Trude Reinfjell

Children with acute lymphoblastic leukaemia: A study of health-related quality of life, mental health and intellectual aspects

Thesis for the degree philosophiae doctor

Trondheim, September 2007

Norwegian University of Science and Technology
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To my children

Camilla, Kai, Victoria and Anna

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ABBREVIATIONS

ALL	Acute Lymphoblastic Leukaemia
CBCL	Child Behavior Checklist
CNS	Central Nervous System
CRT	Cranial Radiation Therapy
CT	Chemotherapy
GHQ	General Health Questionnaire
HRQOL	Health-related quality of life
ICC	Intra Class Correlation
NOPHO	Nordic Society of Paediatric Haematology Oncology
PEDSQL	Pediatric Quality of Life Inventory
PACS	Parental Account of Children's Symptoms
QOL	Quality of life
SDQ	Strength and Difficulties Questionnaire
YSR	Youth Self-Report
WHO	World Health Organization

THE PAPERS ON WHICH THIS THESIS IS BASED

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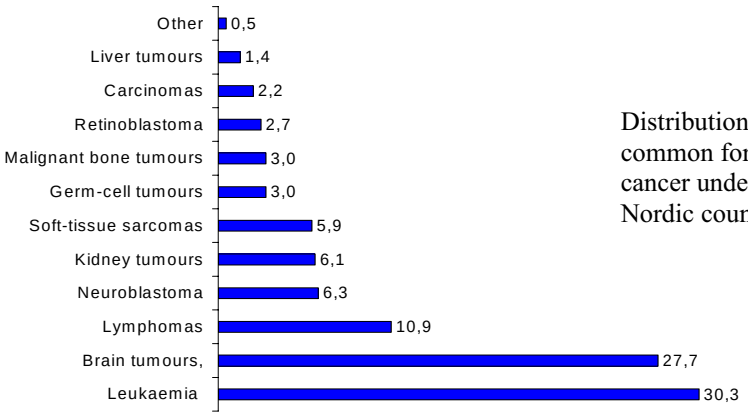
1. INTRODUCTION AND BACKGROUND

1.1 General introduction

Each year in Norway, about 130 children and adolescents under the age of 15 are diagnosed with cancer (incidence 15,3/100.000), and 40 children die annually of cancer [1]. Each year, approximately 40 children and adolescents in this age group are diagnosed with Acute Lymphatic Leukaemia (ALL) (incidence 3,9/100.000) [2]. ALL constitutes nearly 1/3 of all the cases of childhood cancer, and brain tumours about 1/4. Different solid tumours form the rest, as shown in figure 1.

Fig.1



Distribution (%) of the most common forms of childhood cancer under the age of 15 in the Nordic countries, 1985 – 1994.

These are types of cancer that strike children and adolescents at an age when they are very vulnerable, both physically and psychologically. ALL is most typically diagnosed in preschool-age children, with a striking incidence peak at age 2-7 years [3], which is a period of life with rapid brain maturation and development.

New treatments involving a combination of chemotherapy and radiotherapy have resulted in significant improvements in the rate of survival, from about 20 % in 1960 to approximately 80 % in terms of the average 5-years survival in recent years [2, 4]. Thus, about 1 of every 1.000 adults who reaches the age of 20 in developed Western countries will be a long-time survivor of childhood cancer [5]. In developed countries, advances in medical treatment are a result of coordinated and targeted research by specialized groups, e.g., the Children's Oncology Group (in the U.S.), the Cancer Study Group (in the U.K.), and the Société

Internationale d'Oncologie Pédiatrique (SIOP), as well as of centralized treatment in hospitals specializing in paediatric oncology [5]. These efforts have resulted in considerable similarities between treatment protocols and survival rates in different countries. In the Nordic countries, a Nordic Paediatric Haematology and Oncology group (NOPHO) has been established, which ensures that children from the Nordic countries are all treated according to the same protocol [2].

1.1.1 Clinical background

For a ten-year period from 1993-2002 I was employed as a clinical psychologist consultant in the Norwegian Cancer Organization and connected to the Department of Paediatrics at St. Olavs University Hospital in Trondheim. Through this work I became acquainted with many children who had cancer, and with their families, and got to follow them during the different phases of their treatment. I also had the opportunity to observe their efforts to readapt to a normal life with friends, at kindergarten or school, and was able to follow the progress of parents as they returned to work and struggled to establish a normal life again (not least for the siblings), after long periods when their energy was drained by the cancer. ALL is certainly a long-lasting process that poses tremendous challenge to both child and family. It was amazing to see how they were able to cope and find strength to continue their life.

During my clinical work I felt an increasing need to understand more about the impact of cancer such as ALL and its treatment on individuals who live for years after their initial diagnosis. The children often underwent regular and extremely painful procedures during the active treatment phase. The treatment can be aggressive, lengthy and very painful, and they often experienced multiple hospitalizations, physical side-effects and many restrictions in their everyday activities as a result of this. I often wondered what impact such periods of extreme stress might have on a child and on her/his parents and siblings. I also had the opportunity to follow some children after they finished their treatment. It was my experience that some of the children and their families had a hard time finding their way back to a "normal" life, and that they often suffered in silence. Their needs did not seem to be met after their treatment ended. It was these experiences that gave me the motivation to plan a follow-up study about children with ALL, which matured and became a reality the day I got a four year scholarship from the Department of Psychology at the Norwegian University of Science and Technology (NTNU).

1.1.2 Acute Lymphoblastic Leukaemia (ALL)

ALL is the most common form of childhood cancer, and comprises about 85% of leukaemia cases, 10-15% are Acute Myelogen Leukaemia (AML). ALL is a malignant disorder of the lymphoid cells found in the bone marrow: it is a fast-growing cancer of the white blood cells, where malignant white blood cells migrate via the circulatory system to virtually the entire organ system, including the CNS. In cases involving ALL, the bone marrow produces many unformed cells called “blasts” which would normally develop into lymphocytes. However, these blasts are abnormal, do not develop further, and cannot fight infections. The number of abnormal or leukaemia cells grows quickly. They crowd out the healthy red blood cells, white blood cells and platelets that the body needs [6].

The typical symptoms of ALL are: 1) Anaemia, 2) a reduced amount of white blood cells, 3) fever, 4) loss of energy/fatigue, 5) frequent infections, 6) easy bleeding or bruising, and 7) diffuse pain, especially in the bones. Furthermore, during ALL the abnormal cells may collect in the brain or spinal cord (CNS). This may result headaches, sometimes accompanied by vomiting, although most children with the disease do not have these symptoms. Leukaemia cells can also collect in the testicles and cause swelling. The diagnosis is given after an assessment of blood tests and bone marrow aspiration [6, 7].

1.1.3 ALL treatment, physical and psychological side effects

Intensifying the treatment for ALL has improved the overall prognosis [8]. ALL treatment protocols normally involve different combinations of chemotherapy (CT) and, in some very rare cases, cranial irradiation therapy (CRT). The intensity depends on the severity of the ALL. Prophylactic treatment which focused on treating the CNS in order to prevent CNS relapse was central in raising the survival rate. However, its agents are known to have a transiting neurotoxic effect, which is thought to play a central part in the occurrence of persistent brain sequelae [9-14] and neuropsychological function deficits [15, 16]. As documentation on the connection between CRT and cognitive and neuropsychological late effects grew, doses of CRT were reduced from 2400Cgy to 1800Cgy and their usage was restricted to high intensive protocols only. Today, direct CNS treatment is prescribed for older children only, and with a clear CNS-affection. With limits placed on the use of CRT, there was an increased use of CT directed toward CNS. How effective therapy might be depends on

several factors, including what combination of therapeutic agents is used to treat the disease, the intensity of the treatment protocol, and the risk of relapse [17].

The treatment groups for the NOPHO-ALL-1992 protocol are: 1) Standard risk (SR), 2) Intermediate risk (IR), 3) High risk (HR), 4) High risk-1 (HR-1), 5) High risk-2 (HR-2), and 6) Very high risk-1 (VHR). In general, risk group assignment is assessed mainly on the child's age and leukocyte count. The contemporary protocols are more individualized, involving the careful assignment of children to leukemic risk groups. For instance, children who undergo more intensive therapies are classified as HR. For SR patients, most protocols treat the CNS without CRT, achieving comparable efficacy with intrathecal and systemic drug combinations. HR patients, however, may require CRT to provide the CNS with adequate protection against relapse or even to protect against the risk of haematological relapse [6].

The length of treatment for ALL can vary from 2 to 2,5 years [17], and is mostly divided into three or four phases: 1) remission induction (with the induction phase taking up the first 7 weeks of treatment); 2) CNS preventative-/prophylactic therapy; 3) consolidation, and 4) maintenance. The first remission induction phase entails an initial, highly intensive period of treatment, where the disease is brought into remission during a period of intensive drug therapy that typically lasts about 7 weeks. The purpose of the remission induction phase is to rapidly eradicate leukaemia cells from the bone marrow and circulatory system. This phase is then followed by an intensification of the treatment. This prophylactic or preventative phase of therapy can last from weeks to months and is necessary to prevent CNS relapse, because the CNS is known to serve as a sanctuary for occult leukaemia. This treatment may involve CRT in combination with a drug delivered directly into the spinal canal (so-called intrathecal therapy), or, in many institutions, drug therapy on its own. Consolidation may be used to intensify therapy following remission induction. This phase of the treatment continues for several months and is then followed by maintenance therapy which usually lasts for about 2 years. This involves drug therapies only, often with periods of intrathecal therapy. Maintenance therapy is required for prolonged periods (often many months) afterwards because of the possible presence of undetectable and potentially fatal amounts of leukaemia cells [6, 17].

Treatment for ALL involves high levels of acute distress, generally caused by anxiety and pain associated with some of the medical procedures – such as bone marrow aspirations,

lumbar and venous punctions, and injections with chemotherapeutic agents, as well as bouts of nausea and vomiting resulting from chemotherapy and from continued anxiety associated with the treatment [6, 18, 19].

Children undergoing treatment for ALL experience a number of bodily changes. Some side effects, such as weight loss or gain, loss of hair, and mouth ulcers, may be reversible, while others, such as sterility, and organic brain damage, may be permanent. Visible changes to the physical appearance of a child are a constant reminder that she or he is different from other children. The side effects which accompany the treatment continually affect the child's self-image, and concerns about a potential loss of self-esteem brought about by these alterations in body image have been the focus of previous research [18, 20, 21].

Changes to a child's physical appearance can bring about a loss of self-confidence which in turn can lead to regressive behaviour, a withdrawal from her or his peers, and a fear of attending school, all of which can affect the phase of emotional and social adjustment and the level of academic performance. The life-threatening nature of the disease is the most striking aspect of cancer. Studies have shown that the child is fully aware of how serious the disease is, and this awareness is associated with increased anxiety [22-24]. It has been shown that a child's age is a less important factor in how aware he or she is of the potential for a shortened life-span than is her or his experience with the disease and its treatment. Levels of anxiety in a child with cancer seem to increase the longer the disease progresses and the more visits there are to the clinic [22, 25]. For parents, the child's treatment involves emotional as well as practical burdens in addition to the threat of loss. Previous studies have shown an increase in anxiety and depression, feelings of guilt, sleep disturbance, isolation and anxiety about the future, as well as increases in stress and in conflicts between the couples [26-28], in addition to rises in the levels of PTSD symptoms [29-33].

1.2 Late effects

The challenges associated with survivorship have attracted more and more attention as the number of cancer survivors goes up annually. Since these numbers should continue to rise, it becomes even more important to understand the unique needs of this population and to identify those who are most at risk of complications in their treatment, and who might benefit from interventions designed to alleviate or reduce that risk. Considering that they are exposed,

among other things, to treatment such as radiotherapy and chemotherapy, survivors will be vulnerable to a range of late effects [34, 35]. Medical and psychological late effects are defined as occurring after the successful completion of medical therapy, usually two or more years from the time of diagnosis [36].

1.2.1 Somatic complications

Late effects from the new treatment forms may give rise to somatic complications such as reduced fertility (particularly in boys), cardiomyopathy (especially in girls), reduced lung functioning, and osteoporosis. Further complications include reduced linear growth and endocrine disturbances brought about when cranial irradiation is included in therapy, in addition to second cancer (in 2-3 percent of all patients) [3]. A recent meta-analysis showed that children who were survivors of ALL appeared to experience clinically significant declines in neurocognitive functioning [37].

1.2.2 Health-related quality of life (HRQOL), mental health, psychosocial and cognitive outcomes

As the treatment for such cancer can be aggressive and associated with both acute and long-term morbidity [38], the focus in much of the research has changed, with the emphasis now being on the health-related quality of life [39], as well as psychosocial [40], cognitive and neuropsychological outcomes [41]. The study of the health-related quality of life (HRQOL) in children is a relatively new field of research [42]. Such studies can have considerable significance for understanding children's psychosocial functioning and development [43, 44]. The child's risk of mental and psychosocial problems is doubled or tripled in the presence of a chronic condition [45, 46]. Psychosocial outcomes in childhood cancer have been the subject of previous research, but do not generally provide consistent results with regards to psychosocial adjustment. Studies have shown that many survivors function reasonably well, with little difference found between results for survivors and those for their peers or siblings [31, 47, 48]. It is also reported that a considerable proportion of survivors had long-term coping [49, 50], while poorer coping in cancer patients was associated with longer treatment time [49]. Coping styles are more closely described in Paper 5. In addition, other studies have indicated increased risks of maladaptive psychosocial sequels, such as depression, anxiety, problems of self-esteem and fluctuations in mood [20, 51], moderate emotional difficulties (including depression), problems with interpersonal relationships, withdrawal and isolation,

the use of denial as a defence mechanism, strong dependency on parents [50, 52, 53], and symptoms of posttraumatic stress [29, 33]. Controversial findings with regards to childhood cancer and psychosocial adjustment [50, 51, 53] can be explained by methodological restrictions – such as heterogeneity in samples of patients with respect to time since diagnosis, differences in diagnosis, and differences in age at the time of diagnosis with concomitant differences in levels of development [40]. Other explanations can include differences in treatment protocols and intensitivity [54], as well as a lack of sensitivity in the tools of investigation - e.g. self-report instruments for children are still quite limited. In addition, a further problem has been the different criteria used when selecting control groups (norm data/matched control groups of children from a healthy population/ siblings/peers) [37, 55]. Earlier studies have also tended to focus on different domains when it comes to looking at psychological variables, which make it difficult to compare them. All of these aspects place limitations on how useful the findings are with regards to actual adjustment problems for children with cancer [56].

Studies on the cognitive outcomes of CNS prophylaxis yield contradictory results [54], though recent reports suggest that survivors treated with chemotherapy only, also suffered minor cognitive impairment [14, 57-60]. Furthermore, a recent meta-analysis showed that children who survived ALL appeared to experience clinically significant declines in neurocognitive functioning [37], both in global and specific areas of neurocognitive functioning. These effects were thought to have been caused by the treatments used to cure their disease. Interestingly, these declines are less clear when compared to normative data [37]. Hence, continued evaluation of levels of cognitive and learning functioning in children who have been treated for moderate-risk acute lymphocytic leukaemia is recommended [54, 61-62]. Last et al [5] focus on the fact that it is not yet known what happens to aging brains long after they have been exposed to cranial radiation therapy and/or chemotherapy during childhood.

Some previous studies suggest that the risk of CNS toxicity in SR patients can be considerably reduced by treating the CNS without radiation [63]. But the intensive drug therapy required and the neurotoxic potential of these agents raise questions about the extent to which cognition can be spared. For instance, the dexamethasone used in the induction treatment phase has been shown to lessen the risk for CNS relapse and to improve the overall event-free survival, but it has also been suspected of increasing the risk of neurocognitive

damage [3]. In some studies, comparable neuropsychological sequelae have been documented among children treated with and without CRT [64-66].

1.3 Developmental aspects

The implications of cancer vary with each child's cognitive, emotional and social course of development. How children understand the cancer they suffer from is greatly influenced by such developmental aspects as their ability to acquire knowledge, to understand and reflect upon their situation. Both the coping strategies of their families, and the attitudes professionals have to informing the child, will have a further impact on the children's adaptation [25]. In modern developmental psychology, the interactive process between children and their caregivers is considered critical for a child's development and adjustment [67, 68]. This important alliance between the child and caregiver can be disturbed when a child falls ill with cancer, because the parents can have anxieties and worries of their own, and this therefore become a crucial aspect of the child's further development and adjustment [69]. It should therefore be emphasized that caregivers have a separate need of follow-up care, in order to be able to provide good support to their children. How a child copes with her or his illness depends a great deal on the backup they receive from the whole family [70].

A paediatric health-related quality of life (HRQOL) instrument which includes a developmental perspective must therefore be sensitive both to cognitive and emotional changes throughout the age span. Daily functioning in contexts that are relevant for children, such as school and the local community should also be assessed [71]. The following questions are all affected by the child's development: what can I ask; how should I ask; can I ask the child her/himself? What are the important areas children of different ages need to function in? Developmental tasks will vary from age to age, starting with their getting together with peers at the age of 4 to5: the performance of school-related tasks then becomes central, followed by gaining a position among peers and developing romantic relationships during adolescence, with a transition towards autonomy taking place in late adolescence. These are all examples of universal developmental tasks. Having a chronic condition may have a considerable effect on the process and outcome of dealing with these tasks [72].

Developmental issues in HRQOL have not received sufficient attention despite the obvious fact that children and adolescents undergo continuous and quite rapid development [43, 72]. Measuring HRQOL is therefore a task that may need to be assessed in slightly

different ways for children at different ages or for the same child over a certain period of time. And this raises certain questions: can the same definition of HRQOL be used across child development, or should HRQOL address different contents according to the child's point of development? [74] The WHO has stressed that tools of measurement should be child centred, self-reported, age-dependent and cross-culturally comparable [75].

1.4 Assessment of HRQOL in children

The evaluation of HRQOL in adults is well established, and HRQOL measures are routinely included in many clinical trials. From a historical perspective, the measurement of children's HRQOL has received less attention. The question of children's HRQOL did not start to gain momentum until the 1980s [76]. Despite the growing interest in HRQOL outcomes, there are still only a few measures which attempt to assess HRQOL outcomes for children and adolescents [77]. Among the approximately 20.000 publications on HRQOL, around 15 % were related to children (N= 3050). HRQOL is meant to show how the patient functions in everyday life, using physical health as well as emotional, social and educational functioning as the yardsticks. Information about HRQOL in children with cancer might thus provide us with a more comprehensive means of evaluating the outcome of treatment than survival rates and relapse-free intervals alone.

In everyday language, the phrase Quality of life (QOL) can mean several things, and these meanings have the potential to complicate the scientific study of QOL. The term QOL can be synonymous with happiness, or material wealth. Definitions and ideals will be dependent on the specific social, cultural, spiritual and historical circumstances in which we find ourselves.

The term HRQOL is frequently used interchangeably with quality of life (QOL) [78]. However, QOL is considered as a broader and more general conceptual term related to non health-related aspects of life (e.g., the evaluation of the impact of architectural surroundings on general well-being) [79]: and as we have just seen, QOL is often synonymous with happiness or material wealth. The concept of HRQOL refers specifically to the impact that health and illnesses may have on the well-being of an individual, and on her or his ability to function in daily life, with respect to physical health, as well as emotional, social and school functioning, as these are delineated by the World Health Organization [80]. It is often distinguished from the more general and popular meanings of the term. This thesis is centred

on questions of HRQOL, but for the sake of simplicity the abbreviation QOL is also adopted sometimes.

Any instrument used to measure HRQOL must be multidimensional and consist of the physical, psychological (including emotional and cognitive), and social-health dimensions delineated by the World Health Organization (WHO) [80]. The literature shows that there is substantial support for the systematic assessment of HRQOL as an important means of measuring outcome in paediatric populations. Medical efforts to extend the length of children's lives should be augmented by efforts to improve the qualitative aspects of their lives as well. A recent review shows that although HRQOL research has become a major area of interest in paediatric outcome research, studies using HRQOL as an instrument of measurement remain limited [5]. To date, most studies have focused on broad adjustment issues such as depression and anxiety, educational attainment, and social functioning. Only recently have there been studies which focus on QOL [5]. There is a need for including QOL measures in paediatric settings and research trials, particularly given the fact that normal childhood development can be profoundly affected by the toxicities and untoward effects of aggressive medical treatments [81].

However, the lack of valid and reliable measures for children and adolescents does place certain limitations on current HRQOL research [82]. The presence of low concordance between proxy-and self-reports suggests a critical need in paediatric HRQOL measurement for reliable and valid child self-report instruments for the broadest possible age range [83]. Pediatric patient self-report should be considered the standard for measuring HRQOL, but there are times – when a child is too young, too cognitively impaired or fatigued to complete a HRQOL instrument, for example – that parent proxy-report instruments are also needed [84]. A previous review [77] showed that over 50% of studies used parents to report on their child's QOL, and 40% used clinical staff. Only 19% of the studies addressed age differences in QOL, and QOL was assessed more often for older children (13-18 years) than for those between 6 and 12 years.

HRQOL measures are categorized as either generic or disease-specific. Choosing between a generic or specific disease (or perhaps in some cases a combination of both), depends largely on the research question, the patient group in the study, the quality of the measure, or having the possibility to compare with a control group. Generic measures allow us to make comparisons between survivors and either control groups or the general

population. In a study of cancer patients who had been cured, a generic measure might sometimes be preferable to a cancer-specific one, because it provides the possibility of using the same instrument for a control group drawn from the general population. So choosing which tool of measurement is most appropriate has to be related to the overall purpose of the study.

1.4.1 HRQOL measures – methodological aspects

The lack of consensus regarding how to define QOL has previously been highlighted [85]. Koot and Wallander [73] note that QOL is a concept which is difficult to categorize and challenging to operate with. However, some researchers adopt stricter criteria, focusing on more comprehensive measures of QOL for which psychometric data are available. An important factor in selecting a HRQOL measure will be its psychometric adequacy as well as its ability to tap outcomes of primary interest to a particular investigation [81]. The importance of validating new translations should be emphasized, in order to investigate if the psychometric properties can be used further in both clinical practice and research. The two concepts required for a satisfactory measure are validity and reliability [43]. Validity is judged according to whether or not the questionnaire measures what it is supposed to measure, and is related to systematic measurement errors [86], while reliability is evaluated according to random errors and is related to the precision or consistency of the questionnaire (61).

Validity

Various ways of determining validity are discussed in detail elsewhere [86]. In this study we have used content, construct and discriminant validity**. Content validity**, which is related to face validity, is connected to the developmental process of a questionnaire and assesses the degree to which a test appears to measure what it claims to measure. It is meant to demonstrate how well procedures of comprehensive development were followed and documented. For the purposes of QOL assessments, validity usually asks “Does the measure accurately assess the theoretical construct of interest”, and this is thought to be a difficult question to answer, given the inconsistencies in QOL definitions and theoretical models [43, 87].

Construct validity assesses whether or not a test measures the construct it purports to measure – e.g. that a QOL scale succeeds in measuring QOL. It particularly evaluates how

consistently an instrument of measurement relates to the concepts (i.e. constructs) that are being measured. The process of establishing construct validity represents a key element in differentiating the science of behavioural measurement from other, non-scientific, approaches to the analysis of human behaviour [88]. This is a continuous process involving the theory behind the concepts and various psychometric testing. To demonstrate construct validity it is necessary to show not only that a measurement tool correlates highly with other variables with which it should correlate theoretically, but also that it does not correlate with variables from which it should differ. **Discriminant validity**, which involves comparisons with other known group, describes an instrument's ability to discriminate accurately between known groups of patients: the discriminative validity of a measure is investigated by determining whether or not scores on a test accurately distinguish between children and adolescents known to differ in terms of their health status [81].

Reliability

Reliability is a measure of random errors and is usually expressed by a number between 0 and 1, where 1 indicates perfect reliability and 0 indicates the complete absence of any reliability. Reliability tells us about the precision or consistency of the test.

The internal consistency of the questionnaire is related to the number of items within a scale and their covariation when measuring a specific dimension. Internal consistency refers to the extent to which the items of a domain or scale assess the same dimension, and is normally measured using Cronbach's alpha, which estimates the overall correlation between items included in a scale [89]. This is a statistical assessment of the correlation between items within a dimension, and it determines whether or not items within a scale correlate positively (that is to say, that they measure the same thing). The use of Cronbach's alpha as a predictor of reliability proceeds from the assumption that all items reflect the same single underlying concept. An internal consistency of .70 or higher is recommended for measures used to detect between-group differences in clinical trials or outcome research [90].

1.4.2 The PedsQL^{TM}4.0

The Pediatric Quality of Life Inventory (PedsQL) has been translated into many European and other international languages, and is widely used in research. PedsQL was translated into Norwegian during 2002/2003, at a time when no other HRQOL measurements for children were available in Norway [91].

The PedsQL[83] is considered one of the most promising HRQOL instruments for children and adolescents, integrating generic core scales and disease-specific modules into one system of measurement [92]. As a tool, it is particularly effective because it includes a broad age range with developmental sensitivity as well as categories for both parents and the young persons themselves. The PedsQL version 4.0 builds on programmatic instrument development research over the past 15 years, beginning with the measurement of pain and functional status [93]. The 4.0 version was designed to measure the core health dimensions delineated by WHO [80], including role (school) functioning [83], and was developed through focus groups and cognitive interviews [82]. The PedsQL 4.0 has been proposed as a valid and reliable generic paediatric HRQOL measurement that can be used for self-reports and proxy-reports in age groups ranging from 2 to 18 years [83], and can also be used in clinical practice, clinical trials, and other research, as well as in school health settings and community populations [73, 83]. The PedsQL has shown satisfactory psychometric properties [83, 91]. A Cronbach's alpha ≥ 0.77 was obtained for the Norwegian translation of the PedsQL for the age group 13-15, which indicates good internal consistency [91].

