

The role of psychoeducation in improving quality of life for children with leukaemia

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**Abstract**

Leukaemia is diagnosed in 500 children in the UK annually. Treatment takes up to 3 years, involves numerous medical procedures, unpleasant side effects and disruptions to family life. Many children develop long-term physical or psychological problems as a result of their treatment. With survival rates approaching 90% it is important to develop interventions which reduce the burdens of treatment and improve the child’s quality of survival. Psychoeducational interventions have been developed and evaluated for children with other chronic conditions. This thesis will explore the role they might play for children with leukaemia.

A narrative review of psychoeducational interventions delivered to children with cancer showed a lack of rigour in the literature which provides only weak evidence for a number of potentially useful approaches. A systematic review and meta-analysis of psychoeducational interventions (Study 1) found a lack of interventions for children with leukaemia, highlighting the need to develop psychoeducational interventions for this group. The meta-analysis found a differential effect for psychoeducation in different chronic conditions and a larger effect in younger children. The design of a novel psychoeducational intervention for children with leukaemia is then described. Children (aged 7-12 years) were taught about the pathophysiology of leukaemia and its treatment, in small group sessions, in 4 participating hospitals. Study 2 reported the effectiveness and acceptability of this intervention. The intervention resulted in improvements in child quality of life. Acceptability of the intervention was good, but recruitment was low, meaning the trial may have been underpowered to detect effects on the other measures. Recruitment difficulties are common in psychoeducational intervention studies and reduce the quality of the evidence base. Therefore, Study 3 reported the results of an interview study with non-participating families from the leukaemia intervention trial. Time and scheduling problems, lack of priority, lack of relevance and perceived negative impact were identified as barriers to recruitment. The implications for future psychoeducational interventions and research are discussed.

**Contents**

**Introduction……………………………………………………………………………………………1**

**Chapter 1: Leukaemia and its treatment…………………………………………………………5**

* 1. Description of leukaemia………………………………………………………………5
	2. Incidence………………………………………………………………………………..5
	3. Blood cell development………………………………………………………………..6
	4. Symptoms of leukaemia…………………………………………………………….....7
	5. Diagnosis………………………………………………………………………………..7
	6. Treatment………………………………………………………………………………..9
		1. Treatment for ALL………………………………………………………...11
		2. Treatment for AML…………………………………………………….….13
		3. Stem Cell Transplantation…………………………………………..……14
	7. Prognosis………………………………………………………………………….……15
	8. Side effects…………………………………………………………………………….16
	9. Relapse…………………………………………………………………………………17
	10. Late effects…………………………………………………………………………….18
	11. Psychological late effects…………………………………………………………….19
	12. Leukaemia as an acute and chronic illness………………………………………...21
	13. Summary……………………………………………………………………………….21

**Chapter 2: Information needs of children with leukaemia……………………………………23**

* 1. The ‘protective’ approach……………………………………………………………..24
	2. The ‘open’ approach…………………………………………………………………..25
	3. Incorporating open communication into clinical care………………………………26
	4. Factors involved in informing children……………………………………………….27
		1. The family context………………………………………………………..28
		2. The impact of age on cancer disclosure……………………………….28
	5. Communicating with healthcare providers………………………………………….30
	6. Unmet information needs in survivors……………………………………………….31
	7. Summary………………………………………………………………………………..32

**Chapter 3: A risk and resiliency model of adjustment to childhood cancer……………...34**

* 1. Adjustment to illness…………………………………………………………………..35
	2. Quality of Life as a measure of adjustment…………………………………………37
	3. The risk-resistance model…………………………………………………………….38
		1. Disease and disability factors…………………………………………...41
		2. Functional independence………………………………………………..42
		3. Psychosocial stress………………………………………………………43
		4. Intrapersonal factors………………………………………………………44
		5. Socio-ecological factors…………………………………………………..45
		6. Stress processing………………………………………………………….46
		7. Appropriateness of the model……………………………………………48
		8. Limitations of the model…………………………………………………..48
	4. A framework for intervening……………………………………………………………49
	5. Targets for psychoeducational interventions…………………………………………50
	6. Summary…………………………………………………………………………………52

**Chapter 4: Narrative review of psychoeducational interventions for children**

**with cancer………………………………………………………………………………..53**

* 1. Psychoeducation………………………………………………………………………..53
	2. Psychoeducational interventions delivered to children with cancer……………….55
	3. Coping skills interventions……………………………………………………………..56
		1. Coping skills for procedural distress…………………………………….56
		2. Coping skills for illness distress………………………………………….57
		3. Coping skills for survivors………………………………………………...57
	4. Social skills training……………………………………………………………………..58
	5. Knowledge and adherence interventions……………………………………………..59
		1. Interventions to reduce procedural distress…………………………….60
		2. Interventions to increase illness knowledge…………………………….60
	6. Health behaviour interventions………………………………………………………...61
		1. Health behaviour interventions during treatment……………………….62
		2. Health behaviour interventions for survivors……………………………62
		3. Health risk behaviour interventions for survivors………..……………..63
	7. Conclusions and methodological issues……………………………………………...63
	8. Summary…………………………………………………………………………………65

**Chapter 5: Psychoeducation for children with chronic conditions: a systematic review and meta-analysis…………………………………………………………………………………….82**

* 1. The role of meta-analysis in evidence-based practise………………………………83
	2. The comparative burdens of leukaemia and chronic illness………………………..84
	3. The role of psychoeducation in managing chronic illness…………………………..87
	4. Potential moderators of effect………………………………………………………….88
	5. Scope of the meta-analysis…………………………………………………………….89
	6. Methods…………………………………………………………………………………..90
		1. Literature search strategy…………………………………………………90
		2. Inclusion/exclusion criteria………………………………………………..92
		3. Data extraction and management………………………………………..92
		4. Risk of bias assessment…………………………………………………..93
		5. Data synthesis……………………………………………………………...93
	7. Results…………………………………………………………………………………...94
		1. Characteristics of included studies……………………………………….94
		2. Risk of bias assessment………………………………………………….101
		3. Analysis of effect sizes……………………………………………………102
		4. Moderator analyses……………………………………………………….103
	8. Discussion……………………………………………………………………………..104
	9. Limitations of the review……………………………………………………………...110
	10. Summary…………………………………………………………………………….111

**Chapter 6: Design of the leukaemia intervention and RCT evaluation study……………..112**

* 1. Complex interventions………………………………………………………………..112
	2. Background to the design of the intervention……………………………………. 114
	3. Design of the evaluation study………………………………………………………115
	4. Participants…………………………………………………………………………….116
	5. Procedure………………………………………………………………………………117
	6. Design of the intervention…………………………………………………………….119
	7. Outcome measures…………………………………………………………………...122
		1. Quality of life measures…………………………………………………..122
		2. Generic and illness-specific QoL measures……………………………122
		3. Child/parent-reported QoL measures…………………………………...123
		4. The Pediatric Quality of Life Inventory (PedsQl)……………………….124
		5. The generic PedsQl scale………………………………………………..124
		6. The cancer-specific PedsQl module…………………………………….125
		7. The child-reported PedsQl scales……………………………………….126
		8. Caregiver burden………………………………………………………….126
		9. The Strengths and Difficulties Questionnaire (SDQ)………………….127
		10. Child confidence…………………………………………………………..127
		11. Treatment-related anxiety………………………………………………..128
	8. Administration of the questionnaires………………………………………………129
	9. Quantitative analysis………………………………………………………………..129
	10. Qualitative analysis of the intervention…………………………………………..131
	11. Feasibility and acceptability……………………………………………………….132
	12. Summary…………………………………………………………………………….133

**Chapter 7: Evaluation of the leukaemia intervention………………………………………….134**

* 1. Results…………………………………………………………………………………134
	2. Results of the quantitative analysis…………………………………………………137
		1. Primary outcomes…………………………………………………………..137
		2. Secondary outcomes……………………………………………………….142
	3. Clinical improvements………………………………………………………………..153
	4. Qualitative evaluation of the intervention…………………………………………..154
		1. Child evaluation……………………………………………………………..155
		2. Parent evaluation……………………………………………………………157
	5. Discussion…………………………………………………………………………….160
	6. Limitations of the study………………………………………………………………166
	7. Summary………………………………………………………………………………166

**Chapter 8: Barriers to participation in the leukaemia intervention: a qualitative interview study with parents…………………………………………………………………………………..168**

* 1. Problems with recruitment into intervention studies………………………………168
	2. Barriers to participation in intervention studies…………………………………….169
	3. Methods………………………………………………………………………………..170
		1. Participants…………………………………………………………………..170
		2. Data collection……………………………………………………………….171
		3. Data analysis………………………………………………………………...171
	4. Results………………………………………………………………………………….172
	5. Discussion……………………………………………………………………………..178
		1. Mode of delivery of the intervention……….…………………….178
		2. Timing and relevance of the intervention……………………….181
		3. Psychological barriers to participation…………………………..183
	6. Limitations of the study……………………………………………………………….184
	7. Summary……………………………………………………………………………….185

**Chapter 9: General Discussion…………………………………………………………………….186**

* 1. Summary of findings………………………………………………………………….187
	2. Evidence for the effectiveness of psychoeducation for children with leukaemia……………………………………………………………………………….188
	3. Evidence for effective approaches in psychoeducation………………………….192
	4. Evidence for the effectiveness of the leukaemia intervention reported in this thesis…………………………………………………………………………………… 193
	5. Improving psychoeducational provision for children with leukaemia………….. 195
		1. The impact of age on psychoeducational provision…………...195
		2. Tailoring the content and timing of psychoeducation………….197
		3. Additional components……………………………………………200
	6. Addressing potential adverse effects……………………………………………….201
	7. Conclusions and suggestions for future research…………………………………203

**References…………………………………………………………………………………………….205**

**Appendices……………………………………………………………………………………………248**

 Appendix A: Lesson plans for the leukaemia intervention……………………………….248

 Appendix B: Questions used to measure child confidence (section 6.7.10) and treatment-related anxiety (section 6.7.11)…………………………………………………261

Appendix C: Parent and child qualitative questionnaires used to evaluate the workshop programme……………………………………………………………………………………264

Appendix D: Individual plots for parent-reported PedsQl (generic) total score and child-reported PedsQl (cancer) total score………………………………………………………269

Appendix E: Interview schedule for parent interviews exploring barriers to participation…………………………………………………………………………………...271

**List of Figures**

Figure 3.1 Risk-resistance framework of child adjustment to cancer…….……………………...40

Figure 3.2 Targets for interventions suggested by the risk-resistance framework….………….51

Figure 5.1 Web of science search strategy….……………………………………………………..91

Figure 5.2 PRISMA flow diagram showing screening and selection of included studies…………………………….………………………………………………….......95

Figure 5.3 Funnel plot of effect size (SMD) against standard error for studies in the meta-analysis…………………………………………………………………………………..101

Figure 5.4 Summary statistics, effect sizes and forest plot of studies in the meta-analysis…………………………………………………………………………………..102

Figure 6.1 Key elements in the development and evaluation of complex interventions for health…………………………………………………………………………………….114

Figure 7.1 Consort Flow Diagram for flow of participants through the study……………………135

Figure 7.2 Parent-reported PedsQl (generic) total mean scores plotted over time for the immediate and delay group……………………………………………………………138

Figure 7.3 Parent-reported SDQ (total difficulties mean scores) plotted over time for the immediate and delay group……………………………………………………………139

Figure 7.4 Parent-reported PedsQl (cancer) total mean scores plotted over time for the immediate and delay group……………………………………………………………142

Figure 7.5 Child-reported PedsQl (generic) total mean scores plotted over time for the immediate and delay group……………………………………………………………143

Figure 7.6 Child-reported PedsQl (cancer) total mean scores plotted over time for the immediate and delay group…………………………………………………………………………144

Figure 7.7 Parent-reported caregiver burden total mean scores plotted over time for the immediate and delay group……………………………………………………………145

Figure 7.8 Parent-reported child self-confidence total mean scores plotted over time for the immediate and delay group……………………………………………………………146

Figure 7.9 Parent-reported parent treatment anxiety total mean scores plotted over time for the immediate and delay group……………………………………………………………147

Figure 7.10 Parent-reported child treatment anxiety total mean scores plotted over time for the immediate and delay group…………………………………………………………..148

Figure 7.11 Child-reported treatment anxiety total mean scores plotted over time for the immediate and delay group……………………………………………………………149

**List of Tables**

Table 4.1 Coping skills interventions for children with cancer and survivors………….……....66

Table 4.2 Social skills interventions for children with cancer and survivors………….………..70

Table 4.3 Knowledge and adherence interventions for children with cancer……….………....72

Table 4.4 Health behaviour interventions for children with cancer and survivors….………….74

Table 4.5 Systematic reviews of psychoeducational and psychosocial interventions for children with cancer and survivors………………………………………………………….…………………78

Table 5.1 Characteristics of studies included in the meta-analysis………….…………….…….96

Table 6.1 Time flow though the study using study week…………………….…………….…….118

Table 6.2 Time flow through the study using timepoints…………………….…………….……..118

Table 6.3 Content of the four intervention workshops……………………….…………….……..120

Table 6.4 Components of the intervention and modifiable targets………………………….…..121

Table 7.1 Comparison of the baseline characteristics of the immediate and delay groups…………………………………………………………………………………………………136

Table 7.2 Characteristics of the recruited sample compared to general population and chronically ill samples……………………………………………………………………………….137

Table 7.3 Results of the multilevel modelling analysis on the primary outcomes…………….141

Table 7.4 Parameter estimates from the best fit models for the primary outcomes………….141

Table 7.5 Results of the multilevel modelling analysis on the secondary outcomes…………150

Table 7.6 Parameter estimates from the best fit models for the secondary outcomes……....152

Table 7.7 Effect sizes (Cohen’s d) for mean differences on the outcome scores at post-intervention for the immediate group with the delay group acting as control……………….…154

**Introduction**

Leukaemia is a cancer of the blood in which white blood cells divide uncontrollably without reaching maturity. These leukaemia cells block the development of healthy blood cells and cause symptoms which would be rapidly fatal without treatment. Childhood leukaemia is a relatively rare condition with 500 new cases recorded annually in the UK (Cancer Research UK, 2017).

 Treatment takes an extended period of time (up to 3 years) and involves protracted disruptions to family life, repeated hospitalisations and withdrawal from normal school and social activities (Eiser, 2004). Some aspects of treatment (e.g. medical procedures and adverse effects of medication) can be distressing, while side effects can make the child feel extremely unwell. The treatment can also lead to physical and psychological late effects which impact children’s health and well-being many years after treatment ends (Children with Cancer, 2019; Ness et al., 2011). Children treated for leukaemia also have lifelong vulnerabilities to developing secondary malignancies and chronic illnesses (e.g. diabetes and heart problems), which require them to adopt positive health behaviours and continued health screening/monitoring into adulthood (Ness et al., 2011).

Survival rates for childhood leukaemia have improved significantly since the 1970s, as a result of improvements in treatment and supportive care, and now approach 90% for some forms of the illness (Children with Cancer, 2019). This means that the population of children who are surviving leukaemia is growing every year. However, these improvements in treatment often lead to worse side effects and greater long-term health and psychosocial problems (Wang et al., 2016). Minimising the burdens associated with treatment and optimising the quality of survival is essential to improving the outcomes for this substantial group of children and adults.

Childhood leukaemia is a complex condition which many families know little about when their child is diagnosed (Clarke et al., 2005). To add to this uncertainty, the prognosis and exact course of treatment are not known in the early stages. Many children will respond well to treatment, some children will need more intensive treatments, some will relapse, and some children will die. It is not possible to know the child’s outcomes, which side effects the child will experience or whether they will develop long-term physical problems when they are diagnosed. The reason why a child develops leukaemia is also rarely known (Inaba et al., 2013; Pui et al., 2008; Wang et al., 2016). This makes leukaemia a difficult illness to understand and to communicate about, for parents and doctors.

Previous research on how to improve this process of communicating with children has been unable to recommend particular approaches (Ranmal et al., 2008). Even though research shows that open communication with health professionals and within families leads to better outcomes for children, there have been few recommendations for how to support this process. Psychoeducation may be an important method of informing children with leukaemia about their illness which could be explored through developing and evaluating interventions.

This thesis explores the role of psychoeducation in improving quality of life for children with leukaemia by reducing treatment-related burdens. It draws on a risk and resiliency framework for intervening, which involves reducing risk factors involved with poor psychosocial outcomes and increasing resiliency factors which help the child to adjust to their illness.

This evaluation of psychoeducation includes reviews of the existing literature and a detailed evaluation of a novel psychoeducational intervention for children with leukaemia. The thesis will follow Medical Research Council guidelines for evaluating complex interventions (Craig et al., 2008). These guidelines address the challenges of assessing the efficacy of complex interventions, what the best methods are for delivering them and identifying processes of change.

The intervention which is reported in this thesis was originally developed and piloted at Manchester Children’s Hospital by Deema Hussein and Dr Guy Makin. The implementation and evaluation of the intervention was part of an NIHR project which ran between 2012 and 2016 in 4 hospitals. I taught all of the workshops at each of the participating hospitals. All of the data was also collected and analysed by me as part of this thesis.

This is the first time a group psychoeducational intervention to teach children with leukaemia about their illness has been evaluated. A risk and resiliency theory, which highlights potential processes of change, is provided as a framework on which to interpret the components of the intervention. It was not used to develop the intervention. The general discussion will examine whether this risk and resiliency framework was an appropriate model for evaluating this intervention.

 This thesis aimed to explore the potential for psychoeducation to improve quality of life for children with leukaemia by answering the following questions:

1. What is the evidence that psychoeducation is effective for children with leukaemia and is there evidence to support particular approaches?
2. Is the specific psychoeducational intervention described and evaluated in this thesis effective in improving the quality of life of children with leukaemia?
3. What are the barriers to participation associated with recruitment to this psychoeducational intervention and how could these barriers be overcome in future interventions?

To answer these questions required a mixed methods approach. The empirical work included a meta-analysis of existing psychoeducational interventions to assess the efficacy of psychoeducation and explore moderators of effect. The evaluation study of the leukaemia intervention was a randomised controlled trial, using quantitative multi-level modelling of outcomes and a qualitative acceptability analysis. Finally, a qualitative interview study explored in detail the perspectives of a sample of parents who chose not to participate in the leukaemia intervention. This study explored barriers to participation which may be useful for developing and implementing psychoeducational interventions in the future.

**Chapter 1**

**Leukaemia and its treatment**

This chapter will describe the pathophysiology of leukaemia, its treatment, side effects and potential long-term effects on children. It will demonstrate the considerable burdens faced by children with leukaemia and their families, and the potential for treatment to lead to significant distress. For some children, the burdens and distress of treatment will lead to long-term physical and psychological problems. This can have consequences for the child’s health and well-being many years after their treatment ends. Therefore, it is important to identify treatment-related burdens and explore interventions which can reduce their impact.

* 1. **Description of leukaemia**

 Leukaemia is a cancer of the blood in which the white blood cells divide uncontrollably without reaching maturity (Clarke et al., 2016). The two most common types of childhood leukaemia affect different white blood cells: Acute Lymphoblastic Leukaemia (ALL) affects the lymphocytic cells and Acute Myeloid Leukaemia (AML) affects the myeloid cells. Treatment takes 2-3 years for ALL and up to 6 months for AML. ALL and AML make up approximately 95% of childhood leukaemias (Children with Cancer, 2019). Adult leukaemias are treated very differently to childhood leukaemias. Rare chronic forms of childhood leukaemia sometimes occur (e.g. Chronic Myeloid Leukaemia) and are also treated very differently. This thesis refers to the treatment of children with ALL and AML.

* 1. **Incidence**

Cancer is relatively rare in children, making up less than 1% of the total annual cancer cases in the UK. Nevertheless, 1 in every 500 children will be diagnosed with cancer before they are 14 years old (Cancer Research UK, 2019). There were 1,859 new cases of childhood cancer each year (on average) between 2014-2016 in the UK (Cancer Research UK, 2019). Around one third of these cancers (approximately 500 cases per year) were leukaemia, making it the most common childhood cancer (Cancer Research UK, 2019). Acute Lymphoblastic Leukaemia (ALL) makes up approximately 80% of these cases (about 400 per year) and Acute Myeloid Leukaemia (AML) makes up approximately 15% of cases (about 80 cases per year) (Cancer Research UK, 2019). Almost all cases of leukaemia in children are acute which means that the symptoms appear suddenly and progress rapidly.

More than half of all leukaemia cases are diagnosed in children under 5 years old (Connor, 2016). The peak incidence for ALL is between 1-4 years old and the peak incidence for AML is in children under 2 years, with another peak in adolescence (Connor, 2016; Redaelli et al., 2005). Boys have a slightly higher risk of developing leukaemia than girls, with a ratio of 5:4 for AML and 4:3 in ALL (Children with cancer, 2019).

* 1. **Blood cell development**

Leukaemia occurs when normal blood cell development stops working properly. This can happen at a number of different stages in blood cell production (Jin et al., 2017). Blood cells (red blood cells, white blood cells and platelets) develop from stem cells in the bone marrow through a process of division and differentiation. The red blood cells carry oxygen around the body and are the most abundant blood cell, making up approximately 45% of the blood by volume. Platelets (thrombocytes) are involved in blood clotting and prevent excessive blood loss. ALL develops when the lymphoid progenitor cells do not differentiate into mature lymphocytic white blood cells (natural killer cells, T cells or B cells) (Erber, 2010). The lymphocytic cells produce antibodies in response to infections which produces the body’s immunity to diseases such as chicken pox or measles. AML develops when the myeloid progenitor cells do not differentiate into mature granulocytic white blood cells (neutrophils, basophils, eosinophils and monocytes) (Erber, 2010). Granulocytes respond to ‘foreign agents’ (such as parasites or bacteria) in the body by releasing chemicals which kill or ingest them. The immature white blood cells (leukaemia cells) are referred to as ‘blasts’ (lymphoblasts and myeloblasts).

In leukaemia, genetic changes occur in the DNA of one of the progenitor blood cells during development. What causes these changes is not fully understood although it is likely to include both genetic and environmental factors. The changes cause the immature blast cells to divide uncontrollably without maturing into fully developed cells. These blasts build up in the bone marrow and prevent the production of healthy white and red blood cells and platelets (Erber, 2010; Mitchell et al., 2009).

* 1. **Symptoms of leukaemia**

Symptoms of leukaemia are caused by low levels of healthy blood cells and a build-up of blast cells in different parts of the body. Children with leukaemia often have high white blood cell counts but because the blasts are immature they cannot effectively fight disease. Frequent infections and high temperatures are one of the more recognisable indicators of leukaemia. A lack of red blood cells can cause anaemia which presents as tiredness, pale skin, shortness of breath and headaches. A lack of platelets can cause excessive bleeding (e.g. nosebleeds, bleeding gums), bruising and petechiae (dark red spots on the skin, often appearing as a rash). Other symptoms of leukaemia include swollen lymph nodes, bone or joint pain (caused by blast cells accumulating around bones and joints) and swelling of the abdomen (caused by leukaemia cells accumulating in the liver and spleen) (American Cancer Society, 2017; NHS, UK, 2017). More rarely, when the leukaemia cells have already spread to the central nervous system, children can experience severe headaches, dizziness and seizures (Mitchell et al., 2009).

* 1. **Diagnosis**

Leukaemia is often difficult to diagnose because many of its initial symptoms are similar to common viral conditions such as cold and flu. Families often make repeated visits to doctors before leukaemia is diagnosed (Connor, 2016). A systematic review described 95 presenting signs and symptoms of childhood leukaemia with five features present in over half of cases (e.g. hepatomegaly (enlarged liver), 64%; splenomegaly (enlarged spleen), 61%; pallor (pale skin), 54%; fever, 53%; bruising, 52%) and eight features present in over a third of cases (e.g. recurrent infections, 49%; fatigue, 46%; limb pain, 43%; rash, 35%) (Clarke et al., 2016).

Diagnosing leukaemia requires a number of invasive tests. Clinical examinations include a thorough examination of the abdomen, lymph nodes and skin, followed by blood tests (Connor, 2016). Tests may reveal low levels of mature white blood cells and high levels of blast cells in the blood. However, blasts are not always visible in the blood and a more accurate indicator of leukaemia comes from sampling the bone marrow. Bone marrow aspirations involve taking a sample of marrow from a large bone, such as the pelvis. This procedure is usually carried out under general anaesthetic to reduce distress to the child (Mitchell et al., 2009).

Blood and bone marrow tests are carried out in specialist medical centres where haematologists identify the exact type of leukaemia and the genetic changes within individual cells. A lumbar puncture will be carried out to test for leukaemia cells in the cerebrospinal fluid. This involves inserting a needle into the spine and drawing out a few drops of fluid. This is usually done under general anaesthetic. Children may also be X-rayed using Computerised Tomography (CT) scanning to investigate whether leukaemia cells have spread to other parts of the body (Mitchell et al., 2009).

The results of these tests will be considered alongside other characteristics of the child (e.g. age, gender) to allocate a level of risk and determine the child’s initial treatment regimen (Connor, 2016; Zwaan et al., 2015). Approximately 40% children diagnosed with ALL fall into a low risk group. Low risk is associated with a lower white blood cell count at diagnosis, no spread to organs outside the bone marrow and a fast response to treatment. Approximately 51% children are classed as standard risk and 9% as high risk. Higher risk regimens use more intensive chemotherapy treatments and may include other procedures (e.g. Stem Cell Transplant) (Mitchell et al., 2009; Redaelli et al., 2005).

Parents often have a limited understanding of leukaemia when they receive the diagnosis and many fear their child will die (Clarke et al., 2005). Although survival rates have increased to around 90% for some types of ALL, doctors cannot guarantee at this point that the child will survive or predict which side or late effects they might develop due to treatment (Inaba et al., 2013; Pui et al., 2012). As doctors need to explain potential side and late effects as part of gaining informed consent from families, the initial information given around diagnosis can seem overwhelming (Dobrozsi et al, 2019). Parents are likely to experience a great deal of uncertainty about their child’s prognosis and future outcomes. Higher levels of illness uncertainty have been reported to predict greater anxiety and depression in parents of children with cancer (Grootenhuis & Last, 1997) and adolescents with cancer (Neville, 1998).

* 1. **Treatment**

Children are admitted to hospital immediately to begin treatment as leukaemia would otherwise progress rapidly and lead to death (Berg, 2000). This is often a very difficult time for families who must adjust to having a very sick child and adapt family and work responsibilities to having a child in hospital. They may need to give up work which will have financial consequences and may have less time to spend with other children (Eiser, 2004). Having a child in hospital can also mean a lot of travel for families who do not live near to the specialist medical unit. Children with ALL are usually in hospital for around 3-8 weeks initially. The remaining treatment takes 2-3 years and is mostly carried out on an out-patient basis. Treatment for AML takes up to six months and is carried out entirely in the hospital. While they are in hospital children with ALL and AML will miss out on nursery or schooling, and their normal social activities. This can affect future academic performance, social development and lead to feelings of social isolation (Earle & Eiser, 2007).

Treatment involves a number of invasive procedures (such as lumbar punctures, blood tests, catheter insertions) which have been shown to contribute to stress, anxiety and painful memories in parents and children (Barbi et al., 2005; Kazak et al., 2004). The main form of treatment for leukaemia is chemotherapy, which destroys the blast cells and restores normal blood cell production. A combination of chemotherapy drugs and steroids are given in series of stages (Inaba et al., 2013). Chemotherapy drugs are usually administered through a central or peripheral venous catheter which remains in place throughout the initial phases of treatment (Hickman/PICC line). This is a thin plastic tube, inserted into a vein (either in the chest or arm) under general anaesthetic, which allows drugs to be administered without the need to inject into a new vein each time. There are some additional care requirements involved with the line, including keeping it dry while washing, watching out for blockages and keeping it clean to avoid infections (Macmillan, 2017).

Children also receive intrathecal chemotherapy under general anaesthetic, in which drugs are delivered directly into the cerebrospinal fluid, to prevent central nervous system (CNS) relapse. The CNS is a common relapse site because chemotherapy drugs do not effectively cross the blood-brain barrier. When this was recognised in the 1970s it led to the universal use of cranial irradiation to treat leukaemia. However, cranial irradiation is associated with a much greater risk of long-term complications such as neurocognitive impairments and secondary cancers (Vora et al., 2016). Intrathecal chemotherapy has since reduced the risk of CNS relapse considerably (Cooper & Brown, 2015; Pui et al., 1998; Pui et al., 2015) and cranial irradiation is now reserved for very high-risk cases only (Vora et al., 2016). Intrathecal delivery can lead to complications in some cases, including headaches, backache and nausea but these are usually mild and temporary (Keidan et al., 2015).

* + 1. **Treatment for ALL**

The initial hospital stay for children with ALL is between three weeks to two months depending on the child’s side effects and response to treatment. Children then attend regularly for further blocks of chemotherapy but can usually go home between treatments. They will be immunocompromised during this time and may need to be readmitted to hospital if they show signs of having an infection (parents are told to ring the hospital if their child’s temperature goes above 38 degrees Celsius). The treatment for ALL proceeds in three stages (Inaba et al., 2013):

**Induction:** The first stage of chemotherapy uses a combination of chemotherapy drugs to achieve remission where over 95% of the leukaemia cells have been destroyed and normal blood cell development has resumed. This stage is carried out in the hospital. Combinations of chemotherapy drugs are used to minimise the chances of developing drug resistance (Cooper & Brown, 2015). Induction takes between 3-6 weeks depending on how long it takes for the child to respond to treatment and is successful in over 95% of children. The remission rate is 99% in standard and low risk ALL and 88% in high risk ALL (Redaelli et al., 2005). Of the 5% for whom the initial treatment fails, half will die from treatment-related mortality (Cooper & Brown, 2015). Children who do not achieve remission at induction stage can be moved earlier into the consolidation/intensification stage of treatment or offered a stem cell transplant (SCT) (Bhojwani et al., 2009).

During induction the drugs used in chemotherapy are likely to damage healthy white and red blood cells making children less able to fight infections. Many children require preventative antibiotics or medication to prevent fungal infections. Some require blood transfusions to improve levels of red blood cells and platelets. Corticosteroids (steroids) are used to increase appetite, reduce nausea and reduce allergic reactions to the chemotherapy drugs. Current treatment regimes use high-dose Dexamethasone given for up to one month during induction and then once a month for a week until the end of the treatment period (Adams et al., 2016).

**Consolidation/intensification:** In order to entirely eradicate any remaining leukaemia cells, the child will have further blocks of chemotherapy. The drugs used and doses will be adjusted according to how easily remission was achieved in induction. Usually consolidation is done on an out-patient basis but there are more intensive protocols which require hospital-care (Cooper & Brown, 2015). Standard treatment lasts between 6-9 months and involves two further blocks of chemotherapy, often using drugs which were not used in induction (Cooper & Brown, 2015). Time is left between blocks to allow the child’s body to recover and to reduce the risk of developing treatment-related complications. Once the child’s remission is sustained they can enter the maintenance stage of treatment.

**Maintenance therapy:** Maintenance is the longest stage of ALL treatment and aims to prevent relapse once remission has been established (Cooper & Brown, 2015). Prolonged maintenance therapy has shown the greatest benefit for children with all forms of ALL (Redaelli et al., 2005). Males have a greater risk of relapse and require three years of treatment following diagnosis while females require two years (Mitchell et al., 2009). During maintenance, children take chemotherapy drugs orally at home and have monthly injections of chemotherapy drugs in the hospital (Cooper & Brown, 2015; Ness et al., 2011). This stage is carried out on an out-patient basis. Adherence to medication is very important at this stage as even low levels of non-adherence (adherence below 95%) can increase the risk of relapse (Bhatia et al., 2012; Rabin, 2017).

During maintenance the child is usually well enough to return to school although they may have visible side effects from their treatment (including weight changes and hair loss). Chemotherapy and steroids can also affect the child’s ability to remember, concentrate and moderate their behaviour (Buizer et al., 2009). Children are likely to be immuno-compromised from continued chemotherapy and may miss additional school time because of illnesses and hospital appointments. Children will be monitored during and after maintenance treatment to check for signs of relapse and to assess potential long-term complications from treatment (e.g. cardiac or bone/joint problems) (Children’s Oncology Group, 2019).

* + 1. **Treatment for AML**

Length of treatment for AML is shorter than for ALL; usually around six months (Children with Cancer, 2019). Treatment is carried out entirely in the hospital as the chemotherapy drugs used are more intense and leave the child severely immuno-compromised. Intensive chemotherapy is carried out over four or five courses and is associated with a high risk of severe, short and long-term toxicities (Zwaan et al., 2015), including cardiac failure, other organ failure and haemorrhage (Maude et al., 2014; Riley et al., 1999). The main cause of death during treatment for AML is infection, with more intensive treatments increasing the risk (Sung et al., 2009).

**Induction and consolidation:** The drugs used in the induction and consolidation phase of treatment for AML are equally intensive although they may be altered according to response to treatment (Rubnitz, 2017). The child will initially be given one or two blocks of high dose myelosuppressive drugs over a few days with an interval of 1-2 weeks in between. Intrathecal chemotherapy will also be given after each block to administer the drugs directly into the spinal fluid. Remission is assessed after these two blocks of chemotherapy (classified as recovery of normal haematopoesis, with less than 5% blasts in the bone marrow) (Rubnitz, 2017). Using response to treatment and information about the type of AML the child has, they will be assessed for risk of relapse. High-risk children or those who relapse in this initial period are likely to be offered an early stem cell transplant (Zwaan et al., 2015). Low-risk children receive less intensive chemotherapy drugs to reduce the risk of toxicity. There is no maintenance phase in the treatment of AML as it has not been shown to confer any benefit (Zwaan et al., 2015). Once chemotherapy is complete the child will need to be monitored for relapse over a number of years. Children may be offered a stem cell transplant if they do not respond to chemotherapy or relapse early. They may also have cranial irradiation if the leukaemia invades the central nervous system.

* + 1. **Stem Cell Transplantation (SCT)**

Stem cell transplantation is not routinely used in children with leukaemia as it is a risky procedure, with higher risk of fatal infections and toxicity from intense chemotherapy drugs (Leung et al., 2011) and is reserved for children who are at a high risk of relapse (Hochberg et al., 2013; Leung et al., 2011; Rubnitz, 2017). Before transplantation the child’s bone marrow cells are destroyed using high dose chemotherapy or total body irradiation. The child then receives a transplantation of stem cells from a matched donor which restarts the process of haematopoesis in the child’s bone marrow (Hochberg et al., 2013). The transplant is delivered via a central line into the bloodstream. Before the child’s blood system recovers they are extremely susceptible to infection and will be nursed in a controlled environment (an isolation ward with filtered air and barrier nursing). They will also need blood transfusions to replace red blood cells. It takes 2-4 weeks until there are enough white blood cells to fight infection (during which time the child stays in isolation) and up to six months before they can fight off a major infection (during which time they will be monitored but can normally return home).

As well as causing a range of side effects including hair loss, nausea, diarrhoea and inflammation of the lining of the mouth, SCTs can lead to long-term issues including infertility, hypothyroidism, diabetes, osteoporosis and neurosensory impairments (Baker et al., 2010). SCTs increase the risk of mortality for a number of years after transplantation due to late relapse, rejection of the transplanted cells, prolonged immunodeficiency and secondary malignancies (Socie et al., 1999).

* 1. **Prognosis**

Until the development of combination chemotherapy in the late 1960s and 1970s the prognosis for children diagnosed with leukaemia was very poor. Leukaemia was seen as an incurable disease and the emphasis was on palliative care for the child (Chesler et al., 1986; Chesler & Barbarin, 1987). Between 1966-1970 leukaemia had a 5-year survival rate of 9%, which rose to 61% between 1981-85 (Cancer research UK, 2017) and 79% between 1996-2000 (Shah et al., 2008). The 5-year survival rate for children diagnosed with leukaemia has now risen to more than 80%. Children with ALL have the best prognosis with survival rates at around 90% (Hunger et al., 2012; Pui et al., 2015). The 5-year survival rate for AML is lower at around 60-65% (Berbis et al., 2013; Rubnitz, 2017). Survival could also be considered in terms of an overall ‘cure’ rate which is defined as the point at which there is no excess mortality which can be assigned to the disease or treatment (Shah et al., 2008). However, with increasing survival rates, ‘time to cure’ has also risen dramatically. There was an average annual increase of 0.3 years which resulted in an average ‘time to cure’ of 19 years by 2008 (Shah et al., 2008). This increase is due to treating late relapses, secondary malignancies and toxicity related to chemotherapy. Because of the extended period of mortality associated with leukaemia treatment it can be difficult to assess long-term cure rates which is why 5-year survival rates are commonly used.

Improvements in survival rates since the 1980s have occurred through intensifying drug regimes, improvements in risk classification, monitoring the response to chemotherapy, and improvements in supportive care (Rubnitz, 2017). This means there are now an increasing number of adults who are survivors of childhood leukaemia (Ness et al., 2011). However, for some children, leukaemia is still a life-limiting condition (Rubnitz, 2017). Children with ALL who have induction failure have a 33% survival rate. This group makes up around 3-5% of total ALL cases (Cooper & Brown, 2015). Children with AML who have adverse genetic features and poor response to treatment, have a survival rate of less than 20% even with a SCT (Mitchell et al., 2009). Deaths occurring during treatment often result from haemorrhage or infection and are more common in AML due to the intensity of treatment (Slats et al., 2005).

To reduce mortality from infection, children are treated with preventative medicine in hospital and parents monitor the child’s temperature at home, bringing them back into hospital at the first sign of an infection. Neutropenic sepsis (an overwhelming infection) can quickly lead to multi-organ failure. In cases of high temperature children will be prescribed broad spectrum antibiotics and will remain in hospital until their temperature drops (Mitchell et al., 2009).

* 1. **Side effects**

The drugs used in chemotherapy cause a number of side effects because they also damage healthy cells and tissues. Almost all children treated for leukaemia will suffer from some side effects. Treatment regimens aim to reduce this damage as much as possible by targeting drugs according to risk, meaning that high-risk patients are more likely to suffer severe side effects (Pui et al., 2015; Zwaan et al., 2015). The cells most affected by chemotherapy are rapidly dividing cells such as the hair or lining of the stomach so many children experience hair loss, nausea, loss of appetite and diarrhoea. Some side effects (such as hair loss and weight changes) may alter the child’s physical appearance and affect their body image and self-esteem. Chemotherapy also destroys healthy blood cells so children may suffer from anaemia, fatigue, bruising and bleeding and reduced resistance to infections. Skeletal complications, including fractures and osteonecrosis (damage to the bone caused by disruption of blood supply) often start during maintenance treatment (Högler et al., 2007). In a review, up to 13% children with leukaemia presented with osteopenia (lowered bone density) at diagnosis and this rose to 83% within 24 months (Davies et al., 2005).

 The steroids used in leukaemia have side effects such as hyperglycaemia (high blood sugar), hypertension (high blood pressure), mood changes, impaired cognitive function, acne, increased appetite and osteoporosis (Adams et al., 2016; Redaelli et al., 2005). Steroid treatment is associated with internalising (e.g. withdrawal, anxiety and depression) and externalising behaviour problems (e.g. delinquency and aggression) (Liu et al., 2018; Reinfjell et al., 2009). Steroids can affect the child’s ability to sleep and in rare cases can cause steroid-induced psychosis. In some cases, the side effects of steroids are so bad that they are stopped even though this can impact the outcome of treatment (Warris et al., 2016). The mood and behaviour changes associated with steroids (e.g. anxiety, depression, aggression) can have a significant impact on family life as parents may not be able to ‘parent’ or discipline their child as they usually would (Williams & McCarthy, 2015). Parents have reported anxiety in relation to changing parental roles (Willingham-Piersol et al., 2008).

* 1. **Relapse**

Relapse occurs when the leukaemia cells return after initial remission. This can occur early in treatment or after the whole process of treatment has been completed. Around a quarter of children treated for leukaemia will relapse (Abrahamsson et al., 2011; Hunger et al., 2012; Nguyen et al., 2008; Tierens et al., 2016). A relapse rate of 15-20% for ALL has been reported with one third of these going on to have a second relapse (Oskarsson et al., 2016). A relapse rate of 30% has been reported for AML, with only one third of these children going on to be cured (Sander et al., 2010). Relapses are extremely distressing for families as they increase the period and intensity of treatment and reduce the chances of survival considerably. Fear of relapse is a significant stress for families during and after treatment. As most children who relapse will do so in the first two years (Locatelli et al., 2012), this may lessen over time. However, anxiety associated with the possibility of relapse has been reported in survivors many decades after treatment (Zebrack, 2000).

