for the development of the late effects identified in Ellie's case.
- 5 Develop an SCN role description of a Late Effects Care Coordinator.
- 6 Outline the key points a Late Effects Care Coordinator may present to an adolescent group of childhood cancer survivors about the following:
  - self management
  - psychological/emotional care
  - educational opportunities
  - employment opportunities
  - body changes (such as growth)
  - fertility
  - looking forward.

## Childhood cancer relapse

The fear of relapse is present from the day of diagnosis for most families. When parents are advised that their child has relapsed they may experience the same or even more pronounced reactions than those they experienced at diagnosis. Relapse of the child's disease can occur either during treatment, immediately after treatment, or months to years following treatment.

When a child relapses, their long-term prognosis is dependent on the timing of the relapse. Relapses can occur as isolated occurrences in bone marrow, CNS or testicles.<sup>48</sup> Treatment options for a child who relapses shortly after therapy depends on many factors including prior treatment, whether the recurrence is medullary or extramedullary, and individual considerations. Options may include antineoplastic agents plus or minus haematopoietic stem cell transplantation.<sup>27</sup>

The prognosis for a child with ALL whose disease recurs depends on the time from diagnosis, site of relapse, and immunophenotype.<sup>27</sup> Relapse during treatment or immediately after the completion of treatment is associated with poorer prognosis. A relapse more than a year after treatment completion is associated with a better prognosis.<sup>27</sup>

The role of the SCN during relapse is to provide information and support for the child and family about the disease and treatment options. The family should be encouraged to discuss treatment decisions, including any plans to try unconventional treatments, with health professionals.

A key role of the MDT is to provide information about treatment options, to enable parents to make informed decisions. Maintaining open, honest communication between family members and health professionals is an important part of this process. Families need to know that the child will receive quality care, regardless of any decisions they make. Physical comfort must always be maintained and families should be encouraged to spend quality time with their child and plan positive, fun family activities.<sup>12</sup>

Learning activities	
Completed	Activities
<input type="checkbox"/>	1 Outline the signs and symptoms associated with relapse of ALL.
<input type="checkbox"/>	2 Describe the key supportive care needs of the child and the family affected by relapsed disease.
<input type="checkbox"/>	3 Access Treatment of Relapsed Childhood ALL <sup>49</sup> , and summarise treatment options for relapsed ALL.

## References for the paediatric acute lymphoblastic leukaemia (ALL) case based learning resource

1. Australian Institute of Health and Welfare and Australasian Association of Cancer Registries. *Cancer in Australia: an overview, 2010*. 2010 [cited Cancer series no. 60, Cat no. CAN 56; Available from: <http://www.aihw.gov.au/publication-detail/?id=6442472459>].
2. AIHW & AACR. *Cancer in Australia: an overview 2012*. 2012; Available from: <http://www.aihw.gov.au/publication-detail/?id=60129542359&tab=3>.
3. Australian Institute of Health and Welfare. *A picture of Australia's children 2012*. 2012; Available from: <http://www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=10737423340>.
4. Youlden, D., et al. *Childhood cancer in Australia, 1995-2004*. 2010; Available from: [/assets/edcan/files/Childhood\\_cancer\\_survival\\_in\\_Australia\\_1995-2004.pdf](/assets/edcan/files/Childhood_cancer_survival_in_Australia_1995-2004.pdf).
5. Pizzo, P.A. and D.G. Poplack, *Principles and practice of paediatric oncology*. 6th ed. 2011, Philadelphia: Lippincott Williams & Wilkins.
6. Australian Institute of Health and Welfare. *Australia's health 2014*. 2014; Available from: <http://www.aihw.gov.au/WorkArea/DownloadAsset.aspx?id=60129548150>.
7. Australian institute of Health and Welfare. *Australian cancer incidence and mortality books: all lymphoid cancers*. 2010 16.12.2011]; Available from: <https://www.aihw.gov.au/reports/cancer/acim-books/contents/acim-books>.
8. National Cancer Institute (NCI). *Childhood Acute Lymphoblastic Leukemia treatment (PDQ)*. 2011 20.12.11]; Available from: <http://www.cancer.gov/cancertopics/pdq/treatment/childALL/HealthProfessional/page1>.
9. National Cancer Institute. *Childhood Acute Lymphoblastic Leukemia Treatment (PDQ). General Information About Childhood Acute Lymphoblastic Leukemia (ALL)*. 2014 August 2014]; Available from: <http://www.cancer.gov/cancertopics/pdq/treatment/childALL/HealthProfessional>.
10. Robinson, M.J. and D.M. Robertson, *Practical paediatrics*. 6th ed. 2007, New York: Churchill Livingstone.
11. Lanzowsky, P., *Manual of pediatric hematology and oncology*. 5th ed. 2010, Tokyo: Elsevier Academic Press.
12. Hockenberry, M.J. and D. Wilson, *Wong's nursing care of infants and children*. 9th ed. 2011, Canada: Mosby Elsevier.
13. McGrath, P.N. and L. Pitcher, 'Enough is enough': qualitative findings on the impact of dexamethasone during reinduction/consolidation for paediatric acute lymphoblastic leukaemia. *Supp Care Cancer*, 10(2):146-55. *Supportive Care in Cancer*, 2002. **10**(2): p. 146-55.
14. National Collaborating Centre for Cancer. *Guidance on cancer services: improving outcomes in children and young people with cancer*. 2005 02.11.11]; Available from: <http://www.nice.org.uk/guidance/csgcyp>.
15. National Breast Cancer Centre and National Cancer Control Initiative. *Clinical practice guidelines for the psychosocial care of adults with cancer*. 2003 27/10/11]; Available from: [www.nhmrc.gov.au/files\\_nhmrc/file/publications/synopses/cp90.pdf](http://www.nhmrc.gov.au/files_nhmrc/file/publications/synopses/cp90.pdf)
16. MCGregor, L.M., et al., *Pediatric cancers in the new millenium: dramatic progress, new challenges*. *Oncology*, 2007. **21**(7): p. 809-820.
17. Cancer Council Australia. *Position statement: State and Territory travel and accommodation subsidy schemes*. 2004 02.11.11]; Available from: [http://www.cancer.org.au/content/pdf/CancerControlPolicy/PositionStatements/PS-Travel\\_and\\_accommodation\\_subsidy\\_schemes\\_Nov04.pdf](http://www.cancer.org.au/content/pdf/CancerControlPolicy/PositionStatements/PS-Travel_and_accommodation_subsidy_schemes_Nov04.pdf).