1.4.3 The translation process

The translation and linguistic validation of the PedsQL questionnaire followed recommended guidelines [94, 95]. Two independent forward translations were carried out by a psychiatrist and a clinical psychologist, and the translators discussed semantic and conceptual discrepancies before finally developing a consensus forward translation. The back translation, whereby the first version of the PedsQL questionnaire was translated from the target language into the source language, was performed independently by a skilled English speaker with considerable experience of living in countries where English was the native language.

In a following pilot-project, the questionnaire was administered to a total of 10 children, 12 adolescents and 23 parents in order to test how items were interpreted and understood, and response ratings: cognitive interview techniques [94] were used to obtain feedback about both. The questionnaires were then revised in response to feedback from children and parents. A written report was sent to Varni for further review. Relevant changes made during the translation process were checked and authorized by Varni.

1.5 The parental perspective

Good family functioning is one of the strongest contributors to adjustment both in children with chronic health problems [96] and healthy children. A cancer diagnosis poses a considerable threat to normal parent-child relationships [38]. Drotar 1997 [96] points out that in almost every reviewed study where there were non-significant findings related to family/parental functioning and child psychological outcomes, the amount of variance accounted for in children's psychological outcomes was quite low overall – his approximate estimate is by 10-15%. Research shows that high family cohesion and low family conflict consistently predict better adjustment in youths with chronic illness [96], as do adequate support from the family and wider network in combination with effective communication about the illness between parents and children [97, 98] Studies show that negative parental emotional responses, such as depression, are associated with poor adjustment both in children with cancer and children who are healthy [99].

The parent proxy-ratings are often qualitatively different from their children's own rating and even from each other. Most research suggests that mothers are more involved than fathers in handling the emotional and instrumental demands and responsibilities associated with caretaking [97]. Eiser (2005) points out that fathers often remain more involved in everyday life despite the child's illness. This aspect may influence the father's own situation and needs, since by staying at home or at work more during the time the child is being treated, the father will not be able to get adequate help for his own emotional needs, and this may affect his later adjustment. Even as research participants, fathers are less involved longitudinally than mothers [100]. Hanson [97] argues that more data is needed because fathers have not been the subject of many studies. But what is clear is that a chronic condition in the family has different effects: each family member will experience different changes that have an impact on their QOL, at the same time as the family climate as a whole will be altered [97]. Higher levels of anxiety, distress, and/or depression have been found in some parents with children who have chronic conditions: parental adjustment overall has been consistently correlated with levels of support and stress in the family generally [98].

2. AIMS OF THE STUDY

The general aim of the present study was to increase our knowledge about children in remission from ALL, with a particular focus on their HRQOL, mental health, psychosocial and intellectual functioning. This was undertaken in order to contribute to improving the

rehabilitation and follow-up phase for children in remission from ALL, and to help prevent psychosocial problems for children, and their families, after they have been treated for cancer.

Since no HRQOL measures were available at that time in Norway, an important first task was to translate the PedsQL^{TM} 4.0 into Norwegian, and to start investigating the psychometric properties of the newly translated instruments of measurement to ensure that they could be used further in the main study of children in remission from ALL.

The following specific aims evolved:

1. To describe HRQOL in children and adolescents in remission from ALL by assessing both the PedsQL child self-report and parent proxy-report compared to healthy controls, and further to assess intellectual functioning in children in remission from ALL compared to healthy children (Paper I).

2. To explore aspects of mental health and psychosocial adjustment for children in remission from ALL and their parents compared to healthy controls (Paper II).

3. To evaluate the reliability and validity of the Norwegian translation of the PedsQL ^{TM} (version 4.0 generic core scale) in a sample of healthy young adolescents (Paper III).

4. To examine the value of the PedsQL as a tool with which to assess depressive symptoms in a sample of young adolescents – controlling at the same time for recognized risk factors such as adverse and stressful life events as well as social anxiety. (Paper IV)

5. To describe and discuss the theoretical and clinical aspects of the children's adjustment to, and understanding of, their cancer experience. (Paper V).

3. METHODOLOGY

3.1 Study design

The present study is based on a cross-sectional design. The information needed to register treatment related factors was gathered retrospectively from the medical records at the two participating University Hospitals – Rikshospitalet-Radiumhospitalet HF and St. Olavs. The data on HRQOL, mental health, psychosocial and intellectual functioning which was used to provide outcome variables, was gathered during the follow-up period.

3.2 Subjects

The follow-up study of 40 children in remission from ALL between the ages of 8 and 15 years, and their parents, was carried out from the autumn of 2003 to the autumn of 2004, and data from their control group was collated between the autumn of 2005 and the spring of 2006. A validation study of 224 healthy young adolescents and parents was performed in 2003 to corroborate the quality of the translated PedsQL questionnaire used in the follow-up study of children with ALL.

3.2.1 Patient inclusion/exclusion criteria and control group

Children with ALL

Children and adolescents in remission from ALL were recruited from two University Hospitals in Norway: Rikshospitalet-Radiumhospitalet Medical Centre in Oslo and St. Olavs University Hospital in Trondheim. The children were born between 1989 and 1995, had a mean age of 11.8 (range 8.5-15.4), took part 4.2-12.5 years after their ALL diagnosis, and were treated according to the Nordic protocol, The Nordic Society of Paediatric Haematology/Oncology (NOPHO-ALL, 1992): their parents were also invited to participate in the study. Children who suffered relapses, or who had other kinds of severe medical condition (e.g. Down's syndrome) were excluded. Of the 56 children who fulfilled the criteria for participation, a total of 40 (71.4%), comprising 21 girls (52.5%) and 19 boys (47.5%), took part. Parental information was supplied by 36 mothers, whose mean age was 40.0 (range 30-55), and 21 fathers, whose mean age was 43.0 (range 32-58): each parent was asked to give their evaluation of the PedsQL proxy-report separately. Data regarding diagnoses and treatment protocols were collected from the medical records. The average age at the time ALL was diagnosed was 4.0 years (range 0-7.6). The average time since diagnosis was 7.9 years (range 4.2-12.5). The treatment categories were scored according to the Nordic protocol

(NOPHO-ALL, 1992) with the following categories: 1) Standard risk (SR); 2) Intermediate risk (IR); 3) High risk (HR); 4) High risk-1 (HR-1); 5) High risk-2 (HR-2); and 6) Very high risk-1 (VHR). With regards to the small sample in the four last categories, we scored these as one category – high/very high risk. One child had been treated with chemotherapy combined with radiation therapy (1800Cgy), and the remaining children with chemotherapy only. The analyses were also performed without the irradiated case. One child was in the infant-risk group, and treated according to the NOPHO-92 protocol HR-1. Sociodemographic characteristics and treatment-related variables are presented in Table 1 (page 18).

Control group

The children treated for ALL were compared to a group of healthy children with a similar age and gender distribution (n=42) (79,3%) (Table 1), recruited from two elementary schools and two junior high schools in the middle part of Norway, and from both urban and rural areas. Children with a psychiatric diagnosis or with other specific and relevant medical problems such as cognitive dysfunction were excluded. Informed consent was obtained from all of the children and adolescents, as well as from their parents. The study was approved by the Regional Ethics Committee of Medical Research. Characteristics for the control group are shown in Table 1 (page 18).

Table 1. *Sociodemographic characteristics of children with ALL and healthy controls. Treatment variables for children with ALL.*

	ALL (n = 40)	Healthy (n = 42)	t score	P
Gender				
Girl: n (%)	21 (52.5)	21 (50.0)	-.11	.91
Boy: n (%)	19 (47.5)	21 (50.0)		
Age at study				
Mean (SD)	11.8 (1.9)	11.8 (1.9)	.14	.92
Median	11.4	11.6		
Range	8.5-15.4	8.11-15.0		
Family Composition				
Both parents	31 (77.5)	29 (69.0)	-.75	.46
Single mothers	8 (20.0)	12 (28.6)		
Single fathers	1 (2.5)	1 (2.4)		
Parental Characteristics				
Age, median (range)				
Mother	40.0 (30-55)	40.0 (31-52)	-.25	.81
Father	43.0 (32-58)	43.5 (34-72)	-.09	.93
Education, median(range)				
Mother	14.0 (10-19)	13.0 (9-19)	.07	.95
Father	14.0 (10-20)	13.0 (10-19)	.84	.40
Community			.69	.49
Urban	15 (37.5)	18 (42.9)		
Rural	25 (62.5)	24 (57.1)		
Home			.72	.48
Own house	36 (90.0)	39 (92.9)		
Own apartment	3 (7.5)	3 (7.1)		
Renting apartment	1 (2.5)	-		
Economy			-.04	.96
Very satisfying	27 (67.5)	21 (50.0)		
Good	8 (20.0)	21 (50.0)		
Poor	5 (12.5)	-		
Diagnosis and treatment				
Age at diagnosis				
Mean (SD)	4.0 (1.9)	-		
Median	3.1	-		
Range	0-7.6	-		
Years since diagnosis				
Mean (SD)	7.9 (2.0)	-		
Median	7.1	-		
Range	4.2-12.5	-		
Treatment protocols				
Standard risk	15 (37.5)	-		
Intermediary risk	15 (37.5)	-		
High/very high risk	10 (25.0)	-		

3.2.2 Validation study

The validation study included young adolescents (n=425) and their caregivers (n=237), recruited from six junior high schools in Norway –three from urban, and three from rural, areas. A total of 440 questionnaires were distributed of which 425 were returned, which gives a response rate of 96.6%. Self-report forms were completed by 425 adolescents, comprising 235 girls (56%) and 184 boys (44%): six did not report gender. In junior high schools in Norway adolescents between the ages of 13 to 15 are divided into three different grades, and the participants were distributed as follows for the 8th, 9th and 10th grades: 33%, 33% and 34%, respectively. Proxy-reports were completed by 237 (56%) caregivers. The proxy-reports were completed by mothers in 139 (59% of the) cases; by both parents in 69 (29% of the) cases; by fathers in 27 (11% of the) cases; or by other caregivers such as grandparents in 2 (0.8% of the) cases. An adolescent self-report and a parent proxy-report on the PedsQL were available for 229 of the adolescents. Informed consent was obtained from all the children and adolescents, as well as from their parents.

3.2.3 Refusers and missing data

Children with ALL

The final sample included 71.4% of those eligible. In the 16 families that did not participate, there were more girls (n=13) than boys (n=3). Most of them stated they were too busy or distressed, that they were not willing to participate, or that they did not want to relive previous experiences of sickness and hospitalization. Practical reasons such as geographical distance were also a factor.

Validation study

A sample of 440 young adolescents and their parents were recruited from six junior high schools in Norway – three from urban, and three from rural, areas. A total of 440 questionnaires were distributed, of which 425 were returned. Thus, the final sample included 96.6% of these eligible.

Because of the anonymity required during such procedures, more information about non-respondents among the sample of adolescents as well as the sample of parents was not available.

3.2.4 Sample representativity

Norway is a small country, with a total of five University Hospitals. Two of them took part in this study – Rikshospitalet-Radiumhospitalet Medical Centre in Oslo and St.Olavs University Hospital in Trondheim. These two university hospitals diagnosed approximately 77 of 146 children with ALL in Norway during this time span (1989-1995). This is 52.7% of the total sample in Norway.

The validation study supports the idea that the present study is representative, given that the response rate was 96.59%, and given too that response rates were evenly distributed among 13, 14 and 15 year olds. The schools which took part are also representative for both urban and rural areas in Norway.

3.3 Procedures and methods

Procedures for the study of children treated for ALL and their control group

Leaders of the Paediatric departments of Rikshospitalet-Radiumshospitalet (RH) and St. Olavs hospital were contacted and gave us their permission to contact the patients whose names were taken from their patient pool. Written information about the project and consensus formulas for the parents and for the older children were sent to the parents of 56 survivors by ordinary mail, and they were contacted by phone for further information. After informed consent was received from the families, appointments were made by phone for the interview, which was often planned to coincide with their follow-up appointment at the hospital. All assessments of both the children and their parents were carried out at the hospital. The interview session was conducted by a clinical psychologist (the author). The parents of the children treated for ALL were interviewed separately. All children were individually assessed by different standardized instruments in a quiet room. Data regarding treatment protocols were collected from the patient's medical records.

With regards to the control group, the educational sections of two municipal districts were contacted in order to discuss the demographics of different schools and for permission to contact school principals in their county. When informed consent was given in writing by the sections, four school headmasters were contacted and their informed consent was given in turn. Two headmasters in the city of Trondheim were instructed to make a sample by drawing lots based on age and gender matches. Another group from the rural county of Nord-Trøndelag was matched along the lines of gender and the nearest age in month. Lots

were drawn when this became necessary, as when several children matched the age-group. Written information and consent formula were sent to the families by the different principals, and they also contacted the families by phone to inform them about the project. When informed consent was given by the parents and adolescents, the assessments with each child were carried out individually in a quiet room at the schools, using the same procedure as with the children in remission from ALL.

After the assessments each pupil received an envelope, which contained information and a questionnaire for their parents. Parents were asked to fill out the questionnaires separately before returning them in a pre-stamped envelope. When necessary, the participants were further able to contact the researcher by phone to obtain additional information.

The design and methods used in the study were chosen on the basis of clinical experiences and research traditions at the Division of Child and Adolescent Psychiatry, Rikshospitalet-Radiumhospitalet and the Department of Psychology, NTNU. The choice of methods was based on the following criteria:

1) internationally acknowledged methods
2) documented reliability and validity
3) appropriate to the age group concerned
4) closely related to the aims of the study and
5) assessed issues raised by the study with the aid of relevant clinical experience and literature on adolescents with chronic illnesses.

The study used a multi-modal design, combining the methods of (i) interviews with the parents and (ii) questionnaires with both child and parent informants. It was seen as preferable that the HRQOL and psychiatric assessments were performed by an investigator (in this case, the author) who had no prior knowledge of any of the particulars of the ALL treatment. This method eliminated the possibility that answers might have been formulated to please or otherwise to avoid the discomfort of sharing information with, an authority figure responsible for the previous treatment.

Procedures for children in the PedsQL validation study:
Local junior high schools were contacted and teachers distributed written consent forms that the adolescents gave to their parents. Each pupil received an envelope, which contained

information and a questionnaire for their parents. Parents were asked to return the completed questionnaire in a pre-stamped envelope. The participants could further contact the researchers to obtain additional information. Approval forms signed by the parents and returned to the teacher, confirmed that the adolescent had been given permission to participate.

The self-report instruments were administrated and completed in the classrooms.

Children were given verbal and written instructions before completing questionnaires in class, and this was done under the supervision of a research assistant.

3.4 Methods used for children, adolescents and parents:

A general overview of the methods used in this study is given below, and further details are provided in the papers.

3.4.1 Medical treatment protocols

Data on diagnoses and treatment protocols were collected from the medical records. The average age at the time of the ALL diagnosis was 3.4 years (range 0-7). The average time since diagnosis was 7 years (range 4-14). The treatment categories were scored according to the Nordic protocol (NOPHO-ALL, 1992) with the following treatment categories: 1) Standard risk (SR): 2) Intensive risk (IR); 3) High risk (HR); 4) High risk-1 (HR-1); 5) High risk-2 (HR-2); and 6) Very high risk-1 (VHR). With regards to the small sample in the four last categories, we scored these as one category – high/very high risk.

3.4.2 HRQOL

The Pediatric Quality of Life Inventory (PedsQL^{TM}4.0) [82] was used to measure HRQOL in children and adolescents. The 23-item PedsQL, version 4.0 Generic Core Scales, can be grouped into 4 domains of HRQOL: 1) Physical Functioning (8 items); 2) Emotional Functioning (5 items); 3) Social Functioning (5 items); and 4) School Functioning (5 items). The Generic Core Scales are comprised of a child self-report covering ages 5 to 7, 8 to 12 and 13 to 18 years. The parent proxy-report covers ages 2 to 4, 5 to 7, 8 to 12 and 13 to 18, and assesses how the parents perceive their child's HRQOL. The items for self-report and proxy-report are essentially identical, differing in the language that they use, which is developmentally appropriate, and in using the first or third-person pronoun.

The questions ask how much of a problem each item has been during the past 1 month: 0 = never a problem; 1= almost never a problem; 2 = sometimes a problem; 3 = often a problem; 4 = almost always a problem. Respondents are asked how many health problems they have experienced during the past month, and to rate these in terms of degree (e.g. I hurt or ache), activities (e.g. It's hard for me to run), or feelings (e.g. I feel afraid or scared).

Items are reverse-scored and linearly transformed to a 0 to 100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0), so that higher scores indicate a better HRQOL. Scale scores are computed as the sum of the items divided by the number of items answered (this accounts for missing data). In addition to the four subscales, a Total Summary Health score (23 items) can be computed. A Psychosocial Health Summary score (15 items) can be computed as the sum of the items divided by the number of items answered in the Emotional, Social, and School Functioning Subscales, and a Physical Health Summary score (8 items) is the same as the Physical Functioning subscale. The PedsQL^{TM}4.0 provided a very reliable Total Scale score with a Cronbach's alpha $\geq$ 0.89, and it has been shown to differentiate between healthy children and children with chronic health conditions [102]. A Norwegian version of the PedsQL 4.0, geared towards psychometric properties, is presented and described in greater detail in an earlier work [91]. The PedsQL has demonstrated satisfactory psychometric properties [83, 91]. A Cronbach's alpha $\geq$ 0.77 was obtained for the Norwegian translation of the PedsQL for the age group 13-15, which indicates good internal consistency [91].

3.4.3 Children's mental health and psychosocial functioning

Two kinds of outcome measure were used to assess mental health and psychosocial functioning. The reliability and validity of the measurements presented below have been documented to be accurate.

The mental health of the children was assessed using two outcome measures of behavioural and emotional problems based on standardized questionnaires. The Child Behavior Checklist (CBCL) [103] was completed by the parents, and the Youth Self-Report (YSR) [104] questionnaire was completed by children over 10 years old. The Norwegian version has 112 problem items, 90 of which are common to both the CBCL and the YSR. For both forms the questions are scored 0 (no), 1 (sometimes), and 2 (often). Eight syndrome scales are generated, five of which are subdivided into two subscales. The internalizing subscale covers issues such as withdrawal, somatic complaints, and anxiety/depression. The externalizing

subscale includes delinquent and aggressive behaviour. As population norms for these questionnaires have not yet been established in Norway, the present study can only offer raw scores. According to the American norm, corrected for gender and age, the 90th percentile (T-score>63) is used as a cut-off point for total, internalizing, and externalizing scores implying psychiatric problems.

An additional outcome measure was the Strength and Difficulties Questionnaire (SDQ), which is designed to assess the mental and psychosocial health of children and adolescents [105]. The SDQ is a brief behavioural screening questionnaire consisting of 25 items in addition to a supplement on what impact various difficulties might have on the child and family. There are 5 subscales: Emotional Symptoms, Conduct Problems, Hyperactivity, Peer Problems and Prosocial Behaviour: the first four add up to the Total Difficulties Score. Each item uses a 3-point ordinal Likert format and can be answered with: “not true”, “somewhat true” or “certainly true”, rated 0-2 for negatively worded items and rated inversely 2-0 for positively worded items. In this way, and for all items, higher scores indicated greater levels of difficulty. There are similar versions for parents. The SDQ demonstrates satisfactory rates of reliability and validity [105, 106].

3.4.4 Intellectual functioning

The Wechsler Intelligence Scale for Children, Third edition (WISC-III) [107] [108], was used to assess cognitive functioning in the children. The Full Scale IQ summarizes overall performance on the WISC-R, and provides a broad assessment of general intelligence and the ability to do well in school. For the purposes of the present study, we used the Full Scale Intelligence Quotient (FSIQ), the Verbal Intelligence Quotient (VIQ), the Performance Intelligence Quotient (PIQ), as well as the four indexes: the Verbal Comprehension Index (VCI); the Perceptual Organization Index (POI); the Freedom from Distractibility Index (FDI); and the Processing Speed Index (PSI).

3.4.5 Parental interview

Parents were interviewed separately by a child psychologist using a modified version of the standardized, semi structured, investigator-based Parental Account of Children’s Symptoms (PACS) [109]. The PACS includes questions that are relevant for a psychiatric assessment of the index children, and is also helpful in registering sociodemographic factors. The parental

interview also had supplementary questions directed at uncovering the parents experiences and concerns with regards to the child and to her or his siblings, as well as: developmental aspects from birth to early childhood previous to the diagnosis of ALL; the emotional and practical aspects of treatment procedures; the medical follow-up; the family climate; the availability of network and social support; and the parents own subjective experience with respect to the possibility of late effects after ALL treatment.

3.4.6 Parents QOL and mental health

The General Health Questionnaire (GHQ-30) [110] was included to assess parents' own QOL and mental health. The GHQ-30 is the most frequently used screening instrument for distress, psychopathology and quality of life in adults, showing acceptable reliability and validity in studies of medical and psychiatric populations. The GHQ includes both positive and negative questions and its shorter equivalent, the GHQ-30, contains 30 items covering symptoms that are thought to reflect distress and psychopathology. GHQ-30 avoids using physical symptoms as an indicator of distress.

4. STATISTICS

The statistical methods used in the present study are described in greater detail in the various papers. The study took parametric statistics as its starting point (Paper I and II).
To assess differences between two independent groups, the independent t-test was used.
In the methodological part of the study, internal consistencies (Cronbach's alpha) and factor analyses (Paper III) are recorded. Validity was further examined by exploring the intercorrelations between and among the four PedsQL Subscales [111]. In addition, we calculated intraclass correlation coefficients (ICC) to assess parent and child convergence on the PedsQL subscales. ICC takes into account not only the correlation but also differences in intercept and slope between replicant ratings [86]. Paired t-tests were used to assess the extent to which adolescents or their proxies scored systematically lower on the subscales of the PedsQL. In order to evaluate the minimally important difference in scores, we calculated the standardized response mean, a distribution-based approach that compares temporal change by the standard deviation of change [112]. Gender differences in the self-report scales were analyzed with a two-sample t-test. A multiple hierarchical linear regression analysis was conducted to investigate the relationship between depressive symptoms and the HRQOL

scores as measured by the PedsQL when the potential effects of gender, age, SLE and SPAI-C were statistically controlled for. Additional independent multiple hierarchical linear regression analysis was conducted for each of the PedsQL^{TM} summary scales as dependent variables (paper IV). Multicollinearity was tested with the measures of Tolerance and VIF.

The Statistical Package for Social Sciences (SPSS 12.0 and 14.0) statistics program for Windows was used for the analyses (SPSS Inc., Chicago, III, USA), and generally a critical value (α) of 5% or less were considered as statistically significant. In order to reduce the risk of making the Type 1 errors associated with multiple comparisons, a Bonferroni corrected alpha level of 0.004 was chosen (Paper I and IV). Adjustments for multiple comparisons are often performed by the correction of Bonferroni. However, Bonferroni adjustments may cause over-correction of type I errors and a disastrous impact upon type II errors [113]. Choosing a p-value of $p < .01$ as implying statistical significance is more cautious than the usual $p < .05$, and therefore reduces the chance of false positive results. It means that on average only 1 in 100 comparisons would observe such extreme differences purely by chance alone (Paper II).

5. ETHICAL ASPECTS OF THE STUDY

The study was approved by the Regional Ethics Committee for Medical Research, The Central Norway Regional Health Authority. The children and their parents received written information about the study by mail. Informed written consent was obtained from participating children at the age ≥12 and from their parents. Non-responses to the letter were followed up once by telephone. When we did not manage to reach a family, we sent a written reminder. When clinical problems were detected in children, the adolescents and their parents were involved in discussions about possible referrals for further treatment.

6. SUMMARY OF RESULTS

6.1 Synopsis of papers I-V

Paper I

HEALTH-RELATED QUALITY OF LIFE AND INTELLECTUAL FUNCTIONING IN CHILDREN IN REMISSION FROM ACUTE LYMPHOBLASTIC LEUKAEMIA.

In this cross-sectional study we evaluated health-related quality of life (HRQOL) and intellectual functioning of children in remission from Acute Lymphoblastic Leukaemia

(ALL). Children and adolescents treated for ALL (n = 40) (mean age 11.8 years, range 8.5-15.4) and healthy controls (n = 42) (mean age 11.8, range 8.11-15.0) were assessed through a cross-sectional approach using the Pediatric Quality of Life inventory (PedsQL^{TM}) 4.0 and the Wechsler Intelligent Scale for children-III (WISC-III).
Children and adolescents treated for ALL reported on average significantly lower HRQOL compared to healthy controls: the mothers proxy-report showed significantly lower HRQOL for their children, as did the fathers proxy-report, as measured by the PedsQL^{TM} 4.0 Total Scale and Psychosocial Health Scale. Intellectual functioning as measured by the WISC-III Full Scale IQ was below that of the control group, but still within the normal range.
We concluded that significant group differences found between children treated for ALL and their control group for the PedsQL Psychosocial Health Scale may indicate that the complex illness-treatment experience can make children more vulnerable with regards to psychosocial sequels, in spite of otherwise satisfactory physical and intellectual functioning. Follow-up programs which target the psychosocial health of children in remission from ALL should be implemented.