Time from diagnosis is the best predictor of survival rates for relapsed leukaemia. Children who relapse within 18 months have a worse prognosis than those who relapse later (21% 5-year survival in early relapsed ALL) (Nguyen et al., 2008). The relapse rate for children who have a stem cell transplant is between 20-40% and there is only a 5% 1-year survival rate for those who relapse within six months (Haro et al., 2016).

* 1. **Late effects**

Many of the side effects of treatment for leukaemia are temporary. Hair grows back within a few months of treatment, mood changes from steroid use stop once the course is finished and the child’s nausea and diarrhoea go away at the end of chemotherapy. However, because of the cumulative toxicity of the drugs used in chemotherapy, children often suffer from late effects which can contribute to long-term chronic morbidity and early mortality (Ness et al., 2011). Estimates for the incidence of adverse late effects are that they occur in 70-80% of childhood leukaemia survivors (Berbis et al., 2013; Haddy et al., 2009). Many of these effects are associated with particular drugs and are dose-dependent but even those on low doses have an elevated risk (Ness et al., 2011). Late effects of chemotherapy include cardiac problems, osteoporosis and neuropathies (Smith et al., 2015; Vandecruys et al., 2012). Radiotherapy and SCT increase the risk considerably (Petryk et al., 2006; Ness et al., 2011).

 There may be neurocognitive late effects from leukaemia treatment which can affect the child’s reintegration into school and future academic performance. These problems are worst in children treated with cranial irradiation, but impaired attention and executive function are also associated with chemotherapy-only treatment regimens. A study of survivors of ALL found structural changes in the brain, associated with working memory deficits, up to a decade after treatment (Plas et al., 2016). Children treated for leukaemia are below age-adjusted norms for fine motor skills, visual-motor integration skills, verbal skills and visual short-term memory (Balsamo et al., 2016; Moore et al., 2016). A meta-analysis found negative effect sizes over a range of global and specific neurocognitive skills (Campbell et al., 2007).

Leukaemia treatment is also associated with an increased body mass index (BMI) and high blood pressure, caused by steroid use and physical inactivity during chemotherapy. These changes often persist after treatment ends and obesity has been reported at higher levels in survivors than in the general population (Esbenshade et al., 2011; Oeffinger et al., 2003). Late effects such as osteoporosis and neuropathies, affect the child’s mobility, balance and range of motion. This combination of treatment and behavioural risk factors can have a detrimental effect on future lifestyle choices, and long-term health and fitness of childhood leukaemia survivors (Ness et al., 2011).

The risk of a secondary malignancy (e.g. brain tumour, thyroid cancer, skin cancer) is higher in survivors of childhood leukaemia (Maule et al., 2007; Walter et al., 1998). Many late effects caused by damage to organ systems or secondary malignancies will not develop until many years after treatment when the child has entered adulthood (Friedman and Meadows, 2002). It is very important that children are monitored and treated for late effects throughout their lives and that they avoid risk factors for cancer and circulatory disease, such as excessive sun exposure, high levels of drinking, poor diet, lack of exercise and smoking (Gibson et al., 2015; Oeffinger et al., 2003; Rebholz et al., 2012). To do this survivors require an understanding of their diagnosis and the risk factors associated with their specific treatment regimen.

**1.11. Psychological late effects**

Studies suggest that between 20-30% of childhood cancer survivors have long-term psychological issues related to their treatment (Friedman & Meadows, 2002; Patenaude & Kupst, 2005; Vannatta & Gerhardt, 2003). Kunin-Batson et al. (2016) reported 24% and 28% of a sample of 160 ALL survivors had at-risk or clinically elevated levels of anxiety and depression, three months after completing treatment. Kanellopoulos et al. (2013) reported mental, physical and social functioning impairments in 32% of a sample of 285 long-term (7-39 years post-treatment) survivors of ALL.

Post-traumatic stress symptoms (PTS) have been reported in children and parents after the child’s leukaemia treatment. PTS develops in response to traumatic or highly stressful events and includes re-experiencing of the traumatic event (intrusive thoughts/memories), avoidance of reminders of the traumatic event, hyperarousal and depression (Kazak et al., 2004). Kazak et al. (2004) reported diagnostic criteria for PTS in 30% of mothers and 13.7% survivors in a sample of 150 adolescent survivors of cancer and their families. Subclinical re-experiencing symptoms related to cancer treatment were present in 99% of these families. Similar levels of PTS have been reported in other studies; severe symptoms in 12.5% of survivors, 39.7% of mothers and 33% of fathers (Stuber et al., 1996) and 27% families with a lifetime risk of developing clinical PTS (Libov et al., 2002). This may have negative consequences for survivors as PTS and anxiety can interfere with the use of positive health behaviours (Santacroce & Lee, 2006) and lead to avoidance of clinic appointments (Berg et al., 2016).

Problems with behaviour and social relationships can also persist after treatment. Mitchell et al. (2016) reported that 25.8% of ALL survivors had social impairment, three months post-treatment. Social impairments can persist into adulthood. In a study of 102 survivors of childhood ALL, survivors had significantly more problems with romantic and peer relationships as adults than healthy controls (Mackie et al., 2000). Parents might find it difficult to reinstate ‘normal’ parental discipline after the changes associated with steroid treatment, making behavioural problems more difficult to resolve. Schultz et al. (2007) found survivors of childhood cancer had a 1.7 times greater risk of antisocial behaviour than their healthy siblings. Habits related to poor diet and lack of exercise may also be difficult to change once the child finishes treatment.

**1.12. Leukaemia as an acute and a chronic illness**

 Illnesses can be described as acute or chronic. Acute illnesses have a sudden onset of symptoms which worsen rapidly. They usually last for a short time and can usually be cured (e.g. chicken pox, measles, meningitis). Chronic illnesses have symptoms which start gradually and persist over a long period, often with no chance of a cure (e.g. diabetes, asthma, cystic fibrosis). These conditions require long-term management of symptoms and medications. Leukaemia has features similar to acute and chronic illnesses (Eiser, 2004; Turner-Cobb, 2014). Like an acute illness, the symptoms develop and worsen rapidly, and can be ‘cured’. Like a chronic illness, leukaemia requires long-term medical treatment and self-management. Treatment can also lead to chronic late effects which require life-long management. Childhood leukaemia (particularly ALL) has been likened to an acute illness in the early stages of treatment but takes on the features of a chronic illness as treatment progresses (Turner-Cobb, 2014).

**1.13. Summary**

This chapter has described the pathophysiology of leukaemia, its treatment, side effects and potential long-term effects on children. Outcomes have improved for children over the last few decades as a result of combination chemotherapy, targeted treatment regimens and supportive care. Survival rates now approach 90% for some forms of the illness. However, treatment takes place over a protracted period with disruption to family and school life, often leads to unpleasant side effects and includes procedures which can be distressing for children and their families. Treatment may lead to physical and psychological late effects which require long-term management and treatment. Late effects can increase morbidity, early mortality and impact the psychological well-being of survivors many decades after treatment.

As this chapter has shown, the information required to understand leukaemia and its treatment is complex. There is no certainty in the early stages about whether the child will survive, what side effects they might experience or what the long-term effects of treatment might be. This uncertain context can be stressful for families and can make communicating with children about their diagnosis and treatment difficult. Chapter 2 will examine the information needs of children with leukaemia, with a focus on pre-adolescent children who tend to be told less about their illness than older children.

**Chapter 2**

**Information needs of children with leukaemia**

This chapter will discuss the importance of informing children with leukaemia about their diagnosis and treatment. Children have information needs at diagnosis, during treatment and as survivors. Unmet information needs are associated with distress during treatment and poorer psychological and health outcomes as survivors (DeRouen et al., 2015; Millar et al., 2010). Chapter 1 demonstrated that the information required to understand leukaemia is complex. The uncertain course of treatment and outcomes means that informing families is likely to be an on-going process throughout treatment and into survivorship (Gibson et al., 2018; Sisk et al., 2016).

Effective communication with healthcare providers is vital to support children with leukaemia and their families. Being informed about their illness may promote adherence to treatment, compliance with procedures and facilitate informed consent. It may also help the child to prepare for and cope with treatments, communicate their needs to others and feel involved in decisions about their care (Ranmal et al., 2008). Parents usually decide how much information their child should be given, particularly with younger children who are often told less about their illness (Clarke et al., 2005; Young et al., 2003). Psychoeducation may have a role in informing young children about their illness and in supporting family communication.

The literature referenced in this chapter comes from populations of children with leukaemia and pediatric cancer more generally. During the acute phase of treatment, leukaemia has much in common with other forms of pediatric cancer (e.g. treatment via combination chemotherapy and steroids) (NIHR, 2005). Treatment is likely to lead to similar burdens for families, similar side and late effects and have similar implications for health behaviours in survivors. Communicating with all families of children with cancer is likely to convey potentially distressing and uncertain information. Also, because leukaemia is the most common childhood cancer, many studies of paediatric cancer populations will include a large proportion of children with leukaemia.

**2.1. The ‘protective’ approach**

Before combined chemotherapy treatment was developed in the 1960’s and 1970’s, the prognosis for children diagnosed with leukaemia was very poor (DeVita & Chu, 2008). Between 1966-1970 the survival rate for ALL was 9% (Cancer Research, 2019). Healthcare professionals recommended a ‘protective’ approach to communication where children were not told their prognosis. It was believed this knowledge would compromise the child’s ability to cope with treatment and would lead to anxiety and depression (Chesler & Barbarin, 1987). Doctors believed that children did not want to be told their prognosis (Sisk et al., 2016) and parents were advised to maintain normality as much as possible by not discussing the illness with them (Chesler et al., 1986). This approach also ‘protected’ parents and healthcare professionals by allowing them to maintain a sense of control and optimism (Bluebond-Langner, 1978; Chesler et al., 1986; Vernick & Karon, 1965).

As survival rates improved, a more ‘open’ approach to communication was recommended. Between 1981-85 survival rates for ALL had increased to 61% (Cancer Research, 2017). This meant that children were involved in the healthcare system for longer. Developing trusting relationships with health providers and concerns over the child’s long-term health became more important (Cousino et al., 2011).

Problems with the ‘protective’ approach were also highlighted. It was argued that children could tell from the reactions of parents and doctors that they were seriously ill (Bluebond-Langner, 1978; Glaser & Strauss, 1965). Therefore, not talking openly about the illness could make it seem even more dangerous and frightening and reduce the child’s trust in their families and doctors (Eiser, 1994; Vernick & Karon, 1965).

**2.2. The ‘open’ approach**

Evidence started to accumulate that the ‘protective’ approach to communication was leading to poor psychosocial outcomes, even for children who had poor prognoses (Bluebond-Langner, 1978). This evidence came from a number of interview studies with parents and children which compared what the child was told at diagnosis to later psychosocial outcomes (Chesler & Barbarin, 1987; Claflin & Barbarin, 1991; Slavin et al., 1982). Slavin et al. (1982) carried out 116 interviews with long-term survivors of childhood cancer and their parents (mean age at diagnosis = 5.7 years; and at interview = 18.04 years, mean time elapsed= 12.44 years). They also reported a psychiatric evaluation of the child’s self-esteem, anxiety, depression and social adjustment. Early knowledge of the cancer diagnosis (within 1 year, or by 6 years if diagnosed in infancy) was associated with better psychosocial adjustment in survivors, in comparison to those who were informed later or not at all (20% had never been informed by doctors or parents). This suggested that an open communication style at diagnosis had long-term implications for children’s well-being.

A less retrospective study (interviews at 3 months to 3 years from diagnosis), with 56 parents of children with cancer (aged 8-16 years) reported that children who had received early information about their diagnosis and prognosis had lower levels of anxiety and depression at the time of the interview (Last & Van Veldhuizen, 1996). These studies concluded that parents should inform their child as soon as possible after diagnosis and that healthcare providers should support families to do this.

In a historical review of the literature for disclosing cancer to children, Sisk et al. (2016) identified three arguments which were made in favour of disclosing the child’s diagnosis: 1) children were already aware of their illness so any effort to hide the truth was likely to fail, 2) lack of communication from the child might arise from not feeling they could communicate freely (rather than not wanting to) and 3) honest and safe communication provides support for the child. Sisk et al. (2016) also suggested that a context where children can ask questions and express fears may be as important as what they are told.

Contrary to the belief that non-disclosure protected the family, lack of communication within families has been associated with poorer outcomes for children with cancer (Kunin-Batson et al., 2016; Mitchell et al., 2016; Myers et al., 2014; Zheng et al., 2018). In a study of 62 newly diagnosed children with cancer and their families, family cohesion and expressiveness predicted child adjustment (measured using behaviour problems and social competence) over the first 9 months after a cancer diagnosis, after controlling for sociodemographic factors (Varni et al., 1996). Other family functioning variables were not predictive (e.g. conflict, independence, organization, control) suggesting that it was the context of support and open communication which was most important.

**2.3. Incorporating open communication in clinical care**

As a result of the accumulating evidence favouring an ‘open’ approach (e.g. Chesler & Barbarin, 1987; Claflin & Barbarin, 1991; Slavin et al., 1982), professional healthcare bodies have incorporated this into their guidelines for communicating with children. Professional standards in the UK (Department of Health, UK, 2014; NIHR, 2005), Europe (Kowalczyk et al., 2014) and the US (American Academy of Pediatrics, 2014) require thorough communication about the child’s illness and treatment.

Patient involvement in treatment has been associated with improved adherence to treatment and compliance in procedures. Non-adherence to out-patient oral chemotherapy treatment (which is associated with avoidable deaths), has been reported at levels of up to 50%, for children with lymphoma and leukaemia (NICE, 2005). Levels of non-adherence were higher in adolescents, and in children and families with less understanding of their illness. Spinetta et al. (2002) suggested that open and honest communication, according to the age and developmental level of the child, is necessary to promote involvement and reduce non-compliance. In a study of 236 children with cancer (aged 8-12 years), involvement in care (measuring knowledge and participation) was positively associated with treatment compliance and with better psychosocial outcomes (Shoshani & Kanat-Maymon, 2018). Eiser (2004) suggested that children’s compliance around medical procedures may depend on their understanding of why they need the procedure. Without this understanding, unpleasant procedures are more likely to lead to distress.

Psychoeducation has been recognised as an essential part of the process of informing children and families. A review of the evidence for the effectiveness of psychoeducation for children with cancer (including RCTs, qualitative studies and systematic reviews) concluded that there should be a strong recommendation for its inclusion in clinical care (Thompson et al., 2015). Psychoeducation was able to improve knowledge and health locus of control in studies where it was tailored to the needs of families and delivered throughout treatment. It also carried a relatively low risk of adverse outcomes. According to the standard of care which arose from this review, families should receive information about the illness, its treatment, acute and long-term effects, procedures and coping skills (Wiener et al., 2015).

Informational support has also been identified as a universal need for families of children with cancer in the Pediatric Psychosocial Preventive Health Model (PPPHM) (Kazak et al., 2006). This model provides a framework for providing targeted support to families. It recommends that information should be offered to all children and families as it fosters competency at each stage of treatment (diagnosis, active treatment and survivorship).

**2.4. Factors involved in informing children**

 Improved survival rates, the association of open communication with better psychological outcomes, and an emphasis on patient-centred care, has shifted the debate from whether to tell children about their illness, to how to inform them. This includes what information to give, when, and who should be responsible for giving it.

**2.4.1. The family context**

Research has suggested that children should be informed about their illness as soon as possible after diagnosis (Claflin & Barbarin, 1991; Slavin et al., 1982). However, this may be a time when families feel stressed and may be struggling to assimilate information (Cousino et al., 2011). The emotional shock of a leukaemia diagnosis can make it difficult for parents to share information with their child, as they often want to shield children from the life-threatening nature of cancer (Coyne et al., 2016; Ellis & Leventhal., 1993; Young et al., 2003). Although informing children may be burdensome for families, parents still report wanting to be responsible for how and what their child is told (Coyne et al., 2016, Young et al., 2003).

In an interview study, parents identified a number of factors which reduced what they told their child: information overload and emotional turmoil, lack of knowledge/experience and not wanting to burden the child (Badarau et al., 2015). Parents of children with leukaemia have reported finding it more difficult to concentrate and ask questions in consultations with doctors when their child was present (Young et al., 2011). Doctors have also reported finding it difficult when parents want to adopt a more protective approach to communicating with their child (Badarau et al., 2015).

**2.4.2. The impact of age on cancer disclosure**

Age has been shown to be the most important factor in how much information parents tell their child. Parents do not fully inform younger children about their illness as they do not think they will understand it and do not want to overwhelm them (Claflin & Barbarin, 1991; Clarke et al., 2005; Coyne et al., 2016). Pre-school children may be told very little about their illness (Chesler et al, 1986). In an interview study, Claflin and Barbarin (1991) reported that children diagnosed before the age of 9 years had been told significantly less about their illness than older children, with 39% reportedly being told nothing.

An interview study with 55 parents of children newly diagnosed with ALL, reported that parents gave different accounts of leukaemia at different ages. Children were told it was a life-threatening cancer at an average of 12 years, cancer only at 8.73 years, leukaemia at 5.63 years, and ‘poorly blood’ at 4.24 years (Clarke et al., 2005). This suggested that children were not told they had a form of cancer until they were almost 9 years old. A qualitative study of children’s views of cancer found that children aged 8-11 years associated it with dying, rarely talked about the possibility of cure and related its cause to unhealthy behaviours (Knighting et al., 2011). Therefore, finding out later that leukaemia is a form of cancer could lead to misunderstandings and distress. The lack of disclosure for younger children might also be problematic if it sets a context of non-disclosure for the remainder of their treatment and into survivorship. Many children with leukaemia are diagnosed under the age of 5 years but will remain in treatment and follow-up care for many years after that.

Age might also not be the only determinant of how much children can understand about their illness. Context and previous experience may also be important. Eiser et al. (1993) demonstrated that pre-school children could successfully learn information about blood cells if they had previous experience of seeing blood. Gain in knowledge was also not determined by age in a pediatric oncology camp intervention (Bluebond-Langner et al., 1990). Hospitalised children are likely to gain familiarity with their bodies and medical procedures much earlier than healthy children would. Parents and healthcare providers could underestimate what younger children are capable of understanding if they do not also take these experiences into account.

Doctors and parents often use analogies to explain leukaemia treatment to young children. These include the ‘flower garden’ analogy (Jankovic et al., 1994) in which ‘weeds’ (leukaemia cells) need to be killed to allow ‘flowers’ (healthy blood cells) to grow back, or ‘fighting’ analogies such as a battle between ‘good’ and ‘bad’ soldiers. Analogies are intended to make it easier for young children to understand and communicate about their illness (Whaley, 1994). However, they can also lead to misunderstandings if taken literally (Vernick & Karon, 1965). Eiser et al. (1986) suggested that functional analogies (such as invading armies) are not easily understandable for young children. It may be better to provide more realistic explanations using the previous experience of the child to help them to understand. For example, seeing blood/leukaemia cells under a microscope and relating this to their own blood tests may be more understandable to a young child than the concept that weeds are growing inside them.

Barnes (2006) described the development of printed materials for communicating cancer to young children. These materials normalise cancer treatment and explain procedures in an age-appropriate and non-threatening way (e.g. ‘Joe has leukaemia’ ‘Captain Chemo’, ‘Mr Wiggly’) and are widely used in hospitals. However, Barnes (2006) suggested that these materials were designed mainly to improve compliance with procedures and treatment. Therefore, they may not be sufficient to answer all the child’s questions about their illness.

**2.5 Communicating with healthcare providers**

Effective communication with healthcare providers helps the child to understand their illness, prepare for procedures, cope with treatment and communicate their needs (Ranmal et al., 2008). Children have reported wanting to be involved in communication with healthcare providers and in decisions about their care (Coyne et al., 2014, Zwaanswijk et al., 2007). A focus group study with 36 patients, parents and survivors of childhood cancer found that children preferred to communicate face to face with healthcare professionals and be given an opportunity to ask questions (Zwaanswijk et al., 2007).

Studies of child-parent-doctor communication in general healthcare, show that child participation in consultations is often limited (Tates & Meeuwesen, 2001). In a study of 302 video-taped out-patient consultations with families, only 13% of the medical information was directed to the child, with child contributions making up 4% of the encounter (Van Dulmen, 1998). Information about illness management tended to be directed to parents even with older children.

Some children with cancer find the presence of their parents in consultations helpful, in facilitating communication and buffering difficult information (Brand et al., 2017). However, other children find that it hinders their ability to communicate (Coyne et al., 2016; Young et al., 2003; Zwaanswijk et al., 2007). In a focus group study, children with cancer (on-treatment and survivors; aged 8-17 years) reported wanting to be fully and honestly informed about their diagnosis and to be involved in decision-making (Zwaanswijk et al., 2007). Another interview study with children with cancer (aged 7-17 years), reported that children wanted to be informed honestly about their illness, even if the prognosis was poor (Jalmsell et al., 2016). Young et al. (2003) suggested that children can feel marginalised in encounters with doctors where their information preferences are different from their parent’s.

**2.6 Unmet information needs in survivors**

The information needs of survivors of childhood cancer are likely to be different from children on-treatment. Survivors may also have fewer occasions to talk to healthcare providers so misunderstandings and questions may remain unaddressed. Studies have reported that the majority of long-term survivors of childhood cancer have unmet information needs focused around late effects, fertility, risk of relapse and risk of secondary cancers (Cox et al., 2016; McCarthy et al., 2018; Vetsch et al., 2017). Vetsch et al. (2017) used questionnaires (n=322) and interviews (n=70) to investigate associations between unmet needs, sociodemographic factors and clinical characteristics of childhood cancer survivors (average of 19.7 years from diagnosis). Unmet needs were reported by 76.7% of survivors. Of these, 85% wanted more information on late effects and 79.7% wanted information on cancer reoccurrence. In interviews, survivors said that their parents had not passed on information about late effects to them. Unmet needs were associated with lower satisfaction with healthcare, self-reported anxiety and depression, poorer physical health and higher perceived risk of reoccurrence. Unmet information needs have also been associated with higher rates of post-traumatic stress, anxiety and poorer self-management behaviours in survivors of childhood cancer (DeRouen et al., 2015). Millar et al., (2010) reported similar levels of unmet needs in survivors 10 years post-treatment as at 5 years post-treatment, which suggests that these needs may not resolve. Higher unmet information needs have been associated with lower involvement in healthcare and lower health competency (knowledge, skills and confidence) which has implications for survivors’ long-term health (McCarthy et al., 2018).

Survivors of childhood leukaemia need to understand their own illness and treatment regime to be able to manage their late effects, avoid risky health behaviours and optimise their future health (Bashore, 2004). Perceiving health vulnerabilities is a necessary motivation for positive health behaviours but this can be low in childhood cancer survivors (Bashore, 2004). In a study of 635 adult survivors of childhood cancer, only one third realised they had an elevated risk of future health conditions as a result of their treatment (Kadan-Lottick et al., 2002). Less than half knew the drugs they had been treated with and whether their drugs had health implications which required monitoring. In an interview study of 141 child and adolescent cancer survivors (median age at diagnosis: 6.8 years, at interview: 16 years), 70% were not aware of the risk of late effects, 50% did not know the drugs they had been treated with, and 16% weren’t able to correctly identify what type of cancer they had been treated for (Bashore, 2004).

**2.7 Summary**

This chapter has provided evidence that withholding information about the child’s illness and treatment may be harmful. A ‘protective’ approach may not protect the child from difficult information and could cause additional anxiety. Research has suggested that an ‘open’ communication approach leads to better psychological outcomes, improves adherence and compliance, allows the child to take an active role in their care and reduces treatment-related distress.

Psychoeducation might support this process of communication with children with leukaemia, particularly for younger children. Younger children are likely to be at a greater risk of non-disclosure and may not have a context where they can talk openly about their illness or ask questions. Parents may struggle to communicate at an emotionally difficult time and might assume that the child will not understand information about their illness. Young children are also less likely to be involved in communication with healthcare providers and may be given simplistic information using analogies and printed materials. Children who were treated at a young age may then have little understanding of their illness as long-term survivors, which could impact their future health. Therefore, there is a need for age-appropriate psychoeducation.

Chapter 3 will introduce a model of adjustment to illness which has been used to suggest modifiable targets for interventions with children. A number of these targets may be modifiable via psychoeducation. Chapters 4 and 5 will review the evidence for the efficacy of psychoeducation in populations of children with cancer and more general chronic conditions. The leukaemia intervention, which will be described in Chapter 6, was designed to fulfil a need for psychoeducation for children with leukaemia and to provide a context where children could openly communicate and ask questions.

**Chapter 3**

**A risk and resiliency model of adjustment for childhood cancer**

 Chapter 3 will introduce Wallander and Varni’s (1998) risk-resistance model of adjustment to illness which has been used to explain psychological outcomes in children with cancer and to identify modifiable targets for interventions. Quality of Life (QoL) will also be introduced as an important measure of adjustment. QoL has been used to evaluate interventions and to measure the burden of treatment regimes in clinical trials (Eiser, 2004; Varni et al., 1999). In proceeding chapters, it will be used as an outcome measure for a meta-analysis of psychoeducational interventions (Chapter 5) and as a primary outcome measure in the leukaemia intervention (Chapters 6 and 7).

Chapter 1 described the considerable burdens associated with leukaemia treatment for children and their families. These include physical burdens (e.g. side effects, medical procedures), social burdens (e.g. social isolation, missing out on school) and psychological burdens (e.g. mood changes, procedural distress). Leukaemia treatment can lead to adverse psychological outcomes such as anxiety and depression during treatment and there is a considerable subgroup of childhood cancer survivors who develop long-term psychological problems.

 It is important to evaluate interventions which address these burdens and improve the quality of survival for children with leukaemia. The literature describing outcomes for childhood cancer survivors shows that many families do not develop long-term psychosocial impairments (Kazak et al., 2007). This suggests that families are often able to adjust to the child’s illness and treatment. Therefore, a theoretical model which explains the responses of children and families to cancer, needs to include both positive and negative outcomes (Wallander & Varni, 1992; Wallander & Varni, 1998).

This chapter will introduce a risk and resiliency model of adjustment in childhood cancer. The Risk-Resistance Adaptation model (also known as the Disability-Stress-Coping model) (Wallander & Varni, 1992) was originally developed using empirical data from children with chronic illnesses and later applied specifically to paediatric cancer (Wallander & Varni, 1998). The model includes risk factors associated with poor adjustment outcomes and resistance (resiliency) factors associated with positive outcomes. The paediatric cancer literature used to support the model was limited at the time of the 1998 paper. Therefore, further evidence will be considered in light of the model’s predictions. Wallander and Varni (1998) described their model as a problem-solving competency model which could be used to reduce the burdens associated with illness. This is based on the assumption that reducing risk factors and increasing resiliency factors will improve adjustment outcomes. It can, therefore, be used as a framework for intervening with children and families and will be related to targets used in paediatric cancer interventions in the final section of this chapter.

**3.1. Adjustment to illness**

 Adjustment to illness represents the responses of children and families to the burdens of illness and treatment. It is a process which begins at diagnosis and continues throughout treatment and into survivorship (Sharpe & Curran, 2006). Wallander and Thompson (1995) described positive adjustment in children as ‘behaviour that is age-appropriate, normative, and healthy, and that follows a trajectory toward positive adult functioning’ (pp. 125-126). Maladjustment is behaviour which is not age appropriate or is pathological in nature. Models of adjustment recognise the fact that while levels of psychological impairment are often higher in the group as a whole, many families do not develop significant psychological symptoms even with the most serious of illnesses. Adjustment models explain differential outcomes which cannot be directly explained by the biological nature of the illness. Sharpe and Curran (2006) suggested that an understanding of the processes of adjustment could be used to develop interventions for children and families who do go on to have long-term problems. These processes can also be used to provide interventions which are preventative of future problems and to identify families who are at greater risk of poor outcomes.

Risk and resiliency models attempt to explain the processes of adjustment to illness. The illness is conceptualised as a chronic stressor which interferes with health and normal family life and requires constant readjustment in family responses. Resiliency (positive adjustment), can be understood as the achievement of normative emotional, behavioural and psychological outcomes in the face of living with a health condition (Hilliard et al., 2015). Resilience (or protective, resistance) factors are the resources which the child and family can draw on to adapt to the burdens of illness. These might be social (e.g. family or social support), intrapersonal (e.g. self-esteem, problem-solving ability) or stress-processing factors (e.g. positive coping strategies, adaptive cognitive appraisal). Risk factors are those which are likely to exacerbate these burdens and reduce the child and family’s ability to adapt. These might relate to the illness (e.g. disease severity and type), functional impairment (e.g. impaired physical or communicational functioning) or other psychosocial stresses (e.g. repeated hospitalizations, peer problems at school).

Prior to the development of adjustment models, medical-deficit or problem-focused models were commonly used to explain outcomes and focused on negative outcomes. Kazak et al. (2007) suggested that research associated with these models sought out evidence of psychological or social impairments rather than considering that families might be coping well. Therefore, this research failed to identify the psychological and social resources associated with positive outcomes which could be targeted in interventions (Eiser, 1990) and thereby reduced the clinical relevance of the models (Wallander & Varni, 1998). To advance understanding of family adjustment to illness, positive outcome measures and a theoretical framework which incorporated resiliency and competency were needed.

**3.2. Quality of life as a measure of adjustment**

A variety of measures have been used to study outcomes in children with cancer. Traditionally these have included measures such as anxiety, depression and post-traumatic stress. These negative outcomes are sometimes used as proxy measures of adjustment. However, they come from a medical-deficit approach which associates illness with maladjustment and are less able to explore positive outcomes.

Positive adjustment (or resiliency) is described over a range of domains (emotional, social, behavioural and psychological). Therefore, measuring adjustment would either require a variety of separate measures or a multicomponent measure which incorporates all these domains. Attempts to collect data using a series of individual measures may be repetitive and burdensome for families (Eiser, 2007). Instead, quality of life (QoL) measures began to be developed from the 1980s onwards, to fulfil the need for a multicomponent outcome of adjustment.

Concepts of QoL have evolved from the World Health Organisation definition of health (WHO, 1946) which defined health as ‘a state of physical, mental and social wellbeing’. Most QoL measures retain these core domains. The American Cancer Society used them in their definition: ‘Quality of life (QOL) in pediatric oncology is multidimensional. It includes, but is not limited to, the social, physical, and emotional functioning of the child and adolescent’ (Bradlyn et al., 1996, p.1333-34). While measures generally include the same psychological, physical and social domains, there is variety in the items included within these domains (Savage et al., 2009; Anthony et al., 2014). QoL outcomes measure the subjective impact of the illness on children and families. This is important for risk and resiliency models, as objective disease factors are not always strongly associated with adjustment outcomes. For example, an objective medical factor (such as hair loss from chemotherapy) might have different effects on adjustment in different families.

There are a number of reasons to measure QoL as part of cancer treatment. QoL can be used to improve the quality of survival by intervening to reduce the burdens of treatment (Eiser, 2004; Varni et al., 1999). As part of clinical trials, it can be used to modify treatments; balancing the burdens of side and late effects with the prevention of relapses. QoL outcomes can also be used to screen for children at greater risk of later psychological distress (Meeske et al., 2005; Mitchell et al., 2016; Zheng et al., 2018).

Increasingly, it has been argued that clinical trials should include QoL as an outcome alongside traditional clinical endpoints such as survival and toxicities (Savage et al., 2009, Eiser, 2004). In a 1995 review of the use of QoL outcomes in clinical trials, QoL was reported in only 3% of trials, while 75% reported toxicities (Bradlyn et al., 1995). Armstrong & Reaman (2005) have also argued for the inclusion of QoL measurements in all cancer treatment protocols to optimise quality of survival in children treated for cancer.

**3.3. The risk-resistance model**

Wallander and Varni (1992) proposed their risk-resistance model (also known as the Disability-Stress-Coping model) to explain differential adjustment outcomes in children with chronic illnesses. They used evidence from empirical studies examining the predictors of positive and negative psychological outcomes in children with chronic physical conditions to build their model (e.g. Wallander et al., 1989; Wallander & Varni, 1989, Varni et al., 1995). The whole model is complex and includes risk and resistance (resiliency) factors from the intrapersonal to socio-ecological levels. Empirical work has therefore tended to concentrate on components of the model rather than examining it as a whole.

Wallander and Varni evaluated their model using evidence specifically from children with cancer in a later paper (Wallander & Varni, 1998). The model shown in Figure 3.1 has been adapted from this paper with additional outcomes suggested by more recent research (bolded text indicates additional factors, dashed lines indicate additional pathways). Childhood cancer is represented as a chronic stressor which impacts directly on adjustment and indirectly via other psychosocial stresses. The next part of this chapter will evaluate whether additional studies of psychological outcomes in children with cancer support Wallander and Varni’s model. Some measures of negative outcomes are included in this section (e.g. anxiety, PTS) as these are still commonly measured in outcome studies and have been used as proxy measures of adjustment (via maladjustment) (e.g. Van Schoors et al., 2017). Relevant studies will be examined under the six risk and resistance factors described in Wallander and Varni’s model. The first three factors represent the stresses (risk factors) associated with cancer/leukaemia and the last three represent resistance (resiliency) factors as described in the model.

Disease/Disability:

Diagnosis

Severity

Symptoms

**Treatment:**

**Chemotherapy**

**Steroids**

Side effects

Cognitive function

Late effects

Pathways suggested in Wallander & Varni’s Risk-Resistance model

Additional pathways suggested by the research literature

Functional independence:

Activities

Communication

School performance

Social relationships

**Major life events: work, marriage etc…**

Psychosocial stress

Treatment-related problems

Illness-related problems

Other problems (daily + major life events)

e.g. Social isolation

Reintegration/transition

School problems

Illness uncertainty

Adjustment/ adaptation (QoL)

Physical

Psychological

Social

Social-ecological factors

Family functioning

Social support

**Healthcare**

**Community**

**School**

**Ethnicity**

**SES**

Stress Processing

Cognitive appraisal

Coping strategies

Primary vs secondary coping styles

Personal factors

Stable personality factors

e.g. temperament, self-esteem

**Age, gender**

*Figure 3.1* Risk-resistance framework of child adjustment to cancer (adapted from Wallander & Varni, 1998). **Bolded text** indicates suggested predictors not included in Wallander and Varni’s model.

* + 1. **Disease and disability factors**

Wallander and Varni (1998) suggested that disease/disability factors have direct impacts on adjustment, but that this is not the most important pathway in the model. They cited a small number of studies to support this inconsistent relationship. For example, Varni et al. (1996a; 1996b) found no difference on adjustment between children diagnosed with leukaemia compared with other cancers, while a study of long-term survivors of childhood cancer did identify an association between disease severity and degree of maladjustment (Varni et al., 1994a).

Additional research has reported a lack of relationship between disease-factors and adjustment outcomes in cancer survivors. For example, Kupst et al. (1988) found no relationship between medical status, illness duration and coping in 43 families of children with ALL an average of 6.8 years after treatment. Kanellopoulos et al. (2013) found no relationship between type of leukaemia or treatment factors and QoL outcomes, in a study of 285 long-term childhood leukaemia and lymphoma survivors (7-39 years post-treatment).

However, there is also evidence that disease-related factors do have a direct and substantial impact on adjustment for children with cancer, during and after treatment. In a study examining QoL outcomes in children 1 week after the start of a chemotherapy cycle, the main predictor of lower QoL was higher levels of physical symptoms (Baggott et al., 2011). Steroid treatment also has a direct effect on QoL. In a study of 41 children during maintenance treatment for ALL, QoL was more impaired during periods of steroid treatment (DeVries et al., 2008). Externalised behaviour problems have also been associated with periods of steroid use (Marcoux et al., 2012).

Quality of life impairment and psychological impairment is higher in survivors who report current health conditions and cancer-related pain or fatigue (Schultz et al., 2014; Meeske et al., 2005; Ferry et al., 2007). Maurice-Stam et al. (2009) modelled QoL in 353 survivors of childhood cancer and found that current health complaints and late effects, mediated the relationship between disease-related factors and adjustment. In a study of long-term survivors of childhood leukaemia and lymphoma, Kanellopoulos et al. (2013) found no association between disease-related factors and QoL, but there was an association between lifestyle and health factors as a survivor (e.g. obesity, fatigue) and QoL. This suggests that the burden of disease-related factors is greatest during active treatment and in relation to long-term health problems. The impact of cancer may be mitigated over time if health is maintained in survivors.

* + 1. **Functional independence**

In the risk-resistance model, functional independence mediates the relationship between disease-related factors and adjustment. The adverse effect of the disease acts through impairment in the child’s ability to communicate, look after themselves or take part in activities. Wallander and Varni (1998) cited evidence from a study which showed that children on-treatment had more functional impairments and higher emotional distress than children off-treatment (Wallander & Varni, 1998).

Recent evidence also suggests that reduced physical function impacts on adjustment. Myers et al. (2014) found that the risk of psychological impairment in 159 children in their first year of treatment for ALL was highest in those with the worst physical function. Impaired physical function is likely to lead to the child being dependent on others for their care. A qualitative interview study with long-term survivors of leukaemia and lymphoma reported that debilitation and forced dependence on others had a substantial impact on well-being during treatment (Zebrack, 2000). Physical impairment may also impact on social outcomes in adults. Survivors with more serious late effects were significantly less likely to be married and more likely to be living with a parent (Harila et al., 2010). In a longitudinal study of adolescents treated with a stem cell transplant, QoL was most impaired in adolescents with impaired communication (Felder-Puig et al., 2006).

Impaired cognitive function is common in survivors of childhood ALL. Long-term adjustment problems have been shown to be higher in survivors with impaired cognitive function (Kupst et al., 1995; Mackie et al., 2000) and have been associated with reduced educational attainment and higher unemployment in adults (Krull et al., 2013). Lower school performance and higher problem behaviours have been reported in a high-risk treatment group compared to a standard risk group (in 199 children at least 1 year after finishing treatment for ALL) which is likely to reflect the higher treatment burden in the high-risk group (Buizer et al., 2006). Impaired cognitive function has also been shown to impair coping strategies and emotion regulation in children with leukaemia (Campbell et al., 2009; Mackie et al., 2000).

* + 1. **Psychosocial stress**

Psychosocial stress relates to how the child perceives the stressor (i.e. the illness or other stressful events in their life), whether they believe it will be harmful and whether they believe they can cope with it. Wallander and Varni (1998) suggested that in the early stages of treatment, cancer-related problems are the main source of psychosocial stress. Stresses might include hospitalisations, medical procedures, unpleasant treatment and missing out on school and activities. Daily hassles become more important as the child begins to transition back into normal life. They cited a study of 32 children newly diagnosed with cancer to support this. There was no relationship between perceived psychosocial stress and anxiety/depression at 1-month post-diagnosis when the stresses of treatment would be greatest, but there was a relationship at 6 and 9-months post-diagnosis (Varni & Katz, 1997).

There is evidence that individual children experience differential stress responses to their medical treatment. Young children experience different types of stress in relation to medical procedures and changes in physical appearance compared to older children (Dupuis et al., 2016). Varni et al. (1995) reported a direct path between perceived physical appearance and depression/anxiety in 30 children with newly diagnosed cancer. In a longitudinal study of 594 children diagnosed with ALL, Zheng et al. (2018) found normal levels of social functioning during treatment but an increase in impairment as treatment ended which might reflect stresses associated with social and school reintegration.

* + 1. **Intrapersonal factors**

Intrapersonal factors are conceptualised as stable personality traits which affect how the child experiences and processes stress. Wallander and Varni (1998) cited one study which found an indirect path between perceived physical appearance and anxiety/depression which was mediated by self-esteem to support this relationship (Varni et al., 1995).