18. Kosaka, Y., et al., *Infant acute lymphoblastic leukaemia with MLL gene rearrangements: outcome following intensive chemotherapy and haematopoietic stem cell transplantation*. *Blood*, 2004. **104**(12): p. 3527-34.
19. Pieters, R., et al., *A treatment protocol for infants younger than 1 year with acute lymphoblastic leukaemia (Interfant-99): an observational study and a multicentre randomised trial*. *Lancet*, 2007. **370**(9583): p. 240-50.
20. Jaffe, E.S., et al., eds. *World Health Organization classification of tumours. Pathology and genetics of tumors of haematopoietic and lymphoid tissues*. 2001, IARC Press: Lyon, France.
21. Uckun, F.M., et al., *Biology and treatment of childhood T-lineage acute lymphoblastic leukemia*. *Blood*, 1998. **91**: p. 735-746.
22. Ballerini, P., et al., *Impact of genotype on survival of children with T-cell acute lymphoblastic leukemia treated according to the French protocol FRALLE-93: the effect of TLX3/HOX11L2 gene expression on outcome*. *Haematologica*, 2008. **93**(11): p. 1658-1665.
23. Pui, C.-H., et al., *Childhood and Adolescent Lymphoid and Myeloid Leukemia*. ASH Education Program Book, 2004. **2004**(1): p. 118-145.
24. Heerema, N.A., et al., *Prognostic impact of trisomies of chromosomes 10, 17, and 5 among children with acute lymphoblastic leukemia and high hyperdiploidy (> 50 chromosomes)*. *Journal of Clinical Oncology*, 2000. **18**(9): p. 1876-87.
25. National Cancer Institute. *Childhood Acute Lymphoblastic Leukemia Treatment (PDQ). Risk-based Treatment Assignment*. 2014 August 2014]; Available from: <http://www.cancer.gov/cancertopics/pdq/treatment/childALL/HealthProfessional/page2>.
26. National Cancer Institute. *Treatment Option Overview for Childhood ALL*. 2014 September 2014]; Available from: <http://www.cancer.gov/cancertopics/pdq/treatment/childALL/HealthProfessional/page3>.
27. National Cancer Institute (NCI). *Childhood Acute Lymphoblastic Leukemia Treatment (PDQ): General information about childhood Acute Lymphoblastic Leukaemia*. 2011 16.12.2011]; Available from: <http://www.cancer.gov/cancertopics/pdq/treatment/childALL/healthprofessional>.
28. Cancer Council New South Wales. *How clinical trials help people with cancer*. 02.11.11]; Available from: [/assets/edcan/files/CT%2BR\\_NSW\\_LR.pdf](/assets/edcan/files/CT%2BR_NSW_LR.pdf).
29. Group, A.a.N.Z.C.H.O. *Welcome to the Australian Children's Cancer Clinical Trial Registry*. 2009 September 2014]; Available from: <http://www.anzchog.org/clinical-trials-and-research/australian-children-s-cancer-clinical-trials-registry>.
30. Altman, A.J., ed. *Supportive care of children with cancer. Current therapy and guidelines from Children's Oncology Group*. 3rd ed. 2004, John Hopkins University Press: Baltimore.
31. Bryant, R., *Managing side effects of childhood cancer treatment*. *Journal of Pediatric Nursing*, 2003. **18**(2): p. 113-25.
32. Leukaemia Foundation. *Leukaemia Foundation home page*. 2008 23.12.2011]; Available from: <http://www.leukaemia.org.au/>.
33. EviQ: Acute Lymphoblastic Leukaemia BFM 2000 Treatment Overview. 2015; Available from: <https://www.eviq.org.au/Protocol/tabid/66/categoryid/436/id/570/Acute+Lymphoblastic+Leukaemia+BFM+2000+Treatment+Overview.aspx>.
34. Goes, C. and J. Ronan, *Central Venous Access*, in *Supportive Care of Children with Cancer: Current Therapy and Guidelines from the Children's Oncology Group*, A.J. Altman, Editor. 2004, The Johns Hopkins University Press: Baltimore.
35. Hockenberry, M.J., *Symptom management research in children with cancer*. *Journal of Pediatric Oncology Nursing*, 2004. **21**(3): p. 132-6.
36. Hedstrom, M., et al., *Distressing events for children and adolescents with cancer: child, parent and nurse perceptions*. *Journal of Pediatric Oncology Nursing*, 2003. **20**(3): p. 120-32.