Paper II

CHILDREN IN REMISSION FROM ACUTE LYMPHOBLASTIC LEUKAEMIA: MENTAL HEALTH, PSYCHOSOCIAL ADJUSTMENT AND PARENTAL FUNCTIONING

By this stage, we assessed mental health, psychosocial adjustment and parental functioning in children in remission from Acute Lymphoblastic Leukaemia (ALL) compared to healthy controls. In this cross-sectional study 40 children treated for ALL (mean age 11.3 years, range 8.5-15.4), and 42 healthy controls (mean age 11.3, range 8.9-15.0) were assessed using the Youth Self-Report (YSR) and the Strength and Difficulties Questionnaire (SDQ).Their parents completed the Child Behavior Checklist (CBCL) and the SDQ parent-report. The mental health of the parents themselves were evaluated using the General Health Questionnaire (GHQ-30). Children treated for ALL showed on average significantly more symptoms as measured by the CBCL compared to healthy children. Fathers reported more anxiety and depression, as measured by the GHQ-30, compared to healthy controls.
We concluded that adequate rehabilitation and follow-up programs should be implemented for children and parents after treatment. Table 2 (page 28) summarizes the major findings in children in remission from ALL as well as in the control group of healthy children.

Table 2. *Comparison of PedsQL™ scale scores of the 40 children diagnosed with ALL, and the 42 healthy children as controls. Further, comparison of the YSR and the CBCL scale scores.*

	ALL (n =40)		Healthy (n =42)	
	Mean	SD	Mean	SD
PedsQL Child self-report				
Total score	81.70	(12.56)	88.98	(7.57)
Psychosocial health	79.27	(13.99)	87.22	(9.20)
Physical Functioning	86.25	(12.13)	92.26	(6.45)
Emotional Functioning	75.13	(18.69)	83.21	(12.68)
Social Functioning	86.00	(14.11)	92.50	(7.67)
School Functioning	76.63	(16.38)	85.95	(12.98)
PedsQL Mother Proxy-report	ALL (n=36)		Healthy (n=38)	
Total score	79.42	(12.50)	89.62	(10.26)
Psychosocial health	75.86	(14.22)	88.07	(11.28)
Physical Functioning	86.14	(13.69)	92.52	(10.47)
Emotional Functioning	70.28	(15.63)	85.00	(13.46)
Social Functioning	82.81	(15.54)	93.16	(9.89)
School Functioning	74.44	(19.88)	86.05	(14.57)
PedsQL Father Proxy-report	ALL (n=21)		Healthy (n=25)	
Total score	78.05	(12.50)	90.13	(12.24)
Psychosocial health	74.30	(13.95)	88.60	(12.47)
Physical Functioning	84.82	(12.86)	93.00	(12.70)
Emotional Functioning	71.43	(15.01)	86.40	(13.88)
Social Functioning	78.75	(18.98)	91.60	(11.88)
School Functioning	73.09	(16.47)	87.80	(15.82)
YSR raw scores (n=32) Controlgr. (n=30)				
Total behavior score	28.72	(17.74)	20.27	(15.46)
Internalising score	8.94	(6.99)	5.80	(5.46)
Externalising score	8.81	(5.26)	6.00	(5.75)
Clinical range (Total T>63), No.(%)	1	(3.1)	1	(3.3)
CBCL raw scores (mothers) (n=35) Controlgr. (n=38)				
Total behavior score	22.19	(20.31)	11.18	(11.78)
Internalising score	6.83	(6.71)	3.24	(3.13)
Externalising score	6.92	(8.41)	2.92	(4.46)
Clinical range (Total T>63), No.(%)	6	(17.1)	0	(0)
CBCL raw scores (fathers) (n=21) Controlgr. (n=26)				
Total behavior score	23.43	(17.73)	9.54	(13.66)
Internalising score	7.19	(6.49)	2.85	(4.01)
Externalising score	6.38	(5.70)	2.11	(4.77)
Clinical range (Total T>63), No.(%)	5	(23.8)	1	(3.8)

Note. Relevant significant differences between the groups are presented in the papers.

Paper III

MEASURING HEALTH RELATED QUALITY OF LIFE: RELIABILITY AND VALIDITY OF THE NORWEGIAN VERSION OF THE PEDIATRIC QUALITY OF LIFE INVENTORY (PEDSQL™ 4.0)

In this first validation study we evaluated the psychometric properties of the Norwegian translation of the Pediatric Quality of Life Inventory (PedsQL™) 4.0 generic core scale in a sample of healthy young adolescents. This cross-sectional study included 425 healthy young adolescents and 237 of their caregivers participating as a proxy group. Reliability was assessed using Cronbach's alpha. Construct validity was assessed using exploratory factor analysis and by exploring the intercorrelations between and among the four PedsQL subscales for adolescents and their parents. All the self-report scales and proxy-report scales showed satisfactory reliability with the Cronbach's alpha varying between 0.77 and 0.88. Factor analysis showed results that were comparable to the original version, with the exception of the Physical Health scale. On average, monotrait-multimethod correlations were higher than multitrait-multimethod correlations. Sex differences were noted on the emotional functioning subscale, with girls reporting lower HRQOL than boys. We concluded that the Norwegian PedsQL is a valid and reliable generic paediatric Health-Related Quality of Life measurement tool that can be recommended for self-reports and proxy-reports for children in age groups ranging between 13 and 15.

Paper IV

THE PEDIATRIC QUALITY OF LIFE INVENTORY (PedsQL™) 4.0 AS AN ASSESSMENT MEASURE FOR DEPRESSIVE SYMPTOMS: A CORRELATIONAL STUDY WITH YOUNG ADOLESCENTS

This correlation study explored the associations between depressive symptoms in young adolescents and the PedsQL scores when controlling for known risk factors.

An adolescent sample (N=425) filled in a range of different measures, including the PedsQL™ Norwegian version, the Short Mood and Feeling Questionnaire (SMFQ), the Social Phobia and Anxiety Inventory for Children (SPAI-C), and the Stressful Life Events checklist (SLE).

The results indicate a significant moderate correlation between the different measures – PedsQL, SMFQ, SPAI-C and SLE. The presence of depressive symptoms significantly

predicted the PedsQL scores for the adolescents, and explained 17 % of the variance in outcome for the PedsQL Total Scale.

The findings suggest that the PedsQL^{TM} is an adequate instrument of assessment with regards to depressive symptoms in young adolescents, and can be useful in both clinical practice and in further research into children's mental health.

Paper V

CHILDREN WITH CANCER: CHILDREN'S ADJUSTMENT TO AND UNDERSTANDING OF THEIR CANCER

In this article we considered both the clinical and theoretical aspects of how children adapt to life with a serious illness. The main focus was on the developmental changes, emotional and cognitive, undergone by the child during the different age spans. The strategies used by children to cope with their situation are discussed.

This article show that a child's understanding of her or his cancer illness depends a great deal on certain developmental aspects, such as their ability to gain knowledge, as well as to understand and reflect upon their situation. Both the coping strategies of the families and the attitudes professionals have towards informing the child will have a further impact on how well the child manages to adapt. Such knowledge has potential implications for how we inform children about their illness. The interactive process between the child and her or his caregiver is a critical part of this process, and it should be prioritized by health professionals. This paper is presented as a theoretical and clinical background for the thesis.

7. DISCUSSION

The present part of the discussion will look at some of the major findings in the research field, and at links between them, with particular reference to more recent literature: consideration will also be given to methodological limitations and to the implications of both the methodological study (paper III and IV) and the clinical study (paper I and II).

7.1 The methodological study

7.1.1 HRQOL in children and young adolescents as measured by the PedsQL^{TM}4.0

This first validation study of the PedsQL Norwegian version was a pilot study which was carried out with young adolescents, and was part of a larger study with a broader focus on quality of life and mental health in this age group. This study gave us an opportunity to begin the process of validating the PedsQL. We are aware how important it is to include different age groups; not least validation may be more challenging when it comes to younger children. However, when starting a validation process, it can be scientifically and economically useful to first investigate the psychometric properties of one's instruments in a smaller sample – like a pilot – before continuing with a larger sample.

The third article describes the **psychometric properties of the Norwegian translation of the PedsQL^{TM} 4.0** generic core scale in a healthy sample of young adolescents and their caregivers. The results from the present study resemble the findings of the original PedsQL^{TM} [83, 102] and the UK-English version [39] and as such confirm that the measure can be used for both self-reports and proxy-reports in school health settings and community populations. Table 3 (page 32) gives comparison of PedsQL^{TM} scale scores across different studies in large samples of schoolchildren.

Table 3. Comparison of PedsQL™ scale scores across different studies in large samples of schoolchildren

Publication	US version. Varni et al., 2006 [102] .		UK-English version Upton et al., 2005 [92]		Norwegian version Reinfjell et al., 2006 [91]	
Region	San Diego School District, USA		South Wales, Great Britain		3 urban and 2 rural areas in Norway	
Sample characteristics	2,435 children aged 8-18 years; 48% boys, 52% girls; 47% higher school education; 23% middle to high socioeconomic status		1,033 children aged 8-18 years; 51% boys, 49% girls		419 adolescents aged 13-15 years; 44% boys, 56% girls; 72% of parents had higher school education; 95% good to very good household income/assets	
	Mean	SD	Mean	SD	Mean	SD
PedsQL Child self-report						
Total score	80.6	(13.3)	83.9	(11.8)	85.3	(11.1)
Psychosocial health	78.2	(14.9)	81.8	(13.2)	82.2	(12.5)
Physical Functioning	85.2	(13.7)	88.5	(11.6)	91.1	(10.4)
Emotional Functioning	74.3	(18.7)	78.5	(17.9)	77.2	(17.3)
Social Functioning	82.9	(18.5)	87.7	(16.5)	88.1	(13.1)
School Functioning	77.3	(17.0)	78.9	(15.9)	78.0	(15.5)
PedsQL Parent- report						
Total score	76.9	(16.8)	84.6	(11.2)	86.1	(10.2)
Psychosocial health	76.1	(16.3)	82.2	(12.7)	84.7	(10.9)
Physical Functioning	78.5	(22.3)	89.1	(12.3)	88.8	(11.8)
Emotional Functioning	77.0	(17.5)	78.3	(15.5)	80.0	(14.1)
Social Functioning	78.7	(21.1)	86.8	(15.4)	88.1	(13.4)
School Functioning	72.5	(20.2)	81.5	(16.1)	89.0	(12.3)

It should be pointed that there will be fewer points of correspondence with the factor structure obtained in the original PedsQL^{TM} 4.0 publication because the age range in this present study is more restricted. Limitations on the age sample, and comparisons with a healthy population, may compensate for the apparent variability. The results of the factor analysis for items 5, 6 and 7 in the Physical Function scale, as well as items 4 and 5 in the School Function scale, may be typical for healthy samples, and the factor structure should therefore be reinvestigated in clinical samples.

The adolescent-parent agreement did not exceed the preferred intra-class correlation of 0.40, except in the case of the scale measuring School function. A lack of agreement between parents and children may result from differences in how the same situation is perceived, and also differences in how different items are interpreted [114]. As opposed to some previous research [115], our findings did not find higher levels of agreement between parents and adolescents with regards to physical problems. Parents rated the physical function scale lower than the reports of their children. Furthermore, a recent study found that proxy and self-report correlation was higher for children with health problems than for healthy children [39]. Parents and children may be more likely to share information about an issue if it is perceived as a problem [39]. However, the reliability of this agreement has also been challenged in research on children with Cystic Fibrosis [71]. Another explanation for the low concordance between adolescents and parents with respect to physical functioning can be seen in the factor analysis (table 4 and 5) in paper 3: there it emerged that items relating to physical functioning (item 5, 6, 7) were rather diffuse components associated with both physical and emotional domains, and were therefore difficult to distinguish between – something that could further influence both adolescents and parents ratings. Children reported lower HRQOL on the emotional scale compared with their parents, and this supports research carried out previously by Modi & Quittner [71]. There may be several explanations for this: young children may have difficulty expressing their emotions directly to their parents, for example: it is also probable that proxy-reports reflect parental anxiety about their child [39]. This factor should be investigated further using different patient populations, and it confirms the need to measure both child and parent perspectives when evaluating HRQOL. From a clinical perspective, those discrepancies potentially allow for more interventions which reflect the children's subjective ratings, as well as that of their parents [71, 114].

With regards to **gender differences**, we found that girls reported lower levels of emotional functioning than boys. This is consistent with previous research on gender differences in emotional health [116-118]. Differences in response that relate to differences in gender would seem to reflect a genuine disparity between boys and girls: they provide further evidence for the validity of PedsQL^{TM} as a sensitive measure of the emotional functioning of children and adolescents [39].

7.1.2 PedsQL as a measure for depressive symptoms

The results of this study clearly show that depressive symptoms and social anxiety symptoms predict self-reported HRQOL. These results suggest that the PedsQL may in the near future provide an interesting assessment measure for depressive symptoms in young adolescents. The main results indicated that individuals who reported higher levels of depressive symptoms exhibited significantly lower levels of HRQOL as measured by the PedsQL, even when controlling for gender, age, number of stressful life events, and levels of social anxiety symptoms. These results are the same for both the PedsQL Total Score and for all of the four PedsQL subscales. The inherently high correlation between the SMFQ and the PedsQL Total Scale could nevertheless be problematic, since it might possibly indicate that both the SMFQ and PedsQL measure the same phenomena. On the other hand it seems positive that the percentage is not higher than it is, for it suggests that the measures do in fact cover different areas. When looking at the different PedsQL subscales, it is clear that the Emotional Function Subscale has a higher correlation with the SMFQ than with the other subscales, and as such it influences the PedsQL Total Scale. However, the lower correlations for the other subscales (Physical health, Social Functioning and School Functioning) confirm that the PedsQL does measure different areas. This shows how important it is to use the subscales as additional tools of assessment and along with the PedsQL Total Scale when assessing depressive symptoms.
Generally speaking, one would be interested in increasing the HRQOL of adolescents in a clinical setting. The scores on each PedsQL factor may then provide us with valuable information. Individual differences in PedsQL scores should be taken into account when tailoring prevention interventions for mental problems.

The Emotional and School Functioning Subscales all remained significantly associated with levels of depressive symptoms when controlling for gender, age, the occurrence of stressful

life events, and social anxiety. Interestingly, the SMFQ showed significantly stronger rates of prediction for the PedsQL School Functioning Subscale than the SPAI-C. This finding seems to indicate that the PedsQL School Function Subscale is an interesting means of assessing and measuring both depressive and social anxiety symptoms: it also reaffirms the necessity, when evaluating daily functioning, of taking into account contexts that are of relevance to children's lives, such as school and community [71].

7.2 The clinical study

7.2.1 HRQOL, intellectual, mental and psychosocial findings for children in remission from ALL.

HRQOL and intellectual outcome in children treated for ALL

The results showed that children and adolescents treated for ALL report significant lower HRQOL scores for both the Total Scale and the Psychosocial Health Scale as measured by the PedsQL^{TM}4.0. Most of the intellectual scores as measured by the WISC-III were also significant lower for the children treated for ALL compared to controls. For most of the PedsQL Scales parental impressions of the HRQOL were significantly different from those of the control group, and as such confirm a previous and major study which took for its subject the HRQOL of children and adolescents as this was perceived by parents [119]. Interestingly, the children in remission from ALL showed lower scores for the Psychosocial Health Scale compared to the Physical Functioning Health Scale as reported by both the PedsQL self-report and parent proxy-report. This finding confirms the few previous findings which look at children in remission from ALL [23, 24,119]. See Table 4 (page 36). Psychosocial support therefore remains important several years after treatment has ended, even when the overall physical health appears to be good [23].

Psychosocial problems can be caused by several factors, and among these may be a continuing anxiety about possible late-effects or even a recurrence of the cancer. The children may often be afraid on an unconscious level that the disease will recur. In addition to stress experienced during the treatment, they can also be confronted with new problems that develop from the illness and from the long-term side–effects of treatment [24]. Developmental aspects should also be considered. The patients are children for whom about 2.5 years of dynamic psychological and social development is interrupted by serious life threatening illness,

persistent regular hospital visits, compromised immune system, interruption in school attendance and social activities, as well as family crisis. All these factors can influence and interrupt normal psychological and social development and further academic achievement.

Table 4. Comparison of PedsQL^{TM} scale scores across different studies in samples of children with cancer.

Studies	US study. N=73 Age 2-18 Different cancers >1 year off treatment Varni et al., 02 [131]		UK-English study N=45 Age: 8-18 Diagn. ALL ≥ 4 years post diagnosis Eiser et al., 03 [23]		Norwegian study N=40 Age: 8-15 Diagn. ALL ≥ 4 years post diagnosis Reinfjell et al.,07 [133]		Dutch study N= 105 Age 5-20 Different cancers Average 4 years post diagnosis Felder-Puig et al., 04 [132]	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
PedsQL Child self-report								
Total score	77.66	(15.25)	80.97	(12.57)	81.70	(12.56)	82.6	(13.5)
Psychosocial health	76.51	(16.03)	79.07	(13.14)	79.27	(13.99)	-	
Physical Functioning	80.01	(18.66)	86.16	(14.72)	86.25	(12.13)	86.7	(17.1)
Emotional Functioning	77.67	(20.19)	-		75.13	(18.69)	78.6	(19.8)
Social Functioning	79.64	(19.78)	-		86.00	(14.11)	85.8	(18.6)
School Functioning	71.41	(18.12)	-		76.63	(16.38)	79.5	(14.6)
PedsQL Parent- report								
Total score	73.68	(18.63)	76.50	(16.10)	79.42	(12.50)	80.4	(13.4)
Psychosocial health	72.92	(17.98)	73.71	(16.95)	75.86	(14.22)	-	
Physical Functioning	74.96	(24.01)	84.73	(19.73)	86.14	(13.69)	85.0	(16.5)
Emotional Functioning	72.84	(19.85)	-		70.28	(15.63)	73.9	(17.5)
Social Functioning	76.11	(21.66)	-		82.81	(15.54)	83.9	(18.7)
School Functioning	69.06	(23.00)	-		74.44	(19.88)	78.7	(15.7)

On average, children and adolescents treated for ALL show intellectual functioning in the normal range, but below that of the control group. Intellectual functioning in the normal range is considered as a protective factor with regards to the mental and psychosocial health of children and adolescents. However, this study shows that despite adequate intellectual functioning in children in remission from ALL, their levels of Psychosocial Health as measured by the PedsQL are significant lower compared to the control group. This tendency is similar for both the child self-report as well as for the parent proxy-report.

There were significant differences between children with ALL and their healthy controls for three of the WISC-III IQ scales, as well as for two of the different composite factors. In the present study, only one child underwent both chemotherapy and radiotherapy, and this child functioned adequately, while the remaining children underwent chemotherapy. The suggestion that it might be chemotherapy alone which contributes towards cognitive deficits is still a controversial one [54, 61, 64]. Studies have indicated that children and adolescents experience rather vague problems with attention and concentration after treatment, and that these complaints derive from more subtle impairments in processing speed [64]. A recent meta-analysis showed that children who were survivors of ALL appeared to experience clinically significant declines in neurocognitive functioning [37], in both global and specific areas of neurocognitive functioning. The findings were thought to have been a consequence of the treatments used to cure their disease. Interestingly, when compared to normative data, these declines become less clear [37]. Since cognitive deficits may be subtle, continued evaluation of levels of cognitive and learning functioning in children who have been treated for moderate-risk acute lymphocytic leukaemia is recommended [65]. The significant differences found in the present study between children in remission from ALL and their control group should be further assessed with respect to neuropsychological functioning.

Mental and psychosocial outcome in children with ALL

Children treated for ALL showed significantly higher symptom scores on all domains of CBCL and YSR than healthy children. According to the reports of their mothers, six children had a CBCL score ≥ 90 percentile, which is indicative of severe problems, as opposed to none in the control group. The CBCL as reported by the fathers showed that five children scored ≥ 90 percentile, as opposed to only 1 child from the control group. One child scored ≥ 90 percentile on the YSR and was therefore in clinical range, while there was one child in the control group. Our results confirm that children with chronic health conditions occupy the “at

risk" status when it comes to psychiatric difficulties. Although major psychiatric disturbances are not common among long-term survivors of ALL [120], studies have shown that this population has increased risks of mental health and adjustment problems [45]. Based on the meta-analysis, where more than 700 studies were reviewed, it could be concluded that children with chronic physical illness were more likely to exhibit internalizing than externalizing problems, but not to have lower self-esteem [98]. A Swedish study indicates that there is a greater risk of psychosocial problems in the period after treatment than there is during it. Children and adolescents who were no longer being treated reported higher levels of depression and anxiety: seven (14%) reported a high level of depression; six of the children were off treatment [20]. Shelby [101] showed that children treated for ALL were reporting significantly more problems in terms of social competence and internalizing behaviour. In the same study, adolescents exhibited more difficulties in these areas than younger children, there were no differences found between children who had received cranial radiation and those who had not, and the age at the time of diagnosis did not have an impact on their current function. In contrast to the results in this present study, whose significance is measured and confirmed by the instrument CBCL, the SDQ self-report for children showed no statistically significant differences in psychosocial health between children with ALL and their healthy controls. Eiser [38] argues that where there are no differences, a post hoc explanation which needs to be thought about is a lack of sensitivity in the measurements. However, for the mothers of children treated for ALL, the SDQ Parent self-report showed higher scores for Emotional symptoms than did the healthy controls. As such, this finding confirms some of the CBCL findings.

To sum up: taken together, the findings show children in remission from ALL have an at risk status when it comes to potential mental and psychosocial late-effects. Greater awareness of high-risk groups should facilitate more timely identification of problems in the future [53].

7.2.2 HRQOL and mental health in parents of children treated for ALL

Fathers in the present study showed significantly more anxiety and depression as measured by the GHQ-30 compared to healthy controls, while no such differences were found for mothers. Eiser (2005) points out that fathers often remained more involved in everyday life despite the child's illness. This may influence the father's own situation and needs, since by staying at home or at work more during the child's treatment phase, the father will not be able to get

adequate help for his own emotional needs, and this may affect his later adjustment. That fathers in the present study showed more depression and anxiety several years after their child's diagnosis may be an indication of this aspect. Kazak et al. argues that fathers are often underrepresented in paediatric research samples, and her previous studies have found that fathers of childhood cancer survivors have levels of Posttraumatic stress symptom which are nearly as high as those of mothers [121]. Many of the fathers in Kazak's study reported that they were afraid of revealing unpleasant memories, believing that this would be detrimental to other family members. Interestingly, the researchers found by studying a group of 150 families that participants had significantly fewer symptoms of post-traumatic stress after a one-day treatment program employing cognitive-behavioural principles, compared to a control group who did not receive the treatment [122]. Adverse effects on the long-term physical and mental health of parents has also been reported previously [123], with a significant number of parents found to be still suffering from clinical distress five years after treatment [124].Thus, assessing the overall quality of life in survivors should also include the long-term effects for the family as well.

Adequate rehabilitation and follow-up programs should be implemented for both children and parents after treatment. Further research is needed to evaluate the specific areas of parental stress, and to look at how parental coping affects mental health and QOL in these areas.

7.3 Limitations of the study

The methodological study (Paper 3 and 4)

With regards to the Norwegian PedsQL ^{TM} 4.0 validation study, the present findings have several potential limitations. Test-retest reliability and responsiveness are not reported. Information on non-participants was not available, something that can limit generalizability. In the American validation study, the PedsQL differentiated between HRQOL in healthy children and in children with acute or chronic health conditions. This will also be an important future investigative goal for the Norwegian PedsQL version, and is something the authors are taking into consideration. In addition, this study utilized a relatively restricted age range. When in comes to developmental aspects, further research should investigate the psychometric properties of the Norwegian PedsQL versions, focusing on the upper-age range which the adolescent PedsQL was designed for, as well as on younger age-groups.

Furthermore cross-sectional designs can not determine causal relations, and their absence represents an important shortcoming in the present study and implies that the results should be treated with some caution. In further studies using the PedsQL^{TM} 4.0, it will be essential to explore this measure in a prospective, longitudinal design, in order to be able to search for causal factors and to disentangle the true risk and protective factors from mere correlates. In addition, although the depressive measure used in this study is reported to have satisfactory psychometric properties, and moderate to high correlations with a diagnostic interview [125-127], it is not based on DSM-IV or ICD-10 diagnostic criteria for depressive disorder. The future use of diagnostic interviews based on such diagnostic criteria is recommended. However, in epidemiological samples the SMFQ does, distinguish between clinically depressed and not depressed as well as the longer version of the MFQ [125]. Moreover, due to the limited administration time set aside by participating schools, only a selection of acknowledged stressful life events [128-130] were included. The questionnaires used on SLE might therefore lead to an underestimation of the strengths of the findings. The inclusion of full scales assessing stressful and negative life events is recommended. Finally, a relatively high percentage of the parents in the present study have higher education. This might have had an influence on our findings, since children from higher social classes may have a better quality of life. At the same time it should be pointed that the amount of children whose scores were in the clinical range for depressive symptoms is similar to the percentage expected in healthy samples, and as such confirms that the sample is representative.

The clinical study (Paper 1 and 2)

The strengths of our study include how homogenous the sample of children with ALL is with respect to both diagnosis and age-span, and the use of a control group. Drawing control groups from the same local population as the ALL survivors is recommended as an appropriate means of comparison [37]. However, limitations in our study should be noted: it has a cross-sectional design, and we were therefore unable to control for premorbid functioning; the small size of our group of children was another drawback. Cross-sectional designs cannot determine causal relations, and their absence represents an important shortcoming in the present study and implies that the results should be treated with some caution. Furthermore, the psychologist who performed the WISC-III test was not blinded to the ALL diagnosis, and this should also be taken into consideration when interpreting the results. It should also be pointed that the data are less representative for girls compared to

boys. 61.76% of the total eligible sample was girls, while 86.36% were boys. This may also influence the results regarding gender differences.