Other studies have suggested there is a relationship between stable personality traits and adjustment in children with cancer. Sharp et al. (2015) reported a large impact of disposition (personality type) in 255 children with cancer (aged 8-17 years) on anxiety/depression/PTSS. Personality traits (e.g. optimism, extraversion, neuroticism) explained 48% of the variance in depression, 28% in anxiety and 26% in PTS. Negative affect has also been associated with anxiety and depression in a sample of 75 children with cancer (aged 5-17 years) (Miller et al., 2009). It is likely that personality traits affect how the child responds to their illness, although these traits could also lead to maladjustment in children without cancer. These studies do not look at the role of disposition in positive adjustment, but they do suggest a role for screening children and targeting interventions to children who are more at-risk of negative outcomes.

Wallander and Varni (1998) suggested that age and gender were not associated with adjustment in their 1998 paper. However, there is evidence which shows relationships between age, gender and adjustment do exist for children with cancer. The different responses of young children to medical procedures (greater procedural anxiety in young children) would be an example of a differential stress response (Dupuis et al., 2016; Kazak et al., 1996). A qualitative interview study with 32 mothers of children newly diagnosed with ALL suggested that younger children (0-4 years) generally coped better with being ill than older children (10-14 years) (Earle & Eiser, 2007). Older children were more likely to have concerns associated with changes in physical appearance and loss of peer support. Age is likely to impact on adjustment for children with leukaemia as increasing age is associated with higher risks of relapse and death (Webb et al., 2001; Chessells et al., 1998). Female gender has also been associated with higher rates of PTS (Stuber et al., 1997) and less adaptive coping strategies in children with cancer (Maurice-Stam et al., 2009a; Compas, 2012).

* + 1. **Socio-ecological factors**

Family functioning includes measurements in many domains, such as family conflict, cohesion, structure, communication, roles, responsiveness, adaptability, support and involvement (Lewandowski et al., 2010; Alderfer et al., 2009; Van Schoors et al., 2017). Wallander and Varni (1998) described an extensive literature which supported family functioning and social support as predictors of adjustment outcomes. They suggested that family cohesion and expressiveness were particularly associated with positive adjustment (Varni et al., 1996b). Higher perceived classmate support was also associated with lower depression, anxiety, and behaviour problems (Varni et al., 1994b).

Unhealthy family functioning has been associated with higher levels of anxiety, depression and impaired QoL in children with leukaemia (Kunin-Batson et al., 2016; Mitchell et al., 2016; Myers et al., 2014; Zheng et al., 2018). In a study of 144 adolescent cancer survivors (1-12 years post-treatment), 8% of the children had PTS and 75% of these children came from families with unhealthy family functioning (Alderfer et al., 2009). Positive family functioning has also been associated with positive adjustment. In a meta-analysis investigating associations between family functioning and child adjustment after a pediatric cancer diagnosis, greater family cohesion, expressiveness, support and lower conflict were associated with positive child adjustment (measured using anxiety, depression, behaviour problems, social competence, PTS) (Van Schoors et al., 2017). Positive child coping skills have also been associated with positive family relationships and open communication in families of children with leukaemia (Kupst & Schulman, 1988).

There is additional support for the relationship between social support and adjustment. Lower social support available to families has been associated with higher anxiety and depression in children recently completing ALL treatment (Kunin-Batson et al., 2016) and children during the first year of ALL treatment (Myers et al., 2014). Greater perceived social support has been associated with lower PTS in survivors of childhood leukaemia and parents (Kazak et al., 1997), lower anxiety in parents of children with leukaemia (Chen et al., 2015) and lower illness uncertainty in recently diagnosed adolescents (Neville et al., 1998).

* + 1. **Stress processing**

Stress processing is represented as a mediator of the relationship between psychosocial stress and adjustment in the risk-resistance model. Wallander and Varni (1998) described this in terms of the cognitive appraisal and coping strategies used by the parent or child. The stress of the illness comes not from the illness itself, but the child/family’s understanding of it and whether they think they have the resources to cope. Coping reflects the behavioural and cognitive approaches used to manage the stressor.

 Perceptions of threat (cognitive appraisals) are often associated with poor psychological outcomes in survivors of childhood cancer. Subjective appraisals of threat during treatment were more predictive of PTS than objective disease factors, in 186 childhood cancer survivors off-treatment for at least 1 year (Stuber et al., 1997) and in 182 long-term survivors of cancer (Rourke et al., 2007).

 Studies have found that early distress predicts later distress, suggesting that there may be persistent features of child and family stress processing. Myers et al. (2014) reported that anxiety and depression at 1 month were associated with anxiety and depression at 12 months in children in the first year of treatment for ALL. Zheng et al. (2018) reported that emotional impairment at 2 months predicted emotional functioning at 26 months. Parents experiencing high levels of stress and anxiety during leukaemia treatment were also more likely to report increased stress and anxiety after treatment ended (Best et al., 2001). Reciprocal patterns of distress have been reported within families. Survivor and maternal adjustment and coping were strongly correlated in a longitudinal study of childhood cancer survivors, 10 years post-treatment (Kupst et al., 1995) and in a sample of adolescents with cancer and a parent (Trask et al., 2003).

 Studies have also looked at the relationship between coping strategies and child adjustment to illness. Compas et al. (2012) reviewed coping in pediatric chronic illnesses in relation to three types of control coping. Primary control (active) coping involves attempts to act directly on the source of stress (ie. the illness). Secondary control (accommodative) coping involves attempts to adapt to the source of stress. Disengagement (avoidant) coping involves avoidance, denial and wishful thinking. This review suggested that secondary coping was associated with positive outcomes for children with chronic illnesses while results for primary coping were mixed. Secondary coping may be a good fit for the uncontrollable aspects of chronic illnesses, while primary coping may be effective when aspects of the illness can be controlled (e.g. managing side effects). In a meta-analysis of coping and adjustment in children with cancer, approach or problem-focused coping (primary coping) was associated with poor outcomes 6-12 months after diagnosis but with better adjustment 4-5 years later (Aldridge & Roesch, 2007). Therefore, different stages of treatment for leukaemia may require different coping strategies. Avoidance has been shown to be a common coping strategy in children with cancer but is associated with poor outcomes in survivors and in children with other chronic conditions (Compas et al., 2012).

* + 1. **Appropriateness of the model**

The studies summarised in this section suggest that outcomes are generally in line with Wallander and Varni’s model. The risk-resistance model is, therefore, a useful structure to model the burdens associated with cancer and leukaemia treatment. There is evidence which supports the direct and indirect relationships between the risk factors, resistance factors and adjustment which are suggested by the model. This means that these factors may be useful in suggesting targets for intervention to reduce risk factors and support resiliency factors in children with leukaemia.

* + 1. **Limitations of the model**

Although the model is a good approximation of risk and resiliency factors associated with childhood leukaemia, it lacks some specificity. It was not developed specifically for this group and there are additional pathways which could potentially be important. For example, the adverse effects of treatment may be the main disease-related burden during treatment rather than disease-related factors *per se*. The burden of treatment is also related to adjustment in survivors via current health conditions. The adverse effects of treatment were not highlighted in Wallander and Varni’s original model as it was mainly used to explain outcomes for children with chronic illnesses where treatments might be less burdensome. Treatment-related factors may have a greater impact on children with cancer than disease-related factors and have been added to Figure 3.1.

The risk and resistance factors may be more interrelated than they appeared in the original model. Any of the resistance factors in the model could also act as risk factors. For example, unhealthy family functioning and high threat appraisal may reduce the child’s adjustment, even though family factors and cognitive appraisal were described as resistance factors in the 1998 paper. Disease-related factors and functional impairment were also not conceptualised as having an impact on the child’s social context or stress processing. However, steroid treatment has a large impact on family functioning with changes in parenting style. Parental roles may also change as a result of having an ill child. Parents may need to give up work because of their child’s illness which could impact family, financial and social support. Both chemotherapy and steroid treatment can also lead to cognitive impairments and reductions in emotional regulation which can impact on coping skills. Additional pathways were added to Figure 3.1 to show these potential relationships between disease-related factors and socio-ecological factors, and between functional impairment (cognitive) and coping skills.

The model does not include a broad consideration of the child’s social context. The social-ecological factors were limited to family and social support in the original model and did not consider the child’s wider health or social context. There is evidence that social factors have an impact on adjustment outcomes for families of children with cancer. Lower socioeconomic status (SES), unemployment and ethnicity have been linked with poorer adjustment outcomes in survivors (Kunin-Batson, 2016; Myers 2014; Zebrack et al., 2002). Lower SES has been associated with less positive family functioning in the general population (Repetti et al., 2002) which may place an additional burden on families of children with cancer. Minority ethnic groups have also been shown to have worse health outcomes for ALL (Bhatia et al., 2002). SES and ethnicity may therefore be additional risk factors for families of children with cancer.

**3.4. A framework for intervening**

An important aspect of the risk-resistance model is that risk and resiliency factors are modifiable and can be used for intervention development. Varni et al. (1998) described the risk-resistance model as a problem-solving competency model which could be used to develop interventions aimed at solving specific illness problems (e.g. pain management, nausea control, social skills, school reintegration). Other researchers have also used it to develop interventions. Mullins et al. (2015) developed an intervention based on this framework, to modify cognitive stress in parents of children with cancer. They targeted illness uncertainty and used a coping skills intervention to produce changes in cognitive appraisal, coping strategies and use of social support. While only a pilot study, there were trends in reduced parental distress which were associated with lower child internalising behavioural symptoms, even though the child did not attend the intervention (Fedele et al., 2013).

**3.5. Targets for psychoeducational interventions**

The adapted risk-resistance model shown in Figure 3.1 suggests a number of targets for intervention. These have been specified in Figure 3.2 using the risk and resistance factors described above. An important target to reduce disease-related and functional impairments associated with treatment, is to reduce the impact of side effects and late effects. This is an important target in clinical trials and is the reason why it is important to include QoL outcomes. However, this would not be a target for psychoeducation.

A number of targets suggested by the model are potentially modifiable using psychoeducation. These are bolded in Figure 3.2 and fall into four broad areas: 1) coping skills interventions, to manage side effects, alter threat appraisals, promote positive coping strategies and reduce illness uncertainty, 2) social skills training, to reduce social isolation and promote successful social and school reintegration, 3) illness information and treatment adherence interventions and 4) health behaviour interventions, to reduce the impact of late effects and reduce the chance of long-term chronic conditions and secondary malignancies. Psychoeducational interventions in these four areas will be reviewed in Chapter 4.

Stress Processing

**Psychoeducation**

**Coping skills interventions (e.g. promoting positive coping strategies, CBT)**

**Treatment-related distress/threat appraisal reduction e.g. coping with painful procedures**

**Illness uncertainty interventions**

Other

Counselling

Functional independence:

**Psychoeducation**

**Social skills training**

**Communication skills**

**Symptom management**

**Self-management of late effects**

Other

School reintegration interventions

Cognitive skills interventions

Physical training interventions

Disease/Disability/treatment

**Psychoeducation**

**Health behaviour interventions to reduce future health problems**

**Adherence interventions**

Other

Medical interventions: balance the burden of treatment with treatment effectiveness e.g. reduction of steroids in treatment regime

Social-ecological factors

**Psychoeducation**

**Social skills training**

**Communication skills**

**Group interventions**

**Family interventions**

Other

Targeted healthcare interventions e.g. clinical counselling

Screening to social at-risk groups

School reintegration interventions

Personal factors

Targeting interventions to at-risk children

Screening

Age-appropriate interventions

Psychosocial stress

**Coping skills interventions (e.g. promoting positive coping strategies, CBT) Social skills training Communication skills Illness uncertainty interventions**

Other School reintegration interventions Counselling

*Figure 3.2* Targets for interventions suggested by the risk-resistance framework (Wallander & Varni, 1998). **Bolded interventions** may be deliverable via psychoeducation.

**3.6 Summary**

This chapter has discussed the importance of modelling positive adjustment in children with cancer and their families. Research has shown that many families adjust well to having a child with cancer even though treatment is associated with periods of distress. This prompted a change from using medical deficit models to explain family outcomes, to the use of competency models. The example described in this chapter was the risk-resistance model proposed by Wallander and Varni (1992) and evaluated for children with cancer (Wallander & Varni, 1998). The studies reviewed in this chapter have provided additional support for the risk and resistance factors included in the model, and for the direct and indirect pathways to adjustment for children with cancer. It is likely that the relationships are more complex than shown in the original model. However, the structure provides a strong basis to identify modifiable targets and processes of change which can inform the design of psychoeducational interventions. Psychoeducational interventions which have been targeted to children with cancer will be reviewed in Chapter 4. These include coping skills interventions, social skills training, illness information/adherence interventions and health behaviour interventions.

**Chapter 4**

**Narrative review of psychoeducational interventions for children with cancer**

Chapter 3 introduced a model of adjustment to illness based on risk and resistance (resiliency) factors which suggested modifiable targets for psychoeducational interventions. A range of interventions might be appropriate for these targets, including coping skills interventions, social skills training, illness information/adherence interventions, and health behaviour interventions. These interventions aim to reduce the impact of risk factors and increase resiliency factors to improve child adjustment.

This chapter will describe psychoeducational interventions which have been delivered to children with cancer, targeting these modifiable risk and resiliency factors. The interventions are varied in content, method of delivery and population, while their evaluation studies have used different designs and outcome measures. Kazak et al. (2010) highlighted the importance of using evidence-based practise in intervention development and implementation. As well as using research to identify the burdens associated with an illness, and model processes of change (as described in Chapter 3), findings from intervention research should be used to identify strategies and components which have reduced these burdens. Therefore, methods of collating, often large bodies of evidence, are required to identify the effective components of interventions and determine the potential of novel interventions to change outcomes.

**4.1. Psychoeducation**

Psychoeducation had its roots in treating mental health disorders such as schizophrenia and bipolar disorder, but it is now more widely applied, including in a range of physical illnesses such as cancer and diabetes (Hogarty et al., 1986; Barlow & Ellard, 2004). The goal of psychoeducation is to increase the individual’s understanding of their illness and treatment and give them the skills to manage their condition (Barlow & Ellard, 2004). Improving communication with healthcare providers is an important target for psychoeducational interventions (Motlova et al., 2017). Kazak et al. (2006) described the role of information and education in universal pediatric cancer care, as fostering competency and supporting adaptive family coping skills.

Psychoeducation has been defined as ‘an intervention with systematic, structured, and didactic knowledge transfer for an illness and its treatment, integrating emotional and motivational aspects to enable patients to cope with the illness and to improve its treatment adherence and efficacy’ (Ekhtiari et al., 2017, p.239). As this quote suggests, psychoeducational interventions have knowledge transfer and illness management in common. However, the targets and content can vary considerably. Psychoeducational interventions have also taken many different forms; including written information, group interventions, clinic-based counselling sessions, multimedia and internet-delivered content (Barlow & Ellard, 2004).

Psychoeducational interventions might target knowledge about an illness, self-management skills related to treatment, psychological coping skills or motivation to change health behaviours. They could also target a combination of all these factors. Psychoeducational interventions have included interventions which focus on coping skills (e.g. CBT) to manage the psychological, behavioural and emotional aspects of an illness. For example, Schuengel et al. (2011), described a psychoeducational group intervention for children with different chronic conditions which included positive thinking and relaxation, alongside information-seeking and improving compliance to treatment. Here, information-seeking and compliance were promoted as general coping strategies and did not include illness-specific information. Other psychoeducational interventions have focused on information specific to an illness and its management. For example, Pfafflin et al. (2012) described a psychoeducational intervention for children with epilepsy which taught the pathophysiology of epilepsy, its treatment, the importance of diagnostic tests and how to cope with seizures. As well as improving knowledge, the intervention aimed to help children to cope with their illness, reduce illness-related fears and actively participate in their treatment.

Evaluations of psychoeducational interventions also differ in how they measure outcomes. In a review of psychoeducational interventions for children with cancer, Bradlyn et al. (2003) distinguished between interventions which measured improvements in knowledge, and those which measured improvements in health or psychosocial outcomes via knowledge and skills training. This is an important distinction as increases in knowledge are not always associated with changes in health behaviours (Bradlyn et al., 2003; Hudson et al., 2002). Therefore, knowledge gain is often not a primary outcome in evaluations of psychoeducational interventions. Instead, studies tend to use a variety of health outcomes and measures of psychological adjustment (e.g. anxiety, PTS, behaviour, QoL).

The information needed to effectively manage symptoms and treatment is likely to differ for different conditions and may also change over the course of an illness. During the acute phase of treatment, children with cancer may require information related to procedures and managing symptoms. Children in the chronic phase may require information to manage late effects, optimise their health behaviours and cope with re-integration back into school (Landier et al., 2016).

**4.2. Psychoeducational interventions delivered to children with cancer**

This narrative review describes evaluation studies of psychoeducational interventions delivered to children with cancer. Interventions are considered under the four broad areas suggested by the modifiable risk and resiliency factors shown in Figure 3.2. Intervention characteristics for each study (study design, sample characteristics, outcome measures and results) are summarised in Tables 4.1 to 4.4. Relevant systematic reviews are summarised in Table 4.5. These tables are displayed at the end of the chapter.

* 1. **Coping skills interventions**

Cognitive appraisal and coping skills were described in the risk-resistance model (Wallander & Varni, 1998). The child’s perception of the threat from a stressor and their belief about whether they can cope, mediates the relationship between psychosocial stress and adjustment. This means that the child’s perception and response to a stressor is an important target for interventions. Coping skills interventions aim to promote competency and self-efficacy by teaching adaptive coping styles and problem-solving skills in response to an illness (Grey et al., 2009).

* + 1. **Coping skills for procedural distress**

Perception of threat during treatment has been identified as a stronger predictor of long-term psychological distress (PTS) than objective disease or threat measures (Kazak et al., 2007; Stuber et al., 1997). Early distress has also been reported to predict later distress (Myers et al., 2014; Zheng et al., 2018). This highlights the importance of reducing threat appraisal during treatment.

Coping skills interventions (shown in Table 4.1), aimed at reducing procedural distress (associated with lumbar punctures) have improved outcomes (children’s pain, distress and stress; pulse and blood pressure, reduced need for anaesthetic) in a number of studies (Jay et al.,1987; Jay et al., 1995; Kazak et al., 1996). These coping skills were based on CBT and included behavioural rehearsal, breathing exercises, distraction and guided imagery. However, the interventions evaluated by Jay et al. (1987; 1995) used repeated measures studies (with random sequences) rather than RCTs meaning that coping skills (if assimilated) could contaminate the other conditions. Jay et al. (1987) reported that the effects of the intervention did not generalise to future procedures meaning that a therapist needed to coach the child each time. This suggests that the effects of the interventions were limited, and the child was not assimilating these skills. The results were mixed when an intervention for procedural distress was evaluated in an RCT (lower child distress rated by parent/nurse but no effect on perception of procedure or QoL) (Kazak et al., 1996).

* + 1. **Coping skills for illness distress**

Compas et al. (2012) related coping skills to the perceived controllability of an illness and suggested that secondary coping is more adaptive in illnesses where the child cannot control significant aspects of their illness. Coping skills interventions have targeted strategies to cope with the uncontrollable aspects of cancer (e.g. relaxation, mindfulness, distraction) and with aspects that can be controlled (e.g. cognitive reframing, social support, goal setting, symptom-management) (Rosenberg et al., 2018; Wu et al., 2014). Reviews (shown in Table 4.5) have suggested that CBT interventions are effective in improving outcomes such as anxiety, depression and treatment-related distress for children with cancer (Coughtrey et al., 2018; Kazak et al., 2005).

As shown in Table 4.1, Rosenberg et al. (2018) reported improvements in coping and QoL (cancer-specific) but not anxiety or QoL (generic) in an individualised CBT and skills-training intervention for adolescents and young adults (12-25 years). Wu et al. (2014) reported improvements in perceived symptom severity but not coping, in a group intervention with children (aged 9 years and over). It is difficult to compare these two interventions as they were evaluated using different outcomes. However, the greater effects on coping in Rosenberg et al. (2018) could be due to a longer intervention duration (8 weeks as opposed to 1 week), individualised content, or the older age group. It is also possible that the smaller sample size in Wu et al. (2014) meant it was underpowered to detect an intervention effect.

* + 1. **Coping skills for survivors**

Adaptive coping styles may change over the course of an illness, in response to what the child can control (Compas et al., 2012). Aldridge and Roesch (2007) reported that approach, problem-focused coping (primary control coping) was not adaptive shortly after a cancer diagnosis but was adaptive in survivors. Therefore, survivors may be able to focus on more controllable aspects of their illness. They may also need coping skills training to manage physical and psychological late effects of their treatment (e.g. fear of relapse, continuing chronic illness).

As shown in Table 4.1, coping skills interventions for survivors showed some promise but would need to be tested in RCTs. Two interventions that taught coping skills using CBT in group sessions (Maurice-Stam et al., 2009) and in individual telephone sessions (Santacroce et al., 2010), have only been tested for feasibility with small samples. The Surviving Cancer Competently Intervention Program (SCCIP), aimed to identify and reduce the sources of stress associated with leukaemia using family therapy and CBT (e.g. reframing and goal setting). A pilot study identified changes in the expected direction for PTS, anxiety and family functioning (Kazak et al, 1999). However, the findings from a subsequent RCT were less conclusive, with significant improvements on some measures of PTS and father anxiety, but not for mothers or other child outcomes (anxiety, PTS) (Kazak et al., 2004). Kazak et al. (2004) suggested that differential dropout of participants with higher levels of PTS reduced the study’s ability to detect intervention effects.

* 1. **Social skills training**

The risk-resistance model (Wallander & Varni, 1998) suggested that peer issues and school reintegration can cause psychosocial stress which directly impacts adjustment. It also suggested that social support is a resiliency factor which promotes positive adjustment. A number of studies have demonstrated this relationship between social support and positive family adjustment (Kazak et al., 1997; Kunin-Batson et al., 2016; Myers et al., 2014). Eiser (2004) argued that reintegration into normal school and social activities allows the child to access social support. However, children may also have to deal with problems such as teasing and bullying in response to changes in physical appearance. Effective reintegration is therefore an important target for children during and after maintenance treatment. Social skills interventions aim to teach communication skills and problem-solving skills for peer issues (e.g. bullying, teasing) (Varni et al., 1993).

Most social skills interventions have targeted survivors of brain tumours as these children often have poorer social outcomes (Gurney et al., 2009). However, survivors of other forms of cancer also report impaired social functioning and may benefit from social skills training (Mitchell et al., 2016; Mackie et al., 2000).

As shown in Table 4.2, social skills group interventions for survivors of brain tumours have reported improved outcomes (e.g. social competence, social performance, social skills, QoL, internalising behaviour) (Barakat et al., 2003; Barrera & Schulte, 2009; Barrera et al., 2018; Schulte et al., (2014). These interventions targeted nonverbal and verbal communication, empathy and conflict resolution, friendship-making, cooperation, conflict resolution, managing bullying, empathy and assertion. However, most were evaluated using a pre-post design with small sample sizes (n=13-32). A pre/post evaluation (Schulte et al., 2014) was followed up with an RCT, with less conclusive results (Barrera et al., 2018). Improvements were reported in child-reported social competence, but not QoL or parent/teacher-reported social competence.

An RCT of a social skills intervention (targeting problem-solving peer problems, assertiveness and handling teasing) for children newly diagnosed with other cancers (aged 5-13 years) reported mixed results (higher perceived social support and school competence but no improvement in social competence or self-esteem) (Varni et al., 1993). Varni et al. (1993) suggested that it would be better to target children with social impairment as the children’s scores were not generally impaired at baseline.

* 1. **Knowledge and adherence interventions**

The risk-resistance model (Wallander & Varni, 1998) described the direct impact of symptoms and treatment-related burdens on adjustment, and the indirect impact via functional impairment and psychosocial stress. Reducing these physical burdens is an important target of psychoeducational interventions. Improved illness knowledge can promote self-management of symptoms, recognising and treating side effects, avoiding complications and hospitalisations (Landier et al., 2016). Poor adherence has been associated with lower illness knowledge and is associated with poor health outcomes (Bhatia et al., 2012; NICE, 2005). Improved knowledge about procedures may also improve compliance and reduce procedural distress (Eiser, 2004).

* + 1. **Interventions to reduce procedural distress**

As shown in Table 4.3, interventions targeting procedural distress improved some procedure-related outcomes (need for sedation, reduced threat appraisal) (Bisignano & Bush, 2006; Haeberli et al., 2008), using information, rehearsals and familiarity with procedures to reduce threat appraisal and stress. These interventions aimed to reduce cognitive threat appraisal associated with procedural distress. This is a similar approach to the procedural distress coping skills interventions described in section 4.3.1. Here, information and familiarity are utilised as a coping strategy as opposed to the cognitive reframing, relaxation and distraction used in the previous coping skills interventions. A review of interventions which aimed to improve communication for children with cancer, found weak evidence that information-based interventions are effective in reducing distress around painful procedures (Ranmal et al., 2008). The weakness of the evidence reflected a lack of rigour in the evaluations and heterogenous aims and outcomes.

* + 1. **Interventions to increase illness knowledge**

As well as improving adherence, compliance and self-management of symptoms, knowledge about an illness may reduce the stress of illness uncertainty (Fortier et al., 2013). Chapter 2 argued for the importance of informing children with leukaemia about their illness in a context where they can ask questions. Open communication and family expressiveness have been associated with better adjustment in children (Van Schoors et al., 2017; Varni et al., 1996), while children with greater communication impairment have reported poorer QoL (Felder-Puig et al., 2006). Improved communication may allow children to access family and social support, communicate their needs and talk with healthcare professionals (Ranmal et al., 2008). Children may not be able to communicate about their illness unless they have an understanding of it (D’Alessandro & Dosa, 2001). Being involved in treatment-related decisions may also promote the child’s feelings of control and improve their coping skills (Compas et al., 2012).

As shown in Table 4.3, interventions to improve general illness knowledge have mainly been delivered using computer games and evaluated in RCTs (Dragone et al., 2002; Kato et al., 2008; Jones et al., 2010). Two games (designed by the same research team) delivered to children with leukaemia (Dragone et al., 2002) and to children with solid tumours (Jones et al., 2010) increased the child’s internal locus of control but not knowledge, QoL or self-efficacy.

Another computer game delivered to children with cancer, improved knowledge, adherence to medication and self-efficacy, but not locus of control, stress or QoL (Kato et al., 2008). Different results on locus of control and knowledge outcomes might reflect targeting to different age groups. The sample size was also much higher in Kato et al. (2008) and the two outcomes were measured using different scales. Kato et al. (2008) reported low compliance in their intervention (28% used the game for the recommended time) which demonstrates the difficulty of ensuring compliance in remote interventions. Kato et al. (2008) also demonstrated that it is possible to improve knowledge without improving QoL or reducing treatment-related stress. This might reflect the method of delivery. While the game is interactive it might not answer all the child’s questions or address misunderstandings.

* 1. **Health behaviour interventions**

Survivors need different information about their illness than they did during treatment. This includes information about late effects, the importance of adhering to follow-up care and the importance of positive health behaviours to reduce the risk of long-term health problems (Knijnenburg et al., 2010). Current health complaints have been shown to mediate the relationship between cancer and adjustment, which demonstrates the importance of maintaining health in survivors (Maurice-Stam et al., 2009; Kanellopoulos et al., 2013).

 Health behaviour interventions have largely been delivered to groups of survivors of childhood cancer, although a smaller number have targeted children during treatment. Interventions have focused on the prevention of future health problems by targeting health behaviours (e.g. diet, exercise, smoking, sun-related behaviours) and using a variety of methods (e.g. cooking classes, website content).

* + 1. **Health behaviour interventions during treatment**

 As shown in Table 4.4, interventions for children during active treatment, targeting exercise and nutrition, have only been evaluated using small samples and have not yet reported improvements in outcomes (Bruggers et al., 2017; Li et al., 2017). This may be an important area for future intervention development as poor eating and activity habits often begin during active treatment (Tan et al., 2013; Zhang et al., 2016). Braam et al. (2018) suggested that a physical and psychosocial intervention delivered to survivors may have been more effective if it had been delivered during treatment.

* + 1. **Health behaviour interventions for survivors**

As shown in Table 4.4, evaluations of interventions delivered to survivors, targeting exercise and nutrition, have reported a number of significant improvements (e.g. improved negative mood, improved lower body strength, parent-reported pain and procedural anxiety). However, the evidence is inconsistent (Djik-Lokkart et al., 2016; Braam et al., 2018; Howell et al., 2018). A differential effect in favour of older children (14+ years) was reported in a weight loss intervention (Huang et al., 2014) and in a review of lifestyle behaviour interventions (Kopp et al., 2017). A review of nutritional interventions delivered to survivors of childhood cancer, concluded that there was low quality evidence of improvements in health behaviours (Cohen et al., 2016). The low-quality rating reflected the lack of studies, heterogenous targets and outcomes between studies, and a lack of follow-up of health behaviours.

* + 1. **Health risk behaviour interventions for survivors**

Survivors of cancer have a higher risk of developing chronic long-term problems and secondary cancers than the general population (Ness et al., 2011; Smith et al., 2015). To reduce these risks, survivors need to understand their health vulnerabilities and engage in positive health behaviours. Some treatments also have additional implications for health monitoring (e.g. higher risk of neuropathy late effects with Vincristine) (Ness et al., 2011).

As shown in Table 4.4, positive results have been reported for health-risk behaviour interventions, in improving specific health intentions and behaviours (Mays et al., 2011a; Mays et al., 2011b; Tyc et al., 2003). An evaluation of the Survivor Health and Resilience Education (SHARE) program reported significant improvements in bone health behaviours (relating to calcium intake) and sun safety behaviours 1 month after the intervention (Mays et al., 2011a; Mays et al., 2011b). Tyc et al. (2003) reported reduced intentions to smoke, increased perceptions of vulnerability and increased knowledge in childhood cancer survivors (aged 10-18 years), following a risk counselling intervention. However, intentions may not translate into health behaviours. Hudson et al. (2002) demonstrated that increases in perceived vulnerability following a risk counselling intervention did not translate into health behaviours. Health outcomes also need to be followed-up for a longer period to see whether any improvements are incorporated into long-term health behaviours (Cohen et al., 2016).

**4.7 Conclusions and methodological issues**

This narrative review of psychoeducational interventions delivered to children with cancer suggests that interventions have improved outcomes across a range of targets (coping skills, social skills, information and adherence, health behaviours) and outcomes (e.g. anxiety, QoL, health behaviours). However, the differential and often inconsistent results make it difficult to draw generalisable conclusions about the most effective methods of delivering psychoeducation.

Interventions were often evaluated using pre/post designs or using another treatment control group (e.g. computer game vs book in Dragone et al., 2002). Many had small sample sizes which meant they were likely to be underpowered to detect intervention effects. There was also a large amount of heterogeneity in the interventions and in the outcomes used to evaluate them. Over 50 outcome measures were used in these studies, often using different constructs and scales. This makes it difficult to compare even similar interventions.

 It is important for evidence-based practise that intervention research is utilised to guide the development of new interventions (Kazak, 2005; Sackett et al., 1996). A number of reviews have attempted to synthesise the literature on psychoeducational and psychosocial interventions for children with cancer (shown in Table 4.5). Interactive skills-based learning, tailored to specific outcomes and carefully timed, was reported to be more effective in two narrative reviews of psychoeducational interventions for children with cancer and survivors (Bradlyn et al., 2003, Kazak et al., 2005). However, most systematic reviews were unable to recommend any particular approaches (e.g. Brier et al., 2015; Meyler et al., 2010; Ryan et al., 2018). Reviews highlighted significant methodological problems in intervention studies which affected the quality of evidence. These were a lack of interventions (e.g. Kopp et al., 2017; Cohen et al. 2016), a lack of RCTs (e.g. Coughtrey et al., 2018; Richter et al., 2015), a lack of validated, sensitive outcome measures (e.g. Seitz et al., 2009; Ryan et al., 2018), small sample sizes (e.g. Kopp et al., 2017; Brier et al., 2015) and heterogenous aims and outcomes (e.g. Ranmal et al., 2008; Bradlyn et al., 2003). Reviews also highlighted interventions which have been implemented in clinical care without being rigorously evaluated (Seitz et al., 2009; Coughtrey et al., 2018; Kazak et al., 2005). To come to conclusions about the effectiveness of psychoeducational interventions, future reviews would need to focus on methodologically sound studies, validated outcome measures and targets which can be compared across studies.

**4.8 Summary**

This chapter has described psychoeducational interventions which have been delivered to children with cancer. The risk-resistance model (Wallander & Varni, 1998) suggested modifiable risk and resiliency factors which have been targeted in a wide variety of psychoeducational interventions. There is evidence that psychoeducational interventions can improve adjustment in children with cancer on a number of different outcomes (e.g. social competence, QoL, anxiety, cancer knowledge). However, the evidence is inconsistent.

This review has demonstrated the challenges involved in using previous interventions to draw generalisable conclusions about psychoeducation in paediatric cancer. It is important to systematically examine the evidence base to provide recommendations and guidance for the development and implementation of novel interventions (Craig et al., 2008; Kazak, 2005). The inconsistent evidence suggests the need for a systematic review in this area. Meta-analysis is a quantitative approach to synthesising an inconsistent evidence base and exploring the reasons for heterogeneity between studies (Haidich, 2010). Chapter 5 will report a meta-analysis of psychoeducational interventions. This meta-analysis aimed to calculate an overall effect size for psychoeducational interventions and identify the most effective modes of delivery.

Table 4.1

*Coping skills interventions for children with cancer and survivors*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Authors | Intervention | Design | Sample | Time and Duration | Follow-up | Measures | Positive outcomes | Non-significant or adverse outcomes |
| Hinds et al., 2000  | Self-care coping intervention. Individual. | RCT (ac) | 78 newly diagnosed adolescent cancer patients (12-21 years) (I: 40, ac: 38) | 40 minutes in 3 stages: discussion, video, rehearsal | 6 months post-baseline | Hope, locus of control, self-esteem, self-efficacy, symptom distress, treatment toxicity |  | No group difference for any outcome |
| Jay et al., 1987 | CBT vs. pharmacologic. Individual coaching. | 3 treatment conditions: randomised sequence repeated measures | 56 children with leukaemia (3-13 years) during lumbar punctures | 30-45 minutes prior to procedure | Post procedure | Pulse rate and blood pressure, procedural distress (observed), pain (self-report) | CBT: lower pain, distress, pulse rate.  | Did not generalise to future procedures |
| Jay et al., 1995 | CBT vs. general anaesthesia. Individual coaching. | Repeated measures with randomised sequence | 18 leukaemia patients (3-12 years) during lumbar punctures | 45 minutes prior to procedure | Post intervention | Behavioural distress, pain and fear (self-report), pulse rate, anticipatory anxiety, side effects from anaesthesia, behavioural adjustment (parent) | Increased behavioural adjustment in the CBT condition 24 hours after the procedure.  | Increased behavioural distress at the beginning of the procedure in the CBT condition.No differences on pain, fear or preference for conditions. |
| Kazak et al., 1996 | Pharmacological only vs. CBT + pharmacological.Individual coaching. | RCT: pharmacological (PO), pharmacological + CBT (CI), control group (CC) | 162 children with newly diagnosed leukaemia and parents (P0: 45, CI: 47, CC:70) | No time given. Delivered during each procedural lumbar puncture. | 6 months post diagnosis | Child and parent distress, perception of procedures, parent stress, child QoL | Lower child distress before and during procedures (rated by parent and nurse) | No difference for perception of procedures, Qol. No difference on father reported child distress. Parent distress. |
| Kazak et al., 1999 | Surviving Cancer Competently Intervention Program (SCCIP). CBT and family therapy. Group family sessions. | Pre/post trial | 19 adolescent survivors (10-17 years), with parents and siblings | 4 x 1-1.5 hour group sessions in 1 day  | 1 day | PTS, state-trait anxiety (parent), child anxiety, impact of event scale, family functioning  | Decreased PTS symptoms, anxiety (parent, child), family functioning |  |
| Kazak et al., 2004 | Surviving Cancer Competently Intervention Program (SCCIP). CBT and family therapy. Group family sessions. | RCT (wlc) | 150 adolescent survivors (10-19 years), (I=76, wlc=74) parents, siblings | 4 x 1-1.5 hour group sessions in 1 day | 3-5 months post intervention | PTS, Impact of event scale (IES), state-trait anxiety (parent), anxiety (child) | Intrusive thoughts (father), arousal (child), anxiety (father) | IES, PTS (mother), avoidance, arousal, PTS (father), intrusion, avoidance, PTS (child), anxiety (mother and child) |
| Maurice-Stam et al., 2009 | ‘Op Koers’ Onco. CBT/coping skills. Group sessions. | Pre/post pilot study | 11 child survivors (8-12 years) and parents | 6 group sessions | 0-4 weeks post intervention | Social competence, positive thinking, relaxation, information-seeking | Social competence, positive thinking, relaxation, information-seeking |  |
| Maurice-Stam et al., 2014 | ‘Op Koers’ Onco- Online. CBT/coping skills. Individual. | Post-study evaluation | 11 adolescent cancer survivors (11-17 years) | 6 x 90 minutes structured chat sessions. Weekly.  | Post-intervention | Satisfaction & feasibility | Satisfaction & feasibility |  |
| Rosenberg et al., 2018, 2019 | Promoting Resilience in Stress Management (PRISM). CBT and coping skills training. Individual sessions. | RCT (sc) | 92 adolescent and young adults with cancer (12-25 years) (I= 48, sc=44) | 4 x 30-50 minutes. 8 weeks. | 6 months post baseline | Resilience scale, QoL (generic and cancer), psychological distress, anxiety/depression, coping skills | Resilience, QoL (cancer), psychological distress, depression | QoL (generic), anxiety |
| Santacroce et al., 2010 | HERO PLUS Coping skills, CBT and communications skills training. Individual telephone sessions. | Feasibility RCT (sc) | 20 adolescent and young adult survivors (15-25 years) and a parent (I= 9, sc= 11)  | 7 x 30 minutes telephone sessions | 12 week post baseline | Uncertainty in illness, anxiety, PTS, benefit finding, health promotion behaviour | Trends only due to sample size: improvements in benefit finding, small improvements in anxiety, health behaviours and PTS | Sample too small to assess between-groups differences |
| Wu et al., 2014 | Coping skills and experience sharing. Group sessions. | RCT (sc) | 58 children (9+ years) with cancer (I=29, sc=29) | 3 x 60-90 minute modules delivered in group sessions within 1 week | 3 month post intervention | Perceived symptom severity, cancer coping  | Symptom severity: pain management, gastrointestinal symptoms | Cancer coping |

RCT: Randomised controlled trial, CBT: Cognitive behavioural therapy, QoL: Quality of Life, PTS: Post-traumatic stress, I: intervention, wlc: waitlist control group, sc: standard care control group, ac: attention control group.

Table 4.2

*Social skills interventions for children with cancer and survivors*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Authors | Intervention  | Design | Sample | Time and duration  | Follow-up period | Measures | Positive outcomes | Non-significant or adverse outcomes |
| Barakat et al., 2003 | Communication skills: empathy, conflict resolution, cooperation. Group sessions. | Pre/post design | 13 brain tumour survivors (8-14 years) | 6 weekly small group sessions | 9 months | Social skills and competence, internalising, externalising and adaptive behaviour (child, parent, teacher report), QoL | Social competence (child, parent) on QoL scale. Internalising behaviour (child), symptoms.  | Externalising behaviour (child) |
| Barrera & Schulte, 2009 | Social skills training.Group sessions. | Pre/post intervention feasibility study | 32 brain tumour survivors (8-18 years) | 8 x 2 hour weekly sessions | 6 months post-intervention | Social skills, QoL, behaviour, depression, feasibility | Self-control, social skills, QoL, feasibility | Depression |
| Barrera et al., 2018 | Social skills training. Group sessions. | RCT (ac) | 91 brain tumour survivors (8-16 years) (I: 43, ac: 48) | 8 x 2 hour weekly sessions | 6 months post-intervention | Social skills, QoL | Social competence (self-report) | Proxy-report (parent, teacher) social competence, QoL |
| Schulte et al., 2014 | Social problem solving and performance. Group sessions. | Pre/post pilot study | 15 survivors of brain tumours (7-15 years) | 8 x 2 hour weekly sessions | Post intervention | Social performance, problem-solving | Social performance: eye contact and social conversations | Social problem-solving |
| Varni et al., 1993 | Social skills training: problem-solving, assertiveness, teasing. Individual sessions. | RCT: Social skills vs. standard school reintegration program (sc) | 64 children newly diagnosed with cancer (5-13 years) (I= 33, sc= 31) | 3 x 60 minute individual sessions, 2 booster sessions | 9 months | Child depression, anxiety, self-esteem, perceived social support, behavioural and emotional problems, social competence | Higher perceived social support at 9 months, decreased behaviour problems (parent-report), reduced state anxiety at 6 months, school competence at 9 months. | Depression, self-esteem, social competence |

RCT: Randomised controlled trial, QoL: Quality of Life, I: intervention, sc: standard care control group, ac: attention control group.