37. Paediatrics and Child Health Division, T.R.A.C.o.P., *Executive Summary- Management of Procedure-related Pain in Children and Adolescents*. Journal of Paediatrics and Child Health, 2006. **42**(S1): p. S1-S2.
38. Uman, L.S., et al., *Psychological interventions for needle-related procedural pain and distress in children and adolescents*. Cochrane Database of Systematic Reviews, 2006(4).
39. Vessey, J.A. and D.J. Mebane, *Chronic conditions and childhood development*, in *Primary Care of the Child with a Chronic Condition*, P.L. Jackson and J.A. Vessey, Editors. 2000, Mosby: St Louis.
40. Langton, H., ed. *The child with cancer: family-centred care in practice*. 2000, Bailliere Tindall: Toronto.
41. Zebrack, B.J. and L.K. Zeltzer, *Living beyond the Sword of Damocles: surviving childhood cancer*. Expert Reviews in Anticancer Therapies, 2001. **1**(2): p. 163-164.
42. Bradwell, M., *Survivors of childhood cancer*. Paediatric Nursing, 2009. **21**(4): p. 21-24.
43. Oeffinger, K.C., et al., *Chronic Health Conditions in Adult Survivors of Childhood Cancer*. New England Journal of Medicine, 2006. **355**(15): p. 1572-1582.
44. Landier, W. and Children's Oncology Group Nursing Discipline Clinical Practice Subcommittee/Survivorship in collaboration with the Late Effects Committee. *Establishing and enhancing services for childhood cancer survivors: long-term follow up program resource guide*. 2007 02.11.11]; Available from: <http://www.survivorshipguidelines.org/pdf/LTFUResourceGuide.pdf>.
45. Bottomley, S.J. and E. Kassner, *Late effects of childhood cancer therapy*. Journal of Pediatric Nursing, 2003. **18**(2): p. 126-33.
46. National Cancer Institute (NCI). *Late effects of treatment for childhood cancer (PDQ): General information about late effects*. 2009 20.12.2011]; Available from: <http://www.cancer.gov/cancertopics/pdq/treatment/lateeffects/patient/page1>.
47. Shad, A.T. and N. Gossai. *Late effects of childhood cancer treatment*. 2012 September 2014]; Available from: <http://emedicine.medscape.com/article/990815-overview>.
48. Hagedorn, N., et al., *Submicroscopic bone marrow involvement in isolated extramedullary relapses in childhood acute lymphoblastic leukemia: a more precise definition of "isolated" and its possible clinical implications, a collaborative study of the Resistant Disease Committee of the International BFM study group*. Blood, 2007. **110**(12): p. 4022-9.
49. National Cancer Institute. *Treatment of Relapsed Childhood ALL*. 2014 September 2014]; Available from: <http://www.cancer.gov/cancertopics/pdq/treatment/childALL/HealthProfessional/page8>.
50. Australian Institute of Health and Welfare (AIHW) 2017. Australian Cancer Incidence and Mortality (ACIM) books: 2017. Canberra: AIHW. <https://www.aihw.gov.au/reports/cancer/acim-books/contents/acim-books>