To be able to investigate the systematic effects of chemotherapy on HRQOL outcomes and intellectual functioning over a longer period of time, longitudinal designs should be implemented for children treated for ALL, and controls involving other types of cancers should be carried out to control how cancer is experienced more generally.

The findings based on the 21 fathers of ALL patients who participated in our study should also be treated with a degree of caution. But the results may indicate the need to pay attention to the mental health and adjustment of fathers during the time of the child's treatment as well as the rehabilitation phase. The fact that only 21 fathers participated may indicate a common problem in clinical research, namely that more fathers should be included in future research on children with cancer and their parents: ways of making this happen need to be found and implemented.

7.4 Implications of the study

An important aim in the care for children and adolescents with chronic illnesses is to minimize the consequences of the psychosocial difficulties following treatment for ALL. The findings revealed by this study have practical, therapeutic and research-related implications.

The implementation of HRQOL measures in paediatric research

- In this study we have shown that the PedsQL Norwegian version is generally a valid and reliable instrument, and that it reproduces some of the earlier findings for the original version. The Norwegian PedsQL ^{TM} 4.0 version can therefore be recommended as a valuable tool for assessing the HRQOL of young adolescents in Norway.

- The imperfect concordance observed between self-and proxy-reports supports the need to measure the perspectives of child and parent in evaluating paediatric HRQOL. It is important to emphasize the clinical usefulness of looking at child-parent discrepancies, which give us the possibility of measuring both child and parent perspectives. To the

extent that HRQOL is subjective, there are strong arguments in favour of eliciting data directly from children whenever possible.

- The findings suggest that the Paediatric Quality of Life measure (PedsQL^{TM}) is an interesting measure for assessing depressive and social anxiety symptoms in young adolescents, and can be useful in both clinical practice and further research as an outcome measure in studies on the mental health of children.

- The results indicate that HRQOL instruments such as the PedsQL^{TM} 4.0 can be a sensitive outcome measure for how children function after treatment for ALL, and such measures of health and functioning should be included in paediatric settings and research trials. Normal childhood development can be profoundly affected by the toxicity and adverse impact of aggressive medical treatments. Information about the HRQOL of children with cancer may provide us with a more comprehensive means of evaluating the outcome of treatment than survival rates and relapse-free intervals alone. HRQOL measures should be used to predict treatment outcomes, or to evaluate the impact of a treatment or intervention. In a clinical setting one would generally be interested in increasing children's HRQOL. The scores on each PedsQL factor may then be highly informative. Individual differences in PedsQL scores should be taken into account when tailoring preventive intervention and rehabilitation programs for children after treatment.

Practical and therapeutic implications for children in long-term remission from ALL

- The significant group differences found between children treated for ALL and their control group, may indicate that treatment for ALL can make children more vulnerable to late-effects that will have an impact on HRQOL and intellectual functioning. The results indicating impairments in HRQOL compared to the control group show the need for follow-up. Adequate follow-up for children in long-term remission from ALL should be implemented. This presents the healthcare community with several challenges: how to focus on providing appropriate care for the survivors, as well as the need to prevent the long-term psychosocial sequels of cancer and its treatment.

- Several issues need to be addressed, such as educating survivors and healthcare providers with respect to potential late effects. This study shows that problems can be seen several years after diagnosis and treatment, and demonstrates the need for a closer awareness of adjustment issues related to mental health and psychosocial functioning in children after their treatment for ALL. To be able to detect and address actual problems effectively, children should be followed-up from the time they return to school and further into their academic careers. In addition to the medical follow-up given to patients in clinics, outpatient centres should also be addressing these equally vital challenges and needs.

- Psychosocial check-ups should be provided in parallel with the routine and regular medical follow-ups. Professional mental health guidance with a developmental and family perspective should be implemented.

- Information about and counselling for potential late-effects and problems with respect to HRQOL and mental health should be given to both parents and children. Information should be individually adjusted to the child's developmental and cognitive level.

Parents of children in long term-remission from ALL

- The result may indicate the need to pay more attention to the mental health and adjustment of fathers during the time of the child's treatment as well as the rehabilitation phase. The fact that only 21 fathers participated may indicate a common problem in clinical research, namely that fathers should be included in future research on children with cancer and their parents: ways of making this happen need to be found and implemented.

- Further research is needed to evaluate the specific areas of parental stress, and how parental coping affects mental health and QOL in these areas.

- Adequate rehabilitation and follow-up programs should be implemented for both children and parents after treatment.

Implications for further research

- Developing Norwegian norms for the different age spans the PedsQL is designed for should be a priority in future works.

- The children's intellectual functioning was in the normal range, but below that of the control group, and this needs further investigation, particularly with respect to neuropsychological functioning. It is recommended that further research be carried out into the HRQOL of children in remission from ALL, and that this should be implemented for different age-groups.

- To be able to investigate the systematic effects of chemotherapy on HRQOL outcomes and intellectual functioning over a longer period of time, longitudinal designs should be adopted for children treated for ALL, and for controls involving other types of cancers should be carried out to get a more comprehensive perspective on the cancer experience.

- Generally speaking, the standard deviation for the group of children with ALL is high with respect to the subscales for the PedsQL, the CBCL/YSR and the WISC-III, and this could indicate differences in adjustment with respect to the HRQOL, mental health and intellectual functioning of the group of children in remission from ALL. This requires further investigation, with particular attention being paid to the type of treatment protocol, time since diagnosis, age at diagnosis, and difficulties related to HRQOL, mental health and intellectual functioning.

- To be able to determine the relative influence of age, illness, and treatment variables statistically, the size of a research sample has to be adequate. Although large-scale studies may be important in identifying certain risk factors, studies that concentrate on homogeneous subgroups of patients will provide more information about the significance of risk factors involved for that population. In designing these studies, collaboration is needed at the national and international levels. This is further dependent on the availability of parallel forms of measures in different languages.

- Looking at the developmental aspects of emotional functioning in children in long-term remission from ALL should be further investigated using a bigger pool of children, with different age groups represented at both the times of diagnosis and assessment, in order to be able to find subgroups of children who might be especially vulnerable when it comes to emotional functioning. How sensitive the different instruments which measure this aspect are should be the subject of further investigation.

- It would be interesting to obtain information about how the survivors meet developmental tasks in growing up. How survivors function later in life should therefore be investigated in order to yield new insights.

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Paper I

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REGULAR ARTICLE

Health-related quality of life and intellectual functioning in children in remission from acute lymphoblastic leukaemia

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Abstract

Aim: To evaluate the health-related quality of life (HRQOL) and intellectual functioning of children in remission from acute lymphoblastic leukaemia (ALL).

Methods: Children and adolescents treated for ALL (n = 40; mean age 11.8 years, range 8.5–15.4) and healthy controls (n = 42; mean age 11.8, range 8.11–15.0) were assessed through a cross-sectional approach using the Pediatric Quality of Life inventory (PedsQL™) 4.0 and the Wechsler Intelligent Scale for children-III (WISC-III).

Results: Children and adolescents treated for ALL reported on average significantly lower HRQOL compared to healthy controls: the mother's proxy-report showed significantly lower HRQOL for their children, as did the father's proxy-report, measured by the PedsQL™ 4.0 Total Scale and Psychosocial Health Scale. Intellectual functioning as measured by the WISC-III Full Scale IQ was below that of the control group, but still within the normal range.

Conclusions: Significant differences found between children treated for ALL and their control group for the PedsQL Psychosocial Health Scale may indicate that the complex illness-treatment experience can make children more vulnerable with regard to psychosocial sequels, in spite of otherwise satisfactory physical and intellectual functioning. Follow-up programs that target the psychosocial health of children in remission from ALL should be implemented.

INTRODUCTION

Acute lymphoblastic leukaemia (ALL) is the most common form of cancer in children. New treatments involving a combination of chemotherapy and radiotherapy have resulted in significant improvements to rates of survival in recent years, with an approximate 80% average in the 5-year survival rate (1). Late effects from these forms of treatment may include somatic complications, such as reduced fertility (particularly in boys), cardiomyopathy (especially in girls), reduced lung functioning and osteoporosis. Further complications may involve reduced linear growth and endocrine disturbances when cranial irradiation is used as part of the therapy, as well as a second occurrence of the cancer (2–3% of all patients) (2). A recent meta-analysis showed that children who survived ALL appeared to experience clinically significant declines in neurocognitive functioning (3).

Medical and psychological late effects are defined as occurring after the successful completion of medical therapy, and usually 2 or more years from the time of diagnosis (4).

The literature on childhood cancer and psychosocial adjustment has resulted in some controversial findings (5–7), which can be attributed to methodological restrictions in the heterogeneity samples of patients (e.g. differences in diagnoses and time since diagnosis) (7), as well as differences in the criteria for selecting the control groups (3,8). The focus has often been on the degree to which mental health problems are experienced and on maladjustment, instead of on coping and functioning in everyday life (8,9). Paying attention to only the former aspects can potentially limit what we can learn about actual adjustment problems for children with cancer (10).

As the treatment for childhood cancer can be aggressive and associated with both acute and long-term morbidity (11), the research focus has changed in order to emphasize the health-related quality of life (HRQOL) (12). HRQOL measures must be multidimensional and consist of the physical and the psychological (including the emotional and cognitive) dimension, as well as taking into account the social health dimensions delineated by the World Health Organization (WHO) (13). Only recently have there been studies that have focused on HRQOL (14), but such measures of health and functioning should be included in paediatric settings and research trials. Normal childhood development can be profoundly affected by the toxicity and adverse impact of aggressive medical treatments (15). Information about the HRQOL of children with cancer may provide us with a more comprehensive means of evaluating the outcome of treatment than survival rates and relapse-free intervals alone.

Paediatric patient self-report should be considered the standard for measuring HRQOL, although there are circumstances when children are too young, too cognitive impaired or fatigued to complete a HRQOL instrument, and parent proxy-report instruments are needed in such cases (16).

The few previous studies that measured HRQOL show that children in remission from ALL experience considerably compromised psychosocial functioning, even when physical problems diminish in the course of time and the overall health appears to be good (17–19). In addition to measuring HRQOL, in the present study we wanted to assess intellectual functioning, because adequate intellectual functioning is considered as a protective factor in a child's state of psychosocial health (20).

The aim of the present study was (i) to describe HRQOL in children and adolescents in remission from ALL by assessing both the PedsQL child self-report and parent proxy-report in comparison with healthy controls, and (ii) to assess the intellectual functioning in children in remission from ALL compared to healthy controls.

PATIENTS AND METHODS

Patients

Children and adolescents in remission from ALL were recruited from two University Hospitals in Norway: Rikshospitalet-Radiumhospitalet Medical Centre in Oslo and St. Olavs Hospital in Trondheim. The children were born in the period 1989–1995, had a mean age of 11.8 (range 8.5–15.4), took part 4.2–12.5 years after ALL diagnosis and were treated according to the Nordic protocol, The Nordic Society of Pediatric Hematology/Oncology (NOPHO-ALL, 1992); their parents were also invited to participate in the study. Children who suffered relapses, or who had other kinds of severe medical condition (e.g. Down's syndrome) were excluded. Of the 56 children who fulfilled the criteria for participation, a total of 40 (71.4), comprising 21 girls (52.5%) and 19 boys (47.5%), took part. Parental information was supplied by 36 mothers, whose mean age was 40.0 (range 30–55), and 21 fathers, whose mean age was 43.0 (range 32–58): both mothers and fathers were asked to give their evaluation of the PedsQL proxy-report separately. Data regarding diagnoses and treatment protocols were collected from the medical records. The average age at the time ALL was diagnosed was 4.0 years (range 0–7.6). The average time since diagnosis was 7.9 years (range 4.2–12.5). The treatment categories were scored according to the Nordic protocol (NOPHO-ALL, 1992) with the following categories: (i) standard risk (SR); (ii) intermediate risk (IR); (iii) high risk (HR); (iv) high risk-1 (HR-1); (v) high risk-2 (HR-2) and (vi) very high risk-1 (VHR). With regard to the small sample in the four last categories, we scored these as one category—high/very high risk. One child had been treated with chemotherapy combined with radiation therapy (1800 Cgy), and the remaining children with chemotherapy only. One child was in the infant-risk group, treated according to the NOPHO-92 protocol HR-1. Sociodemographic characteristics and treatment-related variables are presented in Table S1.

In the 16 families that did not participate, there were a higher amount of girls (n = 13) than boys (n = 3). Most of them answered that they were too busy or distressed or that they did not wish to be confronted with past experiences of sickness and hospitalisation. Practical difficulties, such as geographical distance were also a factor.

The children treated for ALL were compared to a group of healthy children with a similar age and gender distribution (n = 42; Table S1), recruited from two elementary schools and two junior high schools in the middle part of Norway, and from both urban and rural areas. Children with a psychiatric diagnosis or with other specific and relevant medical problems, such as cognitive dysfunction were excluded. Informed consent was obtained from all the children and adolescents, as well as from their parents. The study was approved by the Regional Ethics Committee of Medical Research. (Table S1).

Procedure

Leaders of the Paediatric departments of Rikshospitalet-Radiumshospitalet and St Olavs Hospital were contacted and gave us their permission to contact the patients whose names were taken from their patient pool. Written information about the project and consensus formulas for the parents and for the older children were sent to the parents of 56 survivors by ordinary mail, and they were contacted by phone for further information. After informed consent was received from the families, appointments were made by phone for the interview, which was often planned to coincide with their follow-up appointment at the hospital.

All assessments of both the children and their parents were carried out at the hospital. The interview session was conducted by a clinical psychologist (the first author). The parents of the children treated for ALL were interviewed separately. All children were individually assessed by different standardized instruments in a quiet room. Data regarding treatment protocols were collected from the patient's medical records.

With regard to the control group, the educational sections of two municipal districts were contacted in order to discuss the demographics of different schools and for permission to contact school principals in their county. When informed consent was given in writing by the sections, four school headmasters were contacted and their informed consent was given in turn. Two headmasters in the city of Trondheim were instructed to make a sample by drawing lots based on age and gender matches. Another group from the rural county of Nord-Trøndelag was matched along the lines of gender and the nearest age in month. Other lots were drawn by necessity, as when several children matched the age group. Written information and consent formula were sent to the families by the different principals, and they also contacted the families by phone to inform them about the project. When informed consent was given by the parents and adolescents, the assessments with each child were carried out individually in a quiet room at the schools, using the same procedure as with the children in remission from ALL.

After the assessments each pupil received an envelope, which contained information and a questionnaire for their parents. Parents were asked to fill out the questionnaires separately before returning them in a pre-stamped envelope.

When necessary, the participants were further able to contact the researcher by phone to obtain additional information.

Measures

HRQOL

The Pediatric Quality of Life Inventory (PedsQL™4.0; 21) was used to measure HRQOL in children and adolescents. The 23-item PedsQL, version 4.0 Generic Core Scales, can be grouped into four domains of HRQOL: (i) physical functioning (8 items), (ii) emotional functioning (5 items), (iii) social functioning (5 items) and (iv) school functioning (5 items). The Generic Core Scales comprised of a child self-report including ages 5–7, 8–12 and 13–18 years. The parent proxy-report covers ages 2–4, 5–7, 8–12 and 13–18, and assesses how parents perceive their child's HRQOL. The items for self-report and proxy-report are essentially identical, differing in the language that they use, which is developmentally appropriate, and in using the first- or third-person pronoun.

The questions ask how much of a problem each item has been during the past 1 month: 0 = never a problem; 1 = almost never a problem; 2 = sometimes a problem; 3 = often a problem; 4 = almost always a problem. In addition to the four subscales, a Total Summary Health score (23 items) can be computed. A Psychosocial Health Summary score (15 items) can be computed as the sum of the items divided by the number of items answered in the Emotional, Social and School Functioning Subscales, and a Physical Health Summary score (8 items) is the same as the Physical Functioning subscale. The PedsQL™4.0 provided a very reliable Total Scale score with a Cronbach's alpha $\geq$ 0.89, and it has been shown to differentiate between healthy children and children with chronic health conditions (22). A Norwegian version of the PedsQL 4.0, geared towards psychometric properties, is presented and described in greater detail in an earlier work (23). The PedsQL has demonstrated satisfactory psychometric properties (23,24). A Cronbach's alpha $\geq$0.77 was obtained for the Norwegian translation of the PedsQL for the age group 13–15, which indicates good internal consistency (23).

Intellectual functioning

The Wechsler Intelligence Scale for Children, Third edition (WISC-III), complete test (25) was used to evaluate intellectual functioning in the children. For the purposes of the present study, we used the Full Scale Intelligence Quotient (FSIQ), the Verbal Intelligence Quotient (VIQ) and the Performance Intelligence Quotient (PIQ), as well as the four indexes: the Verbal Comprehension Index (VCI), the Perceptual Organization Index (POI), the Freedom from Distractibility Index (FDI) and the Processing Speed Index (PSI).

Statistical analysis

A *t*-test for independent samples was used to analyse differences in HRQOL and intellectual functioning between the treatment group and healthy children. Ninety-five percent confidence intervals were calculated for the differences. In order to reduce the risk of making type 1 errors due to multiple comparisons, a Bonferroni corrected alpha level of 0.004 was chosen. The Statistical Package for Social Sciences (SPSS 14.0, SPSS Inc., Chicago, IL) was used for all the analyses.

RESULTS

Health-related quality of life (HRQOL)

The PedsQL™ 4.0 scores for self-reports and for the parent proxy-report for children treated for ALL and for their healthy controls are presented in Table S2. Children treated for ALL showed significantly lower scores for both the PedsQL Total Scale and the Psychosocial Health Scale as these are reflected in both the PedsQL self-report and the parent proxy-report and compared to healthy controls. In addition, the PedsQL parent proxy-report also showed significant lower scores for the Emotional Function Subscale. The PedsQL mother proxy-report was lower for the Social Function Subscale, while the School Function Subscale was lower for the PedsQL father proxy-report compared to healthy controls. Generally, children in remission from ALL showed lower scores for Psychosocial Health Scale overall compared to the Physical Functioning Scale as this was illustrated by both the self-report and the parent proxy-report (Table S2).

Intellectual functioning

The WISC-III scores for children with ALL and their healthy controls are presented in Table S3. Both groups obtained an average FSIQ within the normal range, but there were significant differences between children with ALL and their healthy controls for both the WISC-III FSIQ, the VIQ and the PIQ scale, as well as for two of the different composite factors (Table S3).

DISCUSSION

This study presents descriptive data related to the HRQOL and intellectual functioning in children and adolescents in remission from ALL, and in comparison with healthy children. The results showed that children and adolescents treated for ALL report significantly lower HRQOL scores for both the Total Scale and the Psychosocial Health Scale as measured by the PedsQL™4.0. Most of the intellectual scores as measured by the WISC-III were also significantly lower for the children treated for ALL compared to controls.

The parental impressions of the HRQOL were for most of the PedsQL Scales significantly different from those of the control group, and as such confirm a previous and major study that took for its subject the HRQOL of children and adolescents as it was perceived by parents (18). Interestingly, the children in remission from ALL showed lower scores for the Psychosocial Health Scale compared to the Physical Functioning Health Scale as reported by both the PedsQL self-report and parent proxy-report. This finding confirms the few previous findings with respect to children in

remission from ALL (17–19). Psychosocial support therefore remains important several years after the treatment, even when the overall physical health appears to be good (17).

Psychosocial problems can be caused by several factors, and among these may be a continuing anxiety about possible late-effects or even a recurrence of the cancer. The children may often be afraid on an unconscious level that the disease will recur. In addition to stress experienced during the treatment, they can also be confronted with new problems that develop from the illness and from the long-term side-effects of treatment (17). Developmental aspects should also be considered. The patients are children for whom about 2–5 years of dynamic psychological and social development is interrupted by serious life-threatening illness, persistent regular hospital visits, compromised immune system, interruption in school attendance and social activities, as well as family crisis. All these factors can influence and interrupt normal psychological and social development and further academic achievement.

Looking at developmental aspects with respect to the HRQOL functioning of children in remission from ALL should be investigated using a bigger pool of children, with different age groups represented at both the time of diagnosis and assessment, in order to find subgroups of children who might be especially vulnerable when it comes to the possibility of a reduction in HRQOL.

On average, children and adolescents treated for ALL show intellectual functioning in the normal range, but below that of the control group. Intellectual functioning in the normal range is considered as a protective factor with regard to the mental and psychosocial health of children and adolescents. However, this study shows that despite adequate intellectual functioning in children in remission from ALL, their levels of psychosocial health as measured by the PedsQL are significantly lower compared to the control group. This tendency is similar for both the child self-report as well as for the parent proxy-report.

There were significant differences between children with ALL and their healthy controls for three of the WISC-III IQ scales, as well as for two of the different composite factors. In the present study, only one child underwent both chemotherapy and radiotherapy, and this child functioned adequately, while the remaining children underwent chemotherapy. The suggestion that it might be chemotherapy alone that contributes towards cognitive deficits is still a controversial one (26–28). Studies have indicated that children and adolescents experience rather vague problems with attention and concentration after treatment, and that these complaints derive from more subtle impairments in processing speed (28). A recent meta-analysis showed that children who were survivors of ALL appeared to experience clinically significant declines in neurocognitive functioning (3), in both global and specific areas of neurocognitive functioning. The findings were thought to have been a consequence of the treatments used to cure their disease. Interestingly, when compared to normative data, these declines become less clear (3). Because cognitive deficits may be subtle, continued evaluation of levels of cognitive and learning functioning in children who have been treated for moderate-risk acute lymphocytic leukaemia is recommended (29). The significant differences found in the present study between children in remission from ALL and their control group should be further assessed with respect to neuropsychological functioning.

The strengths of our study include how homogenous the sample of children with ALL is with respect to both diagnosis and age span, and the use of a control group. Drawing control groups from the same local population as the ALL survivors is recommended as an appropriate means of comparison (3). However, limitations in our study should be noted: it has a cross-sectional design, and we were therefore unable to control for premorbid functioning; the small size of our group of children was another drawback. Cross-sectional designs cannot determine causal relations, and represents an important shortcoming in the present study and implies that the results should be treated with some caution. Furthermore, the psychologist who performed the WISC-III test was not blinded to the ALL diagnosis, and this should also be taken into consideration when interpreting the results.

To be able to investigate the systematic effects of chemotherapy on HRQOL outcomes and intellectual functioning over a longer period of time, longitudinal designs should be implemented for children treated for ALL, and controls involving other types of cancers should be carried out to control how cancer is experienced more generally.

CONCLUSIONS

Despite adequate intellectual functioning, the children treated for ALL on average show a lower HRQOL for the Psychosocial Health Scale compared to healthy controls. The children's intellectual functioning was in the normal range, but below that of the control group, and this needs further investigation, particularly with respect to neuropsychological functioning. It is recommended that further research be carried out into the HRQOL of children in remission from ALL. The results indicating impairments in the HRQOL compared to healthy controls show the need for such follow-up. This presents the healthcare community with several challenges: how to focus on providing appropriate care for the survivors of cancer, as well as the need to prevent or eventually treat long-term remission. Several issues need to be addressed, such as educating survivors and healthcare providers regarding potential psychosocial sequels. The kind of psychosocial support offered to the patient during or after the treatment should also be investigated in future longitudinal research.

The results indicate that HRQOL instruments, such as the PedsQL^{TM} 4.0 can be a sensitive outcome measure of a child's functioning subsequent to treatment for ALL. In a clinical setting one would generally be interested in increasing children's HRQOL. The scores on each PedsQL factor may then be highly informative. Individual differences in PedsQL scores should be taken into account when tailoring preventive intervention and rehabilitation programs for children after treatment.