Table 4.3

*Knowledge and adherence interventions for children with cancer*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Authors | Intervention | Design | Sample | Time and duration  | Follow-up period | Measures | Positive outcomes | Non-significant or adverse outcomes |
| Beale et al., 2007 | Computer game intervention (‘Re-Mission’). Individual. | RCT (ac) | 375 adolescents and young adults (13-29 years) with cancer (I: 197, ac: 178) | 3 months (1 hour per week guideline) | 3 months post baseline | Cancer knowledge | Improved cancer knowledge |  |
| Kato et al., 2008: same study as Beale et al., 2007 | Computer game intervention (‘Re-Mission’). Individual. | RCT (ac) | 375 adolescents and young adults (13-29 years) with cancer (I: 197, ac: 178) | 3 months (1 hour per week guideline) | 3 months post baseline | Adherence to chemotherapy, knowledge of cancer, QoL, self-efficacy, stress, locus of control | Adherence, self-efficacy, knowledge | Stress, locus of control, QoL |
| Bisignano & Bush, 2006 | Computer game intervention (‘Spotlight on IV’s’). Individual. | RCT (sc) | 30 children with cancer scheduled for IV (7-18 years) (I= 14, sc= 16) | 20 minutes 1-2 hour prior to procedure | Post-intervention | Threat appraisal, coping strategies, children’s fear and pain self-report, procedural behaviour rating  | Threat appraisal (within groups pre/post), improved cognitive restructuring | Threat appraisal (between groups), fear, pain |
| Dragone et al., 2002 | Computer game intervention (‘Kidz with leukaemia’ space adventure). Individual. | RCT: 2 education arms: CD-Rom vs. book | 31 children with leukaemia (4-11 years) (CD-Rom: 16, Book: 15) | 3 months | Post-intervention | Health locus of control, knowledge of leukaemia treatment | Increased locus of control | Knowledge of leukaemia  |
| Haeberli et al., 2008 | Information and play program (radiotherapy). Individual sessions. | Retrospective control trial (sc) | 223 Children with cancer (up to 18 years) | Before and during procedures. 5-7.5 hours input in total | None | Need for anaesthesia | Lowered need for anaesthesia |  |
| Jones et al., 2010 | Computer game intervention. Individual. | RCT (ac) | 65 children with cancer (solid tumours) (12-18 years) I: 35, ac: 30 | CD-Rom and handbook used at home for 3 months | Post-intervention | Coping strategies, health locus of control, QoL, cancer knowledge, self-efficacy | Increased internal locus of control for the CD-Rom group | No differences on the other measures |

RCT: Randomised controlled trial, QoL: Quality of Life, I: intervention, sc: standard care control group, ac: attention control group, IV: intravenous (needle procedures)

Table 4.4

*Health behaviour interventions for children with cancer and survivors*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Authors | Intervention | Design | Sample | Time and duration | Follow-up | Measures | Positive outcomes | Non-significant or adverse outcomes |
| Bruggers et al., 2018 | Mobile video game ‘Empower Stars’: exercise and empowerment intervention. Individual. | Feasibility study of prototype game | 10 children (7-14 years old) with cancer | 20 minutes exercise as part of 30 mins daily gameplay. ‘One day’ proof of concept evaluation. | None | Acceptability for children, parents and healthcare providers | Good approval ratings | No outcomes measured |
| Dijk-Lokkart et al., 2016, Braam et al., 2018 | QLIM (Quality of Life in Motion): combined physical and psychosocial intervention. Individual sessions. | RCT (sc)  | 68 childhood cancer survivors (8-18 years) (I: 30, sc: 38) | Physical exercise sessions twice weekly (45 minutes), 6 psychosocial sessions (60 minutes), fortnightly.12 week intervention period. | 12 months from baseline | Generic and cancer specific QoL (child and parent report), depressive symptoms, behavioural problems, self-esteem | Improvement in pain and procedural anxiety (parent report) on QoL. At 12 months significantly improved lower body strength. | No improvement in psychosocial function or overall QoL. Both groups improved in QoL over time. |
| Donze et al., 2006, Mays et al., (2011a, 2011b) | The Survivor Health and Resilience Education (SHARE) program. Group session and individual boosters. | Pre/post evaluation (2006), RCT (2011a, 2011b) | 75 adolescent survivors of childhood cancer (aged 11-21 years) (I: 38, wlc: 37) | ½ day workshop plus booster phone calls | 1 month from baseline | Preliminary feasibility and acceptability (2006), bone health behaviours (2011a), sun safety behaviours (2011b) | Feasible and favourable ratings for acceptability. Bone health behaviours (calcium related), sun safety behaviours  |  |
| Howell et al., 2018 | Web-based physical activity intervention. Individual. | RCT (ac: activity monitors and health information) | 78 adolescent survivors of childhood cancer (11-15 years), (I: 53, ac: 25) | Web intervention and activity monitors used over 24 weeks | 24 weeks from baseline | Physical activity (activity monitors), fitness and strength, intelligence, QoL | Higher within-groups improvements in the intervention group in activity, intelligence, strength and QoL | No significant between-groups differences |
| Huang et al., 2014 | Fit4Life: weight loss intervention. Individual.  | RCT (ac group: weight management info via phone and mail) | 38 survivors of childhood ALL (8-18 years) with high BMI (I= 19, ac= 19) | Web (weekly), phone (weekly) and text (daily) delivered over 4 months | Post-intervention | Depression, weight gain, nutrition intake, exercise, blood pressure | Significant reduction in intervention group for negative mood compared to control. Over 14 years had lower weight gain and higher exercise | No effect on metabolic parameters (eg. blood pressure), no effect on the younger children (below 14 years). |
| Hudson et al., 2002 | The Protect Study: health behaviour training. Individual sessions | RCT (sc) | 266 adolescent survivors (12-18 years) (I=131, sc= 135)  | Single session (no duration reported) plus telephone follow-up | 1 year | Health protective behaviours, health knowledge, perceived susceptibility, benefits and barriers | Increased perceived susceptibility to health risks. Females reported more gains in knowledge. Better improvements in targeted health behaviours | Health protective behaviour or beliefs |
| Li et al., 2017 | Nutrition counselling intervention for steroid treatment. Individual sessions | RCT (sc) | 22 children with ALL (7-18 years) (I= 12, sc= 10) | Monthly counselling sessions over 1 year. | Post-intervention | Anthropometrics, dietary intake, oxidative stress | Significantly lower calorific intake from baseline to 12 month follow-up (within groups) | No significant between groups difference in dietary intake, anthropometrics, oxidative stress. No significant within groups change in BMI, waist circumference. |
| Raber et al., 2017 | Healthy cooking classes for childhood cancer survivors. Group sessions. | Pre/post evaluation | 189 survivors of childhood cancer (aged 6-18 years) | 45 minute- 1 hour cooking class delivered in camp or out-patient setting | None | Feasibility, acceptability | Intervention was well attended and well received | No outcomes reported |
| Tyc et al., 2003 | Risk counselling (tobacco use) intervention Individual session | RCT (sc) | 103 childhood cancer survivors (groups), 10-18 years (I: 53, sc: 50) | One 50-60 minute risk counselling session. Educational video. Telephone reinforcement  | 1 year | Knowledge, perceived vulnerability, intentions to use tobacco | Knowledge, perceived vulnerability, intention to use tobacco at 12 months | None of the outcomes were significant at 6 months |

RCT: Randomised controlled trial, QoL: Quality of Life, I: intervention, sc: standard care control group, ac: attention control group, BMI: body mass index.

Table 4.5

*Systematic reviews of psychoeducational and psychosocial interventions for children with cancer and survivors*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Authors | Scope of review | Studies | Findings  | Methodological issues | Recommendations |
| Bradlyn et al., 2003Beale et al., 2003 | Psychoeducational interventions for children with cancerPart 1: information and knowledgePart 2: information and skills training | Narrative review | Interventions most effective where tailored to information and coping needs, interactive and addressing skills as well as information. Multimedia as a promising mode of delivery.  | Lack of interventions with children and interventions addressing adherence. Wide range of outcomes which make it difficult to compare. | More interventions with children. Develop multimedia interventions as a way to reduce cost and increase acceptability and accessibility. Adherence interventions.  |
| Brier et al., 2015 | Psychosocial, health promotion and neurocognitive interventions for survivors of childhood cancer  | 24 | Medium to large effect sizes in 14 studies for a range of health behaviours. No specific intervention characteristics identified as more effective.  | Small samples, heterogeneity of outcomes, study design and follow-up. Lack of studies in middle childhood age range (8-12 years) and late adolescence. | Alternative methods of delivery which reduce burden of participation should be tested (e.g. eHealth, telephone). Look at tailoring to needs of individual children (e.g. developmental stage at treatment, age groups). |
| Cohen et al., 2016 | Nutritional interventions for survivors of childhood cancer | 3 | Lack of studies and very heterogenous in targets and outcomes. Low quality evidence of improvements in health behaviours but not whether it translated into future health behaviours and cardiovascular risk. | Low quality evidence. Lack of studies. Lack of objective measures in studies.  | Need for additional evidence and high-quality studies. |
| Coughtrey et al., 2018 | Psychosocial Interventions evaluated in RCTs for Psychological Outcomes in Pediatric Oncology | 12 | Psychosocial interventions improved psychological symptoms in 9 studies and physical symptoms in 6 (including procedural distress). CBT was effective in reducing psychological symptoms.  | Small number of RCTs in this area. Lack of RCTs used to evaluate treatment modalities used in practise eg. psychotherapy, narrative therapy.  | Need for more RCTs in this area, especially of interventions which are already used in clinical care.  |
| Kazak, 2005 | Interventions for survivors of childhood cancer and families | Narrative review | Interventions for procedural distress were effective. Effective interventions are carefully timed and tailored to specific outcomes. | Little evidence for the consistent application of interventions in medical practise. Lack of interventions for relapsed and palliative patients. Lack of fathers and siblings in interventions. Lack of diversity in samples.  | Need for interventions addressing issues around survivorship. Tailor interventions specifically to cancer populations rather than general psychopathology. Move from deficit to competency models. Target subgroups with problems.  |
| Kopp et al., 2017 | Lifestyle behaviour interventions delivered using technology in childhood, adolescent, and young adult cancer survivors | 6 | Studies primarily targeted physical activity. Mostly delivered via the web. Modest improvements in outcomes and mostly in the older adolescent to young adult group. Moderate study quality. All studies demonstrated high feasibility and acceptability. | Small sample sizes so few significant improvements. Short duration interventions. One study had low adherence to program. | Few interventions have been developed. Opportunity to develop and evaluate more.  |
| Meyler et al., 2010 | Family-based psychosocial interventions for childhood cancer | 21  | Behavioural interventions for procedural distress with family input were effective. Feasible to include family component. Included in a variety of ways. | While many showed beneficial outcomes, the majority were not empirically robust. Small sample sizes, no control group. Small number of studies. Not enough evidence to draw conclusions about best ways to include families. | Inclusion of control groups. Report effect sizes, clinical significance and theoretical basis. Cost effectiveness should be included. |
| Nunns et al., 2018 | Non-pharmacological interventions to reduce procedural distress in children treated for cancer | 15 | Efficacy for interventions using hypnosis on pain and anxiety. Less evidence for non-hypnosis-based interventions. | Non-hypnosis interventions were not rigorously tested. High heterogeneity. | Need for more rigorous testing, especially in the older age range and for non-hypnosis interventions. |
| Pai et al., 2006 | Meta-analysis of psychological interventions in pediatric oncology on psychological distress and adjustment | 12 | Small effects for parent distress and adjustment. Near zero effects for children. | Many interventions unfocused. Many modalities included. Lack of attention control groups. Lack of follow-up and reporting of clinical significance.  | Include attention control groups. Longer follow up periods in interventions. Report effect sizes. Need for theoretical underpinning of interventions.  |
| Ranmal et al., 2008 | Interventions to improve communication for children and adolescents with cancer | 10 | Weak evidence that specific information-based interventions are effective for painful procedures and reintegration into school/activities. | Interventions to improve communication for children with cancer have not been tested widely or rigorously. Heterogenous aims and outcomes of studies. | Lack of evidence. More research needed.  |
| Richter et al., 2015 | Psychosocial interventions for adolescents and young adult cancer patients | 12 | Technology-based, psychoeducational, multicomponent and physical exercise interventions for this age group have very small, non-significant effects. The biggest improvements were in cancer-related knowledge | Difficulties recruiting adequate sample sizes to detect an effect. Lack of interventions for this age range. Pre-post designs cannot be used to evaluate effectiveness. Not possible to do subgroup analyses because of heterogeneity.  | Need for more age-specific interventions. Larger sample sizes and RCT designs.  |
| Ryan et al., 2018 | Interventions to improve the aftercare of survivors of childhood cancer | 29 | Evidence that interventions are effective for children and families but lack of long-term follow-up. Not enough evidence to recommend particular approaches.  | Most interventions were at a pilot stage and had not been evaluated over the long-term. Lack of validated measures. Heterogeneity of outcomes and study design. | Need larger sample sizes in multicentre interventions. Longer follow-ups and more RCTs. Look at whether ehealth interventions can reach enough to make these methods useful.  |
| Seitz et al., 2009 | Psychosocial interventions for adolescent cancer patients | 4 | Lack of research exclusively for adolescents. 1 out of 4 studies reported positive outcomes in reducing distress, improving knowledge and improving body image. No effect in other 3 studies. | Lack of relevant evidence. Few studies. Most included studies were pilot studies with small sample sizes. High refusal rates and selective samples. Heterogenous samples (on, off treatment, tumour types). Possibly insensitive outcome scales.  | Need longitudinal studies with large sample sizes and sensitive instruments. Especially of interventions already being implemented in clinical practise.  |

RCT: Randomised Controlled Trial; CBT: Cognitive Behavioural Therapy.

**Chapter 5**

**Psychoeducation for children with chronic conditions: A systematic review and meta-analysis**

Chapter 4 discussed the potential of psychoeducation to improve outcomes for children with cancer, in a variety of populations, with different targets and different methods of delivery. The evidence from these psychoeducational interventions and systematic reviews suggested that it is possible to improve outcomes, but the qualitative review method could not quantify how effective they are or come to conclusions about which components, targets and modes of delivery are effective in this population. It was also not a systematic and comprehensive review of the literature. It is important to synthesise research on psychoeducation to support the development of novel interventions and to estimate the effect an intervention might have (Sackett et al., 1996). Therefore, this chapter will report a meta-analysis which attempted to comprehensively search the literature, to quantify the effect of psychoeducational interventions for children with leukaemia and to identify the key ingredients for successful intervention. Meta-analysis provides an effective method of systematically and statistically combining results from a large body of inconsistent literature (Borenstein et al., 2009; Haidich, 2010).

The systematic review and meta-analysis reported in this chapter aimed to include interventions delivered to children with leukaemia and other cancers, but also included other chronic conditions. This broader range of illnesses was included to increase the amount of data available as it was not clear how many evaluations of interventions for children with leukaemia would be suitable for inclusion. Drawing on intervention studies from more common conditions might provide insight for how to

effectively intervene for children with leukaemia. This chapter will discuss the overlap of

 82

characteristics between leukaemia and other chronic conditions. Discussion of the

meta-analysis will examine whether it is appropriate to generalise findings from other conditions to children with leukaemia.

As described in Chapter 3, the risk-resistance model provided a framework for understanding how children adjust to illness. This model represented a non-illness specific approach to understanding illness adjustment. Wallander and Varni (1998) stated that ‘despite the biomedical uniqueness of each illness, there is considerable commonality in psychosocial ramifications’ (p.29). This was highlighted in studies of children with cancer which showed that disease-related factors are not the main predictors of adjustment outcomes (Kanellopoulos et al., 2013; Varni et al., 1996a). Therefore, it may not be the physical effects of an illness which are most important for how the child adjusts, but common psychosocial processes which the child utilises to adapt. These processes represent the targets for psychoeducational interventions. This meta-analysis aimed to quantify the effect of psychoeducation for children with leukaemia and also to examine whether this effect was indeed similar across a range of conditions. To reflect this focus on adjustment, the outcome measure used was QoL.

**5.1. The role of meta-analysis in evidence-based practise**

It has been argued that meta-analysis provides the highest quality platform for evidence-based practise (Borenstein et al., 2009; Murad et al., 2016). Meta-analysis collates evidence from a number of comparable studies and can provide a more meaningful estimate of the true effect of an intervention than any one study alone. It can be used to draw generalisable conclusions from what appears to be an inconsistent literature, can increase the power to detect an effect (especially with small samples in individual studies) and can explore the underlying reasons for heterogeneity between studies (Haidich, 2010).

The interventions and reviews considered in Chapter 4 identified the potential of psychoeducation to improve outcomes but suggested few generalisable conclusions. Therefore, there is a need for a review in this area which can address the problems highlighted in previous reviews (e.g. lack of RCTs and small sample sizes). The problem of small sample sizes is reduced by meta-analysis as it quantitatively synthesises results, providing a larger overall sample size than any one study (Borenstein et al., 2009). Meta-analysis focuses on effect sizes rather than statistical significance meaning that all studies have a weighted contribution to the overall conclusion.

The inconsistent evidence from the interventions in Chapter 4 suggested a number of moderators of effect (e.g. age, length of the intervention) could be affecting the outcomes. Examining these moderators systematically in a meta-analysis allows hypotheses to be tested regarding differential effects (Haidich, 2010). For example, analyses could test the hypothesis that psychoeducation is more effective in group interventions than in individual interventions.

However, while meta-analyses can explore heterogeneity, the included studies must be comparable, or the results may be meaningless and obscure otherwise important differences in the effect (Higgins & Green, 2009). Some meta-analyses have been criticised for not comparing ‘like with like.’ For example, Simon and Bellver (2014) argued that the use of poor-quality studies and inappropriate pooling in meta-analyses, has led to medical recommendations which are erroneous and misleading in the context of an unrelated medical procedure (‘endometrial scratching’). One of the main sources of heterogeneity in Chapter 4 was the variety of outcomes used (over 50 different outcomes). In a meta-analysis, only similar outcomes can be pooled to give an overall effect size (Higgins & Green, 2009).

**5.2. The comparative burdens of leukaemia and chronic illness**

 Chapter 1 described chronic conditions as illnesses with symptoms which start gradually and persist over a long period of time. There is usually no ‘cure’ for chronic conditions and children are likely to require long-term medication, medical procedures and involvement with healthcare. Examples of pediatric chronic conditions include diabetes, asthma, cystic fibrosis and epilepsy. Chronic conditions are defined in contrast to acute illnesses which have sudden onset of symptoms, last for a short period of time and can be ‘cured’. As discussed in Chapter 1, childhood leukaemia has features of an acute and chronic illness (Eiser, 2004; Turner-Cobb, 2014). The onset of symptoms in leukaemia is often sudden but the illness and its treatment last for many years during which time children will require medication, medical procedures and regular healthcare appointments.

Wallander and Varni (1998) highlighted the common features of childhood chronic illnesses, including childhood cancer, in the development of the risk-resistance model and developed QoL measures to compare burdens across conditions (Varni et al., 2007; Wallander & Varni, 1992). They also suggested that their model could be used to develop interventions which targeted these common burdens.

 As suggested by the risk-resistance model (Wallander & Varni, 1998), pediatric chronic illnesses lead to impairment in adjustment outcomes (e.g. QoL) regardless of the condition (Beattie & Lewis-Jones, 2006; Varni et al., 2007). Chronic illnesses are a major cause of activity limitations, school absences and anxiety (Holt, 2017; Lozier et al., 2019). Many of the risk factors which were described for children with leukaemia in Chapter 3 (e.g. hospitalisations, medication regimes and unpleasant medical procedures) are also features of other chronic conditions.

Chronic conditions during childhood require long-term management by children and families. Poor self-management behaviours have been associated with higher levels of adjustment impairment (Dean et al., 2010; Lozier et al., 2019) while positive adjustment has been associated with better treatment adherence and effective self-management (McGrady et al., 2015; Piercy et al., 2015). Therefore, the focus of many interventions for children with chronic conditions is on improving treatment adherence, self-management of symptoms and compliance with procedures. Non-adherence has

serious consequences in many conditions. The majority of children with diabetes do not achieve optimal glycaemic control (control of blood sugars) which can have serious long-term health implications, including retinopathy and cardiovascular disease

(Nathan et al., 2009), while children with uncontrolled asthma are at higher risk of mortality (Peters et al., 2006). Suboptimal adherence to chemotherapy for children with leukaemia is also associated with poor health outcomes (Bhatia et al., 2012).

As discussed in Chapter 1 the majority of survivors of childhood leukaemia have physical late effects and health vulnerabilities which require long-term treatment and monitoring (Berbis et al., 2013; Ness et al., 2011). Preventative healthcare, which requires knowledge and perceived vulnerability to future health risks, is also an important part of self-management for children with other chronic conditions.

Children with leukaemia experience unpleasant physical symptoms during treatment and are at a greater risk of developing long-term chronic health conditions. Like other chronic conditions this can impair their physical functioning. Lower levels of physical activity, cardiorespiratory fitness and higher levels of obesity have been reported for children with leukaemia and other chronic conditions (Maggio et al., 2010; Van Brussel et al., 2006). Functional impairment was strongly associated with worse adjustment in Chapter 3. Therefore, encouraging children to maintain physical fitness and general health are a target in many interventions for children in a range of chronic conditions (e.g. Huang & Ness, 2011; Quirk et al., 2014).

Chronic illnesses also share many of the psychosocial stresses which were described with reference to leukaemia in Chapter 3. Chronic illnesses can restrict the child’s normal activities and peer relationships. Children with chronic illnesses often miss school which can affect their academic progress. They may also experience psychosocial stress in relation to peers, body-image and loss of independence (Last et al., 2007). Children with chronic illnesses report higher levels of behaviour problems and social withdrawal than their healthy peers (Martinez et al., 2011; Pinquart & Shen, 2011).

The risk-resistance model highlighted the importance of cognitive appraisal and coping strategies in adjusting to illness. Illness uncertainty has been described as a stressor in cancer and other chronic conditions, in relation to uncertain long-term prognoses and effects of treatment (Hoff et al., 2002; Neville, 1998). In a review of studies of coping strategies, secondary control coping was reported to be a more effective coping strategy for children with cancer and other chronic conditions (Compas et al., 2012). This was related to the uncontrollable and intrusive features of chronic illnesses.

Leukaemia places stress on families because of its life-threatening nature. Fear of relapse and death are common and can make communication within families more difficult (Young et al., 2003; Zebrack, 2000). Other chronic conditions can also lead to early mortality and heightened anxiety in the child and family (LeBlanc et al., 2003). Both asthma and epilepsy cause deaths, and cystic fibrosis reduces the child’s life expectancy considerably (median survival = 36.6 years in 2009, Cystic Fibrosis Trust, 2013).

**5.3. The role of psychoeducation in managing chronic illness**

To improve treatment adherence and self-management in chronic health conditions, the child and family often need to learn complex information and skills. This requires educational input and support from health professionals (Price et al., 2015). Psychoeducation may be able to reduce illness-related burdens by improving knowledge about the illness, improving treatment adherence and self-management, reducing treatment-related distress and improving social and communication skills (Barlow & Ellard, 2004; D’Alessandro & Dosa, 2001).

When children with leukaemia are first discharged from hospital to manage the illness at home, families require knowledge about neutropenic precautions (infections), medication adherence, bleeding precautions, steroid side effects, nutrition, anaemia, chemotherapy side effects, procedures and hospital visits (Haugen et al., 2016). In other chronic conditions families need to understand symptoms, treatment-regimes and how to incorporate illness management into normal activities. For example, asthma management requires knowledge about symptoms, triggers, proper use of medication and inhalers, and how to manage exacerbations (Gardner et al., 2015). Diabetes management involves maintaining optimal levels of blood sugar in a daily regimen of blood monitoring, insulin dose adjustment and meal planning (ISPAD, 2000).

**5.4 Potential moderators of effect**

Systematic reviews of psychoeducational interventions for children with chronic conditions have highlighted improvements in disease-related factors such as symptoms, self-efficacy and self-management with small to medium effect sizes (Boyd et al., 2009; Murphy et al., 2006), according to Cohen’s (1988) conventions. However, results are inconsistent across outcomes and intervention targets (Barlow and Ellard, 2004). Given these inconsistencies, there are likely to be moderators of effect which have not been adequately explored. Chapter 4 identified a number of potential moderators in psychoeducational interventions delivered to children with cancer (e.g. age, inclusion of other family members, intervention length, targeting and setting which can be explored using meta-analysis.

Previous reviews have reported positive outcomes for family interventions in a range of chronic conditions (Feldman et al., 2018; Law et al., 2014; Lohan et al., 2015). As described in Chapter 3, family communication and support were associated with better adjustment in children with cancer (Van Schoors et al., 2017; Varni et al., 1996b). Non-adherence and poor self-management have been associated with negative family functioning and family conflict, particularly during adolescence (Lewin et al., 2006; Lohan et al., 2015). Therefore, psychoeducational interventions might have more potential to improve outcomes in family interventions and for older children (adolescents). Time input (dosage) and the duration of intervention delivery might also moderate intervention effectiveness. The information required for effective self-management is likely to require considerable input. However, there is little evidence for optimal time inputs, with some reviews observing no effect of dosage (Hood et al., 2010).

Reviews of psychoeducational interventions have not been able to reach conclusions about the most effective modes of delivery (Barlow & Ellard, 2004; Murphy et al., 2006). Reviews have often been limited by the existing literature which includes many uncontrolled and underpowered studies, poorly described interventions and inadequate reporting of results (Barlow & Ellard, 2004; Murphy et al., 2006). The use of a wide range of intervention targets and outcome measures has also hampered attempts to summarize the literature for children with chronic illnesses (Hilliard et al., 2016). These are similar concerns to those raised in the systematic reviews reported in Chapter 4, suggesting that the same methodological concerns exist in both bodies of literature.

**5.5. Scope of the meta-analysis**

This meta-analysis included psychoeducational interventions delivered to children with chronic conditions, evaluated in an RCT. The sole inclusion of RCTs reflects the methodological concerns raised by previous reviews in regard to uncontrolled studies (e.g. Richter et al., 2015; Ryan et al., 2018). The inclusion of other chronic conditions extended the evidence base from the paediatric cancer literature reviewed in Chapter 4 and reflects the common burdens of leukaemia and other chronic conditions. Condition was included as a moderator of effect to examine whether psychoeducation had similar effects for children with different chronic conditions.

To reduce heterogeneity arising from different outcomes and to allow the pooling of studies, QoL outcomes were meta-analysed. Other outcomes measuring symptoms, knowledge and self-management are likely to differ according to chronic condition (e.g. glycaemic control in diabetes, lung function in asthma) and are not directly comparable. However, adjustment to illness (operationalised as QoL) is modelled as a feature of all chronic illnesses (Wallander & Varni, 1998).

The psychoeducational interventions described in Chapter 4 included interventions with illness-specific information and interventions with generic coping and

social skills. To reduce heterogeneity in intervention target, this meta-analysis focused on interventions which delivered illness-specific information (coping and social skills could be included alongside this component). While coping skills may provide motivation to apply illness knowledge, self-management of a chronic illness will require the transfer of illness-specific knowledge.

The meta-analysis (1) quantified the effectiveness of psychoeducational interventions across a range of conditions, (2) examined potential moderators of effect, such as chronic condition and mode of intervention delivery (setting, grouping, dose, duration) and (3) considered these results in light of the quality of the evidence. Based on the literature reviewed to this point, the hypotheses tested were 1) that psychoeducational interventions would improve child QoL across a range of chronic conditions (Wallander & Varni, 1992), 2) that age would moderate the effect (larger effects in interventions delivered to older children) (Lohan et al., 2015), 3) that interventions which included a parent/caregiver would have a larger effect (Feldman et al., 2018) and 4) that interventions delivered over a longer duration and/or with a larger dose would have a larger effect (Hood et al., 2010). Due to a lack of evidence on the most effective modes of delivery (grouping and setting) from the pediatric cancer and chronic illness literatures, these were exploratory moderators without directional hypotheses.

**5.6. Methods**

**5.6.1. Literature Search Strategy**

Web of Science, PsycInfo, Medline (via Pubmed) and Cumulative Index of Nursing and Allied Health Literature (CINAHL) databases were searched for interventions published from 1st January 1980 to 12th August 2018. The first QoL scale developed to measure outcomes for children with chronic conditions was used in 1985 (Eiser & Morse, 2001), so the start date ensured all relevant studies would be included. The search strategy used a PICO (Population, Intervention, Comparison group, Outcome) framework for searching the literature, including search terms for Population (children with chronic illnesses), Intervention (psychoeducation), Comparison group (RCT with non-treatment control group) and Outcome (QoL). An example search strategy is provided in Figure 5.1.

Headings represent PICO search terms:

Population: Topic= (Child\* OR adolescent\* OR teen\* OR youth OR young\* OR juvenile OR ped\* OR paed\* OR infant) AND Topic= (“Chronic disease” OR “chronic illness” OR “chronic condition” OR asthma OR diabetes OR epilepsy OR cancer OR leuk\* OR arthritis OR eczema OR rhinitis OR rheumat\*) AND

Intervention: Topic= (Intervention\* OR “pilot study” OR group OR therap\* OR session OR program\* OR training OR skills OR support OR workshop) AND Topic= (Psycholog\* OR psychoeducation\* OR psycho-education\* OR psycho-soc\* OR psychosoc\* OR CBT OR “cognitive behaviour\*” OR education\*) AND

Comparison: Topic= (RCT OR “randomised controlled trial” OR “controlled trial” OR “control group”) AND

Outcome: Topic= (QOL OR “quality of life” OR HrQOL OR “health related quality of life” OR PedsQL OR “child health questionnaire” OR PAQOL)

Timespan: January 1980- August 2018

*Figure 5.1* Web of science search strategy used for identifying eligible studies for the meta-analysis.

**5.6.2. Inclusion/exclusion criteria**

The goal was to identify RCTs of psychoeducational interventions for children with chronic health conditions, which reported QoL using a validated QoL measure. Studies were first eliminated on the basis of age and chronic health condition. Included studies targeted children up to 18 years old with a diagnosed chronic physical health condition. Studies which were not RCTs or did not have a non-education control group were eliminated. Other treatment comparison groups (e.g. motivational interviewing, counselling) were excluded. These studies may underestimate the effect of psychoeducation if the treatment included in the comparison group also improved QoL. Studies which did not use a validated QoL measure (published details were required regarding reliability, applicability and validity of the measure) were the excluded. Measures could be generic or illness-specific and self or parent-reported (self-reported and illness-specific measures were given preference in studies using multiple approaches). Finally, studies which did not report a psychoeducational intervention with illness-specific information were also excluded.

**5.6.3. Data extraction and management**

Titles and abstracts retrieved using the search strategy were screened for relevance. Full text articles were then screened for inclusion with a random 10% sample screened by a second reviewer. This gave an initial 87% agreement rate. All disagreements were resolved through discussion. Data extraction was carried out using a piloted form with a 20% sample audited by another reviewer, which gave an initial 92% agreement rate. Means and standard deviations for the total QoL scale or data from which these could be calculated were extracted for meta-analysis. Authors were contacted if data was omitted. The data for meta-analysis was extracted and audited by a second reviewer. This gave an initial agreement of 80%. The remaining 20% was re-extracted to give a final dataset with full agreement.

**5.6.4. Risk of bias assessment**

Risk of bias was assessed using the Cochrane systematic reviews tool (Higgins et al., 2011). Risk was assessed as high, low or unclear for selection bias (random sequence generation and group allocation concealment), performance and detection bias (blinding of participants and researchers to group allocation), attrition bias (loss of participants during the study), reporting bias (full reporting of planned outcomes) and cluster design bias (cluster randomisation, cluster baseline imbalance and cluster attrition). A random sample of 25% was assessed by a second reviewer which gave an initial agreement of 80.4%. Disagreements were resolved through discussion. A funnel plot (plotting effect size against standard error) was used to check for publication bias (Sterne et al., 2011).

**5.6.5. Data synthesis**

Data analysis was conducted using Revman 5.3 (The Cochrane Collaboration, 2014). Effect sizes were calculated as the Standarized Mean Difference (SMD) between intervention and control groups post-intervention (Cohen’s d) (Cohen, 1988) using a random effects model (Borenstein et al., 2010). To avoid over-weighting cluster RCTs, a design effect was calculated: 1+(M-1)ICC (M= average cluster size, ICC= intraclass correlation). The sample size was divided by this design effect to give an effective sample size (McKenzie et al, 2016). A pooled effect size (SMD) and measure of heterogeneity (I2) were calculated for all analyses. Moderators were tested in subgroup analyses for chronic condition (asthma, diabetes), intervention setting (clinic, school, home), grouping (individual, group) and inclusion of a parent/caregiver (included, not included).

The subgroup analysis for age compared pre-adolescent children (aged up to 12 years) with children aged 12 years and over. Twelve years was used to differentiate between childhood and adolescence, which has been identified as a period of difficulty in managing chronic illnesses (Lewin et al., 2006; Lohan et al., 2015). Age range and mean age were used to allocate studies which had a mixed age range. The cut-off of 12 years reflected the groupings of the included studies and the age range targeted in the leukaemia intervention (described in Chapter 6: 7-12 years). There were insufficient studies to separate the younger children (pre-7 years) into a subgroup.

As there is little evidence for optimal doses of psychoeducational interventions, the subgroups used to distinguish between time inputs were defined pragmatically: 7 studies were up to 3 hours and 7 were over 4 hours. National Institute for Health and Care Excellence (NICE, 2013) guidelines for length of behaviour change interventions were used to distinguish duration subgroups (short: <3 months, medium: 3 months-1 year). Subgroup analyses evaluated biases due to study design (RCT, cluster RCT), type of control group (usual care, wait list, attention), study quality (high risk of bias, no high risk of bias) and outcome reporter (parent, child-report).

Some QoL measures have conventions for calculating a Minimal Clinically Important Difference (MCID) that patients perceive to be beneficial and which would mandate a change in the patient’s management (Jaeschke et al., 1989). Where possible, pre- and post-intervention scores were used to calculate whether an MCID had been achieved.

**5.7. Results**

**5.7.1. Characteristics of included studies**

Database searches and contact with authors identified 19,660 studies as shown in Figure 5.2; PRISMA flow diagram (Moher et al., 2009). Full texts were read for 198 papers and 173 papers were excluded; non-RCTs (49 studies), no child QoL outcome (45), delivered to adults (21), duplicate studies (11), inadequate data (20), not psychoeducation (25), unavailable (2). Attempts to contact authors were made before excluding on the basis of inadequate data or unavailability. The remaining 25 studies are summarised in Table 5.1.

Records identified through other sources: contact with authors
(n = 7)

Records identified through database and reference searching
(n = 19653)

## Identification

Duplicates removed (n=299)

Records excluded
(n = 18617)

Records screened (by title)
(n = 19660)

## Screening

Records screened (by abstract)
(n = 744)

Records excluded
(n=546)

Full-text articles assessed for eligibility
(n=198)

Full-text articles excluded
(n =173)

## Eligibility

Studies included in meta-analysis
(n = 25)

## Included

*Figure 5.2* Prisma Flow Diagram (Moher et al., 2009) showing screening and selection of included studies (searches carried out between 16/7/2018 to 12/8/2018)

Table 5.1

*Characteristics of studies included in the meta-analysis*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Study | Design | Age in years (mean) | Setting/ Instructor | Grouping | Mode of delivery and educational content of intervention | Dose/ duration | QoL scale/ reporting |
| **Asthma studies** |
| Almomani et al., 2017 | RCT, uc | 7-18 (10) | Clinic Dr | Individual (Ch + Cg) | Demonstrations, explanations, phone call follow-up. Symptoms, triggers, inhaler use, medication | 1x 30 min  | PAQLQ; dis-sp, SR |
| Bowen, 2013 | RCT, ac | 8-12 (9) | Clinic Nurse | Group (Ch) | Structured educational program. Pathophysiology, medications, exacerbations, lifestyle | 3x 90 min 3 weeks | PAQLQ, dis-sp, SR |
| Bruzzese et al., 2011 | RCT, wlc | 14-16 (15.1) | School Health educator | Group (Ch) Individual | Structured educational program, individual coaching. Pathophysiology, symptoms, medication, triggers, monitoring, lifestyle | 3x 45-60 min 8 weeks | PAQLQ, dis-sp, SR |
| Butz et al., 2005 | ClRCT, uc  | 6-12 (8) | School Health educator | Group (Ch, Cg) | Interactive workshops, demonstrations, discussion. Pathophysiology, medications, symptoms, inhalers, triggers, action plan | 2x 120 min | PAQLQ, dis-sp, SR |
| Cano-Garcinuno et al., 2007 | RCT, nd | 9-13 (11) | Clinic Dr/nurse | Group (Ch, Cg, Ch+Cg)  | Demonstrations, written materials, instruction. Pathophysiology, triggers, medication, inhalers, triggers, exacerbations | 3x 45-60 min 6 weeks | PAQLQ, dis-sp, SR96 |
| Cicutto et al., 2005 | ClRCT, wlc | 6-11 (8.6) | School Health educator | Group (Ch) | Structured educational program (RAP). Pathophysiology, triggers, medications/inhalers, symptoms, action plans, lifestyle | 6x 60 min 6 weeks | PAQLQ, dis-sp, SR |
| Cicutto et al., 2013 | ClRCT, wlc | 6-11 (8.23) | School Health educator | Group (Ch) | Structured educational program (RAP). Pathophysiology, triggers, medications/inhalers, symptoms, action plans, lifestyle | 6x 45-60 min 6 weeks | PAQLQ, dis-sp, SR |
| Henry et al., 2004 | ClRCT, wlc | 13-14  | School Teacher | Group (Ch) | Structured educational program. Pathophysiology, triggers, medications/inhalers, symptoms, lifestyle  | 3x unsp.  | PAQLQ, dis-sp, SR |
| Horner et al., 2014 | ClRCT, ac | 7-11 (8.78) | School, home Nurse | Group (Ch), Individual  | Demonstrations, instruction, home visit. Symptoms, triggers, pathophysiology, medication, inhalers | 16x 15 min 10 weeks | PAQLQ, dis-sp, SR |
| Praena-Crespo et al., 2017 | ClRCT, wlc | 10-12 (10.5) | School Teacher | Group (Ch) | Structured educational program. Pathophysiology, symptoms, triggers, medication, healthy lifestyle, activity | 3x 45 min 6 weeks | PAQLQ; dis-sp, SR |
| **Diabetes studies** |
| Boogerd et al., 2014 | RCT, uc | 11-21 (15.23) | Home (comp) Nurse | Individual | On-line interactive website. Individualised treatment overview, monitoring, professional interaction | Variable 9 months | PedsQL-DM; dis-sp, SR |
| Christie et al., 2014 | ClRCT, uc | 8-16 (13.1) | Clinic Nurse | Group (Ch + Cg) | Structured educational program. Food, insulin and blood glucose, blood glucose testing, insulin adjustment, lifestyle  | 4x 120 min 2 days | PedsQL-DM, dis-sp, SR |
| Katz et al., 2013 | RCT, uc | 8-16 (12.9) | Clinic RT | Individual (Ch + Cg) | Family teamwork: problem solving, role playing. Blood sugar monitoring, hypoglycaemia, weight | 4x 30 min 12 months | PedsQl, gen, SR |
| Laffel et al., 2003 | RCT, uc | 8-17 (12.1) | Clinic RT | Individual (Ch + Cg) | Family teamwork: responsibility sharing, conflict resolution. Blood glucose monitoring, managing blood sugars  | 4x 15-20 min 12 months | PedsQl, gen, SR |
| Lawson et al., 2005 | RCT, uc | 13-17 (15.2) | Home (tel) Nurse | Individual | Personalised telephone instruction/ discussion. Blood sugar monitoring. Insulin adjustment.  | Variable 6 months | DQOLY, dis-sp, SR |
| Murphy et al., 2012 | RCT, uc | 11-16 (13.1) | Clinic Nurse | Group (Ch + Cg) | Family teamwork: communication, responsibility sharing. Carbohydrate counting, blood glucose monitoring, insulin adjustment, activity, puberty | 6x 90 min 6 months  | DQOLY-SF: dis-sp, SR |
| Price et al., 2015 | ClRCT, uc | 11-16 (13.8) | Clinic Nurse/ dietician | Group (Ch) | Structured educational program. Carbohydrate counting, insulin adjustment, hypoglycaemia, long term complications | 10x unsp. 5 days | PedsQL-DM; dis-sp, SR |
| **Atopic Dermatitis/Eczema studies** |
| Grillo et al., 2006 | RCT, wlc | 0-16 (4.3) | Clinic Nurse | Group (Ch + Cg) | Understanding AE, triggers, investigations and treatment. Practical demonstration of wet wrapping | 1x 120 min 1 day | CDLQI, dis-sp, SR |
| Liang et al., 2013 | RCT, ns | 5-16 (ns) | Clinic Clinician | Group (Ch + Cg) | Treatment and management of AD, food allergy, skin care, the use of emollients | 4 x 120 min 4 weeks | CDLQI; dis-sp, ns |
| Ryu & Lee, 2015 | ClRCT, uc | 8-12 (9.3) | School School nurse | Group (Ch + Cg) | Management and treatment of AD: reduce AD symptoms. Skin care: bathing and moisturising | 2 x 40 min sessions 6 weeks | CDLQI; dis-sp, PR |
| **Juvenile Idiopathic Arthritis studies** |
| Armbrust et al., 2017 | RCT, wlc | 8-13 (9.95) | Home and clinic. Clinicians | Individual and group (Ch + Cg) | Pathophysiology of JIA, physical activity, barriers to exercise, motivation and goal setting | Ns 14 wks | PedsQL; gen, SR |
| Stinson et al., 2010 | RCT, ac | 12-18 (14.5) | Home (comp/tel)Clinicians | Individual (Ch, Cg) | Pathophysiology of JIA: diagnosis, medications, managing symptoms (pain, stiffness, and fatigue), coping skills, exercise, nutrition, splints, lifestyle | Variable 12 weeks | JAQQ; dis-sp, SR |
| **Cystic Fibrosis studies** |
| Christian et al., 2006 | RCT, wlc | 8-12 (9.27) | Home (visit) and Clinic RT | Individual (Ch + Cg) Group (Ch) | Diagnosis, communicating about CF, peer issues, physical activity | Ns 2 weeks | PIES, gen, SR |
| **Epilepsy studies** |
| Dorris et al., 2017 | RCT, wlc | 12-17 (14) | Clinic Nurse/ clinician | Group (Ch) | Epilepsy knowledge, sharing experiences, self-management, adherence, appointments, sleep, diet, coping skills | 6 x 120 min 6 weeks | GEOS, dis-sp, SR |

|  |
| --- |
| **Cancer studies** |
| Kato et al., 2008 | RCT, ac | 13-18 (ns) | Home (comp) RT | Individual | Pathophysiology of cancer, managing side-effects, positive self-care behaviours | Variable 3 mo | PedsQl, gen, SR |

RCT: Randomised Controlled Trial, ClRCT: Cluster Randomised Controlled Trial, uc: Usual Care control group, ac: attention control group, wlc: wait list control group, ns: not specified, comp: computer, tel: telephone; RT: Research Team member, Ch: Child, Cg: Caregiver (parent); unsp: unspecified, min: minutes, PAQLQ: Pediatric Asthma Quality of Life Questionnaire, PedsQL: Pediatric Quality of Life Inventory, DM: diabetes module, PIES: Perceived illness experience scale, GEOS: Glasgow Epilepsy Outcome Scale, CDLQI: Children’s Dermatology Life Quality Index, JAQQ: Juvenile Arthritis Quality of Life Questionnaire, DQOLY: Diabetes Quality of Life for Youth, SF: short form, dis-sp: disease-specific, gen: generic, SR: self-report, PR: parent-report, RAP: ‘Roaring Adventures of Puff’

**5.7.2. Risk of bias assessment**

Eight studies were judged at high risk for attrition bias (Almomani et al., 2017; Boogerd et al., 2014; Butz et al., 2005; Henry et al., 2004; Kato et al., 2008; Murphy et al., 2012; Price et al., 2015; Ryu & Lee, 2015). These studies analysed only completers, had attrition which was high or unbalanced between groups, or where dropout could be related to outcome measures (e.g. worse QoL at baseline). One study had high risk of cluster bias (cluster baseline imbalance) (Ryu & Lee, 2015). Seventeen studies had no identified source of high bias. The funnel plot (shown in Figure 5.3) showed the larger more precise studies were close to the pooled effect size, there was little asymmetry and the small imprecise studies were not over-estimating the effect size. Therefore, there was no evidence of systematic biasing of the estimated effect due to missing studies from the literature (Sterne et al., 2011).