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Supplementary material

The following supplementary material is available for this article:

Table S1 Sociodemographic characteristics of children with ALL and healthy controls: Treatment variables for children with ALL
Table S2 HRQOL of 40 children diagnosed with ALL and 42 healthy children as controls
Table S3 Intellectual functioning of 40 children diagnosed with ALL and healthy children as controls

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Table S1. *Sociodemographic characteristics of children with ALL and healthy controls. Treatment variables for children with ALL.*

	ALL (n = 40)	Healthy (n = 42)	t score	P
Gender			-.11	.91
Girl: n (%)	21 (52.5)	21 (50.0)		
Boy: n (%)	19 (47.5)	21 (50.0)		
Age at study			.14	.92
Mean (SD)	11.8 (1.9)	11.8 (1.9)		
Median	11.4	11.6		
Range	8.5-15.4	8.11-15.0		
Family Composition			-.75	.46
Both parents	31 (77.5)	29 (69.0)		
Single mothers	8 (20.0)	12 (28.6)		
Single fathers	1 (2.5)	1 (2.4)		
Parental Characteristics				
Age, median (range)				
Mother	40.0 (30-55)	40.0 (31-52)	-.25	.81
Father	43.0 (32-58)	43.5 (34-72)	-.09	.93
Education, median(range)				
Mother	14.0 (10-19)	13.0 (9-19)	.07	.95
Father	14.0 (10-20)	13.0 (10-19)	.84	.40
Community			.69	.49
Urban	15 (37.5)	18 (42.9)		
Rural	25 (62.5)	24 (57.1)		
Home			.72	.48
Own house	36 (90.0)	39 (92.9)		
Own apartment	3 (7.5)	3 (7.1)		
Renting apartment	1 (2.5)	-		
Economy			-.04	.96
Very satisfying	27 (67.5)	21 (50.0)		
Good	8 (20.0)	21 (50.0)		
Poor	5 (12.5)	-		
Diagnosis and treatment				
Age at diagnosis				
Mean (SD)	4.0 (1.9)	-		
Median	3.1	-		
Range	0-7.6	-		
Years since diagnosis				
Mean (SD)	7.9 (2.0)	-		
Median	7.1	-		
Range	4.2-12.5	-		
Treatment protocols				
Standard risk	15 (37.5)	-		
Intermediary risk	15 (37.5)	-		
High/very high risk	10 (25.0)	-		

	ALL (n=40)		Healthy (n=42)					
	Mean	SD	Mean	SD	Difference	T score	P	95% CI
PedsQL Child self-report								
Total score	81.70	(12.56)	88.98	(7.57)	-7.27	-3.20	**	-11.80 to -2.74
Psychosocial health	79.27	(13.99)	87.22	(9.20)	-7.95	-3.06	**	-13.13 to -2.77
Physical Functioning	86.25	(12.13)	92.26	(6.45)	-6.01	-2.82		-10.25 to -1.77
Emotional Functioning	75.13	(18.69)	83.21	(12.68)	-8.09	-2.30		-15.08 to -1.10
Social Functioning	86.00	(14.11)	92.50	(7.67)	-6.50	-2.61		-11.46 to -1.54
School Functioning	76.63	(16.38)	85.95	(12.98)	-9.33	-2.86		-15.81 to -2.85
PedsQL Mother Proxy- report	ALL (n=36)		Healthy (n=38)					
Total score	79.42	(12.50)	89.62	(10.26)	-10.20	-3.84	***	-15.48 to -4.91
Psychosocial health	75.86	(14.22)	88.07	(11.28)	-12.21	-4.10	***	-18.15 to -6.28
Physical Functioning	86.14	(13.69)	92.52	(10.47)	-6.38	-2.26		-12.01 to -0.75
Emotional Functioning	70.28	(15.63)	85.00	(13.46)	-14.72	-4.35	***	-21.47 to -7.98
Social Functioning	82.81	(15.54)	93.16	(9.89)	-10.35	-3.44	***	-16.35 to -4.34
School Functioning	74.44	(19.88)	86.05	(14.57)	-11.61	-2.88		-19.66 to -3.56
PedsQL Father Proxy-report	ALL (n=21)		Healthy (n=25)					
Total score	78.05	(12.50)	90.13	(12.24)	-12.08	-3.30	**	-19.46 to -4.71
Psychosocial health	74.30	(13.95)	88.60	(12.47)	-14.29	-3.68	***	-22.13 to -6.45
Physical Functioning	84.82	(12.86)	93.00	(12.70)	-8.18	-2.16		-15.80 to -0.56
Emotional Functioning	71.43	(15.01)	86.40	(13.88)	-14.97	-3.51	***	-23.57 to -6.37
Social Functioning	78.75	(18.98)	91.60	(11.88)	-12.85	-2.78		-22.18 to -3.52
School Functioning	73.09	(16.47)	87.80	(15.82)	-14.70	-3.08	**	-24.32 to -5.09

Table S2. *HRQOL of 40 children diagnosed with ALL and 42 healthy children as controls.*
95% CI =95% confidence intervals at 5% level
Note. *** $p < 0.001$. **$p < 0.004$

Table S3. *Intellectual Functioning of 40 children diagnosed with ALL and healthy children as controls.*
95% CI =95% confidence intervals at 5% level
Note. *** p < 0.001. **p < 0.004.

	ALL (n =40)		Healthy (n =42)					
	Mean	SD	Mean	SD	Difference	T score	p	95% CI
WISC-III								
Verbal scale (VIQ)	93.00	(15.66)	109.60	(12.23)	-16.60	-5.36	***	-22.75 to -10.44
Performance scale (PIQ)	96.60	(16.52)	106.45	(13.03)	-9.85	-3.01	**	-16.37 to - 3.33
Full scale IQ (FSIQ)	93.98	(16.04)	109.10	(12.54)	-15.12	-4.77	***	-21.43 to - 8.81
Verbal comprehension (VCI)	93.90	(15.45)	108.40	(12.92)	-14.51	-4.63	***	-20.75 to - 8.26
Perceptual Organization (POI)	97.98	(17.60)	107.00	(12.54)	-9.03	-2.68		-15.72 to - 2.33
Freedom From Distractibility (FDI)	92.78	(15.40)	108.00	(15.13)	-15.23	-4.52	***	-21.93 to - 8.52
Processing Speed (PSI)	87.00	(15.61)	94.62	(17.76)	-7.62	-2.05		-15.04 to - .20

Abbreviations: HRQOL=Health-Related Quality of Life, PedsQL = Pediatric Quality of Life Inventory, WISC-III=Wechler Intelligent Scale for children-III, FSIQ= WISC-III Full Scale IQ Index.

Paper II

Children in remission from acute lymphoblastic leukaemia: Mental health, psychosocial adjustment and parental functioning

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ABSTRACT

Objective: To assess the mental health and psychosocial adjustment of children in remission from Acute Lymphoblastic Leukemia (ALL) and parental functioning compared to healthy controls.
Methods: A cross-sectional study of 40 children treated for ALL (mean age 11.8 years, range 8.5-15.4) and healthy controls (n = 42) (mean age 11.8, range 8.11-15.0) were assessed by the Child Behavior Checklist (CBCL), the Youth Self-Report (YSR) and the Strength and Difficulties Questionnaire (SDQ). The parent's own mental health was assessed by the General Health Questionnaire (GHQ-30).
Results: Children treated for ALL showed on average significantly more symptoms as measured by the CBCL Total Behavior Score for mother's report (p= .005), and for father's report (p=.004) compared to healthy children. Fathers reported more anxiety (p= .03) and depression (p=.02) as measured by the GHQ-30 compared to healthy controls.
Conclusions: Children in remission from ALL showed on average significantly more problems regarding mental health and psychosocial adjustment as reported by their parents compared to healthy controls. Adequate rehabilitation and follow-up programs should be implemented for children in remission from ALL. The results indicate the need to pay attention to the mental health of fathers during the rehabilitation phase.

Key words: paediatrics; mental health; psychosocial adjustment, children; parents.

INTRODUCTION

Over the last decades survival rates of children treated for Acute Lymphoblastic Leukemia (ALL), have increased dramatically. New treatments involving a combination of chemotherapy and radiotherapy have resulted in significant survival improvements, with an approximate 80 % average in the 5-years survival [1, 2]. This progress in medical treatment has changed the focus toward the illnesses impact on the psychosocial situation of the child and the family during and after treatment [3].

Outcome regarding mental health and psychosocial functioning in childhood cancer has been the subject of previous research, but generally do not provide consistent results regarding adjustment. Studies have shown that many survivors functioning reasonably well, with little difference found between results for survivors and those for their peers or siblings [4-6]. It is also reported that a considerable proportion of survivors had long-term coping [7, 8], while poorer coping in cancer patients was associated with longer treatment time [7]. In addition, other studies have indicated increased risk for maladaptive psychosocial sequels, such as depression, anxiety, problems of self-esteem and fluctuations in mood [9-13], and symptoms of posttraumatic stress [14,15]. However, many studies of the psychosocial effects of surviving cancer have included children with a wide variety of cancers, and often research has failed to separate the results according to type of cancer [13]. Another problem is the use of different criteria for the selection of controlgroups, and a lack of a longitudinal approach [16, 17].

Parental functioning is one of the strongest contributors to adjustment in children with chronic health conditions [18]. Emotional distress among parents remains heightened one year after diagnosis but appears to decrease over time [19]. However, adverse consequences for parents related to long-term physical and mental health has been reported [20], a significant number of parents still suffer from clinical distress five years post treatment [21].Thus, quality of survival should also include the long-term effects for the parents as well.

The objective of the present study was to explore aspects of mental health and psychosocial adjustment of children in remission from ALL and their parents compared to healthy controls. Regarding the length of treatment for ALL that can vary from 2 to 2.5 years, as well as the enormous stress associated with a diagnosis of cancer, and that children with ALL often are isolated from their peer groups for long periods of time, we hypothesized that children in remission from ALL would have more mental and psychosocial symptoms compared to healthy children.

PATIENTS AND METHODS

Patients

Children and adolescents in remission from ALL were recruited from two University Hospitals in Norway: Rikshospitalet-Radiumhospitalet Medical Centre in Oslo and St.Olavs Hospital in Trondheim. The children were born in the period 1989-1995, had a mean age of 11.8 (range 8.5-15.4), took part 4.2-12.5 years after ALL diagnosis, and were treated according to the Nordic protocol, The Nordic Society of Pediatric Hematology/Oncology (NOPHO-ALL, 1992): their parents were also invited to participate in the study. Children who suffered relapses, or who had other kinds of severe medical condition (e.g. Down's syndrome) were excluded. Of the 56 children who fulfilled the criteria for participation, a total of 40 (71.4), comprising 21 girls (52.5%) and 19 boys (47.5%), took part. Parental information was supplied by 36 mothers, whose mean age was 40.0 (range 30-55), and 21 fathers, whose mean age was 43.0 (range 32-58): each parent was asked to give their evaluation of the PedsQL proxy-report separately. Data regarding diagnoses and treatment protocols were collected from the medical records. The average age at the time ALL was diagnosed was 4.0 years (range 0-7.6). The average time since diagnosis was 7.9 years (range 4.2-12.5). The treatment categories were scored according to the Nordic protocol (NOPHO-ALL, 1992) with the following categories: 1) Standard risk (SR); 2) Intermediate risk (IR); 3) High risk (HR); 4) High risk-1 (HR-1); 5) High risk-2 (HR-2); and 6) Very high risk-1 (VHR). With regards to the small sample in the four last categories, we scored these as one category – high/very high risk. One child had been treated with chemotherapy combined with

radiation therapy (1800Cgy) , and the remaining children with chemotherapy only. One child was in the infant-risk group, treated according to the NOPHO-92 protocol HR-1. Sociodemographic characteristics and treatment-related variables are presented in Table 1.

The children treated for ALL were compared to a group of healthy children with a similar age and gender distribution (n=42), drawn by lots based on age and gender matches. (Table 1), recruited from two elementary schools and two junior high schools in the middle part of Norway, and from both urban and rural areas. Children with a psychiatric diagnosis or with other specific and relevant medical problems such as cognitive dysfunction were excluded. Informed consent was obtained from all of the children and adolescents, as well as from their parents. The study was approved by the Regional Ethics Committee of Medical Research.

INSERT TABLE 1 ABOUT HERE

Measures

Children`s mental health and psychosocial functioning

The parents completed the Child Behavior Checklist CBCL [22], while the children completed the standardised questionnaire Youth Self-Report (YSR) [23]. The Norwegian version has 112 problem items, 90 of them are common to both CBCL and YSR. For both forms the questions are scored 0 (no), 1 (sometimes), and 2 (often). Eight syndrome scales are generated; five of them are subdivided into two subscales. The internalising subscale includes withdrawal, somatic complaints, and anxiety/depression. The externalising subscale includes delinquent and aggressive behaviour. As population norms for these questionnaires have yet not been established in Norway, the present study reports raw scores. According to the American norm, corrected for sex and age, the 90^{th} percentile (T-score>63) is used as a cut-off point for total, internalising, and externalising scores implying psychiatric problems..

The Strength and Difficulties Questionnaire (SDQ) was used to assess the mental and psychosocial health in children and adolescents [24]. The SDQ is a brief behavioural screening questionnaire consisting of 25 items in addition to a supplement on the impact of the difficulties for the child and family. There are 5 subscales: Emotional Symptoms, Conduct Problems, Hyperactivity, Peer Problems and Prosocial Behaviour, the first four adding up to the Total Difficulties Score. Each item uses a 3-point ordinal Likert format and can be answered with: “not true”, “somewhat true” or “certainly true”, rated 0-2 for negatively worded items and rated inversely 2-0 for positively worded items. In this way, for all items, higher scores indicated more problematic attributes. The SDQ shows satisfactory reliability and validity [24, 25].

Parental Assessment

Parents were interviewed separately by a child psychologist using a modified version of the standardized, semistructured, investigator-based interview Parental Account of Children`s Symptoms (PACS) [26]. The PACS includes questions relevant for psychiatric assessment of the index children, as well as registration of sociodemographic factors.

Parent`s mental health

The General Health Questionnaire (GHQ-30) [27] were included to assess parents` own mental health. The GHQ-30 [27] is the most used screening instrument for distress, psychopathology and quality of life in adults, showing acceptable reliability and validity in studies of medical and psychiatric populations. The GHQ includes both positive and negative questions and the short version GHQ-30 contains 30 items covering symptoms considered to

reflect distress and psychopathology. GHQ-30 avoids using physical symptoms as indicators of distress.

Statistical Analysis
A T-test for independent samples was used to analyse differences in mental health and psychosocial functioning between the children treated for ALL and healthy children, as well as for their parent's QOL and mental health compared to healthy controls. 95% confidence intervals were calculated for the differences. In order to reduce the risk of making Type 1 errors due to multiple comparisons, a corrected alpha level of 0.01 was chosen, otherwise the significance level was set at $p<0.05$. The Statistical Package for Social Sciences (SPSS 14.0) statistics program for Windows was used for all the analyses.

RESULTS

Mental health and psychosocial functioning in children
The CBCL and YSR for children treated for ALL and their healthy controls are presented in Table 2. Children treated for ALL showed significantly higher symptom scores for the CBCL Total Problem Scale, as well as for the Internalizing and Externalizing Subscales. Six children had a CBCL score of ≥ 90 percentile indicative of severe problems, as reported by the mothers, while none in the controlgroup. The CBCL as reported by the fathers showed that five children scored ≥ 90 percentile, 1 child from the controlgroup. Children treated for ALL showed higher symptom scores for the YSR as well, but these results were not significant when the corrected alpha level of 0.01 was chosen. One child scored ≥ 90 percentile on the YSR, and one child in the controlgroup.

The SDQ self-report for children indicated no statistically significant differences in psychosocial health between children with ALL and their healthy controls. However, the SDQ parent self-report for mothers showed significant differences for the Emotional Symptoms Summary Scale ($t = 2.726$, $p = .008$, CI: 1.41 to 0.22).

INSERT TABLE 2 ABOUT HERE

Parent`s mental health
The fathers showed significantly more anxiety ($t= 2.195$, $p= 0.03$, 95% CI: 0.02 to 0.46) and depression ($t = 2.515$, $p= 0.02$, CI: 0.05 to 0.44) as measured by the GHQ-30 compared to healthy controls, while no such differences were found for the mothers.

DISCUSSION

This study presents descriptive data regarding mental health and psychosocial functioning in children and adolescents in remission from ALL and their parents. The results as reported by the parents confirmed our hypothesis showing that both children's mental health and psychosocial adjustment was significantly lower compared with healthy controls. The fathers's own mental health showed for some areas lower scores compared to controls.

Children's mental health
Children treated for ALL showed significantly higher symptom scores on all domains of the CBCL compared to healthy children. Six children had a CBCL score ≥ 90 percentile indicative of severe problems, as reported by the mothers. The CBCL as reported by the

fathers showed that five children scored ≥ 90 percentile. Children treated for ALL showed higher symptom scores for the YSR as well, but these results remained not significant when the alpha level was corrected to 0.01. One child scored ≥ 90 percentile on the YSR. The severity of a child's problems may appear quite different, and depend on whether the source of information is the parent or child [28]. Mental health professionals regarded mothers as more useful informants than children for both internalizing and externalizing problems [29]. Discrepancies between child and parent agreement in this present study should be further investigated. Although major psychiatric disturbance are not common among survivors of ALL [11], the few earlier studies have shown that this population is at increased risk for mental health and adjustment problems [13, 30]. A previous study indicates that the period after treatment is characterized by a higher risk of psychosocial problems compared to the actual treatment period. Children and adolescents off treatment reported higher levels of depression and anxiety, seven children (14%) reported a high level of depression, six of the children were off treatment [31].

In contrast to the results in this present study, whose significance is confirmed by the instrument CBCL, the SDQ self-report for children showed no statistically significant differences in psychosocial health between children with ALL and their healthy controls. The same tendency was shown for most of the SDQ parent proxy-report scales. This confirms that the choice of adequate instruments when assessing the situation for children treated for cancer should be of concern [32], since the measurements might lack sensitivity [33]. However, the SDQ Parent proxy-report as reported by mothers of children treated for ALL showed higher score for Emotional symptoms than did the healthy controls. As such, this finding confirms some of the CBCL findings.

Parents QOL and mental health

The fathers showed significantly more anxiety and depression as measured by the GHQ-30 compared to healthy controls, while no such differences were found for the mothers. Eiser (2005) points out that fathers often remain more involved in everyday life despite the child`s illness. This aspect may influence the father's own situation and needs, since by staying at home or at work more during the time the child is being treated, the fathers will not be able to get adequate help for his own emotionally needs, and this may affect his later adjustment. Even as research participants, fathers are often underrepresented in paediatric research samples [15, 20]. Many of the fathers in a previous study reported that they had feared that expressing their upsetting memories would be detrimental to other family members [15].

Limitations

The strength of our study includes how homogenous the sample of children with ALL is with respect to both diagnosis and age-span, and the use of a control group. However, limitation in our study should be noted. This study has a cross-sectional design, and we were therefore unable to control for premorbid functioning, the small size of our group of children was another drawback. Cross-sectional designs cannot determine causal relations, and their absence represents an important shortcoming in the present study and implies that the results should be treated with some caution. For the future, longitudinal designs should be emphasised with children treated for ALL, and for controls who have other types of cancers and treatments.

The findings based on the 21 fathers of ALL patients who participated in our study should also be treated with a degree of caution. But the result may indicate the need to pay attention to the mental health and adjustment of fathers during the time of the child's treatment as well as the rehabilitation phase. The fact that only 21 fathers participated may

indicate a common problem in clinical research, namely that more fathers should be included in future research on children with cancer and their parents.

CONCLUSION

This study shows that problems can be seen several years after diagnosis and treatment, and demonstrates the need for close awareness of adjustment related to mental health and psychosocial functioning in children in remission from ALL. To be able to detect and address actual problems effectively, children should be followed-up from returning to school and further into their academic careers. Parallel to the medical follow-up in clinics, outpatient centres should have this aspect of concern as well. Further research should consider within group differences in the group of children treated for ALL, with particular attention being paid to the type of treatment protocol, time since diagnosis, age at diagnosis, and family variables. Indeed, knowing what separates those children with good coping and adjustment from the others is critical.

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Table 1. *Sociodemographic characteristics of children with ALL and healthy controls. Treatment variables for children with ALL.*

	ALL (n = 40)	Healthy (n = 42)	t score	P
Gender			-.11	.91
Girl: n (%)	21 (52.5)	21 (50.0)		
Boy: n (%)	19 (47.5)	21 (50.0)		
Age at study			.14	.92
Mean (SD)	11.8 (1.9)	11.8 (1.9)		
Median	11.4	11.6		
Range	8.5-15.4	8.11-15.0		
Family Composition			-.75	.46
Both parents	31 (77.5)	29 (69.0)		
Single mothers	8 (20.0)	12 (28.6)		
Single fathers	1 (2.5)	1 (2.4)		
Parental Characteristics				
Age, median (range)				
Mother	40.0 (30-55)	40.0 (31-52)	-.25	.81
Father	43.0 (32-58)	43.5 (34-72)	-.09	.93
Education, median(range)				
Mother	14.0 (10-19)	13.0 (9-19)	.07	.95
Father	14.0 (10-20)	13.0 (10-19)	.84	.40
Community			.69	.49
Urban	15 (37.5)	18 (42.9)		
Rural	25 (62.5)	24 (57.1)		
Home			.72	.48
Own house	36 (90.0)	39 (92.9)		
Own apartment	3 (7.5)	3 (7.1)		
Renting apartment	1 (2.5)	-		
Economy			-.04	.96
Very satisfying	27 (67.5)	21 (50.0)		
Good	8 (20.0)	21 (50.0)		
Poor	5 (12.5)	-		
Diagnosis and treatment				
Age at diagnosis				
Mean (SD)	4.0 (1.9)	-		
Median	3.1	-		
Range	0-7.6	-		
Years since diagnosis				
Mean (SD)	7.9 (2.0)	-		
Median	7.1	-		
Range	4.2-12.5	-		
Treatment protocols				
Standard risk	15 (37.5)	-		
Intermediary risk	15 (37.5)	-		
High/very high risk	10 (25.0)	-		

***Table 2**: Mental health in children treated for Acute Lymphoblastic Leukemia and healthy controls.*
Statistical significance is set at p≤.01
95% CI = 95% confidence intervals at 5% level

Abbreviations: CBCL= Child Behavior Checklist, YSR=Youth Self-Report.

	ALL		Healthy					
	Mean	SD	Mean	SD	Difference	T score	p	95% CI
CBCL raw scores (mothers)	(n=36)		(n=38)					
Total behaviour score	22.19	(20.31)	11.18	(11.78)	11.01	2.87	.005	3.36 to 18.65
Internalising score	6.83	(6.71)	3.24	(3.13)	3.60	2.98	.004	1.19 to 6.00
Externalising score	6.92	(8.41)	2.92	(4.46)	3.99	2.57	.012	0.90 to 7.09
CBCL raw scores (fathers)	(n=21)		(n=26)					
Total behaviour score	23.43	(17.73)	9.54	(13.66)	13.89	3.03	.004	4.67 to 23.11
Internalising score	7.19	(6.49)	2.85	(4.01)	4.34	2.82	.007	1.24 to 7.45
Externalising score	6.38	(5.70)	2.11	(4.77)	4.26	2.79	.008	1.19 to 7.34
YSR raw scores	(n=32)		(n=30)					
Total behaviour score	28.72	(17.74)	20.27	(15.46)	8.45	1.99	.051	-0.02 to 16.93
Internalising score	8.94	(6.99)	5.80	(5.46)	3.14	1.96	.054	-0.06 to 6.33
Externalising score	8.81	(5.26)	6.00	(5.75)	2.81	2.01	.049	0.01 to 5.61

Paper III

Health and Quality of Life Outcomes

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Research

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Measuring health-related quality of life in young adolescents: Reliability and validity in the Norwegian version of the Pediatric Quality of Life Inventory™ 4.0 (PedsQL) generic core scales

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Abstract

Background: Health-Related Quality of Life (HRQOL) studies concerning children and adolescents are a growing field of research. The Pediatric Quality of Life Inventory (PedsQL™) is considered as a promising HRQOL instrument with the availability of age appropriate versions and parallel forms for both child and parents. The purpose of the current study was to evaluate the psychometric properties of the Norwegian translation of the Pediatric Quality of Life Inventory (PedsQL™) 4.0 generic core scale in a sample of healthy young adolescents.

Methods: A cross-sectional study of 425 healthy young adolescents and 237 of their caregivers participating as a proxy. Reliability was assessed by Cronbach's alpha. Construct validity was assessed using exploratory factor analysis and by exploring the intercorrelations between and among the four PedsQL subscales for adolescents and their parents.

Results: All the self-report scales and proxy-report scales showed satisfactory reliability with Cronbach's alpha varying between 0.77 and 0.88. Factor analysis showed results comparable with the original version, except for the Physical Health scale. On average, monotrait-multimethod correlations were higher than multitrait-multimethod correlations. Sex differences were noted on the emotional functioning subscale, girls reported lower HRQOL than boys.

Conclusion: The Norwegian PedsQL is a valid and reliable generic pediatric health-related Quality of Life measurement that can be recommended for self-reports and proxy-reports for children in the age groups ranging from 13–15 years.

Background

Mirroring a modern bio-psycho-social orientation toward the concept of health, the development of a multidimensional Health-Related Quality of Life (HRQOL) measurement has been an important concern of research in recent years. It is realized that an instrument measuring HRQOL must consist of the physical, mental, and social health dimensions delineated by the World Health Organization (WHO) [1]. HRQOL studies related to children are a relatively new field of research [2], still there are only a few

measures that assess Quality of life outcomes for children and adolescents [3]. Such studies can have considerable significance for understanding children's psychosocial functioning and development like their perception of illness and its effect on their daily life [4,5]. However, the lack of valid and reliable measures for children and adolescents is one significant limitation of current HRQOL research [6].

Issues related to young persons continuous and often rapid developmental change were initially not sufficiently realized [4,7]. A pediatric health-related quality of life (HRQOL) instrument which includes a developmental perspective must for instance show sensitivity to both cognitive and emotional changes throughout the age span. Daily functioning in contexts relevant for children, such as school and community, should also be assessed [8].

Furthermore, a problem of these scales has been low concordances between proxy-and self-reports on HRQOL instruments. This has been observed in studies of children in both pediatric and psychiatric population [9,10]. Concordances tend to be lower for internalizing problems (eg. depression) than for externalizing problems (eg. hyperactivity) [11]. The presence of low concordance between proxy-and self-reports suggests a critical need in pediatric HRQOL measurement for reliable and valid child self-report instruments for the broadest age range possible [9].

The Pediatric Quality of Life Inventory (PedsQL) [9] is considered one of the most promising HRQOL instruments for children and adolescents, integrating generic core scales and disease-specific modules into one measurement system [12].

The instrument includes a broad age range with developmental sensitivity as well as categories for both parents and the young persons themselves. The PedsQL version 4.0 builds on programmatic instrument development research during the past 15 years, beginning with the measurement of pain and functional status [13]. The 4.0 version was designed to measure the core health dimensions delineated by WHO [1], including role (school) functioning [9], and were developed through focus groups and cognitive interviews [6]. The PedsQL 4.0 has been proposed as a valid and reliable generic pediatric HRQOL measurement that can be used for self-reports and proxy-reports in age groups ranging from 2 to 18 years [9], and can also be used in clinical practice, clinical trials, and research, as well as school health settings, and community populations [7,9].