*Figure 5.3* Funnel plot of effect size (SMD) against Standard Error (SE) for studies in the meta-analysis.

 101

**5.7.3. Analysis of effect sizes**

The pooled effect size (SMD) for all 25 eligible studies (intervention n= 2536, control n= 2372) was 0.14 (95% CI: 0.07 to 0.20). The overall effect was significant (Z=3.91, p= .0001), indicating that psychoeducational interventions significantly improved QoL, with a small effect size (Cohen, 1988). The forest plot for these studies is shown in Figure 5.4. Effect sizes ranged from -0.23 to 0.54. There was heterogeneity in the sample, but this was not significant (χ²= 29.58, p=0.20, I²=19%). However, non-significant heterogeneity does not necessarily indicate an absence of clinical heterogeneity (Groenwold et al., 2010) and the moderator analyses were carried out as planned.



*Figure 5.4* Summary statistics, effect sizes and forest plot of studies in the meta-analysis.

Effect sizes were calculated using post-intervention means and standard deviations. The dots represent the weight of the individual studies. The horizontal error bars represent the 95% confidence intervals. The diamond represents the pooled effect size.

**5.7.4. Moderator analyses**

**Chronic condition**

The included interventions were delivered to children with asthma (10 studies), diabetes (7), juvenile arthritis (2), eczema (3), cystic fibrosis (1), epilepsy (1) and cancer (1) (general cancer population including leukaemia, lymphoma, sarcoma). Other chronic conditions were represented in the literature but could not be included as they were not RCTs or had no QoL measure (e.g. Irritable bowel syndrome, Van den Brink et al. 2016; sickle cell anaemia, Daniel et al., 2015; general chronic illness; Ernst et al., 2017).

It was only possible to subgroup the asthma and diabetes studies. There were insufficient studies in the other conditions, and they could not theoretically be pooled as one group (cystic fibrosis, eczema, cancer, juvenile arthritis, epilepsy). There was a significant subgroup difference between asthma and diabetes (χ²= 6.25, p=.01, I²= 84%). Interventions for asthma were more effective (10 studies, n= 3201; SMD= 0.21, 95% CI: 0.11 to 0.30) than diabetes interventions (7 studies, n= 938; SMD= 0.00, 95% CI: -0.12 to 0.13). The effect of interventions for children with diabetes was estimated at 0. All the asthma studies used the Pediatric Asthma Quality of Life Questionnaire (PAQLQ) (Juniper et al., 1996). Six of the asthma studies had achieved an MCID in the intervention group (calculated as the change from baseline to outcome). The MCID could not be calculated for 3 asthma studies which did not report baseline data or did not use standard scoring. Two studies also reported an MCID in the comparison of baseline and follow-up score for the control group.

**Age**

There was a significant subgroup difference for child age (χ²= 3.81, p=.05, I²= 73.8%) with a larger effect in the younger children (<12 years) (13 studies, n=2877: SMD=0.20, 95% CI: 0.10 to 0.29) compared to the older children (12+ years) (12 studies, n=2031; SMD= 0.07, 95% CI: -0.02 to 0.15).

**Setting, duration (dosage) and group context of intervention**

 Effect sizes did not differ on the basis of setting (school vs clinic vs. home) (χ²= 3.81, p=.15, I²= 47.5%), delivery to individual or group (χ²= 0.00, p=1.00, I²= 0%) or whether a parent/caregiver participated in the intervention (χ²= 0.29, p=.59, I²= 0%). There were no subgroup differences for intervention dose (shorter: up to 3 hours vs. longer: 4 hours and over; 3 studies did not define a time input) (χ²= 0.05, p= .83, I²= 0%) or intervention duration (over 3 months vs. under 3 months) (χ²= 2.51, p=.11, I²= 60.1%). There was a significant difference for intervention dose in the asthma interventions (χ²= 8.47, p= .004, I²= 88.2%). Longer interventions (4 hours and over) had a larger effect (5 studies, n= 1800, SMD= 0.31, 95% CI; 0.22 to 0.41) than shorter interventions (up to 3 hours) (5 studies, n= 1401, SMD= 0.10, 95% CI; 0.00-0.21). There were too few studies in the diabetes subgroup to analyse the effect of intervention dose.

**Study design and sensitivity analyses**

 Effect sizes did not differ between the 16 RCTs (n=1832) and 9 cluster RCTs (n=3076; χ²= 1.17, p=.28, I²=14.9%). Effect sizes did not differ between studies with high risk of attrition bias (8 studies, n= 1543) and those with low or unclear risk (17 studies, n=3365; χ²=.68, p=0.41, I²= 0%), or those using an illness-specific measure of QoL (20 studies, n=4321) and those using a generic measure of QoL (5 studies, n=587; χ²= 1.81, p=.18, I²=44.7%.

**5.8 Discussion**

This meta-analysis aimed to quantify the overall effect of psychoeducational interventions delivered to children with leukaemia and other chronic conditions, using QoL as an outcome. It examined whether the effect of psychoeducation would be comparable across chronic conditions as might be suggested by the risk-resistance model (described in Chapter 3). It also examined potential moderators of effect (e.g. age, family participation in the intervention, dose) and methodological biases.

The searches did not identify any psychoeducational interventions delivered to children with leukaemia, evaluated in an RCT and using a QoL outcome, so no leukaemia interventions were used to calculate this effect. There was only one intervention delivered to children with cancer which was included. Therefore, the results of this meta-analysis are mainly based on other chronic illness groups. Psychoeducational interventions were associated with a small but significant improvement in QoL for children with these other chronic conditions. If psychoeducational interventions have similar effects on QoL across conditions then this outcome might be generalisable to interventions for children with leukaemia. However, a subgroup analysis showed a significant difference between the asthma and diabetes interventions, with a small effect in the asthma interventions and a zero effect in the diabetes interventions. This suggests that not all chronic illnesses are similarly effected by psychoeducation.

The differential effect for asthma and diabetes interventions may reflect differences in the burden of treatment and in the information required for effective self-management. There was a small effect of psychoeducation in the asthma interventions which led to an MCID in 6 out of 7 asthma studies. This may be because the information provided was sufficient to improve adherence to treatment and promote effective asthma self-management. Leukaemia may be like asthma in that children will be following a strict medication regime, managing symptoms and looking out for adverse signs (e.g. high temperatures). If following these guidelines, both sets of children may be able to control their symptoms, avoid adverse effects and experience better QoL.

Psychoeducation led to a zero effect in the diabetes interventions. This might be because the information was too complex or not sufficient to improve the child’s symptoms. Diabetes self-management may be more time-consuming and lead to more activity limitations than asthma self-management (Ziaian et al., 2006). Children with leukaemia are not required to carry out complex calculations as part of their self-management. Therefore, their burden of treatment may be less. On the other hand, children with leukaemia may experience more symptomatic burdens and activity limitations than children with asthma or diabetes.

Leukaemia and diabetes may also feel more difficult to control than asthma. Children with leukaemia will not be able to control whether they have side effects as a result of chemotherapy or mood changes resulting from steroid treatment. It has been argued that tailored interventions which target coping alongside self-management skills are more effective for children with diabetes (Barlow & Ellard, 2004; Charalampopoulos et al.,2017; Hilliard et al, 2016). The need for coping skills might reflect the less controllable aspects of diabetes management (Compas et al., 2012). It is possible that children with leukaemia might also need additional components to improve their QoL.

The lack of studies addressing leukaemia and the evidence that psychoeducation can have different impacts for different chronic conditions limits confidence in the generalisabilty of the other meta-analysis results to interventions for leukaemia. However, the moderator analyses may still provide the basis for hypotheses that can be tested in leukaemia once the literature on intervention evaluation is more developed. The moderator analyses showed that, contrary to the hypothesis that psychoeducation would be more effective for older children, the interventions delivered to the younger group were more effective. This may well be conflated with condition as the majority of asthma interventions were delivered to younger children. However, it could also reflect a real age difference. As argued in Chapter 2, younger children are often told less about their condition and may benefit more from psychoeducation.

QoL tends to be more impaired in adolescents than younger children, in a range of chronic conditions (Moreira et al., 2013; Varni et al., 2007). The greater psychological burden in adolescence might have been an opportunity for larger improvements in QoL after psychoeducational interventions. However, it may be that QoL is more resistant to change in adolescence. Physiological changes, peer issues, increased family conflict, academic pressures and increased risk-taking behaviours during adolescence may independently affect the child’s QoL, impair their illness self-management and make it more difficult to intervene effectively. This would highlight the importance of intervening early with children with chronic conditions. The younger children with diabetes in this review (under 12 years) were included in interventions with adolescents. This might have affected the age-appropriateness of the intervention for both the younger and older children.

Other moderator analyses were inconclusive which means it is not possible to identify the optimal methods for delivering psychoeducation. Two narrative reviews (described in Chapter 4) of interventions for children with cancer reported that interventions which were interactive, targeted and tailored to individual needs and outcomes were more effective (Bradlyn et al., 2003; Kazak et al., 2005). No effect of grouping (group vs individual sessions) was detected in this meta-analysis and there were insufficient studies to examine the effect of targeting in subgroup analyses, particularly as some were targeted according to disease severity and others to socioeconomic risk groups. There was also no effect of including a parent/caregiver as a participant in the intervention. Other reviews have found positive results for family interventions, but the results are often mixed and pathways for their effectiveness have not been identified (Feldman et al., 2018). It is likely that family involvement is effective in some types of interventions, but it did not improve the effect of these psychoeducational interventions.

Communicating with children with cancer about their illness is a process which is seen as vital, but few interventions have been developed to support this process. The lack of rigorously evaluated interventions supporting communication about cancer has been highlighted elsewhere. Ranmal et al. (2008) concluded that, without robust evidence, health providers would need to use their individual judgement about the best ways of delivering information about cancer to children.

Dragone et al. (2002) reported an RCT of a computer game intervention (‘Kidz with leukaemia; a space adventure’) (reported in Chapter 4). However, this study did not report a QoL outcome and did not have a non-educational control group (the control group received information via a book). Interventions which have been delivered to children with leukaemia have mainly targeted side effects of treatment, using interventions such as physical exercise (e.g. Tanner et al., 2017; San Juan et al., 2007), but without a focus on education.

The lack of psychoeducational interventions directed to children with leukaemia might reflect their inclusion in general pediatric cancer interventions. As previously argued, leukaemia is the most common pediatric cancer and often comprises the largest group in these trials. However, there was only one pediatric cancer intervention which met the inclusion criteria. This was also a computer game intervention (‘Re-Mission’; Kato et al., 2008). The effect size calculated for this intervention (SMD= 0.17) was comparable to the overall effect size (SMD= 0.14) reported by this meta-analysis. However, it is not possible to estimate an overall effect of psychoeducation for pediatric cancer from this one study.

As suggested in Chapter 4, attempts to provide illness-specific information to children with cancer and leukaemia have mainly used computer game interventions. Group interventions were used to deliver social skills interventions, some coping skills interventions and some health behaviour interventions. However, this format has not been tested for information-based interventions. This probably reflects the rarity of childhood cancer making it difficult to achieve good sample sizes for group interventions.

Study methodology and quality were analysed to examine whether this influenced the effect size. Results from the funnel plot, risk of bias and methodological subgroup analyses suggest that the evidence is generally good, particularly in comparison to previous reviews (e.g. Barlow & Ellard, 2004; Murphy et al., 2006). The importance of including studies with an RCT design is demonstrated by the improvements in control groups observed in this review. These changes showed that improvements in outcomes might not be intervention-related. Therefore, a design which includes a comparison group and accounts for change over time is essential in evaluating interventions.

The subgroup analysis comparing studies with high risk of bias (attrition bias: 8 studies, clustering bias: 1 study) to those with no high risk of bias was not significant. However, attrition is still problematic. Along with low sample sizes, it means that studies are often underpowered to calculate a precise effect size. The effect sizes reported in psychoeducational interventions have often been small (Harris et al., 2018; Murphy et al., 2006) which means that larger samples may be needed to identify significant effects in individual studies. Even the larger studies in this meta-analysis were run with numbers below their recruitment targets (e.g. Christie et al., 2014; Price et al., 2015). Synthesizing studies using meta-analysis helps to reduce the problem of individual studies being underpowered. However, the information from small studies is a less precise estimate of the pooled effect size than larger studies and these studies contribute little to the overall effect (Turner et al., 2013). It also does not remove the bias from attrition. Attrition is often higher in groups with more severe disease, lower initial QoL, lower socioeconomic status and ethnic minority groups (Charalampopoulos et al., 2017; McGhan et al., 2010). It may be that those with the greatest potential for improvement may be lost, leading to an under-estimation of the potential effect of interventions and reducing the generalisability of findings.

It is important that studies find ways of engaging young people in interventions to improve the recruitment of harder to reach children, particularly those with poor management, low QoL, and those from lower socioeconomic or ethnic minority backgrounds. Not including these children is likely to underestimate the potential of interventions and reduce the generalisability of research. It also indicates potential challenges in translating intervention research into clinical practise.

**5.9 Limitations of the review**

Asthma and diabetes are the most common chronic childhood conditions, so it is unsurprising that they represent the majority of targets for intervention in this review. However, as there were no leukaemia interventions it was not possible to calculate an illness-specific effect size for this condition. The ability to generalise to other chronic conditions is also limited by the small numbers of studies. Psychoeducational interventions have been trialled in pediatric cancer and other conditions, but the lack of RCT designs and QoL outcomes precluded them from inclusion.

More studies across a broader range of conditions would allow an analysis of how well these intervention approaches extend to other chronic illness groups. This is particularly important as a differential effect of condition was reported in this review. There is a need for the inclusion of QoL as an outcome in more intervention studies as this allows the comparative burdens of illness and effects of treatment to be assessed (Eiser, 2004; Varni et al., 2007). If studies only report illness-specific measures this limits the generalisability of their findings. Generalising findings might be particularly important for rarer conditions such as leukaemia.

The sole inclusion of RCTs, was a strength of the review, but it also meant that novel or promising interventions which have not yet been rigorously evaluated have not been included. Hilliard et al. (2016) have suggested that eHealth interventions, delivering psychoeducation via text message or games, represent promising and accessible interventions. However, most are still in the developmental stage and have not yet demonstrated efficacy. This might be particularly important for childhood leukaemia as multimedia games have been the most common format for delivering information interventions. Chapter 4 also identified a number of promising interventions in the pediatric cancer literature which have not yet been adequately evaluated (e.g. Maurice-Stam et al., 2009; Bruggers et al., 2018). Future studies should aim to evaluate promising interventions in RCTs with adequate sample sizes.

**5.10. Summary**

This chapter has demonstrated that psychoeducational interventions had a small but significant effect on QoL in children with chronic conditions. This suggests that psychoeducation is able to improve adjustment in children with chronic illnesses. However, there were no leukaemia interventions with psychoeducation and a QoL outcome which could be included. Only one cancer intervention contributed to the pooled effect. The meta-analysis found a differential effect for psychoeducation in two different chronic conditions (asthma and diabetes). If psychoeducation has a different impact for children with different conditions this might mean these results do not generalise to children with leukaemia.

The differences between chronic conditions might reflect the complexity of self-management information, the ease of applying knowledge and the perceived controllability of the illness. It is also possible that age is an important moderator for the effects of psychoeducation on adjustment outcomes, with younger children more likely to benefit from psychoeducation.

This review suggests that it is vital to develop and evaluate interventions designed to improve communication and information provision for children with leukaemia, as there are very few studies currently in the literature. The next chapter will describe a leukaemia intervention which aimed to improve adjustment in children treated for leukaemia. The intervention included both children on active treatment and survivors.

**Chapter 6**

**Design of the leukaemia intervention and RCT evaluation study**

Previous chapters have described the psychological, social and physical burdens associated with leukaemia treatment and the need to intervene to reduce these burdens. The narrative and meta-analytical reviews described in Chapters 4 and 5 demonstrated the need for well-designed interventions and trials in this area. This chapter will describe the design and content of a leukaemia intervention which aimed to improve adjustment in children. This description will draw on the risk and resiliency framework introduced in Chapter 3, to identify intervention components targeting these risk and resiliency factors. The chapter will also describe the RCT which was designed to evaluate the intervention. This study included quantitative analysis of intervention effectiveness and qualitative analysis of intervention acceptability and feasibility. This chapter will describe the measures included, the analytic framework and the timeframe of the intervention.

**6.1. Complex interventions**

Complex interventions include several interacting components (Campbell et al., 2000; Craig et al., 2008). An intervention may be complex because it has multiple components, it allows flexibility and tailoring to individuals, it targets different behaviours, or it measures multiple outcomes. This means that most, if not all, psychological interventions should be seen as complex interventions. The leukaemia intervention described in this chapter, included different levels of complexity; in components (e.g. information about leukaemia, reducing threat appraisal around procedures), targets (e.g. illness uncertainty, coping skills, health behaviours) and outcomes (e.g. QoL, behaviour problems, treatment-related anxiety). The intervention followed standardised content and lesson plans. However, the small group setting, and duration of each workshop also gave flexibility to tailor the content to individual children. Children were able to ask questions and interact socially with the educator and the other children.

It can be difficult to identify and isolate the active components of complex interventions. The Medical Research Council (MRC), developed guidelines for identifying active components and processes of change in complex interventions (Craig et al., 2008). Figure 6.1 summarises the stages described for this process, adapted to show the key elements in relation to the leukaemia intervention described in this thesis. An initial step of identifying a need was described in Chapters 1 and 2. This is a stepped approach to intervention development which involves a large amount of preliminary and evaluative work, before an intervention could be implemented in clinical practise. A stepped approach has also been recommended by the Children’s Oncology Group (COG) to reduce the burden of time and resources involved in recruiting large numbers of children in preliminary studies (Armstrong & Reaman, 2005). COG recommend an initial pilot study, followed by a limited institution trial and a group-wide trial once effectiveness has been demonstrated.

**Feasibility/piloting**

Testing procedures

Chapter 7: Reporting feasibility of the leukaemia intervention

Chapter 7: Reporting acceptability of the leukaemia intervention

Estimating recruitment/retention

Chapter 7: Reporting recruitment/ retention data

Chapter 8: Interview study with non-participating families

**Development of the intervention**

Identifying an evidence base

Chapter 4: Narrative review of interventions for children with cancer to identify active components

Chapter 5: Meta-analysis of psychoeducation for children with chronic conditions on QoL outcomes

Identifying theory

Chapter 3: Description and relevance of the risk-resistance model for intervening with children with leukaemia

**Evaluation**

Assessing effectiveness

Chapter 7: Quantitative analysis of intervention effectiveness

Chapter 7: Qualitative evaluation of the leukaemia intervention

Chapters 7&9: Discussion of potential processes of change

Implementation and monitoring

*Figure 6.1* Key elements in the development and evaluation of complex interventions for health (adapted from Craig et al., 2008; MRC guidelines), applied to the leukaemia intervention described in this thesis.

Chapters 1-5 of this thesis have provided the theoretical and evidential background for this psychoeducational intervention for children with leukaemia. Future chapters will evaluate the feasibility, acceptability and effectiveness of the intervention.

**6.2. Background to the design of the intervention**

The clinical protocol for the study was registered with the UK’s National Institute of Health Research (NIHR) (R00445P). The study was approved by the University of Sheffield’s Psychology Department Ethics Committee and by the NHS ethics commitees in each participating hospital (Manchester Children’s Hospital, Sheffield Children’s Hospital, Leeds General Infirmary, Alder Hey Children’s Hospital). The intervention had previously been piloted by a different member of the research team, in a series of drop-in sessions in the out-patient clinic for children with cancer at Manchester Children’s Hospital. A prospective sample of 11 children (all under the age of 12 years) and 11 parents filled in a feedback form measuring how interesting, enjoyable, topical, educational and cost-effective the workshop was. The overall feedback was positive. The content of the intervention was modified to be specific to leukaemia and this modified intervention is described in this chapter.

**6.3. Design of the evaluation study**

The intervention was evaluated in a longitudinal Randomised Controlled Trial (RCT). The need to include control groups is highlighted by studies where both the control and intervention group’s outcomes improve during the study. As reported in Chapter 4, interventions evaluated in pre/post designs tend to report better outcomes than when the same intervention is evaluated in an RCT (e.g. Barrera & Schulte, 2009; Barrera et al., 2018). This could be because natural change over time is mistakenly described as an intervention effect in uncontrolled designs. Another reason might be that the control group inadvertently receives an intervention. The control group might receive additional clinical care or might become more motivated to look after their health or learn about their condition.

Research on psychological outcomes for children with cancer suggests that change over time should be taken into account. Impairment in QoL is usually greatest around diagnosis but often improves over time (Adams et al., 2016; Eiser et al., 2005). Other aspects of treatment (e.g. steroid treatment) and daily hassles (e.g. peer/school issues) may also cause psychological outcomes to fluctuate over the course of a study. This means that a longitudinal approach is necessary to effectively monitor change over time. In addition to pre and post intervention measurements of outcomes, the participants also provided data at 3 and 6-months post-intervention.

The study used a wait-list control design, which allowed all participants to receive the intervention. This is often seen as a more ethical approach in medical research as potentially beneficial treatment is not withheld from a control group (Edwards et al., 2011). It also reduces problems with reduced commitment in the control group and increases the sample size of children who receive (and can therefore evaluate) the intervention. This is useful when studying a relatively rare illness as the potential sample pool will be small.

A modified Intention to Treat (ITT) design was used (Gupta, 2011). ITT means that all children recruited and randomised to an intervention are analysed at follow-up regardless of whether they receive the intervention (Wang & Bakhai, 2005). This reduces potential bias from non-analysis of children who withdraw and reflects how an intervention would be implemented in practise. The evaluation study analysed children regardless of whether they attended the workshops. However, to measure change over time, only children who provided baseline data and data for at least one follow-up timepoint could be analysed. This represents the modified ITT design.

**6.4. Participants**

Children aged 7 to 12 years who were undergoing treatment for leukaemia or who had completed treatment in the 4 participating hospitals were eligible. There was no limit to time since treatment, so children had completed treatment up to 11 years previously. Chapter 2 described the need to inform children about their diagnosis and argued that there is a specific need to intervene with this younger age group as they may receive less information from parents and doctors.

Families had to understand verbal and written information in English to give informed consent and to understand the content of the intervention. This was assessed informally during the recruitment phase. Children were excluded if they had another physical condition or psychological problem which could impact their QoL. From a potential sample of 422 children, 74 (17.5%) were recruited, 2 (0.5%) were excluded for having another condition (autism and learning difficulties, PTSD), 78 (18.5%) declined and 268 (63.5%) did not reply to telephone or mail contact. The original power calculations in the study protocol suggested that 120 participants (60 in each group) would have a better than 80% power to detect an effect size of 0.5.

**6.5. Procedure**

Families of children meeting the eligibility criteria were sent printed information about the intervention, which was followed up by telephone. Recruited families gave consent and child assent. Children were randomly assigned to delay or immediate intervention groups using a random number generator by a member of staff at the University of Sheffield who was not involved in data collection or delivering the intervention. Randomisation was stratified using two age groups (7-9 and 10-12 years) to ensure that the groups were mixed. A group which only consisted of older or younger children might alter the content and delivery of the intervention. Age of the child was also a potential moderator of effect which might bias the results if not stratified.

Table 6.1 shows the times for outcome measurement in relation to delivery of the workshops for the two groups. The immediate group received the intervention straight after the baseline assessment (week 1) while the delay group received the intervention 18 weeks after baseline (week 18). During this 18-week period the delay group acted as a control group, providing data on the outcome measures at 2 matched time points to the immediate group (before and after the immediate group’s workshops; weeks 1 and 5). Families provided pre-intervention data in the week before their first workshop and post-intervention data immediately after the last workshop, then at 3 and 6-month follow-ups. In total, 9 blocks of workshops were run between June 2012 and April 2016.

Table 6.1

*Time flow through the study for the immediate and delay groups*

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Study week | 1 | 5 | 18 | 22 | 31 | 35 | 48 |
| Immediate group | Baseline Pre-Int **Int starts** | Post-Int **Int ends** | 3 mo F/up |  | 6 mo F/up |  |  |
| Delay group | Baseline MC | MC | Pre-Int **Int starts** | Post-Int **Int ends** |  | 3 mo F/up | 6 mo F/up |

Int: intervention, MC: matched control timepoint, mo: month, F/up: follow up.

The immediate group received the intervention between study weeks 1 and 5. Delay group received the intervention between study weeks 18 and 22.

Note: time points are matched for the delay and immediate groups up to week 18. Delay groups provide outcome measurements at six time points, immediate groups provide four.

There are two ways of describing time in the study. Table 6.1 shows the study procedures in terms of study week. The study week of outcome collection was matched for the first three data points. After this, data was collected on different study weeks for the two groups. Table 6.2 shows time in terms of the timepoints of the study. As timepoints are comparable for both groups but study week is not, it is timepoints which will be used to compare outcomes in Chapter 7.

Table 6.2

Time flow through the study using timepoints

|  |  |  |
| --- | --- | --- |
| Time point | Immediate group | Delay group |
| 1 | Pre-intervention | Matched Control |
| 2 | Post-intervention | Matched Control |
| 3 | 3-month follow-up | Pre-intervention |
| 4 | 6-month follow-up | Post-intervention |
| 5 |  | 3-month follow-up |
| 6 |  | 6-month follow-up |

**6.6. Design of the intervention**

Chapter 4 reviewed psychoeducational interventions which fell into the broad areas of 1) coping skills, 2) social and communications skills, 3) illness knowledge and adherence and 4) health behaviours. This leukaemia intervention is comparable to the illness knowledge and adherence interventions described in Chapter 4. Its primary aim was to improve child adjustment by increasing the child’s understanding of their illness. However, it also had components which targeted coping skills and health behaviours. The group context might also provide social support and improve the child’s communication skills around their illness. Therefore, research on each of these 4 intervention types is relevant to the content of this intervention.

The intervention consisted of 4 workshops run on consecutive weeks. Each session was approximately 2 hours long and was held in a non-medical area of the hospital (e.g., school room, family area). Groups consisted of 2-6 children and were led by the same researcher for all workshops (MD). Each session included information and demonstrations followed by games and activities to improve the child’s understanding of leukaemia and its treatment. Table 6.3 summarises the content of each workshop. More detailed lesson plans are included in Appendix A.

Table 6.3

*Content of the four intervention workshops*

|  |  |  |  |
| --- | --- | --- | --- |
| Workshop | Exploratory activity | Activity One | Activity Two |
| Workshop One:The human body and the effects of chemotherapy. | Constructing 3-D models of the human body: skeletons and organs. | Let’s Bowl Game: skittles labelled with parts of the body are knocked down with balls representing chemotherapy drugs. Discussion of side effects and managing symptoms. | Changing body image: drawing activity using cards to draw and reconstruct bodies with different body shapes, hair and faces. Discussion of temporary changes in physical appearance due to chemotherapy. |
| Workshop Two:Blood and leukaemia | Models of the heart and circulatory system. Using stethoscopes to listen to heartbeat. | ‘Put it together’ blood activity: models representing the different blood cells: red blood cells, platelets and white blood cells in a blood vessel. Demonstration of what happens with the proliferation of blasts and with chemotherapy to remove blasts.  | ‘Spot the difference’:looking at pictures of ‘normal’ blood and blood from a leukaemia patient to spot the differences between them.  |
| Workshop Three:Cell biology, DNA, leukaemia caused by change in DNA | Looking at slides of blood from leukaemia patient under the microscope. Compared to ‘normal’ blood cell slides.Cell models. | ‘Cell factory’ game:Making a model of the cell and matching the function of organelles to parts of a factory. Role of the nucleus and DNA. | ‘DNA chain’ activity: demonstrate the structure of DNA using a model.Using beads with letters show that a change in sequence means that the sequence no longer makes sense. |
| Workshop Four:The sensory system and pain. Healthy living for the future. | ‘Exploring the senses’ activities: touch, smellModels of the eye and ear. | ‘Rope and donut’ exercise: demonstrate how messages are sent by nerves to the brain using normal and painful messages. How you respond affects the pain you feel. Discussion of coping strategies during procedures. | Discussion of the importance of staying healthy.‘Healthy living’ exercise:collect the stars to identify components of a healthy lifestyle.Choose 3 changes to improve future health. |

Chapter 3 described modifiable targets for intervention suggested by the risk-resistance model (Wallander & Varni, 1998). Table 6.4 shows how these targets could be addressed by the content and components of this leukaemia intervention. These targets can be summarised as 1) improving illness-related communication skills, 2) reducing illness uncertainty, 3) reducing threat appraisal and improving coping skills, 4) promoting treatment adherence and compliance, 5) promoting positive health behaviours and 6) social support.

Table 6.4

*Components of the intervention and modifiable targets*

|  |  |
| --- | --- |
| Component | Target |
| Understanding the pathophysiology of leukaemia (changes to blood cells, DNA)  | * Increase illness-related communication skills
* Reduce illness uncertainty
 |
| Understanding what treatment does and why it is important (chemotherapy, steroids, tests) | * Increase familiarity with treatment and procedures
* Increase illness-related communication skills
* Increase treatment adherence and compliance
* Reduce threat appraisal (e.g. chemotherapy, blood tests)
 |
| Understanding the side effects of treatment | * Managing symptoms (e.g. coping with effects of steroids, nausea)
* Increase illness-related communication skills
* Reduce stress related to changes in appearance
 |
| Coping with painful procedures | * Reduce threat appraisal/ anticipatory anxiety
* Promote positive coping strategies
 |
| Healthy living | * Increase adherence to treatment (survivors)
* Promote positive health behaviours
* Perceive vulnerability to late effects
* Promote positive coping through health behaviours
* Future orientation/motivation
 |
| Small group setting | * Increase illness-related communication skills
* Social support
 |
| Interactive | * ‘Hands-on’ learning
* Information-seeking
* Address misunderstandings
* Age-appropriate explanations
 |

**6.7. Outcome measures**

The MRC guidelines for developing complex interventions, suggest that a range of outcomes are needed to evaluate data from interventions, including outcomes which could identify unintended consequences (Craig et al., 2008). The primary outcome measure is the most important outcome in the study and the outcome on which efficacy will be assessed (Andrade, 2015). Secondary outcomes measure additional efficacy and potential adverse effects. Setting primary measures at the design stage reduces the risk of Type 1 errors arising from using large numbers of outcomes to assess efficacy.

Parent-reported QoL and behavioural problems were primary outcomes and a number of other measures of adjustment (child confidence, caregiver QoL) and impairment (treatment-related anxiety) were included as secondary outcomes. These measures allowed both positive and negative outcomes to be measured.

**6.7.1. Quality of life measures**

The primary outcome for the intervention was parent-reported child QoL, with other QoL measures included as secondary measures (including child-reported and caregiver versions). As discussed in Chapter 3, QoL is a subjective measure of adjustment to illness which measures positive and negative outcomes, rather than focusing only on deficit. This is appropriate for children with leukaemia because many children and families do not show impaired psychological outcomes, especially towards the end of treatment, or as survivors.

**6.7.2. Generic and illness-specific QoL measures**

QoL measures can be generic or illness-specific. Illness specific scales contain items tailored to the specific condition and are likely to be more sensitive to illness-related changes. Generic scales allow comparisons to be made between conditions and to population norms. A generic measure of QoL is likely to be more appropriate for a population which includes survivors, and this was included as the primary outcome measure. An illness-specific version was included as a secondary measure. Attempts have been made to develop illness-specific measures specifically for survivors of childhood cancer. However, these measures have usually been aimed at an older group (adolescent and adult survivors) and are often not psychometrically sound (Klassen et al., 2010; Zebrack & Chesler, 2001).

**6.7.3. Child/parent-reported QoL measures**

Qol scales are often available in child self-report and parent proxy-report versions. Eiser and Morse (2001) argued that both versions should be included in evaluations as parents and children often report their QoL differently. As QoL is a subjective measure of the impact of an illness, both viewpoints should be seen as valid but conveying different information. Children may interpret the impact of their illness differently from parents, based on a different understanding of the illness, different interpretations of questions and different time perspectives.

Agreement between parent and child report is often higher for children with cancer than in healthy populations, although parents tend to rate their child’s QoL slightly lower than the child (Parsons et al., 2012; Russell et al., 2006). Agreement was shown to be better in a sample of children with cancer (on and off treatment) and a parent, compared to healthy controls (n=307) (Russell et al., 2006); 0.344-0.592 for children on-treatment and 0.384-0.677 for children off-treatment, compared to 0.204-0.483 for the healthy controls. All subscales were correlated for the children with cancer, while 8/10 were significantly different for the healthy group. A study which evaluated agreement in self and proxy-reported QoL for children with cancer (n= 141) concluded that parents of children younger than 12 are able to give valid information about their child’s QoL (Chang et al., 2005), where children cannot or do not want to report their QoL due to the burdens of illness or treatment. In the present study, a parent-reported scale was included as the primary outcome and a child-reported scale as a secondary outcome.

**6.7.4. The Paediatric Quality of Life Inventory (PedsQl)**

There are many QoL measures available. Although most include the core domains of physical, social and psychological functioning, there is considerable heterogeneity in the items they include, number of items, response scales and targeted populations (Savage et al., 2009; Anthony et al., 2014). The PedsQl (Varni et al., 2001) has been identified as a psychometrically sound and age-appropriate QoL scale for children with cancer in a number of reviews of available measures (Klassen et al., 2010; Savage et al., 2009; Eiser & Morse, 2001). The PedsQl is widely used in studies, which allows comparisons to be made between different interventions and populations. A review of QoL measures used in pediatric cancer research identified 10 available scales. The PedsQl was used most often (generic version: in 58/130 studies, cancer module: in 28/57 studies) (Anthony et al., 2014).

Varni et al. (2001) developed the PedsQl from a previous cancer-specific measure of QoL (Pediatric Cancer Quality of Life; PCQL; Varni et al., 1998) which was designed for use in clinical trials. The items were generated from literature searches, interviews with parents and healthcare professionals and were based on the risk-resistance model described in Chapter 3. The PedsQl (generic) was the primary outcome used in this RCT. Other PedsQl scales were included as secondary measures; the parent-reported PedsQl (cancer-specific scale) and the child-reported PedsQl (generic and cancer-specific scales).

**6.7.5. The generic PedsQl scale**

The PedsQL (generic) scale has been validated over a range of conditions (Marcus et al., 2009, Seid et al., 2010, Varni et al., 2013). It includes 23 items measuring 4 scales: 1) physical functioning (8 items), 2) emotional functioning (5 items), 3) social functioning (5 items) and 4) school functioning (5 items). The questions ask how much of a problem each item has been in the last four weeks for example, ‘In the past 4 weeks, how much of a problem has your child had with walking down the road a little bit?’ using a 5-point Likert scale for response (0=never a problem, 1= almost never a problem, 2= sometimes a problem, 3= often a problem, 4= almost always a problem). Items are reverse-scored and linearly transformed to a 0-100 scale (0=100, 1=75, 2=50, 3=25, 4=0) so higher scores indicate a higher quality of life. Scale scores are computed as the mean of the component items. The reliability and validity of the PedsQl has been demonstrated for use in paediatric cancer research (Varni et al., 2002). Internal consistency was reported to be acceptable for the parent-reported generic scale (α=.93). Validity was demonstrated using the known-groups method with the PedsQL able to distinguish between healthy children and children with cancer and between those on and off treatment. The scale has a minimal clinically important difference of 4.5 (MCID) (Varni et al., 2003). The MCID represents the minimum improvement in scores which a patient would perceive as beneficial and, in the absence of adverse effects or excessive costs, would warrant a change in the patient’s management (Jaeschke et al, 1989). The MCID can be used alongside statistical tests to assess whether an intervention has made a clinically important difference to patients.

**6.7.6. The cancer-specific PedsQl module**

Parent-reported cancer-specific child QoL was a secondary outcome. The cancer-specific module of PedsQL (Varni et al., 2002) includes 27 items measuring 8 scales: 1) pain and hurt (2 items), 2) nausea (5 items), 3) procedural anxiety (3 items), 4) treatment anxiety (3 items), 5) worry (3 items), 6) cognitive problems (5 items), 7) perceived physical appearance (3 items) and 8) communication (3 items). The questions ask how much the items have been a problem in the last 4 weeks using the same 5-point Likert scale and scoring system as the generic scale; for example ‘In the past 4 weeks, how much of a problem has your child had with having a lot of pain?’ Internal consistency has been reported to be acceptable (α= .87) (Varni et al., 2002).

**6.7.7. The child-reported PedsQl scales**

The 23-item child-reported PedsQl generic and the 27-item child-reported PedsQl cancer specific module were included as secondary outcomes (Varni et al., 2002). These versions have the same number of items, the same item content (phrased for self-report), and the same response and scoring system as the parent versions. Internal consistency has been reported to be acceptable for the generic core scale (α=.88) and the cancer-specific module (α=.72) (Varni et al., 2002). An MCID of 4.4 has been reported for the child-reported generic scale (Varni et al., 2003). In a review of available measures for use with children on-treatment and survivors, the cancer-specific PedsQl was described as psychometrically sound and suitable for use with both groups (Klassen et al., 2010).

**6.7.8. Caregiver burden**

To measure caregiver burden, a modified version of the Paediatric Asthma Caregiver’s Quality of Life Questionnaire (PACQLQ) (Juniper et al, 1996) was included as a secondary outcome. The PACQLQ is reported to have good discriminatory properties, correlates with the child’s health status and child QoL, and has satisfactory internal consistency (α=.93) (Juniper et al., 1996). There are 12 items in the modified questionnaire, which like the original PACQLQ, refer to activity limitations (3 items) and to emotional problems (9 items). These items have been modified to relate to the experience of having a child with cancer. For example, ‘In the past 4 weeks, did you feel your child’s illness interfered with your job or work around the house?’. Responses were recorded on a 7-point scale (1=all of the time, 2=most of the time, 3= quite often, 4= some of the time, 5= once in a while, 6= hardly at all, 7= none of the time). Scores were reversed so higher scores indicated greater caregiver burden. This modified scale was used as part of an evaluation of the UKALL 2003 treatment protocol and demonstrated satisfactory internal consistency at each timepoint (α=.87-.92) (Eiser et al., 2017).

**6.7.9. The Strengths and Difficulties Questionnaire (SDQ)**

The SDQ is a widely used measure of child mental health and has been used as a screening tool for mental health and adjustment in children during treatment for leukaemia (Reinfjell et al., 2009) and in survivors of childhood cancer (Eilertson et al., 2011). Williams et al. (2013) highlighted the need for screening tools such as the SDQ to identify children requiring additional psychological input. Parent-reported SDQ was included as a primary outcome measure in this study, to measure mental health difficulties and behavioural adjustment over the course of the study. The parent-reported total difficulties scale was used which is appropriate for children aged 4-16 years (Goodman, 1997). The SDQ is less reliable as a self-reported measure in younger children, where unsatisfactory internal consistencies have been demonstrated in the conduct and peer problems subscales (alpha= .45, .36 respectively in a sample aged 8-10 years) (Mellor, 2004; Muris et al., 2004). The parent-reported SDQ includes 25 items in 5 subscales: 1) conduct problems, 2) hyperactivity, 3) emotional symptoms, 4) peer problems and 5) prosocial. The total of the first 4 scales is summed to give a total difficulties score. Responses are recorded on a 3-point scale (1= not true, 2= somewhat true, 3= certainly true) with higher scores reflecting greater difficulties. For example: ‘Often has temper tantrums or hot tantrums’. The SDQ total difficulties score has been shown to discriminate between samples of young people with or without mental health problems (Goodman, 2001; Husky et al., 2018), to have satisfactory internal consistency, test-retest stability and good parent youth agreement (α=.73) (Goodman, 2001; Muris et al., 2004).

**6.7.10. Child confidence**

To measure parental perception of the child’s confidence regarding their illness and treatment, parents completed 7 questions based on items from the Self Efficacy Questionnaire for Children (SEQ-C) (Muris, 2001), modified for parent-report and related to issues around leukaemia treatment (shown in Appendix B). For example; ‘How confident is your child that he/she can ask your doctor about matters of concern?’ Responses were recorded on a 5-point scale (from 0= not at all confident to 4= totally confident). These questions were developed for this study as there was no available measure. The original scale includes 3 subscales: social self-efficacy, academic self-efficacy and emotional self-efficacy. The items in the modified questionnaire relate to self-efficacy around illness-related communication (3 items) and managing symptoms (4 items). The SEQ-C shows satisfactory internal consistency and correlated with other measures of psychological impairment (such as depression) (Muris, 2001). These 7 items demonstrated satisfactory internal consistency in this study (α=.89) and correlated with other scales (e.g. parent reported PedsQl (generic) and SDQ total difficulties scale).

**6.7.11. Treatment-related anxiety**

Parents answered 6 items developed for this study as there was no suitable validated measure available (shown in Appendix B). These items measured the parent’s and child’s treatment-related anxiety over the last 4 weeks. The questions asked about anxiety levels related to clinic appointments, Vincristine injections and lumbar punctures over the last 4 weeks. For example, in comparison to previous treatment, ‘thinking about coming to clinic appointments, I have felt (or my child has felt) …’. The responses were recorded on a 7-point scale (1= much less anxious than usual, 4= the same as usual, 7= much more anxious than usual). Children answered the same 3 questions asking about their treatment-related anxiety. Responses were recorded on a 5-point scale (1= much less anxious than usual, 3= the same as usual, 5= much more anxious than usual). These scales demonstrated satisfactory internal consistency in this study (α= .85-.91) and correlated with other study measures (e.g. parent and child-reported PedsQl.

**6.8. Administration of the questionnaires**

Parents and children filled in separate questionnaire booklets at each timepoint. The parent’s questionnaire was titled ‘You and your child’, and the child’s was titled ‘Your thoughts and feelings’. The questionnaires were identical at each timepoint and contained a total of 103 questions for parents and 53 for children. The post-intervention questionnaire was given out during the final workshop. All other questionnaires were mailed to families. Families completed questionnaires at home and returned them by mail. Families were followed up by telephone if questionnaires were not returned.

**6.9. Quantitative analysis**

To assess levels of impairment in the sample, baseline QoL scores (using the parent and child-reported PedsQl scales) were compared to a large sample of healthy, acutely ill and chronically ill children treated in pediatric speciality clinics (e.g. diabetes, cardiology) outpatient clinics and scheduled well-child clinics (Varni et al., 2001). Behavioural and emotional problems, as measured by the SDQ, were compared to a normative sample of children from the general population (Meltzer et al., 2000).

To analyse intervention effectiveness, change over time in the outcome measures was analysed using longitudinal multilevel modelling (MLM) in SPSS Statistics for Windows (Version 21.0. Armonk, NY: IBM Corp). MLM is used to analyse data which is hierarchical (i.e. where the sample is nested within another structure). In longitudinal designs the hierarchy results from the use of repeated measures over time (Hox, 2017). The repeated measures (lowest level variable) are nested within the individual participant (higher level variable). As with standard regression, MLM calculates how the outcome variable (e.g. QoL) varies in relation to the other variables (e.g. the intervention). In MLM, a series of models are applied to the data, with one or more aspect or predictor changing each time. The first model contains no predictors. In a longitudinal design, this baseline model partitions the variance into variance due to differences over time (within groups variance) and variance between individuals (between groups variance). At each stage the more complex model can be compared to the previous model to examine whether it is a better fit to the data. The contribution of individual predictors to explaining variance in the data can be calculated for each model. MLM has a number of advantages over repeated measures ANOVA which are relevant to this RCT (e.g. it can handle missing data and does not require equal time intervals between data points). Repeated measures ANOVA uses least squares estimation which means that all of a participant’s data is excluded if a single timepoint is missing. MLM uses maximum likelihood estimation which means that MLM can make use of all available data from participants (Enders, 2011). This is particularly useful for ITT studies where missing data can be problematic in reducing statistical power and in introducing bias. Kwok et al. (2008) cite a number of reviews which suggest that mishandling of missing data is a major issue in published reports of clinical trials.

To analyse the effectiveness of the leukaemia intervention, repeated outcome measurements over time (lower level units) were nested within children (higher level units). To prepare the data for MLM, dummy variables were added which distinguished groups (0= delayed, 1= immediate) and whether participants had received the intervention at each time point (0= not received, 1= received). As outcomes have been reported to improve over time for children treated for leukaemia (Eiser et al., 2005), time elapsed between diagnosis and baseline was included as a control variable.

Seven models were fitted sequentially for each outcome measure.

1) Unconditional (baseline) model: no predictors. This partitioned the total variance into within-groups variance (representing changes within children across time) and between-groups variance (representing differences between children).

2) Control model: introduced time elapsed between diagnosis and baseline.

3) Change over time model: introduced study week as a continuous predictor.

4) Main effect of intervention model: introduced the dummy intervention variable as a predictor.

5) Main effect of group: introduced the dummy group variable (delay or immediate groups) as a predictor.

6) Intervention modelled as a random effect: the dummy intervention variable was modelled as a random effect. This allowed it to vary for the higher-level units (children), so the intervention could have different effects for different children.

7) Group x intervention interaction: an interaction term was introduced to test whether there was a differential effect of the intervention in the immediate and delay groups.

At each step the improvement in model fit was measured using the reduction in the -2xLog-Likelihood (-2LL) measure of deviance. This measures the amount of unexplained variation in the model with higher values representing more unexplained variance. Therefore, the reduction in -2LL reflects how much variance has been explained by each model. The significance of reduction in -2LL was tested by comparing it to the -2LL of the previous model using the chi-square distribution.

**6.10. Qualitative evaluation of the intervention**

Qualitative questionnaires (included in Appendix C) were given to children and parents at their final workshop with the post-intervention outcome questionnaires. These qualitative questionnaires were designed for the study and included a combination of closed and open questions. In the child questionnaire, the closed questions rated the workshops on a range of properties (e.g. easy, boring, friendly, interesting, fun) and provided picture prompts to the activities in the workshops. The open questions allowed the child to indicate aspects of the workshops they had found memorable or enjoyable.

The adult questionnaire included a number of open questions on the subjects of participation (barriers and reasons for participating), the effects of the workshops on the children (benefits, changes to understanding, what their child told them about the workshops) and recommendations (additional topics, suggestions for improvements, whether they would recommend the workshops to other families). Analysis of the surveys used descriptive statistics for the closed questions and simple coding for the open questions.

**6.11. Feasibility and acceptability**

 MRC guidelines suggest that feasibility and acceptability should be evaluated alongside measures of intervention effectiveness (Craig et al., 2008). According to a review of acceptability measurement in healthcare interventions, this should include measuring the participants’ attitude towards the intervention, perceived burden, perceived effectiveness, ethical consequences (side effects of the intervention) and satisfaction with the intervention (Sekhon et al., 2017). The qualitative questionnaires included items which measured these facets of acceptability for children and parents.

 Feasibility of an intervention reflects how well it could be run in practise. Different aspects of interventions can be assessed (e.g. demand for the intervention, how well it could be implemented as planned and practical issues around implementation) (Bowen et al., 2009). Feasibility will be assessed in terms of the recruitment rate, reasons for non-participation, attrition, attendance at the workshops, return of questionnaires and practical issues in relation to organising the workshops.

**6.12. Summary**

This chapter described the MRC framework for developing and evaluating complex interventions. Previous chapters have discussed the theory and evidence supporting provision of a psychoeducational intervention for children treated for leukaemia. This chapter described how the leukaemia intervention addresses modifiable targets from the risk-resistance model, as discussed in Chapter 3. The design of the RCT to evaluate the effectiveness of the intervention has also been described. Chapter 7 will report the outcomes for this evaluation study.

**Chapter 7**

**Evaluation of the leukaemia intervention**

This chapter will describe the results of the leukaemia intervention described in Chapter 6. It will report the quantitative multilevel modelling analysis and the qualitative questionnaire evaluation to assess the effectiveness of the intervention.

**7.1 Results**

Figure 7.1 shows the CONSORT study flowchart of participants through the study with 422 eligible families contacted by the research team and 74 families recruited into the study. Of these 74 families, 58 provided baseline data (shown in Table 7.1): 55 participants with ALL and 3 with AML. Of 35 participants randomised to the immediate intervention group, 9 withdrew before baseline and 26 provided baseline data (50% male, mean age = 8.81 years, sd = 1.79). Average time since diagnosis was 4.35 years (sd = 2.63). Nine participants were currently undergoing treatment and 17 had completed treatment, on average 3.38 years prior to the workshops (SD = 2.26 years). Of 39 participants randomised to the delayed intervention group, 7 withdrew before baseline (10 further participants were lost to follow-up during the study). Thirty-two participants provided baseline data (66% male, mean age = 9.41 years, sd=1.81). Average time since diagnosis was 4.71 years (SD = 3.31). Twelve of these participants were still receiving treatment, 2 relapsed during the workshop period and 18 had completed treatment, on average 4.03 years previously (SD = 2.70 years). Thirty-three families provided outcome data at 3 months and 36 at 6 months.

The final sample size of families providing follow-up data was 45. This was well below the target sample size of 120. Full attendance of all 4 workshops for children who started the workshop programme was 85%, with 90% of children attending 3 or more workshops. There were no significant differences in baseline measures for the

Met inclusion criteria and were contacted (n= 422)

Randomized (n= 74)

immediate and delay groups. There were no significant differences between those who did and did not provide follow-up data on any of the baseline measures. Two out of 3 of the children with AML in the study withdrew and did not provide follow up data due to relapses. Out of the 45 families who were analysed, 187/218 (86%) child questionnaires and 188/218 (86%) parent questionnaires were returned.

*Figure 7.1* CONSORT Flow Diagram (from Moher, Schulz & Altman, 2001) describing the flow of participants through the study

Analysed (n=19)
Excluded from analysis (no post-intervention scores recorded) (n=3)

Analysed (n=26)
Excluded from analysis (no post-intervention scores recorded) (n=0)

## Analysis

Withdrew during the workshops (n=3)

No reason (1), illness (1), scheduling (1)

Did not provide data: post-intervention (n=4), 3 mo (n=6), 6 mo (n=10)

Still in study after workshops: (n=22)

Withdrew during the workshops (n=0)

Did not provide data: post-intervention (n=0), 3 mo (n=1), 6 mo (n=3)

Still in study after workshops: (n=26)

## Allocation

Allocated to immediate intervention (n=35)

Withdrew before baseline/workshops (n= 9)

Provided baseline data (n=26)

Attended workshops: (n=26)

Reasons for withdrawal:

Time commitments: 5

Could not contact: 3

Illness: 1

Allocated to delay intervention (n=39)

Did not return baseline data (n=7)

Provided baseline data (n=32)

Withdrew before the workshops (n= 7)

Attended workshops: (n=25)

Reasons for withdrawal:

Time commitments: 5

Illness: 1

Child changed mind: 1

Excluded (n= 348)

Declined to participate (n= 78)

Did not reply to contact (n=268)

Excluded for having another condition (n= 2)

## Enrollment

Table 7.1

*Comparison of the baseline characteristics of the immediate and delay groups*

|  |  |  |  |
| --- | --- | --- | --- |
|  | Immediate group (N=26) | Delay group (N=32) | Test on group difference\* |
|  | Means (SD) | Means (SD) | t-test (df) |
| Age (years) | 8.81 (1.79) | 9.41 (1.81) | 1.262 (56) |
| Time since diagnosis (years) | 4.35 (2.63) | 4.71 (3.31) | 0.451 (56) |
| Parent reported outcomes: |  |  |  |
| PedsQL (generic) | 62.65 (19.58) | 61.74 (20.04) | -.164 (56) |
| PedsQL (cancer module) | 73.25 (18.26) | 71.17 (19.99) | -.388 (56) |
| SDQ (total) | 12.08 (7.88) | 12.84 (6.14) | .383 (56) |
| Caregiver burden | 4.76 (1.64) | 4.16 (1.65) | -1.302 (56) |
| Child treatment anxiety | 4.07 (1.19) | 3.62 (2.01) | -.977 (56) |
| Parent treatment anxiety | 3.79 (1.52) | 3.95 (1.56) | .371 (56) |
| Child self-efficacy | 2.4 (1.06) | 2.57 (.79) | .647 (56) |
|  |  |  |  |
| Child reported outcomes: |  |  |  |
| PedsQL (generic) | 63.79 (17.41) | 61.94 (22.29) | -.331 (56) |
| PedsQL (cancer module) | 78.55 (10.75) | 78.14 (12.98) | -.123 (56) |
| Child treatment anxiety | .71 (.52) | .74 (.6) | .191 (56) |
|  | Count (no.) | Count (no.) | Fisher’s exact test |
| Male  | 13 | 21 | .288 |
| ALL Regimen: A | 15 | 16 |  |
|  B | 5 | 0 |  |
|  C | 5 | 14 |  |
| AML | 1 | 2 | Nc |
| On-treatment (number) | 9 | 14 | .592 |
| Attrition | 9 | 17 | .145 |

Nc: test not calculable on treatment regimen (zero value), ALL: Acute Lymphoblastic Leukaemia, Treatment Regimen A= low risk treatment for ALL, Regimen B= moderate risk treatment for ALL, Regimen C= high risk treatment for ALL, AML: Acute Myeloid Leukaemia, PedsQL: Pediatric Quality of Life Inventory, SDQ: Strengths and Difficulties Questionnaire.

\* No t-tests or Fishers exact tests on differences between the immediate and delay groups were statistically significant.

Table 7.2 shows the participants had significantly lower parent and child-reported QoL and higher levels of emotional and behaviour problems at baseline than comparison samples. This shows that there was potential for the intervention to improve these outcomes.

Table 7.2

*Quality of life in recruited sample compared to general population and chronically ill samples*

|  |  |  |
| --- | --- | --- |
|  | Current sample | Comparison sample |
| Scale | N | Mean (SD) | Population | N | Mean (SD) | Test\* (df) |
| PedsQL parent | 48 | 62.21 (19.59) | Healthy1 | 717 | 87.61 (12.33) | t(763)=13.2 |
|  |  |  | Chronically ill1 | 662 | 74.22 (18.40) | t(708)=4.35 |
| PedsQL child | 48 | 62.90 (19.70) | Healthy1 | 401 | 83.00 (14.79) | t(447)=8.56 |
|  |  |  | Chronically ill1 | 367 | 77.19 (15.53) | t(413)=5.80 |
| SDQ | 51 | 12.45 (7.02) | General population2 | 10298 | 8.4 (5.8) | t(10347)=4.97 |
|  |  |  |  |  |  |  |

\*all significant at p<.001 1Varni et al. (2001) 2Meltzer et al. (2000)

Increasing time since diagnosis was correlated with higher parent and child-reported PedsQL scores on the generic (r=.43, r=.38) and cancer specific scales (r=.42, r=.28), lower caregiver burden (r=-.41) and lower parent and child anxiety (r=-.33, r=-.25). This supported the inclusion of time since diagnosis as a control variable.

* 1. **Results of the quantitative analysis**

**7.2.1. Primary outcomes**

Figures 7.2 and 7.3 plot changes in parent-reported PedsQl (generic) and SDQ total difficulties over the study period. Higher PedsQl scores indicate better QoL while lower SDQ scores indicate lower behavioural problems.

**PedsQl (generic)**

|  |  |  |
| --- | --- | --- |
| Time point | Immediate group | Delay group |
| 1 | Pre | Mc |
| 2 | Post | Mc |
| 3 | 3 mo | Pre |
| 4 | 6 mo | Post |
| 5 |  | 3 mo |
| 6 |  | 6 mo |

*Figure 7.2* Parent-reported PedsQl (generic) total mean scores plotted over time for the immediate and delay groups.

Study week is matched for the delay and immediate groups up to Time 3: see Table 6.1. Time 1: week 1, Time 2: week 5, Time 3: week 18. Key shows stages for both groups at each time point. Pre: pre-intervention, Post: post-intervention, Mc: Matched control, 3 mo: 3 month follow-up, 6 mo: 6 month follow-up. PedsQl: Pediatric Quality of Life Inventory. Error bars represent 95% confidence intervals for group means (solid line for immediate group, dashed line for delay group).

Figure 7.2 shows that scores for parent-reported PedsQL (generic) were similar in the immediate and delay groups at baseline. Scores showed an initial improvement in the immediate group after receiving the intervention (time 2) whereas there was no similar increase in the delay group in this period. The immediate group’s scores continued to improve at 3-month follow-up (time 3) before falling slightly at the 6-month follow-up (time 4). The delay group’s scores improved before receiving the intervention and then improved further during the intervention period (time 3 to time 4). The delay group’s scores remained similar at 3 month and 6-month follow-ups (time 5 and 6).

**SDQ (total difficulties)**

|  |  |  |
| --- | --- | --- |
| Time point | Immediate group | Delay group |
| 1 | Pre | Mc |
| 2 | Post | Mc |
| 3 | 3 mo | Pre |
| 4 | 6 mo | Post |
| 5 |  | 3 mo |
| 6 |  | 6 mo |

*Figure 7.3* Parent-reported SDQ (total difficulties) mean scores plotted over time for the immediate and delay groups.

Study week is matched for the delay and immediate groups up to Time 3: see Table 6.1. Time 1: week 1, Time 2: week 5, Time 3: week 18. Key shows stages for both groups at each time point. Pre: pre-intervention, Post: post-intervention, Mc: Matched control, 3 mo: 3 month follow-up, 6 mo: 6 month follow-up. PedsQl: Pediatric Quality of Life Inventory. Error bars represent 95% confidence intervals for group means (solid line for immediate group, dashed line for delay group).

Higher scores represent higher prevalence of behavioural difficulties so a reduction in scores represents improvements in this outcome. Figure 7.3 shows that SDQ scores were similar in the immediate and delay groups at baseline. Difficulties decreased in the immediate group after receiving the workshops (time 2) while difficulties increased slightly in the delay group over the same period. The immediate group’s scores continued to decrease at 3-month (time 3) but then showed a marked increase in difficulties at 6-month follow-up (time 4). Difficulties in the delay group fell before receiving the intervention (time 3) but increased slightly after the workshops (time 4), then decreased slightly at 3 month (time 5) and increased slightly at 6-month follow-ups (time 6).

**Multilevel modelling**

As described in Chapter 6, seven models were fitted sequentially to the data for each outcome. These 7 models were: 1) an unconditional model with no predictors, 2) a control model with time elapsed from diagnosis, 3) a change over time model, 4) the main effect of the intervention model, 5) the main effect of group model, 6) the random effect of the intervention model, 7) the group x intervention interaction model. At each step the significance of improvement in model fit was calculated and the predictors of the best fit models are reported below.

**PedsQl (generic)**

Table 7.3 shows that time elapsed between diagnosis and baseline (the control model) and change over time were significant predictors of the PedsQl (generic) scale. The model with the best fit (bolded in Table 7.3) contained the main effect of the intervention. Further additions to this model did not significantly improve fit. The parameter estimates from the best fit model are shown in Table 7.4. Longer time since diagnosis was associated with higher PedsQl scores. Scores improved over the course of the study (study week). Receiving the intervention was associated with higher PedsQl (generic) independently of the overall effect of study week.

**SDQ (total difficulties)**

Table 7.3 shows that change over time (study week) was the model with the best fit. Table 7.4 shows increasing study week was associated with decreasing SDQ difficulties. Time elapsed between diagnosis and baseline (the control model) did not significantly improve fit. There was no main effect of the intervention on SDQ scores.

Table 7.3

*Results of the multilevel modelling analysis on the primary outcomes*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Model | Deviance (-2LL) | Change in Deviance, change in df |  Residual variance | Child level intercept variance | Child level slope co- variance  | Intercept slope covariance |
| Parent-report PedsQL (generic) |
| Unconditional | 1583.376 |  | 71.947 | 274.915 |  |  |
| Control model | 1565.661 | 17.715\*, 1df | 71.526 | 197.893 |  |  |
| Change over time  | 1528.106 | 37.555\*, 1df  | 55.634 | 199.350 |  |  |
| **Main effect of intervention**  | **1522.355** | **5.751\*, 1df** | **53.444** | **200.445** |  |  |
| Main effect of group | 1521.605 | .75, 1df | 53.436 | 197.645  |  |  |
| Intervention as random effect  | 1519.294 | 2.311, 2df  | 49.892  | 198.754  | 12.547 | -20.811 |
| Group\*Int interaction | 1519.205 | .089, 1df | 49.892 | 198.754 | 12.547 | -20.811 |
| Strengths and Difficulties Questionnaire (SDQ) (total difficulties) |
| Unconditional | 1243.678 |  | 13.140 | 34.493 |  |  |
| Control model | 1241.670 | 2.01, 1df | 13.135 | 33.175 |  |  |
| **Change over time**  | **1237.586**  | **4.084\*, 1df**  | **12.852** | **32.722** |  |  |
| Main effect of intervention  | 1237.084 | .502, 1df  | 12.778 | 32.986 |  |  |
| Main effect of group | 1236.730 | .354, 1df | 12.778 | 32.753  |  |  |
| Intervention as random effect  | 1231.497 | 5.233, 2df  | 11.099 | 33.602  | 5.983 | -6.192 |
| Group\*Int interaction | 1231.449 | .048, 1df  | 11.101 | 33.580 | 5.942 | -6.112 |

-2LL: -2 log likelihood, df: degrees of freedom.

Bolded model is the model with the best fit. \* indicates a significant improvement in the model, tested using Chi-square distribution on reduction in -2LL deviance

Table 7.4

*Parameter estimates from the best fit models for the primary outcomes*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Parameter | Estimate | SE | Df | T | Significance (p value) |
| Parent-report PedsQL (generic) |
| Intercept | 50.481 | 3.734 | 63.891 | 13.518 | .001 |
| Time since diagnosis | 3.047 | .666 | 58.552 | 4.576 | .001 |
| Change over time  | .151 | .060 | 155.566 | 2.539 | .012 |
| Intervention | 4.222 | 1.742 | 151.581 | 2.423 | .017 |
| Strengths and Difficulties Questionnaire (SDQ) (total difficulties) |
| Intercept | 13.864 | 1.499 | 57.125 | 9.250 | <.001 |
| Time since diagnosis | -.385 | .271 | 54.504 | -1.419 | .162 |
| Change over time  | -.038 | .019 | 152.199 | -2.031 | .044 |

SE: Standard Error, Df: degrees of freedom, T: t test

* + 1. **Secondary outcomes**

Figures 7.4 to 7.11 plot changes in the secondary outcomes: parent-reported PedsQl (cancer), child-reported PedsQl (generic), child-reported PedsQl (cancer), parent-reported caregiver burden, parent-reported child self-confidence, parent-reported parent treatment anxiety, parent-reported child treatment anxiety and child-reported treatment anxiety. Higher scores on the PedsQl and confidence scales indicate higher QoL and confidence. Lower scores on the anxiety scales and the caregiver burden scale represent lower burden and lower anxiety.

**Parent-reported PedsQl (cancer)**

|  |  |  |
| --- | --- | --- |
| Time point | Immediate group | Delay group |
| 1 | Pre | Mc |
| 2 | Post | Mc |
| 3 | 3 mo | Pre |
| 4 | 6 mo | Post |
| 5 |  | 3 mo |
| 6 |  | 6 mo |

*Figure 7.4* Parent-reported PedsQl (cancer) total mean scores plotted over time for the immediate and delay groups.

Study week is matched for the delay and immediate groups up to Time 3: see Table 6.1. Time 1: week 1, Time 2: week 5, Time 3: week 18. Key shows stages for both groups at each time point. Pre: pre-intervention, Post: post-intervention, Mc: Matched control, 3 mo: 3 month follow-up, 6 mo: 6 month follow-up. PedsQl: Pediatric Quality of Life Inventory. Error bars represent 95% confidence intervals for group means (solid line for immediate group, dashed line for delay group).

Figure 7.4 shows that scores for parent-reported PedsQl (cancer) were similar for both groups at baseline. Scores improved for the immediate group after receiving the intervention (time 2), continued to improve at 3-month (time 3) but decreased at 6-month follow-ups (time 4). The delay group’s scores had improved before receiving the intervention (time 3), continued to improve after the intervention (time 4) and at the 3-month and 6-month follow-ups (times 5 and 6).

**Child-reported PedsQl (generic)**

|  |  |  |
| --- | --- | --- |
| Time point | Immediate group | Delay group |
| 1 | Pre | Mc |
| 2 | Post | Mc |
| 3 | 3 mo | Pre |
| 4 | 6 mo | Post |
| 5 |  | 3 mo |
| 6 |  | 6 mo |

*Figure 7.5* Child-reported PedsQl (generic) total mean scores plotted over time for the immediate and delay groups.

Study week is matched for the delay and immediate groups up to Time 3: see Table 6.1. Time 1: week 1, Time 2: week 5, Time 3: week 18. Key shows stages for both groups at each time point. Pre: pre-intervention, Post: post-intervention, Mc: Matched control, 3 mo: 3 month follow-up, 6 mo: 6 month follow-up. PedsQl: Pediatric Quality of Life Inventory. Error bars represent 95% confidence intervals for group means (solid line for immediate group, dashed line for delay group).

Figure 7.5 shows that scores for child-reported Pedsql (generic) were similar for both groups at baseline. After receiving the intervention, the immediate group’s scores improved (time 2), continued to improve at 3-month (time 3) and fell slightly at 6-month follow-ups (time 4). Scores improved for the delay group before receiving the intervention (times 2 and 3), then fell slightly during the intervention period (time 3 to time 4). Scores improved at the 3-month and 6-month follow-ups (times 5 and 6).

**Child-reported PedsQl (cancer)**

|  |  |  |
| --- | --- | --- |
| Time point | Immediate group | Delay group |
| 1 | Pre | Mc |
| 2 | Post | Mc |
| 3 | 3 mo | Pre |
| 4 | 6 mo | Post |
| 5 |  | 3 mo |
| 6 |  | 6 mo |

*Figure 7.6* Child-reported PedsQl (cancer) total mean scores plotted over time for the immediate and delay groups.

Study week is matched for the delay and immediate groups up to Time 3: see Table 6.1. Time 1: week 1, Time 2: week 5, Time 3: week 18. Key shows stages for both groups at each time point. Pre: pre-intervention, Post: post-intervention, Mc: Matched control, 3 mo: 3 month follow-up, 6 mo: 6 month follow-up. PedsQl: Pediatric Quality of Life Inventory. Error bars represent 95% confidence intervals for group means (solid line for immediate group, dashed line for delay group).

Figure 7.6 shows that scores for child-reported PedsQl (cancer) were similar for both groups at baseline. Scores for the immediate group improved after receiving the intervention (time 2), continued to improve until the 3-month follow-up (time 3) and fell slightly at the 6-month follow-up (time 4). Scores for the delay group had improved slightly before receiving the intervention (time 3) and improved further after receiving the intervention (time 4). The delay group’s scores fell at the 3-month follow-up (time 5) and improved slightly at the 6-month follow-up (time 6).

**Caregiver burden**

|  |  |  |
| --- | --- | --- |
| Time point | Immediate group | Delay group |
| 1 | Pre | Mc |
| 2 | Post | Mc |
| 3 | 3 mo | Pre |
| 4 | 6 mo | Post |
| 5 |  | 3 mo |
| 6 |  | 6 mo |

*Figure 7.7* Parent-reported caregiver burden total mean scores plotted over time for the immediate and delay groups.

Study week is matched for the delay and immediate groups up to Time 3: see Table 6.1. Time 1: week 1, Time 2: week 5, Time 3: week 18. Key shows stages for both groups at each time point. Pre: pre-intervention, Post: post-intervention, Mc: Matched control, 3 mo: 3 month follow-up, 6 mo: 6 month follow-up. PedsQl: Pediatric Quality of Life Inventory. Error bars represent 95% confidence intervals for group means (solid line for immediate group, dashed line for delay group).

Higher scores on the caregiver burden scale represent lower burden. Figure 7.7 shows that caregiver burden was slightly higher in the delay group at baseline. Scores in the immediate group improved after receiving the intervention (time 2), fell at 3-month (time 3) and improved at 6-month follow-ups (time 4). Scores in the delay group had improved before receiving the intervention (time 3). Scores remained stable after receiving the intervention (time 4), fell at the 3-month (time 5) and improved at 6-month follow-ups (time 6).

**Parent-reported child confidence**

|  |  |  |
| --- | --- | --- |
| Time point | Immediate group | Delay group |
| 1 | Pre | Mc |
| 2 | Post | Mc |
| 3 | 3 mo | Pre |
| 4 | 6 mo | Post |
| 5 |  | 3 mo |
| 6 |  | 6 mo |

*Figure 7.8* Parent-reported child self-confidence total mean scores plotted over time for the immediate and delay groups.

Study week is matched for the delay and immediate groups up to Time 3: see Table 6.1. Time 1: week 1, Time 2: week 5, Time 3: week 18. Key shows stages for both groups at each time point. Pre: pre-intervention, Post: post-intervention, Mc: Matched control, 3 mo: 3 month follow-up, 6 mo: 6 month follow-up. PedsQl: Pediatric Quality of Life Inventory. Error bars represent 95% confidence intervals for group means (solid line for immediate group, dashed line for delay group).

Figure 7.8 shows that scores for parent-reported child self-confidence were similar for both groups at baseline. Scores improved for the immediate group after receiving the intervention (time 2) and continued to improve at the 3-month (time 3) and 6-month follow-ups (time 4). Scores improved for the delay group before receiving the intervention (time 3), then fell after the intervention (time 4) and at 3-months (time 5), before recovering slightly at the 6-month follow-up (time 6).

**Parent-reported parent treatment anxiety**

|  |  |  |
| --- | --- | --- |
| Time point | Immediate group | Delay group |
| 1 | Pre | Mc |
| 2 | Post | Mc |
| 3 | 3 mo | Pre |
| 4 | 6 mo | Post |
| 5 |  | 3 mo |
| 6 |  | 6 mo |

*Figure 7.9* Parent-reported treatment-related anxiety (parent) total mean scores plotted over time for the immediate and delay groups.

Study week is matched for the delay and immediate groups up to Time 3: see Table 6.1. Time 1: week 1, Time 2: week 5, Time 3: week 18. Key shows stages for both groups at each time point. Pre: pre-intervention, Post: post-intervention, Mc: Matched control, 3 mo: 3 month follow-up, 6 mo: 6 month follow-up. PedsQl: Pediatric Quality of Life Inventory. Error bars represent 95% confidence intervals for group means (solid line for immediate group, dashed line for delay group).

Higher scores on the anxiety scales represent higher anxiety. Figure 7.9 shows that scores on the parent-reported parent treatment anxiety scale were similar for both groups at baseline. The immediate group’s anxiety scores improved after receiving the intervention (time 2) and continued to improve at the 3-month (time 3) and 6-month follow-ups (time 4). The delay group’s anxiety had fallen before receiving the intervention (time 3), continued to fall after the intervention (time 4) and at the 3-month follow-up (time 5) before increasing slightly at the 6-month follow-up (time 6).

**Parent-reported child treatment anxiety**

|  |  |  |
| --- | --- | --- |
| Time point | Immediate group | Delay group |
| 1 | Pre | Mc |
| 2 | Post | Mc |
| 3 | 3 mo | Pre |
| 4 | 6 mo | Post |
| 5 |  | 3 mo |
| 6 |  | 6 mo |

Figure 7.10 Parent-reported child treatment-related anxiety total mean scores plotted over time for the immediate and delay groups.

Study week is matched for the delay and immediate groups up to Time 3: see Table 6.1. Time 1: week 1, Time 2: week 5, Time 3: week 18. Key shows stages for both groups at each time point. Pre: pre-intervention, Post: post-intervention, Mc: Matched control, 3 mo: 3 month follow-up, 6 mo: 6 month follow-up. PedsQl: Pediatric Quality of Life Inventory. Error bars represent 95% confidence intervals for group means (solid line for immediate group, dashed line for delay group).

Figure 7.10 shows that scores for parent-reported child treatment anxiety were slightly higher in the immediate group at baseline. The immediate group’s scores fell after receiving the intervention (time 2), remained stable at 3-months (time 3) before falling slightly at the 6-month follow-up (time 4). The delay group’s scores had fallen before receiving the intervention (time 3), continued to fall after the intervention (time 4), at the 3-month (time 5) and 6-month follow-ups (time 6).

**Child-reported treatment anxiety**

|  |  |  |
| --- | --- | --- |
| Time point | Immediate group | Delay group |
| 1 | Pre | Mc |
| 2 | Post | Mc |
| 3 | 3 mo | Pre |
| 4 | 6 mo | Post |
| 5 |  | 3 mo |
| 6 |  | 6 mo |

Figure 7.11 Child-reported treatment-related anxiety total mean scores plotted over time for the immediate and delay groups.

Study week is matched for the delay and immediate groups up to Time 3: see Table 6.1. Time 1: week 1, Time 2: week 5, Time 3: week 18. Key shows stages for both groups at each time point. Pre: pre-intervention, Post: post-intervention, Mc: Matched control, 3 mo: 3 month follow-up, 6 mo: 6 month follow-up. PedsQl: Pediatric Quality of Life Inventory. Error bars represent 95% confidence intervals for group means (solid line for immediate group, dashed line for delay group).

Figure 7.11 shows that scores for child-reported treatment anxiety for the immediate and delay groups were similar at baseline. Scores for the immediate group did not improve straight after receiving the intervention (time 2) but improved at the 3-month (time 3) and 6-month follow-ups (time 4). The delay group’s anxiety increased at time 2 but fell before receiving the intervention at time 3. Scores continued to fall after receiving the intervention (time 4), increased at 3-month (time 5) and decreased at 6-month follow-ups (time 6).

**Multilevel modelling for secondary outcomes**

The multilevel models and parameter estimates for the models with the best fit for the secondary outcomes are presented in Tables 7.5 and 7.6. Time elapsed between diagnosis and baseline significantly improved model fit in all secondary outcomes (parent-report PedsQl (cancer), caregiver burden, parent-reported child confidence and treatment-related distress, child-report PedsQl (cancer and generic) and child-report treatment-related distress). The main effect of the intervention was not a significant predictor for any secondary outcome. The best fit model for parent-reported PedsQl (cancer) and child-reported PedsQl (generic) contained the intervention modelled as a random effect suggesting that the effect of the intervention was different for different participants. Individual plots for these 2 outcomes are provided in Appendix D. The change over time model was the best model for child-reported QoL (cancer), caregiver burden, parent-reported child confidence and parent and child reported treatment-related anxiety. Scores improved over the course of the study but not as a direct result of receiving the intervention.