The PedsQL is translated into many European and other international languages, and widely used in research. PedsQL was translated into Norwegian during 2002/2003, at that time no other HRQOL measurements for children were available in Norway. When selecting a HRQOL measure it will be important to examine its psychometric adequacy as well as its ability to tap outcomes of primary interest to a particular investigation [14]. The importance of validating new translations should be emphasized to investigate the acceptability of the psychometric properties for further use in both clinical practice and research. This first validation study of the PedsQL Norwegian version is a pilot study with young adolescents, and is part of a larger study with a broader focus on young adolescent's quality of life and mental health.

The objective of the current paper was to evaluate reliability and validity of the Norwegian translation of the PedsQL™ (version 4.0 generic core scale) in a sample of healthy young adolescents. The focus in the present paper is therefore on the scales that are relevant for adolescents.

Methods

Participants

A sample of 440 young adolescents and their parents were recruited through five junior high schools in Norway, three from urban and two from rural areas. A total of 440 questionnaires were distributed and 425 were returned, which gives a response rate of 96.6%.

Self-report forms were completed by 425 adolescents, 235 girls (56%) and 184 boys (44%), six did not report gender. In junior high schools in Norway adolescents between 13 to 15 years of age are separated in three different grades and participants were distributed as follows for 8th, 9th and 10th grade; 33%, 33%, 34%, respectively.

Proxy-reports were completed by 237 (56%) caregivers. The proxy-reports were completed by 139 (59%) mothers, by both parents in 69 (29%) of the cases, by 27 (11%) fathers, or by other caregivers such as grandparents 2 (0.8%). For 229 adolescents both adolescent self-report and parent proxy-report on the PedsQL were available. Information about non-response in the sample of adolescents as well as the sample of parents was not available, because of the anonymity required. Sociodemographic characteristics of the sample are given in Table 1. The Data Inspectorate and the Regional Committee for Medical Research Ethics approved the study. Written parental informed consent and child assent were obtained.

Measures

The 23-item PedsQL, version 4.0 Generic Core Scales, can be grouped into 4 domains of HRQOL: 1) Physical Functioning (8 items), 2) Emotional Functioning (5 items), 3) Social Functioning (5 items) and 4) School Functioning (5 items). These scales are feasible for child self-report including ages 5 to 7, 8 to 12 and 13 to 18 years. Parent

Table 1: Sociodemographic characteristics of 419 adolescents and their parents

Adolescents	**N**	**%**
Total sample	419	
Girls	235	56.1
Boys	184	43.9
School grade:		
8th grade	140	32.9
9th grade	142	33.4
10th grade	143	33.7
Parental education and economy		
Mothers	216	
Mothers education:		
Elementary school	10	4.7
Highschool graduate	51	23.6
Post high school	155	71.7
Fathers	110	
Fathers education:		
Elementary school	5	4.4
Highschool graduate	25	22.8
Post high school	80	72.8
Economy	235	
Very satisfying	26	11.1
Good	198	84.2
Poor	11	4.7

proxy-report includes ages 2 to 4, 5 to 7, 8 to 12 and 13 to 18, and assesses parent's perceptions of their child's HRQOL.

The items for self-report and proxy-report are essentially identical, differing in developmentally appropriate language, and first or third person tense. The instructions ask how much of a problem each item has been during the past 1 month. A 5-point response scale is utilized across child self-report for ages 8 – 18 and parent proxy-report (0 = never a problem; 1= almost never a problem; 2 = sometimes a problem; 3 = often a problem; 4 = almost always a problem). Subjects are requested to rate how much problems they experienced during the past month with health (eg. "I hurt or ache"), activities (eg. "It's hard for me to run"), or feelings (eg. "I feel afraid or scared").

Items are reverse-scored and linearly transformed to a 0 to 100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0), so that higher scores indicate better HRQOL. Scale scores are computed as the sum of the items divided by the number of items answered (this accounts for missing data). In addition to the four subscales, two summary scores can be computed. Physical Health Summary score (8 items) is the same as the Physical Functioning subscale, and Psychosocial Health Summary score (15 items) is computed as the sum of the items divided by the number of items answered in the Emotional, Social, and School Functioning subscales.

The translation and linguistic validation of the PedsQL questionnaire followed recommended guidelines [15,16]. Two independent forward translations were conducted by a psychiatrist and a clinical psychologist, the translators discussed semantic and conceptual discrepancies and finally developed a consensus forward translation. The translation of the first reconciled forward version of the PedsQL questionnaire back into the source language was done by a skilled english speaking person with experience from living in English speaking countries.

In a following pilot-project, the questionnaire was administrated to 10 children, 12 adolescents and 23 parents to test the interpretation and understanding of items and response ratings. Cognitive interview techniques [15] were used to obtain feedback about the interpretation and understanding of items and respons ratings. The questionnaires were then revised in response to feedback from children and parents. A written report was sent to Varni for further review. The relevant changes in the translation process were reviewed and authorised by Varni. In addition to the PedsQL 4.0, the questionnaires included information about children's socio-demographic characteristics.

Procedure

Local junior high schools were contacted and teachers distributed written consent forms that the adolescents presented to their parents. Each pupil received an envelope, which contained information and a questionnaire for their parents. Parents were asked to return the completed questionnaire in a pre-stamped envelope. The participants could further contact the researchers to obtain additional information. Approvals signed by the parents and returned to the teacher, confirmed that the adolescent had permission to participate.

The self-report instruments were administrated and completed in the classrooms. Children were given verbal and written information before completing questionnaires in class, under the supervision of a research assistant.

Statistical analysis

Scale internal consistency reliability was determined by calculating Cronbach's alpha coefficient [17]. Scales with reliabilities equal to or greater than 0.70 were considered satisfactory and are also recommended for comparing patient groups [18,19].

We used exploratory factor analysis to examine the structure of relationships between the items of the PedsQL™

4.0 and to compare the factor structure in the present study with the structure reported for the original PedsQL™ [9]. Regarding Varni's results where the school functioning items loaded on two separate factors, we expected to find a five factor structure. To extract the factors we applied Principal Component Analysis, with oblique rotation (Direct Oblimin). Factors with an eigenvalue less than 1 were disregarded.

Validity was further examined by exploring the intercorrelations between and among the four PedsQL Subscales [20]. To strengthen faith in the validity of the PedsQL version 4.0, multitrait-monomethod correlations (eg. correlations among subscales within self-report and proxy-report) should be lower than monotrait-multimethod correlations (eg. concordance between self-report and proxy-report for the same subscale). Correlations are designated as small (0.10–0.29), medium (0.30–0.49), and large (=0.50) [21]. Given shared method variance [18] and that the PedsQL items were developed to measure an integrated multidimensional construct (pediatric HRQOL), it was expected that heterotrait-monomethod correlations among the Subscales would be medium to large (0.30–0.50). Proxy/child concordance for the same subscale was furthermore expected to demonstrate medium to large effect sizes.

Based on previous literature [9] it was anticipated that the Physical Functioning Subscale would demonstrate the largest concordance, and heterotrait-heteromethod concordance was expected to be small. In addition, we calculated intraclass correlation coefficients (ICC) to assess parent and child convergence on the PedsQL subscales. ICC takes into account not only the correlation but also differences in intercept and slope between replicant ratings [22]. Paired t-test were used to assess the extend to which adolescents or proxies systematically scored lower on the subscales of the PedsQL. As a measure of the minimally important difference in scores, we calculated the standardized response mean, a distribution-based approach that compares temporal change by the standard deviation of change [21]. Standardized response mean of 0.2–0.5, 0.5–0.8, and >0.8 are regarded as small, moderate, and large, respectively. Gender differences in the self-report scales were analysed with two-sample t-test. For all analyses, we used SPSS statistical software version 12.0 (SPSS Inc., Chicago, III, USA) and a critical value (α) of 5%.

Results

Scale-level analysis

Mean scale scores, percentage of scores at the floor and ceiling and Cronbach's alpha are shown in Table 2. All the self-report scales and proxy-report scales exceeded the minimum reliability standard of 0.70. No floor effects were found on self or proxy-report for this healthy sample of adolescence. Ceiling effects existed and ranged from minimal (eg. 2.6% and 3.4% for self and proxy-report, respectively for Total score) to moderate (eg. 26.5% and 24.2% for self and proxy-report for Physical Functioning). The largest effect was found for Social Functioning (43% and 46% for self and proxy-report). Table 2 gives information about scale descriptives and internal consistency reliability for the PedsQL 4.0.

Further, for all 23 items, item means for self-report ranged from 67.9 to 99.9 with 12 of 23 items falling within a 10-point range. Item means for proxy report ranged from 67.8 to 98.9, with 13 items falling within a 10-point range. Two items from the Physical health scale have a relatively small standard deviation namely: 1.2 (item 5) and 9.6 (item 1) for the self-report, 8.2 (item 5) and 8.8 (item 1) for the proxy report. The remaining standard deviations ranged from 13.3 to 25.8 for self-report items and 14.8 to 23.7 for proxy-report items.

Construct validity

Adolescent-parent report

Monotrait-multimethod correlations are all statistically significant but generally modest. Table 3 shows the intercorrelations between and among the four subscales of the PedsQL.

For the subscale School Functioning we found moderate (>0.40) intercorrelations between adolescents and parents. All multitrait-multimethod correlations were lower than the monotrait-multimethod correlations. However, some of the multitrait-multimethod correlations are higher than the convergent correlations of the other three subscales, in particular for Emotional functioning and Social functioning. The average convergent correlation is 0.31 and the average off-diagonal correlation is 0.22. This indicates that on average the monotrait-multimethod correlations are higher than the multitrait-multimethod correlations. The intraclass-correlation (ICC) was relatively low for all scales, indicating poor to fair (<0.40) child-proxy agreement for all scales but one. Moderate agreement (ICC = 0.41) was found for the sub scale measuring School functioning. Lowest agreement was found for the emotional functioning scale (ICC = 0.21). The results of the paired t-tests suggested that parents scores were systematically higher than that of adolescents for Emotional functioning ($t = 2.32$; $df = 228$; $p = 0.02$) and School functioning ($t = -5.28$; $df = 228$; $p < 0.001$). Conversely, parents reported lower on the subscales for Physical functioning ($t = 2.9$; $df = 233$; $p = 0.004$) and Psychosocial health scale ($t = -2.7$; $df = 231$; $p = 0.007$). The scores on the Social Functioning scale did not yield statistically significant differences between parents and adolescents ($t = 1$; $df = 228$; $p = 0.268$). Only the difference found for

Table 2: Scale Descriptives and Internal Consistency Reliability for PedsQL 4.0

Scale	Items	N	Mean	SD	Percentage floor	Percentage ceiling	Cronbach's alpha
Adolescent self-report							
Total score	23	414	85.29	11.11	0	2.6	.84
Physical health	8	422	91.12	10.35	0	26.5	.78
Psychosocial health	15	416	82.16	12.50	0	3.1	.82
Emotional functioning	5	424	77.15	17.32	0	10.4	.79
Social functioning	5	424	88.12	13.11	0	43.6	.80
School functioning	5	424	78.02	15.47	0	8.3	.73
Parent proxy-report							
Total score	23	232	86.10	10.20	0	3.4	.77
Physical health	8	236	88.83	11.76	0	24.2	.80
Psychosocial health	15	234	84.66	10.92	0	4.3	.88
Emotional functioning	5	238	79.98	14.13	0	12.7	.78
Social functioning	5	238	88.05	13.37	0	46.0	.82
School functioning	5	238	88.97	12.37	0	13.5	.75

School Functioning corresponded to a small effect size (0.35), the other differences between parents and adolescents all have effect sizes below 0.20.

Gender differences

A statistically significant gender differences was found on the emotional subscale, with girls on average scoring lower than boys (t = 4,79; df = 416, p < 0.001). However, the mean score for girls (73.92 and sd = 17.53) as well as for boys (81.85 and sd = 15.83) were at the high end of the scale. No statistically significant gender differences were found for the remaining scales.

Factor analysis

The results of the factor analysis for self-report and proxy-report are shown in table 4 and 5.

An eigenvalue cutoff of 1.0 resulted in a five factor solution for self-report and proxy-report, accounting for 56 % and 61 % of the variance. The school functioning items split into two different factors, like the originally version. For physical functioning, item 5 ("hard to take bath or shower"), item 6 ("hard to do chores around the house") and item 7 ("hurth or arche") split into different factors. The items related to emotional and social functioning are consistent with the original PedsQL™ version [23].

Discussion

This article describes the psychometric properties of the Norwegian translation of the PedsQL™ 4.0 generic core scale in a healthy sample of young adolescents and their caregivers. The results from the present study resemble the findings of the original PedsQL™ [9] and the UK-English version [24] and as such confirm that the instrument can be used for self-reports and proxy-reports in school health settings and community populations.

Reliability

Internal consistency was satisfactory with Cronbach's alph coefficient >0.70 for all four subscales. No floor effects were found for any of the scales. The presence of ceiling effects in the present study may be expected in generic HRQOL instruments, because they are made to be applicable to a wide range of populations [24]. This could be a

Table 3: Intercorrelations between and among PedsQL subscales

	Adolescent self-report				Parent proxy-report		
Adolescent self-report	1	2	3	4	5	6	7
1 Physical functioning							
2 Emotional functioning	**0,65**						
3 Social functioning	**0,66**	**0,61**					
4 School functioning	**0,56**	**0,54**	**0,46**				
Parent proxy-report							
5 Physical functioning	0,35	*0,12*[ns]	*0,21*	*0,35*			
6 Emotional functioning	0,25	0,22	*0,29*	*0,30*	**0,52**		
7 Social functioning	*0,20*	*0,12*[ns]	0,28	*0,25*	**0,51**	**0,50**	
8 School functioning	*0,17*	*0,15*	*0,19*	0,42	**0,53**	**0,54**	**0,49**

Notes: N = 229; NS = Not significant at 5% level; Multitrait-monomethod correlations are in bold; monotrait-multimethod correlations are underlined; multitrait-multimethod correlations are italicised.

Table 4: PedsQL 4.0 Norwegian version Factor Loadings for Adolescents Self-Report

Scale/Item	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5
Physical Functioning					
1. Hard to walk more than one block	,079	**,702**	-,356	,086	,299
2. Hard to run	,327	**,887**	-,359	,145	,270
3. Hard to do sports or exercises	,375	**,851**	-,322	,142	,240
4. Hard to lift something heavy	,251	**,568**	-,484	,052	,363
5. Hard to take bath or shower	-,036	,039	,041	**,509**	-,195
6. Hard to do chores around house	**,497**	,255	-,363	-,008	,421
7. Hurth or arche	**,562**	,460	-,441	,229	,436
8. Low energy	,531	**,595**	-,474	,131	,371
Emotional Functioning					
1. Feel afraid or scared	**,723**	,344	-,479	,183	,323
2. Feel sad or blue	**,799**	,419	-,385	,092	,387
3. Feel angry	**,742**	,210	-,363	,027	,418
4. Trouble sleeping	**,553**	,301	-,249	,182	,305
5. Worry about what will happen	**,641**	,387	-,492	,035	,489
Social Functioning					
1. Trouble getting along w/peers	,500	,349	**-,730**	,032	,219
2. Other kids not wanting to be friend	,481	,369	**-,770**	,164	,213
3. Teased	,450	,299	**-,583**	,163	,161
4. Doing things other peers do	,201	,401	**-,772**	,061	,341
5. Hard to keep up when play with others	,247	,400	**-,799**	,019	,412
School Functioning					
1. Hard to concentrate	,377	,326	-,341	,129	**,825**
2. Forget things	,435	,335	-,330	,024	**,799**
3. Trouble keeping up with schoolwork	,418	,387	-,317	,100	**,825**
4. Miss school – not well	,462	,287	-,161	**,571**	,286
5. Miss school – doctor appointment	,109	,105	-,163	**,791**	,251

Eigenvalue cutoff: 1.0; Total Variance Explained for Adolescents Self-Report: 57%; Bold = highest factor loading for each item.

sample specific phenomenon, and should be further explored through the administration of PedsQL™ to children with different health issues including those children and adolescents experiencing acute health problems.

Regarding single item descriptives, it is interesting to note the low standard deviation for two items from the Physical health scale. These results are challenging the requirements of equivalent item means and variance. However, this finding may be typical for the way PedsQL behaves in a healthy sample.

Validity

Our results showed that on average the monotrait-multimethod correlations are higher than the multitrait-multimethod correlations. This high multitrait-multimethod correlations indicate that the different traits measured in the four subscales show considerable overlap. For example, three items in the physical functioning scale ("hard to take bath or shower", "hard to do chores around the house", and "hurt or ache") are loading on another factor than the other physical functioning items. This could be more related to a fatigue component, which seems more relevant for a chronically ill patient population than healthy adolescents. A confirmatory factor analysis could provide further insight in the degree of overlap between items hypothesized to measure different constructs, and also in the equivalence of factor loadings on the items within a single factor.

The adolescent-parent agreement did not exceed the preferred intra-class correlation of 0.40, except for the scale measuring School function. Lack of agreement between parents and children may result from differences in perception of the same situation, and also differences in interpretation of different items [11], or may be due to the young adolescents becoming more independent from the parents. As opposed to some previous research [25], our findings did not find higher agreement between parents and adolescents regarding physical problems. Parents rated the physical function scale lower than their children's reports. Further, a recent study found that proxy and self-report correlation was higher for children with health problems than for healthy children [24]. Parents and children may be more likely to share information about an issue if it is perceived as a problem [24]. However, the strength of this agreement has also been challenged in research on children with Cystic Fibrosis [8].

Table 5: PedsQL 4.0 Norwegian version Factor Loadings for Parent Proxy-Report

Scale/Item	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5
Physical Functioning					
1. Hard to walk more than one block	,151	**,808**	-,143	,190	-,263
2. Hard to run	,322	**,816**	-,364	,305	-,149
3. Hard to do sports or exercises	,302	**,812**	-,392	,326	-,196
4. Hard to lift something heavy	,230	**,774**	-,260	,225	-,253
5. Hard to take bath or shower	,003	**,687**	-,152	,196	-,210
6. Hard to do chores around house	,052	,309	-,272	,291	**-,738**
7. Hurth or arche	,491	,339	-,202	,279	**-,664**
8. Low energy	,428	,421	-,426	,384	**-,692**
Emotional Functioning					
1. Feel afraid or scared	**,775**	,187	-,281	,294	-,263
2. Feel sad or blue	**,716**	,338	-,471	,367	-,411
3. Feel angry	**,597**	,166	-,293	,420	-,387
4. Trouble sleeping	**,680**	,158	-,159	,180	-,112
5. Worry about what will happen	**,715**	,344	-,432	,391	-,141
Social Functioning					
1. Trouble getting along w/peers	,327	,316	**-,833**	,279	-,259
2. Other kids not wanting to be friend	,337	,231	**-,905**	,358	-,118
3. Teased	,237	,277	**-,776**	,359	-,169
4. Doing things other peers do	,241	,530	**-,618**	,462	-,013
5. Hard to keep up when play with others	,170	,359	-,545	**,618**	,026
School Functioning					
1. Hard to concentrate	,321	,278	-,296	**,852**	-,222
2. Forget things	,222	,267	-,222	**,761**	-,370
3. Trouble keeping up with schoolwork	,363	,207	-,369	**,841**	-,214
4. Miss school – not well	,408	,250	-,108	,352	**-,661**
5. Miss school – doctor appointment	**,386**	,147	-,135	,348	-,263

Eigenvalue cutoff: 1.0; Total Variance Explained for Proxy-Report: 60%; Bold = highest factor loading for each item.

Another explanation for the low concordance between adolescents and parents regarding physical functioning can be seen in the factor analysis (table 4 and 5) which indicated that items concerning physical functioning (5, 6, 7) were rather diffuse components related to physical as well as emotional domains, and therefore difficult to distinguish, something that could further influence both adolescents and parents ratings. Children reported lower HRQOL on the emotional scale compared with their parents, and corresponds to the previous research of Modi & Quittner [8]. Young children may have difficulty expressing their emotions directly to their parents, another factor could be the likeliness that proxy-report reflect parental anxiety about their child [24]. This aspect should be further investigated in different patient populations, and confirms the need to measure both child and parent perspectives when evaluating HRQOL. Clinically, those discrepancies give a potential for interventions emphasizing the children's subjective ratings, as well as their parents [8,11].

Regarding gender differences, we found that girls reported lower levels of emotional functioning than boys. This is consistent with previous research regarding gender differences in emotional health [26-28]. The gender differences would seem to reflect a genuine disparity between boys and girls and therefore gives further evidence for the validity of PedsQL™ as a sensitive measure of the emotional functioning of children and adolescents [24].

The result of the factor analysis resembles Varni's five-factor structure in the original PedsQL™ version, except for some items. Like the results of Varni *et al.* [9] two of the five items (4 and 5) related to school functioning were loading to another factor. A natural explanation for this could be that the three first items related to school functioning (eg. "hard to concentrate", "forget things", "trouble keeping up with schoolwork") are more likely to have a cognitive component, while the others are more related to physical aspects (eg. "miss school because not feeling well", "miss school because of doctor appointment").

All items related to social functioning had a clear factor loading, as well as the items related to emotional functioning. The physical items seem to split into three factor loadings (see Table 4). Item 1 ("hard to walk more than a block"), item 2 ("hard to run"), item 3 ("hard to do sports or exercises"), item 4 ("hard to lift something heavy") and item 8 ("low energy") are all loading on factor 2. Further, item 6 ("hard to do chores around the house", item 7

("hurth or arche") on factor 1. Item 5 ("hard to take bath or shower") on factor 4. In the results of Varni *et al*. [9] the loading for the four first items for the physical functioning scale is similar to our results. The factor loadings for the proxy-report also indicate that the physical factor loadings seem to have the same pattern, most of the factor loadings are similar to the child self-report. It should be pointed that comparisons to the factor structure obtained in the original PedsQL™ publication may be restricted and less comparable due to the restricted age range in this present study. The restricted age range, with a healthy population, may attenuate the variability achieved. The results from the factor analysis regarding item 5, 6 and 7 in the Physical Functioning scale, as well as items 4 and 5 in the School Function scale may be typically for healthy samples, the factor structure should therefore be reinvestigated in clinical samples.

Limitations

Concerning the Norwegian PedsQL™ 4.0 validation study, the present findings have several potential limitations. Test-retest reliability and responsiveness are not reported. Information on non-participants was not available, something that can limit generalizability. In the American validation study, the PedsQL differentiated HRQOL between healthy children and children with acute or chronic health conditions. This will also be an important future goal to investigate for the Norwegian PedsQL version, and is something the authors are taking into consideration. In this study the age range utilized was quite restricted. Regarding developmental aspects, further research should investigate the Norwegian PedsQL versions' psychometric properties concerning the upper-age range which the adolescent PedsQL was made for, as well as younger age-groups.

Conclusion

The PedsQL Norwegian version is generally a valid and reliable instrument, replicating some of the earlier findings for the originally version. The Norwegian PedsQL™ 4.0 version will be a valuable tool for assessing the HRQOL of young adolescents in Norway.

The imperfect concordance observed between self-and proxy-reports supports the need to measure the perspectives of child and parent in evaluating pediatric HRQOL [9,29]. It would be important emphasizing the clinically usefulness regarding child-parent discrepancies still when challenging the validity of measures.

Competing interests

The author(s) declare that they have no competing interests.

Authors' contributions

TR made contribution to the study design, data collection, statistical analysis, interpretation of data and the drafting of the paper. THD contributed to the study design, interpretation of the data, drafting and revising the manuscript. MV contributed to the statistical analysis, interpretation of the data and manuscript drafting. AV has contributed the interpretation of the data and manuscript drafting. All authors read and approved the final manuscript.

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Paper IV

The Pediatric Quality of Life Inventory (PedsQL™) 4.0 as an assessment measure for depressive symptoms: A correlational study with young adolescents

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ABSTRACT

Background: Health-related quality of life (HRQOL) is today considered as an important assessment measurement, but still only a few measures assess HRQOL outcomes for children and adolescents. One of them is the Pediatric Quality of Life Inventory (PedsQL™). This correlation study explored the associations between depressive symptoms in young adolescents and the PedsQL scores when controlling for known risk factors.
Methods: An adolescent sample (N=425) completed a battery of measures including the PedsQL™ Norwegian version, the Short Mood and Feeling Questionnaire (SMFQ), the Social Phobia and Anxiety Inventory for children (SPAI-C), and the occurrence of Stressful Life Events (SLE).
Results: The results showed a mild to moderate correlation between the measures PedsQL, SMFQ, SPAI-C and SLE. The presence of depressive symptoms significantly predicted the PedsQL scores for the adolescence, and explained 17 % of the variance in outcome for the PedsQL Total Scale.
Conclusion: The findings suggest that the PedsQL™ is an adequate assessment instrument regarding depressive symptoms in young adolescents, and can be useful in both clinical practise and further research as an assessment measure regarding children's mental health.

Key words: Health-related quality of life; depression; young adolescents.

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BACKGROUND

Depression, both symptoms and disorders, increases throughout adolescence with a marked of increase in early and middle adolescence [1, 2]. Studies have shown that 8 % of Scandinavian adolescents aged 13-18 years were having a moderate, and 2% a severe depressive symptom level [3]. This is consistence with other international studies [4], and

further a lifetime prevalence estimated to range from 15% to 20% among adolescents [5]. A relatively high correlation is found between depressive and anxiety symptoms. Studies of social anxiety in childhood show that anxiety symptoms predict later depression [6, 7].