Table 7.5

*Results of the multilevel modelling analysis on the secondary outcomes*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Model | Deviance (-2LL) | Change in Deviance, change in df | Residual variance | Child level intercept variance | Child level slope covariance  | Intercept slope covariance |
| Parent-reported PedsQl (cancer module) |
| Unconditional | 1438.168 |  | 78.941 | 203.539 |  |  |
| Control model | 1419.298 | 18.87\*, 1df  | 78.116 | 140.662 |  |  |
| Change over time  | 1394.359 | 24.939\*,1df  | 64.387 | 144.931 |  |  |
| Main effect of intervention  | 1393.408 | .951, 1df  | 63.947 | 144.866 |  |  |
| Main effect of group |  1392.867 | .541, 1df  | 63.987 | 142.970 |  |  |
| **Intervention as random effect**  | **1385.141** | **7.726\*,2df**  | **56.477** | **146.317**  | **29.740** | **-46.587** |
| Group\*Intervention interaction | 1384.943 | .198, 1df | 56.500 | 146.193 | 29.408 | -46.721 |
| Child-reported PedsQl (generic) |
| Unconditional | 1621.855 |  | 113.355 | 243.968 |  |  |
| Control model | 1608.018 | 13.837\*, 1df  | 112.476 | 186.564 |  |  |
| Change over time  | 1592.293 | 15.725\*, 1df  | 101.570 | 185.838 |  |  |
| Main effect of intervention  | 1590.574 | 1.719. 1df  | 100.366 | 186.212 |  |  |
| Main effect of group | 1589.907 | .667, 1df | 100.405 | 183.353  |  |  |
| **Intervention as random effect**  | **1583.790** | **6.117\*, 2df**  | **87.727** | **186.918**  | **44.477** | **-45.237** |
| Group\*Intervention interaction | 1582.121 | 1.669, 1df | 87.393 | 186.370 | 40.705 | -43.341 |
| Child-reported PedsQl (cancer) |
| Unconditional | 1298.107 |  | 59.451 | 114.114 |  |  |
| Control model | 1288.188 | 9.919\*, 1df | 58.667 | 94.629 |  |  |
| **Change over time**  | **1278.602** | **9.586\*, 1df**  | **54.237** | **95.902** |  |  |
| Main effect of intervention  | 1277.054 | 1.548, 1df | 53.652 | 95.582 |  |  |
| Main effect of group | 1277.033 | .021, 1df | 53.661 | 95.488 |  |  |
| Intervention as random effect  | 1273.890 | 3.143, 2df  | 48.914 | 96.309 | 17.387 | -15.278 |
| Group\*Intervention interaction | 1273.269 | .621, 1df | 48.951 | 96.323 | 15.905 | -15.035 |
| Caregiver burden |
| Unconditional | 641.216 |  | .946 | 1.626 |  |  |
| Control model | 624.737 | 16.479\*, 1df | .942 | 1.146 |  |  |
| **Change over time**  | **618.733** | **6.004\*, 1df**  | **.900** | **1.167** |  |  |
| Main effect of intervention  | 618.731 | .002, 1df | .900 | 1.167 |  |  |
| Main effect of group | 617.100 | 1.631, 1df  | .898 | 1.132 |  |  |
| Intervention as random effect  | 616.033 | 1.067, 2df | .831 | 1.152 | .248 | -.042 |
| Group\*Intervention interaction | 614.856 | 1.177, 1df | .830 | 1.154 | .217 | -.043 |
| Parent-reported child confidence |
| Unconditional | 418.452 |  | .279 | .499 |  |  |
| Control model | 411.899 | 6.553\*, 1df | .278 | .438 |  |  |
| **Change over time**  | **407.712** | **4.187\*, 1df**  | **.270** | **.442** |  |  |
| Main effect of intervention  | 407.592 | .12, 1df | .270 | .443 |  |  |
| Main effect of group | 407.526 | .066, 1df  | .270 | .443 |  |  |
| Intervention as random effect  | 405.094 | 2.432, 2df | .235 | .454 | .129 | .013 |
| Group\*Intervention interaction | 402.562 | 2.532, 1df | .236 | .458 | .099 | .070 |
| Parent-reported parent treatment-related anxiety |
| Unconditional | 430.243 |  | 1.226 | 1.300 |  |  |
| Control model | 419.415 | 10.828\*, 1df | 1.201 | .957 |  |  |
| **Change over time**  | **414.876**  | **4.539\*, 1df**  | **1.148** | **.948** |  |  |
| Main effect of intervention  | 414.840 | .036, 1df | 1.148 | .949 |  |  |
| Main effect of group | 414.835 | .005, 1df  | 1.148 | .949 |  |  |
| Intervention as random effect  | 414.196 | .639, 2df  | 1.190 | .986 | .097 | .309 |
| Group\*Intervention interaction | 414.034 | .162, 1df  | 1.181 | .989 | .089 | .297 |
| Parent-reported child treatment-related anxiety |
| Unconditional | 429.389 |  | 1.606 | .698 |  |  |
| Control model | 423.702 | 5.687\*, 1df | 1.575 | .583 |  |  |
| **Change over time**  | **417.869** | **5.833\*, 1df**  | **1.497** | **.561** |  |  |
| Main effect of intervention  | 417.550 | 0.319, 1df | 1.487 | .572 |  |  |
| Main effect of group | 417.372 | .178, 1df  | 1.486 | .567 |  |  |
| Intervention as random effect  | 416.548 | .824, 2df | 1.410 | .578 | .287 | .201 |
| Group\*Intervention interaction | 414.739 | 1.809, 1df | 1.407 | .567 | .209 | .226 |
| Child-reported treatment-related anxiety |
| Unconditional | 161.064 |  | .113 | .160 |  |  |
| Control model | 154.588 | 6.476\*, 1df | .112 | .140 |  |  |
| **Change over time**  | **145.432** | **9.156\*, 1df**  | **.103** | **.134** |  |  |
| Main effect of intervention  | 144.838 | .594, 1df | .103 | .134 |  |  |
| Main effect of group | 144.692  | .146, 1df  | .103 | .134 |  |  |
| Intervention as random effect  | 144.655  | .037, 2df | .103 | .135 | .000 | -.007 |
| Group\*Intervention interaction | 143.996 | .659, 1df | .103 | .135 | .000 | -.006 |

PedsQl: Pediatric Quality of Life Inventory. \* indicates a significant improvement in the model, tested using Chi-square distribution on reduction in -2LL deviance.

Table 7.6

*Parameter estimates from the best fit models for the secondary outcomes*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Parameter | Estimate | SE | Df | T | Significance |
| Parent-reported PedsQl (cancer module) |
| Intercept | 63.920 | 3.508 | 60.200 | 18.220 | <.001 |
| Time since diagnosis | 2.554 | .551 | 52.360 | 4.639 | <.001 |
| Change over time  | .183 | .066 | 123.559 | 2.776 | .006 |
| Main effect of intervention | 2.531 | 2.154 | 107.429 | 1.175 | .243 |
| Main effect of group | -1.962 | 3.298 | 53.665 | -.595 | .554 |
| Child-reported PedsQl (generic) |
| Intercept | 57.101 | 4.102 | 62.639 | 13.920 | <.001 |
| Time since diagnosis | 2.847 | .651 | 57.535 | 4.376 | <.001 |
| Change over time  | .140 | .078 | 135.538 | 1.793 | .075 |
| Intervention | 3.191 | 2.498 | 118.041 | 1.277 | .204 |
| Group | -4.471 | 3.878 | 57.238 | -1.153 | .254 |
| Child-reported PedsQl (cancer) |
| Intercept | 71.763 | 2.790 | 60.191 | 25.721 | <.001 |
| Time since diagnosis | 1.595 | .494 | 57.110 | 3.227 | .002 |
| Change over time  | .136 | .043 | 131.613 | 3.158 | .002 |
| Caregiver burden |
| Intercept | 3.760 | .302 | 61.182 | 12.458 | <.001 |
| Time since diagnosis | .235 | .056 | 56.736 | 4.204 | <.001 |
| Change over time  | .013 | .005 | 147.753 | 2.480 | .014 |
| Parent-reported child confidence |
| Intercept | 2.194 | .180 | 59.644 | 12.178 | <.001 |
| Time since diagnosis | .084 | .033 | 56.168 | 2.585 | .012 |
| Change over time  | .006 | .003 | 150.342 | 2.060 | .041 |
| Parent-reported parent treatment-related anxiety |
| Intercept | 4.450 | .332 | 45.865 | 13.386 | <.001 |
| Time since diagnosis | -.228 | .069 | 43.497 | -3.314 | .002 |
| Change over time  | -.016 | .008 | 94.932 | 94.932 | .034 |
| Parent-reported child treatment-related anxiety |
| Intercept | 4.055 | .309 | 44.326 | 13.127 | <.001 |
| Time since diagnosis | -.141 | .062 | 37.292 | -2.264 | .029 |
| Change over time  | -.021 | .009 | 96.742 | -2.445 | .016 |
| Child-reported treatment-related anxiety |
| Intercept | .973 | .113 | 54.804 | 8.640 | <.001 |
| Time since diagnosis | -.054 | .021 | 50.588 | -2.540 | .014 |
| Change over time  | -.007 | .002 | 106.122 | -3.080 | .003 |

PedsQl: Pediatric Quality of Life Inventory.

**7.3 Clinical improvements**

By the end of the study (6 months follow up) mean parent-reported PedsQl had improved from 62.21 (SD: 19.59) to 71.25 (SD: 17.96), mean child-reported PedsQl from 62.90 (19.70) to 73.00 (SD: 18.08) and mean SDQ from 12.45 (sd: 7.02) to 11.08 (sd: 6.66). These values remain below the healthy and chronically ill samples reported in Table 7.3. However, the improvements in QoL scores represent more than twice the MCIDs (4.5 for the parent-reported scale and 4.4 for the child-reported scale) defined by Varni et al. (2003). These improvements include changes due to the intervention and natural improvements over time.

Table 7.7 shows the mean scores for the outcome measures comparing the immediate group immediately after the workshops, with the delay group before they received the intervention (time 2). This represents data which would be reported in an RCT with a non-intervention control group and might be useful for future meta-analyses. The data for child-reported PedsQl (cancer module) is the data which would have been included in the meta-analysis reported in Chapter 5. The effect size of 0.16 is comparable to the effect size (SMD=0.14) reported there, for the chronic conditions combined.

Table 7.7

*Outcome results at time point 2 for immediate and delay groups*

|  |  |  |  |
| --- | --- | --- | --- |
|  | Intervention group N=23Mean (SD) | Delay group N=22Mean (SD) | Cohen's d  |
| Parent reported outcomes |
| PedsQL (generic) | 69.18 (18.5) | 59.69 (18.12) | .54 |
| PedsQL (cancer module) | 79.86 (17.64) | 72.97 (18.04) | .40 |
| SDQ (total) | 10.82 (7.94) | 13.3 (7.55) | .33 |
| Caregiver burden  | 5.23 (1.52) | 4.96 (1.68) | .17 |
| Child treatment anxiety | 2.91 (1.51) | 3.56 (1.6) | .43 |
| Parent treatment anxiety | 3.53 (1.99) | 3.61 (1.75) | .04 |
| Child confidence | 2.57 (.93) | 2.63 (.81) | .07 |
|  |  |  |  |
| Child reported outcomes |
| PedsQL (generic) | 74.18 (15.9) | 65.33 (19.15) | .52 |
| PedsQL (cancer module) | 81.34 (15.32) | 79.1 (14.18) | .16 |
| Child treatment anxiety | .74 (.62) | .82 (.48) | .15 |

PedsQL: Pediatric Quality of Life Inventory, SDQ: Strengths and Difficulties Questionnaire

Cohen's d (calculated on differences in means between intervention and delay group at timepoint 2; post-intervention for immediate group and pre-intervention for delay group)

**7.4 Qualitative evaluation of the intervention**

Parents and children each filled in a questionnaire after their final workshop to assess acceptability and feasibility of the workshop program.

**7.4.1. Child evaluation**

The qualitative questionnaire was completed by 42 children. The satisfaction ratings were high; 95% rated the workshops as very enjoyable, 92.5% as very interesting and 98.3% as very friendly. The majority of children stated the workshops were not difficult although 21.4% found some aspects difficult to understand (most commonly cells and DNA). All of the children said that the workshops would be helpful for other children with leukaemia (90.5% very helpful, 9.5% a bit helpful). In response to what they most enjoyed about the workshops, 22 recalled particular games or activities (the bowling game was mentioned most often), 5 liked the social aspect of making friends and being able to talk to others with the condition, 10 mentioned learning about specific topics (eg. blood, how the body works). The children made few critical judgements. Only 1 commented that there was an aspect they didn’t enjoy (‘answering hard questions’). Six said they would make changes to the workshops; more or longer sessions (4), more activities (1), more complex content for the older children (1).

Answers to open-ended questions were given by 28 children and highlighted improvements in knowledge of leukaemia and its treatment. Twenty-one children said the workshops had filled in gaps in their previous knowledge, with some saying they had known little about leukaemia beforehand (7):

*I understood why I was having treatment for 3 years (2001)*

*I wondered what leukaemia is, but now I understand (5005)*

Four children said this had made them feel less worried and scared about their illness:

*It makes you understand what is going on in your body and less scared about what will happen (1203)*

*If you and your family are worried, the workshops can help you understand a bit more about your treatment and how you may feel but it will also help you relax (5002)*

Although one child noted that knowledge could also make children worry more:

*In a way it would be helpful for children to know what's happening in their body and how the chemo will affect them. As well it might be worse because it might worry them about what will happen to them in the future (3007)*

Two of the older children said they already understood leukaemia before the workshops, but that attending the workshops would be useful for younger or less-informed children*:*

*I feel more confident about the information I already knew. As a family we talked a lot about cancer. Not all families have this prior knowledge and it would be helpful for them to do the workshops (6006)*

Three children said that the fun, interactive nature of the workshops made it easier for them to learn:

*It's a bit easier to understand what's wrong with us as children by doing activities rather than just listening to words all the time (8001)*

Four children said that understanding leukaemia made it easier for them to talk about it:

*I enjoyed telling my friends about blood and blasts (1204)*

*I understand more now. I can tell my friends all about the white blood cells and how they went wrong and caused my ALL (8001)*

**7.4.2. Parent evaluation**

The qualitative questionnaire was completed by 44 parents. All of the parents stated that they would recommend the workshops to other families.

**Difficulties participating**

Twenty-two parents said they had one or more difficulties in attending the workshops; scheduling around other family activities (6), scheduling around work commitments (7), missing school (6), child illness (3) traffic, travel or parking problems (6).

**Reasons for participating**

Twenty-six parents chose to take part as they thought the intervention would have positive benefits for their child through; improved understanding of their condition and treatment during (10) and after (8) treatment, the opportunity to talk about leukaemia (3) and ask questions (2), increased confidence (3), meeting other children in the same position (3) and seeing that children get better (3). Seventeen parents said they chose to participate to contribute to research which could lead to future improvements in treatment.

**Benefits of the workshops**

Parents said that their child had benefitted from the workshops because they enjoyed the activities (30) and had learned information about their illness, treatment and the importance of staying healthy (34). Some parents said their child had very little or no understanding of leukaemia before the workshops (3) or had worried it was their fault they got leukaemia (3).

*she is happier knowing she didn't do anything to give herself leukaemia and she was also very interested in how the medicine worked against it (3007)*

Some parents had struggled to explain the illness to their child or answer their questions, and thought the workshops had provided this information (3):

*From experience (child’s name) worried about her illness and found school and friends a challenge. As a parent you try and keep family on a normal par and sometimes forget about explaining the important issues of leukaemia as they have aged. This has provided (child’s name) with the knowledge at a level she understands (4002).*

**Opening up communication**

Ten parents said the workshops had helped the child and parents to talk to each other about leukaemia:

*He is a different child completely. I just wish we didn't have to wait so long for him to attend this. And we advise as a family to talk about it and don't brush it under the carpet. It's part of your life (1007).*

*He is a little more honest about the level of pain he is actually experiencing which is good so we can help him more. Before he was keeping it in and he is too young to suffer in silence (8005).*

Fifteen parents said it helped the child to tell other people (often peers) about their illness. They had become more confident in explaining because they understood their illness better. Some of these children did not talk about it at all before the workshops:

*It has helped him to explain to friends what was wrong with him as he wouldn't talk about it before (1007)*

*They really benefitted (child’s name), they taught her things she didn't know about her illness and she feels happier about telling people about it because she can explain more (3007).*

*He talks and explains to other children what he had in his own words and other kids just sit and listen to him (8001).*

Seventeen parents said they and their child benefitted from meeting other families and children who had been through the same thing; children enjoyed the social aspects of the workshops (14), enjoyed taking part in activities where they could be ‘normal’ children (3), where they could see other children who had had treatment and were now well (3), and where they could improve in confidence by doing activities away from their parents (3).

 **Suggestions for improvements**

Parents made a small number of suggestions for how to improve the workshops: different setting (non-hospital) and timings (4), more sessions over a longer period (3), sessions for parents and siblings (2) and additional content (more information on the effects of steroid treatment and long-term health problems (3).

**Adverse effects**

Two parents mentioned adverse effects; the hospital-setting was a reminder of treatment (1) and the workshops and outcome measurements may have added to the child’s anxiety (1).

*I worry that it may have made him think/focus on it more. (Child’s name) is relapsed and we have always benefitted from his 'happy go lucky' attitude. As he gets older I fear he worries more and not sure how the course helped with his emotional/ 'worry' factor. He enjoyed it though and it definitely benefitted his understanding (1203)*

**7.5 Discussion**

This study evaluated the effectiveness of a psychoeducational intervention delivered to children treated for leukaemia; on QoL, behavioural problems, child self-confidence and treatment-related anxiety. Key strengths of the study were the longitudinal measurements, the RCT design and multi-level approach to analysis, which allowed the effects of the intervention to be distinguished from natural improvements in QoL over time. Improvements in QoL have been reported for children over the course of leukaemia treatment (Adams et al., 2016; Eiser et al., 2005) which can make interventions difficult to interpret (Kazak et al.,1996). Time since diagnosis significantly predicted all outcomes, except for SDQ, in this study, which may reflect these expected improvements over time. In all outcomes, the delay group improved before receiving the intervention. This highlights the importance of using a comparison group and analysis which takes change over time into account.

Another strength of the study was the recruitment of a sample with a treatment need. The QoL of our sample (as measured by parent and child-reported PedsQL (generic) was significantly more impaired than a chronically ill sample. Other studies have reported recruiting samples with very little impairment at baseline, which limits the potential of the intervention to improve outcomes (Christie et al., 2009; DeWit et al., 2008; Ryu & Lee, 2015).

There was a main effect of intervention for the primary outcome measure of parent-reported PedsQL (generic), which suggests that the intervention led to a significant improvement in child QoL (measuring social, emotional, school and physical functioning). Over the course of the study QoL increased by more than twice the MCID for this scale. This suggests that this psychoeducational intervention was able to improve a generic measure of adjustment in a mixed group of survivors and children on-treatment by clinically significant levels.

For those on-treatment, the workshops explained why their side effects occur, the symptoms of leukaemia, how treatment removes leukaemia cells and the importance of making healthy choices for the future. There are several mechanisms through which this could improve the child’s QoL. Being better informed may reduce stress associated with illness and treatment uncertainty (Santacroce & Lee, 2006). It may also improve the ability and confidence of the child in communicating with doctors, family and peers, allowing them to make choices and to utilise social support (Ranmal et al., 2008). Improving the child’s secondary coping strategies which target adjustment to illness rather than the illness itself, has been associated with improved outcomes in paediatric cancer (Compas et al., 2012). The child may perceive leukaemia as uncontrollable, but the intervention may improve feelings of control around symptom management and treatment. Further studies would be required to test whether improvements in QoL could improve long-term health outcomes. This intervention provided information through a series of hands-on activities which could be tailored to the child’s information needs and cognitive level. Interactive and individualised interventions were reported as the most effective mode of delivery in a review of psychoeducational interventions for children with cancer (Bradlyn et al., 2003).

The intervention may also provide information, social support and coping strategies for survivors, who may have been too young or distracted during treatment to fully assimilate illness information. Uncertainty remains high in survivors, especially in relation to future health problems and the possibility of relapse (Decker et al., 2007; Santacroce & Lee, 2006). These children may have less contact with healthcare providers and less opportunities to ask questions or address misunderstandings. Therefore, the intervention may have provided an opportunity to seek information. Survivors are often less likely to use health protective behaviours (such as healthy eating and exercise) or have relatively high levels of risk-taking behaviours (such as smoking and substance use) even though their risk of long-term chronic health conditions and secondary cancers are higher than for healthy peers (Bauld et al., 2005, Tyc et al., 2001). The intervention provided information on the vulnerability of children to late effects and the importance of positive health behaviours. This may have provided some understanding and motivation to address their on-going health needs. However, this was only a small component of one workshop. Further work would be necessary to explore whether positive health choices made in an intervention could be incorporated into behaviour and maintained over the long-term.

The random effects model was the best model for the parent-reported PedsQl (cancer module) and the child-reported PedsQl (generic) suggesting that the intervention effects differed for individual children and parents. A potential explanation for this differential effect might be the inclusion of survivors and children on-treatment. Both groups have information needs regarding their leukaemia treatment. However, it may be that the intervention was more suitable for children on treatment, especially as it targeted treatment-related distress. The burdens of leukaemia are different in the acute phase (on-treatment) than they are in survivorship and one intervention may not be as effective for both groups.

 Many of the outcome scores improved during the study but not as a direct result of receiving the intervention. Natural improvement over time might not explain all of these improvements. Many of the outcomes showed a large improvement in the delay group between time points 2-3 (e.g. child-reported PedsQl; generic and cancer scales), immediately before receiving the intervention. It is possible that preparing for the intervention and filling in outcome measures could have increased motivation in this group or increased communication in families. It has been suggested that increased involvement with healthcare and open communication in families improves adjustment (Ranmal et al., 2008; Van Schoors et al., 2017). QoL monitoring has also been used as an intervention for children with diabetes as it raised issues which could then be addressed by families and doctors (DeWit et al., 2008). This might mean that the wait-list control design obscured some of the effects of the intervention.

Measurement may also have been affected by disease status. The PedsQl (cancer module) is specific to issues around cancer-treatment so may not be as relevant to issues around survivorship. This may explain why changes were detectable using the parent-reported generic scale but not the cancer-specific scale. Had the intervention only included children on-treatment, improved scores on the cancer-specific scale may have been demonstrable. Other outcome measures were also less relevant to those not on-treatment. Questions about Vincristine injections (in the treatment anxiety scale) could not be answered by children off-treatment, meaning that the sample size for this scale was smaller.

While there is evidence of improvement in QoL, there was little evidence of improvement in emotional and behavioural problems (as measured by the SDQ) scores associated with the intervention. Scores had improved slightly over the course of the study, but this change was not significant, and scores were still well below those of the healthy sample (shown in Table 7.3). This was the only outcome not to be associated with time since diagnosis, which suggests that behaviour does not necessarily improve after treatment ends. Behaviour problems are a substantial burden during leukaemia treatment. Steroid use is particularly associated with mood problems. The effects of steroids are often experienced as the most difficult aspect of leukaemia treatment for children and families and can affect the ability of parents to maintain normal discipline (Adams et al., 2016). Steroid and chemotherapy treatments were not recorded as part of the outcome measurements. Therefore, it is also possible that steroid treatment during the study period might have affected QoL.

The effects of steroids were explained in workshop one, as a side effect of treatment. However, the psychological effects of this may not have been dealt with in enough detail to impact behavioural problems associated with their use. Two families said they would have liked more information about steroids to be part of the intervention. It is also possible that the child and other family members need coping skills training in addition to information to be able to cope with the effects of steroids. Behaviour problems can persist in survivors, including increased rates of antisocial behaviour (Schultz et al., 2007) and lower behavioural inhibition (Campbell et al., 2009). These problems may reflect changes which occur in family functioning during treatment and may require other interventions to improve outcomes (e.g. family teamwork). There may also be changes in brain function caused by chemotherapy which change executive function and coping strategies (Campbell et al., 2009).

There were no effects of the intervention on caregiver burden or parent-reported child confidence. These outcomes were assessed using adapted versions of questionnaires as there were no measures specific to paediatric cancer. The lack of effect may be because the intervention is not effective in improving these outcomes, or because the study was underpowered to detect an effect. It is also possible that these measures are not sensitive enough to identify changes. A systematic review found no measures of caregiver burden for paediatric cancer which had been adequately evaluated, and which captured the changing roles and responsibilities in families (Shilling et al., 2016).

Acceptability of the intervention was high. Attendance at the workshops was 85% for the complete program of 4 workshops. Parents and children universally rated the intervention as useful, enjoyable, interesting and friendly. All families said they would recommend the intervention to other families in the same position. Learning in a social and interactive environment, where children could ask questions, was seen as a benefit of the intervention. Some of the families said that their child had known little about leukaemia before the intervention or had worried they had done something themselves to get the illness. Parents sometimes struggled to answer their questions. This highlights the need for information directed to children with leukaemia, even in the years after treatment where the child may have less opportunities to ask questions. Some of these children had been treated when they were very young and may not have understood the illness at the time.

Many of the families said that learning about leukaemia had helped their child to communicate with others. Some children on-treatment were able to communicate their needs better, while survivors talked more about leukaemia with family and friends. These improvements in communication could help to improve QoL through improving symptom management, communicating with health providers, and improving family or peer relationships. Open communication in families and perceived social support have been associated with better child adjustment after a pediatric cancer diagnosis (Van Schoors et al., 2017; Kazak et al., 1997; Kupst & Schulman, 1988).

The results from the PedsQl generic and cancer-specific scales favouring a random effects model, may suggest that it is more appropriate to deliver the intervention to children on-treatment only. However, the mix of children on and off-treatment was often seen as a benefit by families and had been a reason for participation for some. Parents of children on-treatment wanted their child to see others who had gone through the same thing and ‘come out the other side’.

Almost half of the families (21/44) said they had some scheduling or travel issues relating to attending the intervention. Travelling to the hospital for 4 workshops on consecutive weeks was a substantial time commitment, especially when balancing other family and work commitments. While it was feasible to run the workshops, the commitment asked from families was high and probably deterred some from participating. The workshops were run at various times to fit in with families; including during school hours, holidays, weekends and evenings. However, no time was perfect for all families and this remained a challenge throughout the recruitment process. It was especially problematic for the delay group who had to commit to the workshops 3 months in advance. There may be ways to run the workshop program to reduce this burden, such as reducing to 2 longer workshops, or an all-day program. For the children still receiving treatment it might be more effective to run the workshops alongside existing clinical appointments.

**7.6 Limitations of the study**

A limitation of the study was the small sample size. As well as reducing the power to detect effects it prevented the examination of potentially important moderators of effect such as stage of treatment, treatment regimen or age of the child. The study achieved a 17.5% recruitment rate. As shown in Figure 1, 63.5% of the targeted sample were not contactable by phone and did not reply to mailings. This may represent difficulties in recruiting children no longer receiving treatment, as some of the contact details were not current. Of the 3 children with AML recruited to the study, 2 withdrew due to illness. This reflects the increased burden of AML treatment and means that the results of this study may not generalise beyond ALL. There is a need for more interventions aimed at children with AML as the burdens associated with treatment may be different. This would have additional implications for recruiting an adequate sample as AML is much rarer than ALL. It might, therefore, require a different mode of delivery such as eHealth (computer or telephone) as children would need to be recruited over a wider area.

**7.7 Summary**

This study has provided evidence of improvements in QoL following a psychoeducational intervention for children treated for leukaemia. Psychoeducational interventions designed to improve knowledge have been evaluated in many chronic conditions. However, no similar group interventions delivered specifically to children with leukaemia and based on education rather than coping skills have been identified in the literature. It is encouraging that preliminary results suggest this may be effective in this group, and that the intervention was rated as highly acceptable and beneficial by families.

This study also demonstrates the difficulty of recruiting samples of sufficient size for relatively rare conditions. Various methods were used to improve recruitment; including repeated attempts to contact families, involvement of family support Facebook groups, arrangement of workshop schedules to fit in with families and using a multicentre approach. Even using these approaches the study fell short of its recruitment target. Examining barriers to participation may suggest ways to improve recruitment and would increase the generalisability of intervention research. Chapter 8 will report the results of an interview study with a sample of families who chose not to participate in this intervention, in an attempt to identify these barriers.

**Chapter 8**

**Barriers to participation in the leukaemia intervention: A qualitative interview study with parents**

Psychoeducational interventions delivered to children with cancer and other chronic conditions are often limited by small sample sizes, typically failing to reach recruitment targets. As described in the previous chapter, the evaluation of the leukaemia intervention reported difficulties with recruiting an adequate sample of children with leukaemia. Even using a multisite approach, flexibility in intervention scheduling and different ways of reaching families, the actual sample was well below the targeted sample size. As interventions need to be evaluated using good quality studies, efforts to improve recruitment are important. The MRC guidelines for evaluating complex interventions state that studies should consider barriers to participation as part of their evaluation (Craig et al., 2008). To inform future recruitment, this interview study investigated reasons for non-participation in a selection of families who chose not to take part in the leukaemia intervention. This chapter will report the results of this qualitative study.

**8.1. Problems with recruitment into intervention studies**

A number of methodological problems have made collating evidence on the effectiveness of psychoeducational interventions difficult. Failure to recruit sufficient numbers is a significant problem as it often leads to underpowered studies which are unlikely to detect intervention effects (Tercyak et al., 2006). Difficulties in recruiting populations with rare conditions and high treatment burdens (such as leukaemia) have been reported (Annett & Erikson, 2009; Olechnowicz et al., 2002). Systematic reviews often highlight the problems of low sample size and high attrition in reducing the quality of evidence for intervention efficacy (Richter et al., 2015; Ryan et al., 2018). The meta-analysis reported in Chapter 5 identified high risk of attrition bias in 8 of the 25 included studies.

Children with poorer disease indicators and psychological outcomes are less likely to be recruited into intervention studies (Christie et al., 2009; Ryu & Lee, 2015) meaning that interventions often do not target the groups most likely to benefit. This reduces the generalisability of findings and the clinical relevance of research. Frameworks for intervening with families often propose that families at the greatest risk of poor outcomes should be targeted (Kazak et al., 2007). Therefore, it is necessary to include valid target groups in intervention research. However, there is little information about the best ways to enrol participants and increase the accessibility of research to at-risk groups (Tercyak et al., 2006).

**8.2 Barriers to participation in intervention studies**

Exploring reasons for non-participation may provide a better understanding of effective ways to present interventions to participants, especially to at-risk groups. Existing research suggests several barriers to participation in psychosocial interventions, from the families’ perspective, including time commitment, travel and scheduling issues (Butler et al., 2008, Patel et al., 2009), perceived relevance and priority of the intervention (Santacroce et al., 2010; Terycak et al., 2006), and study burden (e.g. hospital appointments, randomisation, repeated measures) (Brier et al., 2015; Kazak et al., 2005a).

Psychological factors may also be important as children with lower QoL, higher anxiety and symptoms of PTS have lower rates of recruitment into interventions (DeWit et al., 2008; Graue et al., 2005). Adverse psychological factors such as fear, denial, distress and stigma at feeling different from peers may reduce the likelihood of participation in interventions (Buchanan et al., 2014; Seitz et al., 2009). While studies have reported barriers to participation identified during the recruitment process, few have spoken in-depth to non-participants. Interview studies which have addressed non-participation in psychological and behavioural interventions for children, highlighted lack of time, lack of priority and perceived negative impact of the intervention (Levickis et al., 2013; Read et al., 2009).

This chapter reports the first interview study to explore reasons for non-participation in a psychoeducational intervention for children with leukaemia. Detailed interviews addressed the perceived barriers to participation for parents who declined participation in the leukaemia intervention described in Chapter 6. The results from this study may be used to inform the development and evaluation of future psychoeducational interventions. This includes improving the relevance of interventions, increasing accessibility for families and improving the recruitment of at-risk groups.

**8.3 Methods**

**8.3.1. Participants**

Parents were contacted by telephone as part of the broader recruitment strategy for the psychoeducational intervention study (described in Chapter 6) at Manchester Children’s Hospital in the UK. Parents who declined participation in the intervention often gave brief reasons for their decision. In the final two blocks of recruitment, non-participating parents were asked if they were interested in taking part in this interview study. Parents were told they would not be asked to change their minds about participation in the intervention but would be asked about non-participation for the purpose of improving relevancy and accessibility of the intervention for other families. Of 22 families who were asked to participate, 10 families provided informed consent. All chose to be interviewed at home. Children were not present during the interviews.

**8.3.2. Data collection**

Semi-structured interviews were carried out by the author with one or both parents. The interview schedule covered reasons for non-participation in the leukaemia intervention and other key areas which may have influenced decisions. The interview schedule is provided in Appendix E. Questions asked about the impact of leukaemia on the family, how families had communicated with their child about leukaemia, and how families had sought and understood leukaemia related information. Parents were asked for suggestions of how the intervention or recruitment process could have been improved to make it more accessible and relevant to families in the future. The interviewees were asked the same questions, but the order of questions followed the flow of conversation. Parents were also encouraged to raise issues they thought were important. Interviews were audiotaped and transcribed verbatim.

**8.3.3. Data analysis**

The methodology employed in this study was broadly essentialist and phenomenological in nature (Harper, 2011). As the aim was to understand the parents’ perspectives, reports were treated as true representations of how parents understand these experiences. Data was analysed thematically, using template analysis (Brooks et al., 2015; King, 1998). Template analysis involves developing a coding template on the basis of a subset of the data which is then applied to the remaining data and refined.

 Initial coding was performed using qualitative data management software (NVivo 10; QSR international, 2012). A hybrid method was used which allowed deductive codes to be applied and inductive codes to be derived from the data (Brooks et al., 2015; Fereday & Muir-Cochrane, 2006). Areas of interest such as practical barriers to participation and the impact of leukaemia provided structure in the interviews and were pre-existing codes in the data. However, unpredictable themes could also be described. Initial analysis involved transcribing and reading the interviews to give an overall sense of the data and emerging themes. Memos were added to identify ‘codable moments’ (Boyatzis, 1998) and were summarised under codes to construct a preliminary coding frame (Crabtree & Miller, 1999). This template was re-applied to all the interviews until all ‘codable moments’ could be described (Brooks et al., 2015). Saturation was achieved when no new codes were necessary to fully code the data (Guest, 2006). A coding book and code tree were written to include descriptions of the codes, exclusions, examples and their structure under the superordinate themes. The coding frame and three full transcripts were coded independently by the author and another independent reviewer. The meanings of codes and themes were discussed to evaluate the reliability and application of these to the data. Differences in coding were discussed to ensure data were not being missed or misinterpreted by either coder. The code book and code tree were edited in light of these discussions and reapplied to the data. Regular meetings with other team members were held to discuss the data and themes during the analysis phase.

**8.4. Results**

Parents gave a range of specific reasons for non-participation. They also described the significant burdens and challenges of caring for a child with leukaemia which provided additional insight into their decisions around participation. Reasons for non-participation were divided into 5 subthemes: travel issues and scheduling, timing and relevance, perceived negative impact of the intervention/information on the child, getting back to normal, and child anxiety/avoidance.

**Theme 1: Travel issues and scheduling**

Parents described family engagements, school and work commitments as reasons for non-participation. Parents did not want the child to miss any time from school or social activities as they had already missed a lot during treatment. Additional hospital visits for the workshops were described as ‘*too much’* by parents whose children were still receiving treatment. Having to travel, often considerable distances and at inconvenient times (e.g. rush hour), were also mentioned as reasons for non-participation.

**Theme 2: Timing and relevance of the intervention**

Timing and relevance were reasons for non-participation in 7 out of 8 families of survivors. These 7 families said they would have participated in a psychoeducational intervention if the child was still receiving treatment, as it would help the child to understand their treatment and explain their illness and side effects to others.During treatment, familiarity with medication and procedures was seen as an important part of the child’s ability to cope with their illness. A lack of child-friendly explanations and opportunities to talk to healthcare providers during treatment was associated with short and long-term anxiety and misunderstandings by some families:

*‘I genuinely believe that if she’d have had…more support more opportunity to talk about it…more opportunity to have things explained to her I do honestly believe I’m not saying it would have…she wouldn’t have gone on to have any panic attacks or any anxiety but I do honestly believe that that contributed a lot…to how…you know it impacted her once the treatment finished…’* (Interview 4).

However, a psychoeducational intervention about leukaemia was often not seen as relevant to children who had finished treatment. In some cases, this was because children were treated at a very young age and had no memory of their treatment. Families did not see any purpose in the child learning about leukaemia in this case. Other survivors did remember their treatment and asked questions about their illness. Some children wondered why they got leukaemia or ‘*how they caught it’.* Children still wondered why the medicine had made them so poorly, when medicine was meant to make you feel better. Some parents wanted their child to attend the intervention to address these questions, but the child did not want to participate.

**Theme 3: Perceived negative impact of the intervention and protection from distressing information**

Five families of survivors chose not to participate as they worried the intervention would bring back bad memories for their child. These families were often unsure what their child could remember as they did not talk about it. Some saw unanswered questions as a potential future problem. However, while they recognised the need to address underlying information needs, parents wanted to avoid causing their child distress:

‘*he had a lot of horrible things happen to him… earlier on...I don’t know how much he remembers really. And that’s the thing I think…is it going to bring back those memories…make him more aware of something…is it creating a memory that he didn’t have almost… I just think with him there’s obviously something ticking along inside his head about the whole thing…and at some point I know it will all come out…and that’s the bit that I’m thinking…how do we handle it…’* (Interview 7)

These painful memories often related to invasive procedures during the child’s treatment. Children and parents had experienced intense distress during these procedures. While children often did not remember them, parents worried that the intervention might bring the memories back.

All the families described wanting to protect the child from potentially distressing information about leukaemia, at different stages of treatment. They worried that ‘too much’ information during treatment would reduce the parent’s and child’s ability to cope. All families talked about controlling the amount and type of information they sought as a coping strategy.

 *‘I think just because I didn’t want to scare myself to the point where I wouldn’t be able to deal with what was happening….or that I knew too much…and if I knew that, would I be worse off, because would I have got myself in too much information and not been able to handle it’* (Interview 9).

Parents often avoided sharing information with the child which mentioned the potentially life-threatening nature of leukaemia and did not tell children about deaths of other children on the wards. Parents of survivors avoided telling children that some physical effects of treatment might be permanent. Three parents worried about their child’s long-term health vulnerabilities but did not share these worries with their child.

**Theme 4: Getting back to normal**

The desire to move on and get back to normal life was a reason for non-participation in 5 families. Parents had already devoted considerable time to leukaemia treatment and wanted to move on from this distressing period of their lives. Families described trying to get back to normal as soon as possible after treatment, reinstating normal parental discipline, taking part in family activities, getting back to school and not making leukaemia their ‘*whole focus in life’* (interview 8). Transitioning into survivorship was a challenging period for families, with a shift in priorities from treatment to coping with the demands of normal life. For one family, moving on from leukaemia, involved stopping thinking and talking about leukaemia while the child was still on maintenance treatment:

 *‘I think that he’s done, I think we’ve had it non-stop and I don’t know what, whether I’m either on to him about things, whether you need to maybe talk less about it and do other things and try and get back to normal.’* (Interview 8)

Families also talked about the stigma of illness and not wanting their child to feel different from other children. Families had often been upset and embarrassed by the reactions of other people to their child’s physical appearance during treatment. Children had been treated differently during treatment and families of survivors wanted their child to be treated as a normal child once treatment ended. For some families, attending an intervention was seen as an unwanted reminder of leukaemia and a marker of difference:

*‘we’ve kind of drawn a line under that really…. I don’t really want her to get into this…where’s she’s different…if you know what I mean…so I don’t want her to…she kind of got a lot of special treatment for being unwell.’* (Interview 10)

Many children did not tell their peers they had been ill as this was not part of their identity as a ‘well’ child. This also meant the intervention did not seem relevant to some survivors:

 *‘And he’s in a group of boys at school…, they’re into football, they’re all competitive, and quite boyish boys, and I guess that, being ill doesn’t fit with that, so he’s kind of moved on.’* (Interview 7)

**Theme 5: Child anxiety or refusal to talk about leukaemia**

Child anxiety was given as a reason for non-participation in 6 families. Three families of survivors said their child would not talk about leukaemia or look at photos of themselves during treatment. Parents said it was difficult to address their child’s unanswered questions or anxiety because of this. One child had originally been enrolled in the intervention but had been put off participating after filling in the first set of study questionnaires. Her parents said she did not want to address the issues raised and the questions made her worry about what would happen in the intervention:

*‘she didn’t like answering the questions…at all….so..I mean she did do it in the end but she just wanted to have it done and get rid of it…and not talk about it anymore…. yeah so whereas I’d put that’s an issue she’d no it’s not….thinking right ok…you know so just the complete opposite…so if you ask her something yeah it’s fine…when really it’s not fine at all…’* (Interview 1)

Some children were anxious about clinic visits because other ill children and medical procedures reminded them of their own treatment. Other children had developed anxiety related to illness (e.g. feeling hot or other children being sick) or worried that normal illnesses would lead to the leukaemia coming back:

 *‘I think it’s just the whole thing of…that…big thing of being poorly again….you know she just..she just worried that…if I’m ill will it go to be being that again…’ (interview 2).*

Parents also experienced anxiety around clinic appointments and associated being at hospital with the distress they experienced during treatment:

*‘I absolutely hate going. Because as much as I can look at her, I know she’s got no bruises, rashes, and she’s perfectly healthy, ….in my head I’m still thinking, oh my god… and it kind of reminds you of them times when you’ve been sat there and not knowing what on earth is going to come back, so…’ (interview 10).*

Some children had struggled to adapt to the demands of normal life at the end of treatment. In some cases, these challenges were almost as difficult as the experience of leukaemia treatment. Going back to school was a particular stress in 6 families and children often felt anxious in unfamiliar situations where they felt they had no control. Therefore, parents did not want to burden their child with the additional stress of attending an unfamiliar intervention. Some parents suggested their child would have been more confident if they had known exactly what they would be expected to do in the intervention. Conversely, one family said their child would have been better if they had known nothing in advance and had just ‘dropped in’.