Developing measures that can reliably identify protective factors for psychiatric disorders with high prevalence such as depression is of general interest [8], especially since an early onset of depression has been shown to predict poor prognosis [9-11]. However, little attention has been paid to the health-related quality of life (HRQOL) in children and adolescents with psychiatric disorders [12, 13]. Despite the growing interest in HRQOL outcomes, there are still only a few measures assessing HRQOL in children and adolescents [12]. Among 20.000 publications on HRQOL , approximately 13 % were related to children (N= 3050). More recent research has emphasised the assessment of HRQOL in psychiatry as an important part of the diagnostic process because it can give insight into the areas of functioning in which a child is suffering the most. [14]. Finding [13] show that having a psychiatric problem is at least as large on HRQOL as the impact of having a chronically physical disorder. Improvement in the quality of everyday life should therefore be an important treatment goal [14], and can further give information regarding HRQOL areas that can be of a protective value. The concept of HRQOL could also be used to define outcome variables in treatment outcome research.

The term HRQOL is frequently used interchangeably with quality of life (QOL) [15]. However, QOL is considered as a broader general conceptual term related to non health-related aspects of life (e.g., the evaluation of the impact of architectural surroundings on general well-being) [16], further QOL is often used synonymous with happiness or material wealth. The concept of HRQOL refers specifically to the impact health and illnesses may have for the individual well-being and functionality in daily life, with respect to the physical and the psychological (including the emotional and cognitive), as well as the social health dimensions delineated by the World Health Organization [17].

The Pediatric Quality of Life Inventory (PedsQL^{TM}) [18-21] is presenting one of the most promising HRQOL instruments for children. This is because it integrates generic core scales and disease-specific modules into one measurement system [22]. The PedsQL 4.0 has been proposed as a valid and reliable generic pediatric HRQOL measurement instrument that can be used for self-reports and proxy-reports in age groups ranging from 2 to 18 years [21], and can also be used in clinical trials, research, clinical practice, as well as school health settings, and community populations [21, 23]. A Norwegian version of the PedsQL 4.0, showed adequate psychometric properties in earlier work [24].

Several important risk factors that influence levels of depressive symptoms have been identified, such as adverse life events in adolescents [10], and that also seems to play a vital role in later episodes of depression independent of previous symptoms [25, 26]. Previous studies have indicated that the occurrence of a serious life event or an accumulation of damaging experiences (e.g., loss of social support systems, loss of a parent, a childhood history of physical or sexual abuse), are important risk factors for depression in adolescence [10, 11]. When exploring the associations between depressive symptoms and HRQOL scores, it is thus important to control for known risk factors such as adverse life events and social anxiety.

In this first phase to examine the value of the PedsQL as an assessment measure regarding young adolescent's mental health, the association between depressive symptoms and HRQOL will be investigated. The purpose of this study was to examine the value of the PedsQL as an assessment instrument regarding depressive symptoms in a sample of young adolescents when controlling for known risk factors such as adverse stressful life events and social anxiety.

METHODS

Procedure

Six randomly selected schools were invited to participate, one school declined. Three of the schools were localized in Trondheim, and two in the surrounding villages in the countryside of Norway. Local junior high schools were contacted and teachers distributed written consent forms that the adolescents presented to their parents. Each pupil received an envelope, which contained information and a questionnaire for their parents. Parents were asked to return the completed questionnaire in a pre-stamped envelope. The participants could further contact the researchers to obtain additional information. Approvals signed by the parents and returned to the teacher, confirmed that the adolescent had permission to participate. The self-report instruments were administrated and completed in the classrooms.

Children were given verbal and written information before completing questionnaires in class, and a research assistant was available to answer potential questions regarding the scales. Written parental informed consent and child assent were obtained. The Data Inspectorate and the Regional Committee for Medical Research Ethics approved the study.

Participants

A total of 440 questionnaires were distributed and 425 were returned, which gives a response rate of 96.6%.

Self-report forms were completed by 425 adolescents, 235 girls (56%) and 184 boys (44%), six did not report gender. In junior high schools in Norway adolescents between 13 to 15 years of age are separated in three different grades and participants were distributed as follows for 8th, 9th and 10th grade; 33%, 33%, 34%, respectively.

Information about non-response in the sample of adolescents as well as the sample of parents was not available, because of the anonymity required. Sociodemographic characteristics of the sample and information about the young adolescent's experience of stressful life events (SLE) are given in Table 1.

INSERT TABLE 1 ABOUT HERE

Measures

Pediatric Quality of Life inventory ™ (PedsQL™) 4.0 Norwegian version

The 23-item PedsQL, version 4.0 Generic Core Scales, can be grouped into 4 domains of HRQOL: 1) Physical Functioning (8 items), 2) Emotional Functioning (5 items), 3) Social Functioning (5 items) and 4) School Functioning (5 items). The Generic Core Scales are comprised of child self-report included ages 5 to 7, 8 to 12 and 13 to 18 years. Parent proxy-report includes ages 2 to 4, 5 to 7, 8 to 12 and 13 to 18, and assesses parent`s perceptions of their child`s HRQOL.

The items for self-report and proxy-report are essentially identical, differencing in developmentally appropriate language, and first or third person tense. The instructions ask how much of a problem each item has been during the past 1 month. A 5-point response scale is utilized across child self-report for ages 8 – 18 and parent proxy-report (0 = never a problem; 1= almost never a problem; 2 = sometimes a problem; 3 = often a problem; 4 = almost always a problem). Subjects are requested to rate how much problems they experienced during the past month with health (eg. "I hurt or ache"), activities (eg. "It's hard for me to run"), or feelings (eg. "I feel afraid or scared").

All items are reverse-scored and linearly transformed to a 0 to 100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0), so that higher scores indicate better HRQOL. Scale scores are

computed as the sum of the items divided by the number of items answered. The PedsQL has shown adequate psychometric properties [21, 24]. A Cronbach's alpha ≥ 0.77 was obtained for the Norwegian translation of the PedsQL, which indicates good internal consistency [24].

Stressful life events (SLE)

Adolescents were asked for the lifetime occurrence of the following stressful life events: death in family, illness in family or self, divorce in family, open category of negative life event and bullying. Prior to the item tapping the occurrence of bullying, there was a short ingress that defined and differentiated bullying from teasing in accordance with the definition given by Solberg and Olweus [27]. All items had a dichotomous response format. The SLE score is simply the sum of the total number of stressful life events reported for each adolescent. The selected life events are all in the Life Event Scale of Holmes and Rahe [28] and in the Life Events Checklist [29-32], and they are frequently selected as severe adverse life events reported by adolescents [33, 34].

Social Phobia and Anxiety Inventory for Children (SPAI-C)

The SPAI-C is a 26-item self-report instrument designed to assess social anxiety and social anxiety disorder among children and young adolescents [35, 36]. High scores reflect higher severity of social anxiety. Items assess a range of potentially anxiety-producing situations (i.e. reading aloud, performing in play, eating in the school cafeteria) including physical and cognitive symptoms as well as avoidant behaviours. Each item is rated on a 3-point Likert scale ("never or hardly never", "sometimes", "most of the time or always"). The SPAI-C has been found to possess adequate psychometric properties and acceptable convergent and discriminant validity [36]. A Cronbach's alpha of 0.91 was obtained for the Norwegian translation of the SPAI-C, which indicates good internal consistency [37].

Short Mood and Feeling Questionnaire (SMFQ)

The brief 13 item screening version of the Mood and Feeling Questionnaire (MFQ) was used. All items are negatively phrased on a three-point Likert scale. High scores reflect higher severity of depressive symptoms [38-40]. The SMFQ is an unifactorial scale with adequate reliability (Cronback's alpha = .90) [41]. It correlates highly with more extensive evaluations like the Childrens' Depression Inventory (CDI) [42] with a correlation of $r = .67$, and the Diagnostic Interview Schedule of Children (DISC) [43] with a correlation of $r = .51$ [39]. The SMFQ differentiates between referred child psychiatric subjects and unselected paediatric controls, and between depressed subjects and non-depressed subjects in a general population sample [39].

Statistical analysis

The study used a cross-sectional design. Correlations between the included variables were calculated. A multiple hierarchical linear regression analysis was conducted to investigate the relationship between depressive symptoms and the HRQOL scores as measured by the PedsQL when the potential effects of gender, age, SLE and SPAI-C were statistically controlled for. The following independent variables were entered in separate steps as predictors: 1) gender, 2) age 3) stressful life-events (SLE), 4) depressive symptoms (SMFQ), 5) social anxiety (SPAI-C), 6) SMFQ and SLE.

Additional independent multiple hierarchical linear regression analysis was conducted for each of the PedsQL^{TM} summary scales as dependent variables: a) physical health, b) emotional function, c) social functioning and d) school functioning. Multicollinearity was tested with the measures of Tolerance and VIF.

RESULTS

Descriptive findings and correlations

The means, standard deviations, and correlations between the PedsQL™ scores, SMFQ, SPAI-C and SLE are presented in table 2. Using cut-off criteria of 12, 43 participants (10.1%) demonstrated possible clinically relevant levels of depressive symptoms.
Table 2 displays that the correlations between the young adolescents self-report on the instruments PedsQL, SMFQ, SPAI-C and SLE, was mild to moderate. The percentage of missing values for the PedsQL was calculated. For the adolescents self-report, the percentage of missing responses was 0.2% respectively.

INSERT TABLE TWO ABOUT HERE

Multiple regression

The multicolleniarity tests were acceptable for the further regression analyses (Tolerance =1.0052 and VIF factor=0.995).
Separate hierarchical multiple regression analyses were conducted to examine the contribution of each of the independent variables (see Table 3). HRQOL as measured by the PedsQL was used as the dependent variable. Gender was entered in the first step, age in the second step, SLE-scores in the third step, SPAI-C-scores score in the fourth step, and SMFQ in the fifth step. The interaction between the SMFQ score and the SLE was entered on the sixth step.

INSERT TABLE THREE ABOUT HERE

The results indicated that gender was significantly associated with level of the PedsQL Total Scale, as well as for the subscales Physical Functioning and Emotional Functioning. (see Table 3). Girls were on average scoring lower than boys on the Emotional Function Subscale (t =4,79, p<0.001), as well as for the Total Scale (t =2.65, p<0.01) and Physical Functioning (t =1.95, p=0.05). Age was not significantly associated with level of PedsQL Total Score outcome for any of the subscales. No statistically significant gender differences were found for the remaining subscales.

The SPAI-C was found to significant predict strongest for the PedsQL Total Scale, as well as for three of the PedsQL Subscales (see Table 3), while the SMFQ predicted strongest for the PedsQL School Functioning Subscale.

The SMFQ was significantly predicting levels of the PedsQL Total Score, as well as the other PedsQL-Total Scores for Physical Health, Emotional Function, Social Function and School Functioning (see Table 3). The interaction between the SMFQ score and the SLE were significantly predicting for the PedsQL Social Functioning Subscale.

DISCUSSION

The results from this study show that depressive symptoms and social anxiety symptoms predict self-reported HRQOL. This may indicate that the PedsQL can be an interesting assessment measure for depressive symptoms in young adolescents. The main results indicated that individuals who reported higher levels of depressive symptoms exhibited significantly lower levels of HRQOL as measured by the PedsQL, even when controlling for

gender, age, number of stressful life events, and levels of social anxiety symptoms. These results apply to both the PedsQL Total Score and all of the four PedsQL subscales.
The inherently high correlation between the SMFQ and the PedsQL Total Scale may be problematic because this could indicate that both the SMFQ and PedsQL possibly measure the same phenomena. On the other hand it might be positive that the percentage is not higher than it is, accounting for the measures covering different areas. When looking at the different PedsQL subscales it is clear that the Emotional Function Subscale have a higher correlation with the SMFQ compared to the other subscales, and as such influence the PedsQL Total Scale. However, the lower correlations for the other subscales: Physical health, Social Functioning and School Functioning confirms that the PedsQL are covering different areas. This show the importunateness of using the subscales as assessment issues in addition to the PedsQL Total Scale when assessing depressive symptoms.

Generally, in a clinical setting one would be interested in increasing adolescents' HRQOL. The scores on each PedsQL factor may then be highly informative. Individual differences in PedsQL scores should be taken into account when tailoring preventive intervention for mental problems.

The interaction term between stressful life events and depressive symptoms were significant for the PedsQL Social Functioning Subscale with an explained variance of 2%. This result indicates that individuals reporting higher levels of depressive symptoms along with higher number of stressful life events are more likely to report lower levels of social functioning as measured by the PedsQL. This finding confirm the strong connection between depressive symptoms and stressful life events, and may together operate as potentially risk factors for young adolescents reporting lower HRQOL regarding social functioning.

The Emotional and School Functioning Subscales remained all significantly associated with levels of depressive symptoms when controlling for gender, age, the occurrence of life events, and social anxiety. Interestingly, the SMFQ showed a stronger significant prediction for the PedsQL School Functioning Subscale as compared to the SPAI-C (see Table 3). This finding may indicate that the PedsQL School Function Subscale is an interesting assessment measure regarding both depressive and social anxiety symptoms, and also highlights the importance of assessing the daily functioning in contexts relevant for children, such as school and community [44].

The results showing that girls reported more depressive symptoms than boys, is consistent with other studies concerning gender differences in emotional health [22]. Further, studies have also proposed that this gender differences is rooted in adolescence [45, 46]. Previously studies have found a significant increase in depressive symptoms between the ages 14 to 15 [5, 47]. However, no such increase with age was found in our study, and is therefore identical with a previous study from the middle part of Norway regarding youth and mental health [1]. However, the lack of significant age effects may be due to the limited age range, and further studies including a broader age range are therefore needed. Another explanation could be that the increase in depressive symptoms may already have occurred. An earlier study [48] found a gender specific increase for girls in depressive symptoms between the 13 and 14 years of age, in a nationwide sample of 12 000 Norwegian adolescents. One explanation for this increase in depressive symptoms was the fact that girls were more developmentally challenged with the onset of pubertal development. In our study such differences were already seen in the age-group 13, and may therefore indicate a decreasing age onset of depressive symptoms for girls.

The study contains some limitations that should be mentioned. First, cross-sectional designs can not determine causal relations, which are an important limitation with the present study and implies that the results should be treated with some caution. In the further studies of

the PedsQL™ 4.0 it is essential to explore this measure in a prospective, longitudinal design to be able to search for causal factors and to entangle the true risk and protective factors from mere correlates. Second, although satisfactory psychometric properties and moderate to high correlations with a diagnostic interview have been reported for the depressive measure used in this study [38, 39, 41], it is not based on DSM-IV or ICD-10 diagnostic criteria for depressive disorder. Use of diagnostic interviews based on such diagnostic criteria is recommended. However, the SMFQ does in epidemiological samples, distinguish between clinical depressed and not depressed as good as the longer version of the MFQ [39]. Third, due to limited administration time set by participating schools, only a selection of acknowledged stressful life events [29, 31, 33] were included. The questionnaires used regarding SLE might therefore lead to an underestimation of the strengths of the findings. The inclusion of full scales assessing stressful and negative life events is recommended. Further, a relatively high percentage of the parents in the present study have a higher education. This aspect might affect the results, since children from higher social classes may have a better quality of life. At the same time it should be pointed that the amount of children scoring in clinical range for depressive symptoms are the similar percentage that is expected to be found in healthy samples.

CONCLUSION

The findings suggest that the Pediatric Quality of life measure (PedsQL™) is an interesting assessment measure regarding depressive and social anxiety symptoms in young adolescents. Using the PedsQL as an assessment instrument can be useful in clinical practise when tailoring an intervention for the individual, as well as for further research measuring children's mental health.

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Table 1. *Sociodemographic characteristics of 425 adolescents and 237 caregivers*

Adolescents	**N**	**%**
Total sample	425	(100)
Female	235	(56.1)
Male	184	(43.9)
School grade:		
8th grade	140	(32.9)
9th grade	142	(33.4)
10th grade	143	(33.7)
Stressful Life Events (SLE):		
Death in family	161	(37.9)
Divorce	83	(19.5)
Child seriously illness	15	(3.5)
Family seriously Illness	74	(17.4)
Other difficulties	55	(12.9)
Missing	37	(8.8)
Parents/primary care giver		
Total sample:	237	(55.8)
Mothers	216	(50.8)
Mothers education:		
Elementary school	10	(4.7)
Highschool graduate	51	(23.6)
Post high school	155	(71.7)
Fathers	110	(25.9)
Fathers education:		
Elementary school	4	(4.4)
Highschool graduate	25	(22.8)
Post high school	80	(72.8)
Economy:		
Very satisfying	26	(11.1)
Good	198	(84.2)
Poor	11	(4.7)

Table 2. *The Means, Standard Deviations, Reliability and Pearson Product Moment Correlation between All instruments.*

	PedsQL Total	PedsQL Physical	PedsQL Emotion	PedsQL Social	PedsQL School	SMFQ	SLE	SPAI-C
PedsQL Total score	-							
PedsQL Physical score	-.87**	-						
PedsQL Emotional score	-.87**	-.65**	-					
PedsQL Social score	-.77**	-.63**	-.59**	-				
PedsQL School score	-.81**	-.56**	-.60**	-.46**	-			
SMFQ	-.70**	-.56**	-.69**	-.53**	-.55**	-		
SLE	-.21**	-.20**	-.22**	-.13**	-.13**	.21**	-	
SPAI-C total	-.62**	-.52**	-.56**	-.65**	-.38**	53**	15**	-
No. of items	23	8	5	5	5	13	5	26
N	424	424	424	424	424	412	424	415
M	85.23	91.12	77.15	88.12	78.02	4.95	.91	6.4
SD	11.11	10.35	17.32	13.11	15.47	4.96	.82	7.6

** Correlation is significant at the 0.01 level (2-tailed)

Abbreviations: PedsQL= Pediatric Quality of Life inventory - Children, SMFQ= Short Mood and Feeling questionnaire, SPAI-C=Social Phobia and Anxiety Inventory for Children, SLE=Stressful Life Events

Table 3

Summary of the Separate Hierarchical Multiple Regression Analyses using PedsQL Total Scale, Physical, Emotional, Social and School Function Scale as the dependent variables, and Gender, Age, SLE, SPAI-C, SMFQ and SMFQ-SLE interactionscore as Predictor Variables.

		PedsQL total scale			PedsQL physical scale		
		Adolescent (N = 424)			Adolescents (N = 424)		
Step		F cha	R^2 cha	B	F cha	R^2 cha	B
1	Gender	8.68†	.02	-.15	4.35‡	.01	-.10
2	Age	.08	.00	-.01	.01	.00	.01
3	SLE	15,84*	.04	-.19	14.37*	.03	-.19
4	SPAI-C	241.95*	.36	-.61	136.68*	.25	-.51
5	SMFQ	162.31*	.17	-.50	51.86*	.08	-.35
6	SMFQ – SLE interactionscore	3.08	.00	-,06	3.22	.00	-.08

		PedsQL emotional scale			PedsQL social scale		
		Adolescent (N = 424)			Adolescents (N = 424)		
Step		F cha	R^2 cha	B	F cha	R^2 cha	B
1	Gender	25.85*	.06	-.25	1.80	.00	-.07
2	Age	.60	.00	-.04	2.35	.01	.08
3	Stressful life events (SLE)	17.54*	.04	-.20	8.41†	.02	-.14
4	SPAI-C	176.21*	.28	-.54	271.68*	.40	-.64
5	SMFQ	163.59*	.18	-.52	36.83*	.05	-.27
6	SMFQ-SLE interactionscore	1.59	.00	-.05	14.90*	.02	-.15

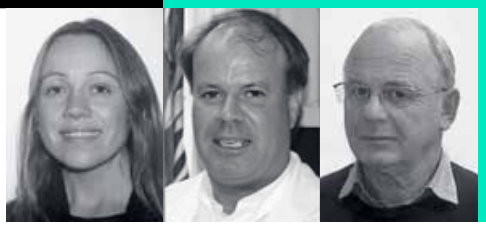
		PedsQL school functioning		
		Adolescent (N = 424)		
Step		F cha	R^2 cha	B
1	Gender	.70	.00	-.04
2	Age	1.82	.00	-.07
3	Stressful life events (SLE)	4.87‡	.01	-.11
4	SPAI-C	64.24*	.14	-.38
5	SMFQ	94.27*	.16	-.49
6	SMFQ-SLE interactionscore	1.10	.00	.05

Note: * $p < .001$, † $p < .005$, ‡ $p < .05$

Abbreviations are the same as for Table 2

Paper V

Fagartikkel



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Barn og kreft: Barns tilpasning til og forståelse av alvorlig sykdom

Hvilke faktorer er spesielt betydningsfulle for å fremme barns forståelse og tilpasning til alvorlig sykdom? Hvordan kan dette vektlegges i klinisk praksis?

Innledning

I Norge er det nå årlig om lag 130 nye tilfeller kreft hos barn under 15 år. Kreft i barneårene er fortsatt den hyppigste dødsårsak av sykdom hos barn mellom 1 og 15 år i den vestlige del av verden, og ca. 40 barn dør hvert år. Insidensen har vært stabil (Kreftregisteret, 2002). Leukemi (blodkreft) utgjør vel en tredel av alle tilfellene med barnekreft, og hjernesvulst utgjør knapt en firedel. Resten er forskjellige solide svulster. Dette er krefttyper som rammer individer i en fysisk og psykisk meget sårbar alder. I en slik fase kan en kreftbehandling påføre barna skader med helsemessige og psykososiale implikasjoner for årtier framover (Nygaard, 1999). Nye behandlingsformer kombinerer kjemoterapi (cellegift), stråling og kirurgi, og fra ca. 20 % overlevelse i 1960-årene er den gjennomsnittlige fem års overlevelse i dag steget til 80 % for barn med blodkreft (leukemi) (Gatta, Capocaccia, De Angelis, Stiller, Coebergh & the EUROCARE Working Group, 2003). På verdensbasis har Skandinavia den høyeste overlevelsesraten. Varigheten av kreftbehandling vil variere med type diagnose, for den vanligste kreftformen akutt lymfatisk leukemi varer behandlingen opp til 2– 2.5 år (Mathisen, 2000).

Somatiske komplikasjoner er i dag grundig dokumentert, og omfatter nevrologiske fortstyrelser, sanseskader, vekthemning, sterilitet, hormonelle forstyrrelser og mer isolerte organskader av hjerte, kar, lever og urinveier (Hawkins & Stevens, 1996; Nygaard, 1991; Wallace & Green, 2004). Fysiske senskader kan grupperes i fire store problemkomplekser knyttet til hjernens funksjoner, vekst, seksualutvikling og kjønnsfunksjoner, inkludert evnen til å få barn (fertilitet), og ny kreftsykdom (Nygaard, 1999).

Barn som får diagnosen kreft, gjennomgår ofte langvarig behandling preget av mye smerte, ubehag og uvisshet. Familiens totale livssituasjon vil i stor grad påvirkes. Den enkelte i familien vil måtte gjennomgå mange og nye utfordringer for å tilpasse seg de praktiske forandringer i hverdagen, den medisinske situasjonen og ikke minst de emosjonelle påkjenningene.

Studier viser at kronisk sykdom hos barn gir 2–3 ganger høyere risiko for psykososiale vansker (Gortmaker, Walker, Weitzman & Sobol, 1990; Wallander & Thompson, 1995). Psykososiale vansker omfatter emosjonelle problemer og atferdsforstyrrelser, redusert funksjon på skole og arbeid, negativt kroppsbilde, vanskeligheter i interpersonlige relasjoner, omfattende bruk av benektning som forsvarsmekanisme og overdreven avhengighet av foreldrene (Koocher & O'Malley, 1981; Mackie, Hill, Kondryn & McNally, 2000; Zeltzer et al., 1997). Men mange av studiene er vanskelige å generalisere på grunn av små og heterogene utvalg og mangel på kontrollgrupper (Dyregrov, 1996; Zebrack, 2002).

Det antas også at kreft hos barn kan predisponere enkelte individer til lettere å få noen av symptomene som er karakteristiske for posttraumatisk stressforstyrrelse (PTSD). Kreft blir assosiert med en trussel til livet og mange angripende og smertefulle prosedyrer (Stuber, Christakis, Houskamp & Kazak, 1996). Kupst og medarbeidere (1995) påpeker viktigheten av å finne barna og familiene som befinner seg i en risikogruppe for å utvikle tilpasningsproblemer.

Kognitiv og nevropsykologisk funksjonssvekkelse omfatter konsentrasjonsvansker og distraksjon, nedsatt hukommelse, mental treghet og svekket IQ. Barna kan ha både generelle og spesifikke lærevansker (Anderson, Godber, Smibert, Weiskop & Ekert, 2000; Mennes et al., 2005; Nygaard, 1999).

Graden av aktuelle senfølger vil være avhengig av både grunnsykdom og type behandling barna har gjennomgått. Senskader som fører til læreproblemer, har i stor grad vært observert hos barn som har vært behandlet for hjernesvulst, og strålebehandling av hjernen blir sett på som en viktig årsak til slike problemer (Nygaard, 1999). Strålebehandling i tidlig alder kan gi alvorlige kognitive og nevropsykologiske senskader. Kognitive vansker forbundet med kjemoterapi har fått økt oppmerksomhet, men antas å gi mer diffuse senfølger enn de som er forbundet med stråling (Mennes et al., 2005). Eiser (1998) påpeker at det foreligger flere grunner til å forvente redusert kognitiv fungering hos barn med kreft, ut fra at barn med kreft opplever hyppig og utstrakt skolefravær. Stråling eller kjemoterapi kan også ha en direkte effekt på læring.