**8.5 Discussion**

This study aimed to explore barriers to participation in a psychoeducational intervention delivered to children treated for leukaemia, and potential ways to improve the acceptability and relevance of psychoeducation for families. This qualitative interview approach allowed an in-depth exploration of the parent’s perspectives in making these decisions.

**8.5.1. Mode of delivery of the intervention**

MRC guidelines for designing complex interventions (Craig et al., 2008) suggest that evaluations should consider the burdens which interventions place on families and how acceptable and feasible they are to implement. Like a number of other evaluation studies, scheduling and travel issues were barriers to participation in recruiting for this intervention (Butler et al., 2008; Patel et al., 2009). Families found it difficult to fit the workshops into their family, school and work schedules, especially as some families were a considerable distance away from the hospital (up to 100 miles for one family in this study). This was also an issue for families who did agree to participate in the intervention. The first block of the intervention was run during school hours, but many families declined because of this. Therefore, further blocks were run in the evening, at weekends and during school holidays according to the best times for the recruited families. Even with flexibility, this remained an issue throughout the study. The qualitative evaluation reported in Chapter 7 found that half of the participating families experienced scheduling or travel difficulties related to attending the workshops.

 Travel and time commitment should also be considered alongside existing burdens for families of children during treatment. These families are likely to be making journeys to the hospital on a regular basis and having to make adjustments to their normal activities and routines because of this. Two parents said that if the workshops had coincided with an existing appointment they would have been more likely to participate. There are issues with running interventions alongside treatments, including illness, side effects, mood issues from steroid treatment and scheduling around procedures. However, reducing the burden of travel and family disruption would be likely to improve recruitment. Another approach to reducing this burden might be to reduce the number of sessions or run the sessions as a one-day workshop.

It has also been suggested that electronic/computer interventions can reduce barriers to participation, reduce intervention burdens and improve the recruitment of widely dispersed populations (Kopp et al., 2017). As mentioned in Chapter 7, this could be especially important for children with AML as their condition is rarer and the burden of treatment is greater. The relative convenience of the multimedia format may be reflected in the use of computer game delivery for psychoeducational interventions for children with leukaemia and cancer, reported in Chapters 4 and 5 (Dragone et al., 2002; Kato et al., 2008; Jones et al., 2010).

However, multimedia delivery also has drawbacks. Compliance can often be low in these interventions (e.g. 28% in Kato et al., 2008) and it may restrict the tailoring of information to individuals. Social context might also be an important part of an intervention. The qualitative evaluation of the leukaemia intervention, reported in Chapter 7, suggested that both children and parents valued the group context and the opportunity to see children who had already been through treatment. Therefore, burdens need to be considered alongside the importance of potential active components.

It might be possible to compare different modes of delivery of the intervention, for example, by comparing a multimedia format, to the group context evaluated in Chapter 7. Comparing modes of delivery has been attempted by Dragone et al. (2002) and Jones et al. (2010) who compared a computer game to a book format. Both studies suggested that the computer game condition increased the child’s internal locus of control but not knowledge. This might suggest that both conditions pass on information, but the computer game condition gave the child a greater sense of control over their illness. Other computer technologies (such as video-conferencing software) might also make it possible to incorporate an interactive social component, rather than relying on a more passive game format.

It is also important to recognise that some of the children were anxious about social interaction and might be more likely to participate in an intervention without this aspect. Some children who did not want to take part in the intervention asked their parents questions about their illness. It might be possible to provide a facility for the child to ask questions without attending a group. This may be important for survivors who have less opportunity to communicate with healthcare professionals. Asking families about their preferred mode of delivery for a psychoeducational intervention might be a useful way forward.

 Some families also chose not to participate because their child was anxious about what would happen in the intervention. Children worried about unfamiliar situations or thought they would have to talk about their experiences in front of other people. Some parents thought their child would have been more likely to attend if they had had a better idea of what would be expected of them during the workshops. This suggests that clearer explanations of workshop content and delivery may have been necessary to reassure some children. Two families also suggested that taster sessions might be useful for the child to see what was going to happen and allay fears before the intervention started.

All of the recruitment was done through parents. It might have been more effective to direct some communication to the child (with the parent’s consent), allowing them to ask questions and feel involved with the recruitment process. This would also have been a good fit with the aim of the intervention to improve the child’s communication and feelings of empowerment in relation to their illness. Children have reported wanting to receive information and be involved in decisions about their care (Coyne et al., 2014; Spinetta et al., 2003).

 Both parents and children expressed some anxiety in relation to illness and hospitals. Therefore, the hospital setting may have influenced some family’s decisions not to take part, especially as recalling bad memories was a concern for a number of families. It is possible that a different setting, away from the hospital, might have been more acceptable for some families.

**8.5.2. Timing and relevance of the intervention**

Timing and relevance were important considerations for families. The content of the intervention was seen as more relevant to children who were receiving treatment. As described in Chapter 6, the intervention explained the pathophysiology of leukaemia, the role of chemotherapy in treating leukaemia and causing side effects and the importance of being healthy. Some families of survivors did not see any reason to revisit treatment issues now that the child had completed treatment. This suggests that targeting the intervention to children on-treatment would be more appropriate. During active treatment, children are in a routine of hospital visits and will be able to relate what they learn in the intervention to their immediate treatment, side effects and physical symptoms. This is also likely to be a time when anxiety related to procedures and illness uncertainty will be greater. Therefore, parents are more likely to see the relevance of the intervention at this stage of treatment.

Targeting children on-treatment might also reduce the problem of non-contactable families. These families represented 63.5% (n=268) of eligible families identified by participating hospitals (n=422). In many cases this was because of the time elapsed since the child’s treatment and changes in contact details. Families of children receiving treatment would have up-to-date contact details and would be more accustomed to contact from hospitals.

Evaluating this intervention in a larger sample of children on-treatment might have improved the recruitment rate, although this would involve additional challenges in terms of recruitment through the reduced potential sample pool. It might also be appropriate to consider children on-treatment and survivors as different targets for psychoeducation, requiring tailored approaches to contact and intervention delivery.

Psychoeducational interventions are often targeted to groups of cancer survivors to improve social skills and positive health behaviours (e.g. Barrera et al., 2018; Tyc et al., 2003). Therefore, considering ways of improving recruitment of survivors is also important. Tailoring the intervention to be more relevant to survivors would be likely to improve their uptake. Leukaemia had been such a major part of families lives that they were keen to move on once treatment had ended. Priorities shifted towards a return to family and school activities and an emphasis on normality for the child. Therefore, interventions offered to survivors would need to acknowledge this, and perhaps address how they could support families in this transition. Many families talked about the enduring effects of leukaemia; physical late effects, problems with peers, communication problems, school reintegration issues. A psychoeducational intervention more tailored to these issues might have seemed more relevant to families of survivors.

Highlighting the positive outcomes of being informed and the importance of information in relation to future health behaviour, might have encouraged parents of survivors to recognise this as an important need for their child. Health behaviour interventions have reported higher consent rates than psychosocial interventions, possibly because their relevance to the child’s wellbeing is clearer (Brier et al., 2015). The relevance of the intervention could also have been explained in relation to burdens which the families identified (e.g. addressing questions or misunderstandings, giving children the communication skills to talk to peers). It would be useful to involve families in expressing needs they would like an intervention to address. This could be used to tailor the content of an intervention and to target advertising materials to highlight relevance and maximise participation.

Additional methods of contacting families may be required to recruit long-term survivors into research studies. Possible methods might include online family support groups and advertising via social media (Burton-Chase et al., 2017).

**8.5.3. Psychological barriers to participation**

Psychological issues, such as anxiety, have been associated with lower recruitment rates in interventions (DeWit et al., 2008; Graue et al., 2005). The importance of improving participation in groups of children with greater psychological problems has also been highlighted (Kazak et al., 2007). Anxiety was one of the main reasons for non-participation in this study. Some children refused to talk about their illness, parents wanted to avoid causing their child distress by exposing them to potentially upsetting information and some children had developed phobias and generalised anxiety.

In presenting interventions to families of children with leukaemia, it is important to recognise that anxiety around illness and treatment is likely. Families may need reassurance about how any difficult issues might be addressed. For some families, reassurance that the intervention would not revisit medical procedures or that the child would not be expected to talk about their experiences of treatment, may have been sufficient.

Some families talked about wanting the intervention to reassure their anxious child. This might represent a difficult balance for interventions which address the child’s future health risks, as a recognition of health vulnerabilities is necessary to motivate positive health behaviours. One method might be to emphasise the role of positive action in improving health. However, it would be useful to involve parents in addressing any worries they might have about the content of the intervention beforehand.

Many children also wanted to appear ‘normal’ in front of peers and did not tell their friends they had been ill. This active avoidance of leukaemia means these survivors would be very unlikely to participate in an illness-related intervention. This pressure to be ‘normal’ has been described in other chronic conditions such as diabetes and has been associated with poorer self-management and psychosocial outcomes (MacLeod & Austin, 2003; Lambert & Keogh, 2015). This is most problematic in adolescence and means adolescents often have lower adherence to treatment and lower enrolment in interventions and clinical trials (Buchanan et al., 2014). Various methods have been employed to try to overcome this barrier in interventions, including using peer leaders (Al-Sheyab et al., 2012) or the internet (Mulvaney et al., 2010) to deliver the intervention. Intervening before adolescence may also be important.

**8.6 Limitations of the study**

The main limitation of this study is the small sample size, which reduces how far these findings can generalise to other families. The parents who agreed to be interviewed might also not be representative of other families who declined participation in the intervention but did not want to talk about their reasons. It is possible that there are other reasons for non-participation in the population that were not recorded here. The representativeness of the sample is also reduced as 63.5% of the eligible families in the intervention study were not contactable. It is possible the reasons for non-participation in the non-contactable group would have been different from the families who were interviewed in this study.

However, this study did recruit a reasonable percentage (45%) of those who were contacted and declined participation in the final blocks of the intervention. Also, the families who were interviewed repeated many of the reasons which non-participating families had informally mentioned during previous blocks of intervention recruitment. Although not collected formally as data, families often said that practical issues (e.g. scheduling and travel), child anxiety about what would be expected of them, not wanting to bring up bad memories, wanting to move on from the leukaemia experience, and lack of relevance because the child did not remember their treatment were reasons why they did not want to participate. This suggests that they had similar concerns to the families interviewed in this study.

**8.7 Summary**

This chapter has explored barriers to participation in a sample of non-participating families from the leukaemia intervention (as reported in Chapter 7). Improving recruitment of children with rare conditions, such as leukaemia, into intervention studies is an important way of improving the evidence base. This chapter has suggested practical ways of improving recruitment, such as delivering alongside clinical care and tailoring interventions according to relevance and the child’s stage of treatment. It has also highlighted psychological barriers to participation (e.g. anxiety, avoidance, illness stigma) which need to be considered, especially in relation to recruiting at-risk groups.

 This evaluation suggests that the leukaemia intervention was more suited to children during active treatment, mainly because of relevance but also because other psychological barriers in survivorship made children less likely to participate. It might also be appropriate to tailor an intervention for survivors which might include different intervention content, a different mode of delivery and different methods of contacting families. Issues around tailoring the intervention to different groups will be explored further in the general discussion of the thesis in the next chapter.

**Chapter 9**

**General Discussion**

This thesis aimed to explore the role of psychoeducation in improving the QoL of children with leukaemia. It used quantitative and qualitative methodologies to analyse the existing evidence base for psychoeducation, evaluate the effectiveness of a novel intervention and explore barriers to participation in the intervention, from a family perspective. As described in the introduction, this thesis addressed the following questions:

1. What is the evidence regarding the effectiveness of psychoeducation for children with leukaemia and is there evidence that some approaches are more effective than others?
2. Is the specific psychoeducational intervention described and evaluated in this thesis effective in improving the QoL of children with leukaemia?
3. What are the barriers to participation associated with recruitment to this psychoeducational intervention and how could these barriers be overcome in future interventions?

The mixed methods approach used in this thesis allowed complementary data on the effectiveness and acceptability of the leukaemia intervention to be collected. Systematic review and meta-analytic methodologies allowed the efficacy of interventions in the literature to be identified and evaluated in a synthesised approach. A rigorous quantitative methodology was used to evaluate the efficacy of the leukaemia intervention (reported in Chapter 7). The perspectives of families who participated and who chose not to participate (Chapter 8) were also elicited. The MRC guidelines for developing and evaluating complex interventions highlights the importance of exploring the perspectives of those who are expected to use these interventions (Craig et al., 2008). Only then can efforts be made to improve the relevance, acceptability and feasibility of interventions.

**9.1** **Summary of findings**

 Chapter 5 reported a meta-analysis of psychoeducational interventions delivered to children with chronic conditions. This followed a narrative review of psychoeducational interventions for children with cancer which showed a large but inconsistent literature. The meta-analysis aimed to calculate the effect of psychoeducation on adjustment (QoL) for children with leukaemia using methodologically sound studies (RCTs). However, no leukaemia interventions were available in the literature, with a QoL outcome and evaluated in an RCT. The meta-analysis reported a significant improvement in QoL for children with chronic conditions. It also reported a significant difference for the effect of psychoeducation between children with asthma and diabetes. This reduced the generalisability of the findings for children with leukaemia and suggested that psychoeducation might have different effects for different chronic conditions. The study also reported a larger effect for psychoeducation in younger children.

 Chapter 7 reported the quantitative and qualitative evaluation of a novel psychoeducational intervention delivered to children with leukaemia. The recruited group had significantly impaired QoL at baseline which improved by more than twice the MCID for the scale over the course of the study. The intervention led to significant improvements in parent-reported child QoL but not for the other measures. This study reported substantial difficulties in recruiting an adequate sample of children with leukaemia and therefore may have been underpowered to detect intervention effects. The qualitative evaluation was positive. Parents and children reported high levels of satisfaction with the intervention and improvements in child knowledge and communication.

 Chapter 8 reported an interview study which addressed the issues arising from recruitment and attrition reported for the leukaemia intervention. Twelve parents of children who did not participate in the intervention were interviewed. Parents reported travel and scheduling issues, lack of relevance and priority, and anxiety as reasons for non-participation. These barriers are largely compatible with previous studies of non-participation and may provide suggestions for developing and implementing novel interventions.

**9.2 Evidence for the effectiveness of psychoeducation for children with leukaemia**

There are two approaches to examining the potential of psychoeducation to improve outcomes for children with leukaemia (Craig et al., 2008; Kazak et al., 2010). One is to examine previous interventions delivered to children with leukaemia (or other potentially similar conditions). The other is to use theory to identify the modifiable burdens and processes of change which could be targeted in interventions. The first four chapters of this thesis attempted to examine this from both perspectives.

A strong method for identifying the potential effect of a psychoeducational intervention on children with leukaemia would be to examine existing interventions and derive generalisable conclusions. However, the reviews in Chapters 4 and 5 identified few psychoeducational interventions for children with leukaemia in the literature. The lack of interventions which specifically address methods of informing children with leukaemia about their illness is surprising, given the emphasis on open communication which was described in Chapter 2. However, it concurs with Ranmal et al. (2008), who concluded that there was insufficient evidence to identify the best methods of communicating with children about cancer. Therefore, this leaves a gap in the literature regarding this important process.

 There are a number of possible explanations for the lack of leukaemia interventions in the literature. One is its relative rarity. Although 500 children are diagnosed in the UK every year, these children are distributed around centres all over the country. Therefore, getting enough children to take part in interventions may be difficult. Families and doctors might also be more focused on the child’s treatment rather than the psychosocial aspects in the early stages. Researchers have identified difficulties recruiting children with rare conditions and high treatment burdens such as leukaemia (Annett & Erikson, 2009; Olechnowicz et al., 2002).

Another possibility is that the process of informing children has not been considered a target for interventions. Doctors give families information at diagnosis, including the printed materials described in Chapter 2, and families choose how the illness is explained to the child. This might be a more likely explanation as there were also few interventions for cancer more generally which concentrated on informing children about their illness.

Psychoeducational interventions delivered to children with leukaemia have tended to address specific health or treatment-related behaviours (e.g. nutrition, exercise, procedural distress), rather than providing information about the illness itself. This might also reflect doctors’ and families’ priority of treating the illness at this point. There is some limited evidence that information-based interventions can reduce distress around procedures (Haeberli et al., 2008) but little evidence for the effectiveness of health behaviour interventions during treatment (Bruggers et al., 2018; Li et al., 2017).

There was evidence in the qualitative evaluation of the workshops (Chapter 7) and the interview study (Chapter 8) that some children had not completely understood their illness. Some children wondered how they had caught it or thought it would come back if they were ill. Some children asked why medicine made them feel poorly rather than better. This showed that, at least for these children, there were some fundamental misunderstandings which arose because they were comparing leukaemia to more common childhood illnesses. Many of the families (34/44) whose child took part in the intervention said that the workshops had filled in gaps in their child’s knowledge (reported in Chapter 7) while parents in the interview study (Chapter 8) thought their child had unanswered questions which would come out at some point. Some of the parents in the interview study (Chapter 8) suggested that if their child had had better explanations during treatment, they might not have gone on to develop anxiety as a survivor. This suggests that for some children, opportunities for psychoeducation during treatment, might have improved their outcomes. However, some older children who took part in the intervention said that they had already known about leukaemia (Chapter 7), so this might depend on the age children were treated and the amount that they were told by their parents at the time.

The lack of interventions specifically for children with leukaemia makes it difficult to assess the effectiveness of psychoeducation directly. Examining psychoeducational interventions delivered to children with cancer (described in Chapter 4), showed that the literature is inconsistent. Reviews have compared different types of interventions with a large amount of heterogeneity. These reviews have often concluded that there is evidence for an effect (e.g. for information interventions for procedural distress and health promotion interventions) but the lack of methodological rigour of the included studies reduces the quality of this evidence. Reviews have also been unable to identify the most effective methods of delivering interventions (e.g. Cohen et al., 2016; Ranmal et al., 2008).

The reviews in Chapters 4 and 5 highlighted the need to test promising interventions in well-designed RCTs (e.g. Richter et al., 2015; Seitz et al., 2009). Interventions are often piloted but do not go on to be tested in a larger trial. This meant that no interventions for leukaemia and only one for cancer could be included in the meta-analysis in Chapter 5. There might be a number of reasons for this. It is relatively inexpensive to carry out pilot studies with a small number of participants, while RCTs require a larger sample and a control group design. For rare conditions such as leukaemia this makes it much more difficult to run an adequate trial. As discussed in Chapters 7 and 8, control groups add additional burdens to trials. The design of the intervention in Chapter 7 meant that the delay group had to make a commitment to attend 3 months in advance, which led to some families dropping out of the study before the intervention began. Families have also reported finding randomisation difficult to understand and burdensome (Kazak et al., 2005a).

Pilot studies tend to find that interventions are effective while evidence from RCTs can indicate weaker effects. This was demonstrated in the studies reviewed in Chapter 4. Pilot studies that do not include a control group may overestimate intervention efficacy by mistaking natural improvements over time for the influence of the intervention. Therefore, reviews may be examining evidence which is misleading. This demonstrates the importance of the RCT design and of improving recruitment into these studies. This inconsistent literature means that it is difficult to evaluate the effectiveness of psychoeducation just using the paediatric cancer literature.

An alternative approach might be to examine how psychoeducational interventions are delivered in other conditions to examine whether there are generalisable conclusions which could be applied to leukaemia. As described in Chapters 3 and 5, the risk-resistance model (Wallander & Varni, 1998) was constructed using outcomes from a range of chronic conditions, specifically as a non-illness-specific model for intervening. This could be an important approach for rare conditions such as leukaemia. However, the meta-analysis (Chapter 5) suggested that there was a significant difference between the effect of psychoeducation for children with asthma and diabetes which reduced confidence in the generalisability of findings across conditions.

This suggests that a generic approach to categorising the burdens of illness and intervening with children with chronic diseases might not be appropriate. Although all children with chronic illnesses might have burdens related to disease, functional impairments and psychosocial stress this might not specify or quantify the distinct burdens associated with different conditions or the most effective methods of intervening. Some of the risk and resiliency factors associated with adjusting to chronic illnesses may be universal (e.g. social support, family cohesion, secondary coping skills) (Compas et al., 2012; Kazak et al., 1997; Van Schoors et al., 2017) while others might be specific to conditions (e.g. perceived threat appraisals associated with medical procedures, illness specific self-management skills). Therefore, with inconsistent evidence from reviews and a lack of leukaemia interventions to include in meta-analysis, it is important to design and implement novel interventions and evaluate their efficacy.

**9.3 Evidence for effective approaches in psychoeducation**

 Like previous reviews (e.g. Barlow & Ellard, 2004; Ranmal et al., 2008) the meta-analysis in Chapter 5 was not able to identify the most effective methods of delivering psychoeducational interventions, in terms of setting, family inclusion or grouping (individual or group). However, it did suggest that psychoeducation might be more effective when delivered to younger children.

The interview study (Chapter 8) suggested methods of delivery which might be more appropriate and less burdensome for families. These burdens agreed with previous literature on non-participation, highlighting time commitments and potential burdens of the intervention (e.g. hospital appointments, repeated measures outcomes) (Brier et al., 2015; Kazak et al., 2005a) as barriers to participation. The interview study also highlighted the importance of relevance and priority. This agrees with previous reviews which have suggested that psychoeducation is most effective when it is carefully timed to the needs of families at different stages of treatment (Bradlyn et al., 2003; Kazak et al., 2005).

This suggests that intervention design should aim to reduce the potential burden on participants. For example, this might involve delivering an intervention using an electronic format or delivering a group intervention alongside existing clinic appointments. Although a multimedia format might reduce intervention burdens it is also important to examine the benefit of a group context. Social support and open communication have been identified as resiliency factors in the risk-resistance framework and have been associated with better outcomes for children with cancer (Myers et al., 2014; Van Schoors et al., 2017). Parents and children both rated the group context as a positive aspect of the intervention (reported in Chapter 7). Children enjoyed socialising with other children at different stages of treatment and parents enjoyed meeting other families. However, these were children who chose to take part in a group intervention and there may also have been children who were put off by the social context (Chapter 8). Therefore, it is important to seek the views of participants on appropriate methods of delivery and possibly offer and evaluate more than one. This might also highlight difficulties with other approaches (such as low compliance in multimedia interventions, e.g. Kato et al., 2008). It might also be possible to improve communication skills and the ability to seek social support without necessitating delivery using a group context.

**9.4 Evidence for the effectiveness of the leukaemia intervention reported in this thesis**

There was some evidence of effectiveness for the intervention reported in Chapter 7. It led to an improvement on one of the two primary outcome measures (parent-reported generic child QoL). However, the results were inconclusive for the other QoL outcomes. The results of the MLM analysis suggested that a random effects model was the best fit for the data for parent-reported cancer-specific QoL and child reported generic QoL. This suggests that the intervention had a different effect on different children. One explanation for these differences might be the inclusion of survivors and children on-treatment in the sample and suggests that evaluating the intervention with one of these groups would be more appropriate. Another explanation might be that psychoeducation is not universally effective for all children. The potential for adverse effects will be discussed further below.

The lack of effect of the intervention on the other outcomes might reflect the small sample size. Chapter 7 also reported that the delay group’s scores often increased just before receiving the intervention. It was suggested that this could arise from natural improvements over time or might reflect improvements arising from QoL monitoring and enhancing communication in families. The problems of not including a control group have been discussed, but potential control group effects also need to be taken into account when evaluating interventions (Ayling et al., 2015).

The results from the evaluation of the intervention in Chapter 7 are consistent with the effect size reported in the meta-analysis in Chapter 5. The meta-analysis calculated an effect size for psychoeducation using illness-specific child-reported measures of QoL, calculated using post-intervention mean differences. The child-reported scale was used because interventions primarily reported these scales and only occasionally reported a parent-reported version. All but 5 studies in the meta-analysis used an illness-specific measure which is why these were used to calculate the pooled effect. There was no evidence of a significant difference between illness-specific and generic QoL measures in the meta-analysis.

The scale which would have been entered in the meta-analysis from the leukaemia intervention (Chapter 7) was the child-reported PedsQl (cancer module). In the meta-analysis the overall effect size was 0.14, and in the leukaemia intervention, using this outcome, the effect size would be 0.16 (see Table 7.7). However, the effect size would have been larger if calculated using the generic QoL scale in the leukaemia intervention (shown in Table 7.7) than using this illness-specific scale (PedsQl: cancer module). Using parent-reported generic QoL to calculate a post-intervention mean difference, would have given a medium effect size (SMD=0.54) (Cohen, 1988). There would also be a medium effect using the child-reported generic scale (SMD=0.52) (see Table 7.7). The use of the generic scale in the leukaemia intervention reflected the inclusion of survivors in the sample.

Acceptability and attendance were high for those who took part in the intervention evaluated in this thesis. Parents and children reported that the child enjoyed the intervention, gained knowledge about leukaemia and were more able to communicate about their illness following the intervention. However, this may not be surprising. These families had made a considerable time commitment to attend the intervention and were likely to be a highly motivated group.

It is important that studies consider the whole process of intervention design and implementation to evaluate their effectiveness (Craig et al., 2018). Therefore, the intervention was not feasible in its present form as it was not able to recruit an adequate sample size even with multiple attempts and methods. Improving recruitment would be the most important way to improve the evaluation of the leukaemia intervention reported in this thesis. It would also improve the evidence base more generally.

**9.5 Improving psychoeducational provision for children with leukaemia**

 It is important to consider how this intervention could be improved using the evidence in this thesis, both to increase its effectiveness and to improve its recruitment rates. These findings may then be tested for generalisability to psychoeducational interventions for other chronic conditions.

**9.5.1. The impact of age on psychoeducational intervention effectiveness**

 It has been suggested in a number of areas of this thesis that age may play an important role in the effectiveness of psychoeducation. A hypothesis tested in the meta-analysis in Chapter 5 was that psychoeducation would lead to greater improvements in the adolescent group as these children have been reported to have poorer QoL. However, the interventions delivered to the younger group (up to 12 years old) had significantly larger effects than for the older children. While there could be an effect of condition (many of the asthma interventions were delivered to younger children), it is also possible that age explained the relatively better performance of the asthma interventions. Chapter 2 suggested that younger children with leukaemia might be told less about their illness than older children. Young children were given simplistic explanations about their illness and had less opportunities to control communication in encounters with healthcare professionals (Clarke et al., 2005; Young et al., 2011). It is possible that this is also the case in other chronic conditions.

Adolescents might have other psychosocial pressures which reduce the impact of psychoeducational interventions and require additional components to improve their adjustment to illness. This is supported by evidence showing poorer coping in adolescents with cancer than younger children (Earle & Eiser, 2001) and lower adherence to treatment in cancer and a range of other chronic conditions (Lohan et al., 2015; Bhatia et al., 2012). Adolescents may need different interventions which reflect their need for more complex information and coping skills to deal with psychosocial stresses associated with this period of development (Charalampopoulos et al., 2017). The interview study in Chapter 8 also suggested that stigma around illness had an impact on older children. Some of the children did not want to attend the intervention or did not tell friends about their illness, as they did not want to feel different. This pressure to be the same as peers during adolescence has been identified as a problem for self-management in other conditions (MacLeod et al., 2003; Wallander et al., 1989). In leukaemia it is likely to be particularly burdensome for children who have changes to their physical appearance as a result of their treatment.

The qualitative evaluation of the leukaemia intervention in Chapter 7 and the interview study in Chapter 8 also suggested that the leukaemia intervention was seen differently by children of different ages. Some of the older children said that the information was too simplistic. The format of activities and games may not have been age-appropriate for 12-year olds. One parent in the interview study (Chapter 8) said their child thought the workshops sounded ‘babyish’ and did not want to do an intervention with 7-year olds.

The impact of psychoeducation at different ages is important for children with leukaemia for a number of reasons. Active treatment takes up to 3 years and children carry on being monitored and treated for late effects many years after that. This means that the opportunities to deliver psychoeducation can occur at many different developmental stages. If psychoeducation is more effective before adolescence it is important that interventions start before this time if possible. It is also important that informational content be age-appropriate at each stage. The age range included in the leukaemia intervention may have been too wide to allow tailoring to different levels of understanding. While the older children found some parts simplistic, some concepts such as cell structure and DNA may have been too abstract for the younger group to understand. In the qualitative evaluation of the intervention (Chapter 7) cells and DNA were most commonly described as difficult to understand. Interventions targeted to smaller age ranges could cover similar information but at more age-appropriate levels.

It might also be possible to adapt some information for a younger age group. As described in Chapter 1, the peak incidence for leukaemia is in the under 5’s. Anxiety around procedures is particularly distressing for parents and children in this younger group and is related to a lack of understanding of procedures (Dupuis et al., 2016). Research also suggests that children treated at a young age are told less about their future health vulnerabilities once their treatment ends (Vetsch et al., 2017). Therefore, the needs of very young children to be informed about their illness also needs to be taken into account.

**9.5.2. Tailoring the content and timing of psychoeducation**

 The findings from the meta-analysis (Chapter 5) and interview study (Chapter 8) suggest that interventions should be more tailored to the child’s needs, to increase relevance to families and to address differential burdens at different stages of treatment. Chapter 3 highlighted some adaptations which could be made to the risk-resistance model (shown in Figure 3.1) in light of evidence from children with leukaemia. These adaptations reflected burdens which were specific to children with leukaemia, such as the considerable treatment burdens (Adams et al., 2016; Baggott et al., 2011) and cognitive impairments related to chemotherapy treatment (Plas et al., 2016; Campbell et al., 2007).

The need for a more specific framework for intervening was suggested by the differential effect of psychoeducation in the meta-analysis (Chapter 5). The finding of a zero effect of psychoeducation for children with diabetes suggests that these interventions did not reduce risk factors or improve resistance factors, possibly because diabetes is a more complex condition to control than asthma. This suggests a focus on different targets is required to improve outcomes for children with diabetes, possibly targeting coping skills or psychosocial stresses associated with peer issues.

Specifying the most relevant burdens for particular conditions might be taken a step further to specify important targets at different stages of leukaemia treatment. As described in Chapter 3, at diagnosis and during early treatment, the greatest burdens were associated with treatment (chemotherapy and steroid treatment (Adams et al., 2016; Baggott et al., 2011) and illness uncertainty regarding the child’s diagnosis (Neville, 1998). For survivors, much of the effect of disease-related burdens were mediated through present health complaints (Maurice-Stam et al., 2009; Schultz et al., 2014). Unmet information needs also focused on late effects and ways of maximising health (McCarthy et al., 2018; Vetsch et al., 2017). This suggests that information about the illness and its treatment is likely to be most effective for children in early treatment, while information focused on health is likely to be important for survivors.

The changing burdens and priorities of families were also highlighted in the interview study in Chapter 8. Families experienced the illness itself as the greatest burden initially, but this was replaced by other stresses once treatment ended (e.g. school reintegration, peer issues, late effects) which were reflected in the families’ desire to ‘move on’ from their experience of leukaemia. Zheng et al. (2018) identified increased social anxiety towards the end of leukaemia treatment which might reflect stresses associated with transitioning into survivorship. These changing priorities and the fact that information about the illness itself was no longer seen as relevant for survivors meant that some families chose not to participate in the intervention.

A focus on survivors would mean tailoring the information to their needs. This would include a larger role for the health promotion component described in the leukaemia intervention (described in Chapter 6). This component was taught as part of the final workshop and encouraged children to make healthy choices in light of their increased vulnerability to future health problems. The narrative review of health behaviour interventions in Chapter 4 suggested that interventions may be more effective when targeted to specific health behaviours and to children’s needs. Interventions are also likely to need considerable follow-up to help children to incorporate health intentions into health behaviours. The health component of the leukaemia intervention described in Chapter 6 was very short and was not specific to targets. Therefore, it is not likely to have made an impact on the child’s long-term health behaviours. An intervention for survivors would need to provide more of a focus on health behaviours. As described in Chapter 8, this would also provide relevance to the intervention for survivors and might help to improve recruitment rates.

 Interventions could also be tailored to the needs of children on different treatment regimens or with different types of leukaemia. Children on high-risk treatment regimens, those who require a Stem Cell Transplant or those who have relapsed may require different information and support to a child who is on a low-risk regimen and suffering relatively few side effects. Children with AML may also have different needs to a child with ALL. As described in Chapter 1, AML requires more intensive treatment which is associated with worse side and late effects and has a less positive prognosis. Children with AML are hospitalised for longer and are likely to be more socially isolated in the early stages of treatment. Due to the rarity of the condition and the greater burden of the illness (2 out of 3 children with AML relapsed during the workshop programme), the leukaemia intervention was only delivered to one child with AML. Therefore, it is impossible to say whether this psychoeducational intervention was effective for children with AML. Chapter 7 discussed the need to explore other methods of delivering interventions for children with AML. Group interventions may be very difficult to run as AML is much rarer than ALL and the treatment burdens are greater. Group interventions would also be impossible for children having a Stem Cell Transplant as they would be severely immunocompromised.

As well as tailoring to different groups, it is important to address relevance in the recruitment process. Many of the benefits mentioned by families in the qualitative evaluation of the workshops (Chapter 7) matched the concerns of families in the interview study (Chapter 8). This suggests that the issues used to balance burdens and benefits were similar in both groups. For example, some families who participated in the intervention study (Chapter 7) said their child talked more about their illness after the intervention (sometimes for the first time) and were able to communicate their needs better. Conversely, some families in the interview study (Chapter 8) worried that their child did not communicate about their illness or express their worries. Families in both groups also talked about their child’s misunderstandings of how they got leukaemia (i.e. whether they had done something to get leukaemia or whether they could catch it again). Highlighting these potential benefits might have helped to increase the perceived relevance and priority of the intervention for some families.

**9.5.3 Additional components**

 The meta-analysis in Chapter 5 argued that additional coping skills components may be needed to target the non-controllable aspects of an illness (Charamlampopoulos et al., 2017; Compas et al., 2012). In leukaemia uncontrollable aspects might include the effects of steroids, coping with changes in physical appearance, feeling different from peers and fear of relapse. It has been argued that the effects of psychoeducational interventions might not be comparable across conditions. However, it might be possible to look at how specific burdens have been addressed in different conditions. For example, stigma was highlighted as an issue in the interview study (Chapter 8) and has been identified as a burden for children with other chronic conditions (e.g. MacLeod et al., 2003). Research on reducing stigma for children with other chronic conditions may also be relevant to children with leukaemia.

**9.6 Addressing potential adverse effects**

 The focus of this thesis has been on providing psychoeducation to improve the adjustment of children with leukaemia. However, the potential of information to lead to adverse effects also needs to be considered. Some aspects of communicating about leukaemia could lead to anxiety; such as addressing fear of relapse or talking about the child’s perceived vulnerability to late effects. In the interview study (Chapter 8), some parents talked about wanting the leukaemia intervention to reassure their child, which may be difficult in a context where definite answers cannot be given. Parents also talked about not wanting to share information with their child which might be upsetting.

The outcomes in Chapter 7 suggested that the intervention did not increase anxiety in the recruited children. Treatment-related anxiety decreased over all the groups during the study, although this was not directly associated with receiving the intervention. Children in the qualitative evaluation said that the intervention had made them feel less worried about their illness. However, this might be because children who were more likely to be anxious were less likely to be recruited into the study. There were also a small number of potential adverse effects reported, including the possibility that information would make children worry more (Chapter 7), or the hospital setting might bring back memories of treatment (Chapters 7 and 8). The random effects model which was the best fit for 2 of the QoL outcomes (parent-reported child QoL: cancer and child-reported QoL: generic) also suggests that some children could have been adversely affected by the intervention.

 The potential of the questionnaires to cause anxiety was also highlighted by a number of families. Items in the cancer-specific QoL scale asked if the child worried their medical treatment was not working or if they worried they might relapse. One family stopped their child doing the questionnaires as they worried it was upsetting them. Other families said the questionnaires made their child worry about what was going to happen in the intervention. It is possible that this anxiety led to some of the attrition between baseline and receiving the intervention in the delay group.

 Anxiety is likely to be experienced by all families of children with leukaemia. Diagnosis is associated with shock, psychological impairment and illness uncertainty (Neville et al., 1998) which affects how parents communicate with their child. Parents often want to protect their child from distressing information (Clarke et al., 2005; Young et al., 2003). Fear of relapse can impact families for decades after treatment (Zebrack, 2000). The impact of anxiety was demonstrated in the interview study (Chapter 8) which identified anxiety as an important reason for non-participation in the intervention. This demonstrates the potential difficulty of recruiting children with anxiety into interventions and might be an argument for intervening early with children with leukaemia to reduce distress before it becomes a long-term problem.

On the other hand, there may be a subgroup of children with leukaemia for whom a psychoeducational intervention would always be more likely to lead to anxiety. Levels of avoidant coping have been reported at higher levels in children with cancer (Compas et al., 2012). Controlling the information which parents sought and shared with their child was also a coping strategy for all of the families in the interview study (Chapter 8). Interview studies with children with cancer and survivors also report subgroups who wanted to know as little as possible about their illness (36% in Last and Van Veldhuizen, 1996, 21% in Slavin et al., 1982). Some children prefer information to be buffered by their parents and use avoidance as a coping strategy (Coyne et al., 2016; Zwaanswijk et al., 2011).

Avoidant coping should not necessarily be seen as maladaptive during leukaemia treatment. Distraction and ‘blocking out’ treatment are avoidant coping methods which are sometimes used in procedural distress interventions. However, avoidance has been associated with poorer health and psychosocial outcomes in survivors of childhood cancer (Compas et al., 2012) and children with preferences for avoidant coping are more likely to have psychological impairment (Slavin et al., 1982).

While it might be necessary to intervene with children most at-risk of negative psychosocial outcomes and anxiety, it is unlikely that a psychoeducational intervention based on information about leukaemia will be the most effective method. Kazak et al. (2007) identified information as a universal need for families of children with cancer, supplemented by targeted interventions for families with identified clinical needs. This might be an appropriate approach here and suggests an important role for screening families. At-risk families may be identifiable in the early stages of treatment as early distress often predicts later distress (Myers et al., 2014; Zheng et al., 2018) and distress is often reciprocal in families (Kupst et al., 1995; Trask et al., 2003). Dispositional effects of personality traits such as negative effect and neuroticism have also been linked to anxiety, depression and PTS (Sharp et al., 2015; Miller et al., 2009).

**9.7 Conclusions and suggestions for future research**

This thesis suggests that there is a need to examine ways to improve the communication of illness-related information for children with leukaemia. Unmet information needs can lead to illness uncertainty and distress during treatment and to anxiety and poorer health outcomes in survivors. There are few interventions which have attempted to improve this process for children with leukaemia and results from other chronic conditions may not be directly comparable to interventions for leukaemia. The novel intervention described and evaluated in this thesis showed potential to improve the QoL of children with leukaemia but there were some methodological issues which affected the results and conclusions. Most importantly, the recruitment was lower than expected meaning that the study was likely to have been underpowered. Children with anxiety were also likely to have been underrepresented in the sample as they would have been least likely to participate. The interview study suggested a number of barriers to participation which might be used to improve recruitment into future interventions. This includes tailoring to the needs of families at different stages of treatment, reducing the burdens of the intervention and considering the potential negative impacts on the child.

Future interventions could modify this intervention for separate delivery to children on-treatment and to survivors. Different modes of delivery might also be evaluated and the preferences of families for these methods should be explored. Interventions should be age-appropriate and consider the use of additional components which might allow the child to cope with the less controllable aspects of their illness. More effective methods of recruiting families will also be required which effectively communicate the relevance of interventions for families.