Med utviklingsperspektivet som teoretisk utgangspunkt vil en sykdom kunne ha ulik påvirkning på barnet avhengig av barnets alder og modenhet. En stor begrensning i forskningslitteraturen er at barn og ungdommer har vært behandlet som en homogen gruppe (Eiser, 1995). Dette gjør det vanskelig å spesifisere hvordan barns forståelse av sin sykdom varierer som en funksjon av barnets alder. Tidligere forskning har også i stor grad vært begrenset på grunn av mangel på relevante måleinstrumenter som tar hensyn til barnets utviklingsmessige status, og av bruken av foreldre og ikke barna selv som informanter. Oppmerksomheten har oftest vært rettet mot den kognitive forståelsen, og i mindre grad mot de emosjonelle og sosiale konsekvensene av sykdommen (Eiser, 1998).

Denne artikkelen vil belyse kognitive og emosjonelle forandringer i barns forståelse av sykdom. Vi vil påpeke hvilke kliniske implikasjoner et slikt utviklingspsykologisk perspektiv kan ha for å fremme forståelse og innsikt hos barn som gjennomgår alvorlig sykdom. Faktorer som påvirker barns tilpasning til alvorlig sykdom, og mestringsstrategier barn benytter for å unngå de mest alvorlige konsekvensene av en truende livssituasjon, blir belyst. Sentrale problemstillinger er: Hvilke faktorer er spesielt betydningsfulle for å fremme barns forståelse og tilpasning til alvorlig sykdom? Hvordan kan dette vektlegges i klinisk praksis? Hvilke metodiske tilnærminger kan anvendes for å ivareta barnets ståsted?

Et historisk tilbakeblikk vil belyse hvordan våre antagelser om barns behov er knyttet til den kunnskap vi til enhver tid har. Vi vil presentere relevante utviklingspsykologiske teorier, og et teoretisk begrepsapparat for mestring av stress knyttet til kreft.

De kliniske illustrasjonene er hentet fra førsteforfatterens kliniske arbeid ved en barneavdeling på et somatisk sykehus.

ABSTRACT

Children and cancer: Children's adjustment to and understanding of their cancer

During cancer treatment, most children experience unpleasant physical side-effects, behavioural and emotional problems have also been identified. Children's understanding of their cancer illness depends on developmental aspects, such as their ability to gain knowledge, as well as to understand and reflect upon their situation. Both the families' coping strategies and professionals' attitudes towards informing the child, will further influence the children's adaptation. This article focuses on children's adaptation regarding living with a serious illness. The main focus is on the developmental changes through the child's age spans, emotionally and cognitively. Such knowledge has implications for how to inform children about their illness. The interactive process between the child and their caregiver is a critical aspect, which should be emphasised by health professionals.

Keywords: cancer, children, adolescents, developmental psychology, stress, coping

Historisk tilbakeblikk

Tre tidsepoker innenfor forskning vedrørende barn med kreft reflekterer forandringer i det gjeldende teoretiske perspektivet (Eiser, 1994). Dette har påvirket hvilke spørsmål som har blitt stilt, og måten de profesjonelle og familier har forholdt seg til sykdommen på. De teoretiske perspektivene har preget ivaretagelsen av barnets situasjon og behov både i en klinisk og en forskningsmessig sammenheng.

1950- og 1960-årene

I løpet av 1950- og 1960-årene var man først og fremst opptatt av omsorg for det døende barnet. I denne tidsperioden levde bare én prosent av barna med leukemi fem år etter at de fikk diagnosen. Familiene hadde derfor et helt annet utgangspunkt enn dagens familier. Den psykologiske hjelpen var rettet mot å beskytte barnet fra viten om at sykdommen nesten alltid var dødelig, og å forberede familien på barnets død.

Det teoretiske utgangspunktet var tilknytningsteori (Bowlby, 1969), med oppmerksomhet på den tidlige relasjonen mellom mor og barn. Bowlbys tilknytningsteori bidro til økt forståelse for tilknytning og separasjon i forhold til barn på sykehus. Teorien fikk stor innflytelse, og i kjølvannet av dette ble praksisen ved norske sykehus endret (Killingmo, Auestad & Nyhus, 1975). Barn ble ikke lenger utsatt for det traumet det er å skilles fra foreldrene i lange perioder på grunn av sykehusinnleggelse.

Innflytelse av sykdom på andre familiemedlemmer, inkludert søsken, ble ikke viet oppmerksomhet. Tidlige studier dokumenterte vanskene familiene opplevde, som angst og depresjon blant foreldre, spesielt mødre (Koocher & O'Malley, 1981). En frarådet informasjon til barnet om sykdommen og prognosen, fordi en antok at det ville være for truende og forårsake unødvendig stress og angst og begrense barnets evne til mestring (Share, 1972 og Plank, 1964 i Eiser & Havermans, 1994). Det ble på den tiden rapportert at noen foreldre, spesielt de med små barn, mente at det var umulig for barn å forstå informasjon om sykdommen og dens prognose, og at de derfor må spares for dette (Chesler, Paris & Barbarin, 1986).

1970- og 1980-årene

I de to neste tiårene skjedde det et skifte fra et ensidig fokus på døden som eneste utfall til hvordan en kunne leve med en livstruende tilstand. Prognosen ble for-

Oppfatningen nå er at ærlig og åpen kommunikasjon er avgjørende for å fremme psykisk helse hos barn og bringe fortrolighet med behandlingen

bedret gjennom medisinske framskritt i form av kjemoterapi (cellegift), stråling og kirurgi. Varigheten av kjemoterapi ble spesialisert i forhold til krefttype. Foreldrene måtte lære om sykdommen og behandlingen av den, og i større grad ta del i de praktiske prosedyrene. Det ble mer åpenhet rundt sykdommen i samfunnet, og informasjon ble gitt til både familie, venner og lærere. Barnet levde med sin kreftsykdom og trengte tilrettelegging i skolen.

Igjen fikk et perspektivskifte betydning for forskningen på feltet. Studier ble rettet mot tilpasning og mestring hos familiene til barn med kreft, og det ble utført sammenligninger med relevante kontrollgrupper (Goggin, Lansky & Hassanein, 1976; Kellerman, Zeltzer, Ellenberg, Dash & Rigler, 1980).

I denne perioden fikk kognitive teorier økt oppmerksomhet, og man antok at den påvirkning sykdommen har, er avhengig av barns kognitive utviklingsstadier (Cerreto, 1986; Perrin & Gerrity, 1984). Disse antagelsene var basert på oppfatningen om at visse utviklingsmessige utfordringer må være løst innenfor et gitt aldersområde (Erikson, 1964), og løsningen av disse oppgavene ble betraktet som essensielle for den normale friske utvikling. Dette ble sett på som en interaksjon mellom modning og erfaringer som gjorde barnet i stand til å gjennomføre bestemte oppgaver og dermed gå videre til neste stadium. Fysiske, psykologiske og miljømessige prosesser ble antatt å vanskeliggjøre det normale forløpet, og kronisk sykdom ble sett på som en slik utfordring.

Dette skiftet i teoretisk perspektiv ga også nye oppfatninger i forhold til betydningen av å informere barna. Kliniske observasjoner ga et bilde på at barna forsto og fanget opp forhold fra samtaler mellom de voksne eller diskuterte med andre barn (Binger et al., 1969). Spinetta og Deasey-Spinetta (1981) viste gjennom sin forskning i forhold til døende barn at mange følte seg isolert fra familien sin på grunn av all hemmeligholdelse. Barna med kreft var fullstendig klar over sin situasjon, men ikke i stand til å stille spørsmål vedrørende sine bekymringer, eller dele informasjon med andre.

Kognitive teorier hadde stor innflytelse når det gjaldt å bestemme hvor langt man skulle informere barna om alvorlighetsgraden av sykdommen deres. Det var antatt at barn mellom 7 og 11 år bare var i stand til å forstå informasjon i en veldig «konkret» form. Denne vektleggingen bidro derfor til en bedring av informasjon vedrørende rent konkrete fakta. De emosjonelle konsekvensene av det å bli informert om en mulig dødelig sykdom ble i mindre grad vektlagt.

Bruner (1986) påpeker at utviklingsteorier generelt har operert med en splitting av kognitive og affektive prosesser, og at dette i stor grad har ført til teoretisk stagnasjon i forståelsen av utvikling. Men spedbarnsforskning har vist betydningen av å betrakte utvikling som en kontinuerlig konstruksjonsprosess (Hansen, 1991). Denne utviklingsprosessen, med vekt på sentrale begreper som affektiv inntoning og intersubjektivitet, innebærer at påvirkning av sykdom avhenger av mer enn barnets alder og modenhet. Dagens utviklingspsykologi fremstiller barnets selvopplevelse og selvforståelse som forankret i en dialogisk matrise, basert på aktiv interaksjon med andre mennesker (Bruner, 1975; Hansen, 1991a, 1991b; Stern, 1985; Trevarten, 1980; Zeanah et al., 1989). Samhandlingen mellom barnet og omsorgspersonen betraktes som grunnleggende for barnets utvikling og tilpasning. Når et barn rammes av alvorlig sykdom, kan dette samspillet forstyrres, blant annet på grunn av foreldrenes angst og bekymring, og derfor være en risikofaktor for barnets videre utvikling. Dette gir oss et annet perspektiv når det gjelder barnets utvikling, enn de tradisjonelle utviklingsmodellene, som har hatt et mer egosentrisk perspektiv hvor barnet ser omgivelsene ensidig fra seg selv og ikke er i stand til å ta andres perspektiv (Bruner, 1986). Vi får et mer nyansert bilde av foreldrenes behov når et barn får kreft, og et grunnleggende spørsmål er derfor: Hva trenger foreldrene selv for å kunne være til stede for barnet og gi det en trygg relasjon?

1990- og 2000-årene

Den senere tiden har vært preget av mer intensiv behandling av kreft og økt overlevelse. Men intensiveringen av behandlingen har bidratt til en større økning av sykelighet og morbiditet som følge av behandlingen (Nygaard, 1999). Den generelle oppfatningen er nå at ærlig og åpen kommunikasjon er avgjørende for å fremme psykisk helse hos barn og bringe fortrolighet med behandlingen.

I motsetning til tidligere modeller viser dagens teorier et større mangfold. De tar hensyn til en rekke sosiale, kulturelle, familie- og sykdomsvariabler som naturlig kan influere på barns tilpasning til sykdommen (Eiser & Havermans, 1994). Det utviklingspsykologiske perspektivet har fått større innflytelse når det gjelder forståelse og ivaretagelse av barnets situasjon og behov. Målet er ikke bare å informere barna, men også å involvere dem i bestemmelser om behandlingen og gjøre dem mer delaktige i behandlingsprosedyrer. Betydningen av interaksjon står derfor mer sentralt innenfor moderne tenkning om barns behov for ivaretagelse når de rammes av sykdom. Det har skjedd store endringer i form av å inkludere hele familien. Det er i dag økt oppmerksomhet på den påvirkning og belastning alvorlig sykdom har på foreldre og søsken når et barn rammes. Det er også økt oppmerksomhet på betydningen av å involvere barnets naturlige nettverk som skole, barnehage, venner og fritidsaktiviteter. Dette har igjen fått betydning for utvikling av helhetlige modeller i omsorgen for familier til barn med kreft sammenlignet med tidligere (Eilertsen, Reinfjell & Vik, 2004). Studier viser at barn ønsker mye informasjon om alle aspekter ved sykdommen (Ellis & Levent-

hal, 1993). Men åpenhet er fremdeles ingen selvfølge når et barn dør etter langvarig sykdom. En svensk studie viser at mange foreldre angret på at de ikke hadde snakket med barnet om døden (Kreicberg, Valdimarsdottir, Oneløv, Henter & Steineck, 2004).

Barns tilpasning til kreftsykdom

Forskning viser at barns tilpasning til kronisk sykdom påvirkes av:

1) karakteristika ved sykdommen (i hvilken grad den er livstruende, og begrenser bevegelse og sosiale aktiviteter eller opplevelser).
2) situasjonelle faktorer som stressorer i barnets behandlingshverdag (behandlingsprosedyrer, bivirkninger og komplikasjoner).
3) karakteristika ved barnet (alder, kjønn, personlighet eller mestringsstil, og tidligere erfaringer).
4) karakteristika ved familien (problemløsningsevne eller kommunikasjonsferdigheter, og grad av åpenhet i familien), og sosial støtte fra venner og familie (Kupst & Schulman, 1988; Van Dongen-Melman, Pruyn, Van Zanen & Sanders Woudstra 1886; Varni, Katz, Colegrove & Dolgin, 1993).

Van Dongen-Melman et al. (1986) presenterer et teoretisk begrepsapparat for mestring av stress, knyttet til kreft. Modellen kan hjelpe oss til å forstå hvordan kreftsykdom påvirker et barns liv. Den er basert på to psykososiale teorier om menneskers atferd: attribusjonsteori (Kelley, 1967, 1971 i Van Dongen-Melman et al., 1986) og sosial sammenligningsteori (Festinger, 1954; Schachter, 1959, i Van Dongen-Melman et al., 1986). Modellen beskriver strategier mennesker benytter for å unngå de mest alvorlige konsekvensene av en truende livssituasjon.

Begrepet stressor beskriver stimuli som virker truende på personer. Karakteristika ved personen og den aktuelle situasjonen avgjør opplevelsen av fare (Lazarus, 1966).

Viktige personlige variabler er barnets alder, kognitivt og psykososialt nivå, samt barnets diagnose. Viktige situasjonskarakteristika er graden av støtte fra hjelpeapparatet, familie og venner. Ut fra modellen til Van Dongen-Melmann et al. (1986) blir stimuli opplevd som en stressor når den er årsak til usikkerhet, gir barnet en følelse av mangel på kontroll og negative følelser, og truer selvaktelsen.

> Negative følelser, som sinne, skyld, skam, ensomhet, apati, bitterhet og forvirring, observeres ofte hos barn med kreft

Usikkerhet defineres som mangel på informasjon om et viktig verdisystem for personen. Mangel på informasjon reduserer personens muligheter til å oppleve forutsigbarhet. Barn med kreft vil oppleve mye uvisshet forbundet med sin sykdom og behandling: om de kommer til å overleve, engstelse for behandlingen, om medisinene kommer til å virke, om de må være lenge på sykehuset, og om de kommer til å miste håret. Angst, sinne og ubalanse i humøret er vanlige reaksjoner. Barna kan bli usikre på seg selv og egne følelser. De kan oppleve uvisshet i forhold til hvordan venner vil reagere på dem og sykdommen deres, om vennene vil trekke seg tilbake, og hvordan det skal gå på skolen.

Tap av kontroll defineres som manglende evne til å påvirke det som skjer. Behandlingen kan bidra til at barn får opplevelsen av å miste kontroll over sitt eget liv. Sykdommen krever kontinuerlig medisinsk tilsyn, og pasientene blir ofte konfrontert med at de er avhengige av andre. De må innordne seg sykehusreglene og mister sitt privatliv i form av at intimitetsgrenser overskrides. Mange barn kan oppleve at naturlig og aldersadekvat bluferdighet krenkes av undersøkelser og behandling. Videre blir de pålagt restriksjoner som begrenser aktivitetene, og er ofte overbeskyttet av foreldrene. Pasienten må akseptere intensive behandlingsprosedyrer og bivirkninger som følger disse.

En persons selvaktelse knyttes til oppfatningen av egen kropp, emosjonelle tilstand og evne til å fungere sosialt. Van Dongen-Melman et al. (1986) påpeker at områder av betydning for utviklingen av en positiv selvoppfatning kan bli negativt påvirket hos barn med kreftsykdom. Barnet kommer inn i en ny rolle som syk eller annerledes. Kreftsykdom og behandling forandrer barnets utseende, og fører til kvalme, smerte, tretthet og svakhet. Barnets kroppsbilde kan derfor komme til å bli kontinuerlig endret. Slike endringer minner barnet på at det er annerledes enn andre barn. Ungdommer bekymrer seg for utseendet og sammenligner seg negativt med jevnaldrende. Barn som mangler selvtillit på grunn av endret utseende, kan trekke seg tilbake fra jevnaldrende og skolen og kan få problemer med emosjonell og sosial tilpasning.

Negative følelser, som sinne, skyld, skam, ensomhet, apati, bitterhet og forvirring, observeres ofte hos barn med kreft. Dette kan bidra til isolasjon. En finner ofte symptomer på depresjon hos barn med kreft. Mange er redde for at sykdommen kan slå til igjen, og for døden.

Mestringsstrategier. Mestringsstrategier benyttes for å minske eller eliminere problemene som er nevnt ovenfor: å søke informasjon, støtte og trøst, lete etter årsaker til hendelser, forandre situasjonen, benekte og unngå, og å akseptere situasjonen. Strategiene benyttes for å redusere følelsen av usikkerhet, for å oppnå og beholde en form for kontroll over situasjonen, for å opprettholde og beskytte selvaktelsen og for å redusere negative følelser.

Å søke informasjon. Informasjonsinnhenting benyttes for å redusere usikkerhet og negative følelser. Dette kan være kunnskap som barnet henter fra de ansatte på sykehuset, primærlegen eller andre fagpersoner, og bøker og TV-programmer. Hvis denne framgangsmåten ikke når fram, tyr personen til uformelle kilder. Å sammenligne sin egen situasjon med andre som har opplevd noe tilsvarende, er en vanlig måte å skaffe seg kunnskap på. Barn legger ofte merke til endringer i nære personers følelser, eller forandringer i sykehusrutiner og behandlingsforløp. Van Dongen-Melman et al. (1986) viser til studier som har dokumentert at innhenting av nøyaktig informasjon kan redusere usikkerhetsfølelse og tendenser til depresjon.

Å søke støtte og trøst. Barn har ofte utbytte av å søke støtte hos jevnaldrende med samme sykdom, og trøste hverandre ved å dele erfaringer og opplevelser. Men slik sammenligning kan også forverre de negative følelsene, særlig hvis barnet sammenligner seg med en som er dårligere, eller hvis kameraten dør. Trøst og støtte hentes også fra sykepleiere, venner og sosialarbeidere. Følelsen av støtte er avhengig av at venner og hjelpearbeidere forstår barnerts situasjon. Foreldre blir en god støtte ved å snakke om følelser, angst og håp, og ved å dele barnets bekymringer med sykdommen. Det å motta støtte og trøst vil styrke pasientens følelse av kontroll, og virke positivt inn på selvaktelsen.

Å lete etter årsak til hendelser. Ved å lete etter og finne forklaringer på det som skjer, blir det mulig å skape en logisk, forståelig og til en viss grad forutsigbar verden. Når barn får en kreftdiagnose, kan de begynne å lete etter en grunn til at de har fått sykdommen. I sin søken etter forklaringer og årsaker kan barnet finne dette i seg selv (intern attribusjon) eller utenfor seg selv (ekstern attribusjon). Et eksempel på intern attribusjon er at barnet tror at det har fått sykdommen som straff for dårlig oppførsel. Det er oftest mer positivt for en person å finne eksterne forklaringsmåter, fordi disse tillater at en opprettholder sin selvaktelse. Et eksempel er at radioaktivt nedfall i naturen antas å være årsak til kreftsykdommen.

Å forandre situasjonen. Forsøk på å forandre situasjonen er den mest aktive mestringsstrategien, og inkluderer alle aktiviteter som har til hensikt å fjerne forventede trusler (Lazarus, 1966). I sammenheng med sykdom kan det å forandre situasjonen bety å ta medisin, å dra til sykehuset og å etterkomme det terapeutiske opplegget. Forsøk på å fjerne negative konsekvenser av sykdommen forsterker følelsen av mestring og bygger opp igjen selvaktelsen.

Å benekte og å unngå. Benektelse av sykdommen forutsetter en mangel på oppmerksomhet i forhold til den. Unngåelse innebærer at en er oppmerksom på sykdommen, men forsøker å undertrykke eller unngå å bli konfrontert med konsekvensene av den. Dette er atskilte strategier, men ligner hverandre i måten de opptrer og fungerer på. Begge kan være passende måter å takle uunngåelige stressorer på, som i denne sammenhengen, der hovedstressoren er en livstruende sykdom. Begge strategiene beskytter mot angst, slik at barnet kan fungere så normalt som mulig, samt opprettholde sin selvaktelse. Strategiene blir ofte observert like etter at barnet har fått kreftdiagnosen, og fortsetter å fungere helt til barnet makter å takle stressoren på en bedre måte.

Å akseptere situasjonen. Fordi de har begrenset innflytelse på livstruende sykdom, kan barn med kreft avfinne seg med situasjonen ved å akseptere den. Dette er en strategi som ofte blir brukt etter en periode med benektelse og følelsesmessig utilpasshet. Akseptering kan gjøre det lettere for barna å tilpasse seg en ny virkelighet som krever at en tar en dag om gangen.

Avslutningsvis bringer Van Dongen-Melman et al. (1986) inn to mestringsstrategier til, impulsiv handling og kognitiv restrukturering. Impulsive handlinger karakteriseres ved plutselige følelsesutbrudd, som gråt eller sinne. Dette kan være en metode for å redusere negative følelser og følelsen av tap av kontroll. Kognitiv restrukturering kan være en hjelp til å redusere negative stressorer som følger kreftsykdommen. Et barn kan for eksempel benytte seg av selvinstruksjoner for å redusere angst når det gjennomgår intensive medisinske prosedyrer.

Compas, Banez, Malcarne og Worsham (1991) oppsummerer i tråd med Lazarus (1966) sin gjennomgang av andres forskning på dette feltet, med at relasjonen mellom stressorer og mestringsstrategier må sees på som en prosess. Valg av mestringsstrategier avhenger av person og situasjon. Barns mestring av sykdom vil dessuten være påvirket av diagnose, medisinske prosedyrer og hvordan sykdomsforløpet utvikler seg. I tillegg må det tas hensyn til utviklingsperspektivet når en skal studere barn og mestring. Barnas alder og deres kognitive kapasitet vil påvirke hvordan de forholder seg til og takler stressfylte situasjoner. I tillegg vil valg og utføring av mestringsstrategier være avhengig av hvor mye støtte de har i familie og nettverk.

Barns forståelse av alvorlig sykdom

Litteraturen viser som nevnt at det er store forskjeller på hvordan man har betraktet barnets utviklingsmessige forutsetninger. Dette kan ha sammenheng med at oppmerksomheten oftest har vært på den kognitive forståelsen, på bekostning av de emosjonelle konsekvensene (Eiser, 1998).

Emosjonsregulering er evnen til å overvåke og kontrollere emosjonell erfaring og emosjonelle uttrykk hos seg selv og tilpasse uttrykkene i henhold til sosiale og kulturelle forhold (Campos, Campos & Barrett, 1989). Denne evnen øker som et resultat av kognitiv utvikling og erfaring med varierte sosiale og fysiske miljøer (Saarni, 1997). Reguleringen omfatter intensiteten i emosjonene, typen av emosjonell atferd eller uttrykk, og situasjonen følelsene forekommer i. Forskningen på dette feltet har vært opptatt av de spesifikke følelsene hos mennesker som rammes av alvorlig sykdom. I den tidlige utviklingen er foreldre og andre nære omsorgspersoner viktige støttespillere som kan gi barnet kunnskap om en situasjons emosjonelle betydning og handlingsmuligheter, og hjelpe barnet til å forstå egne og andres reaksjoner. I ungdomstiden blir venner sentrale støttespillere (Tetzchner, 2001).

Førskolebarn

Førskolebarn regulerer stort sett emosjoner gjennom handling eller ved å søke hjelp av andre, trekke seg vekk fra en stressende situasjon eller be en voksen om trøst. Barn kan oppleve mye smerte og ubehag i forbindelse med en kreftbehandling, og for de yngste barna vil det å ikke forstå årsaken til smerten være forvirrende. Når det gjelder barn og smerteopplevelse, har oppmerksomheten først og fremst vært rettet mot de større barna (Eiser, 1995). Innenfor den kognitive tilnærmingen har spesielt to antagelser vært vektlagt – hvordan forklare årsaken til sykdommen og rasjonalet for behandlingen for barnet, og hvordan involvere barnet i en tilpasset selvpleie. Tankegangen er fremkommet på bakgrunn av en

Magisk og egosentrisk tenkning kan lede barn til å tro at det som skjedde, oppstod på grunn av deres tanker eller handlinger

generell modell basert på synspunkter vedrørende kognitiv utvikling, først fremmet av Piaget (1929) og videre anvendt spesielt i forhold til sykdom av Bibace og Walsh (1980) og Perrin og Geritty (1981), hvor grunnantagelsen er at forståelse av sykdom blant barn mellom to og syv år er overinfluert av deres umiddelbare persepsjon. Årsaken til sykdom blir sett på som et eksternt og konkret fenomen av barnet. Det er ingen forståelse av årsak og virkning. Eiser (1995) understreker tilnærmingens begrensninger med hensyn til vurdering av små barns forståelse. Dette kan forklare hvorfor oppmerksomheten og ivaretagelsen spesielt har vært rettet mot de større barna, mens små barns behov kan ha blitt undervurdert.

Småbarn er avhengige av hjelp fra voksne når de opplever stress og emosjonell belastning. Tetzchner (2001) påpeker at det ikke er noe klart skille mellom emosjonell utvikling og kognitiv utvikling. Følelsesmessige reaksjoner forutsetter alltid en vurdering av situasjonen, om den er trygg eller farlig, gir grunn til sorg eller glede. McGrath og McAlpine (1993) konkluderte med at 18 måneder gamle barn er i stand til å uttrykke at smerte gjør vondt, lokalisere smerten, legge merke til smerte hos andre og gjøre forsøk på å unngå det som gjør vondt. Barn er oppmerksomme på hvordan de kan lindre smerten gjennom klemmer, kyss og å spørre om medisin. Ved 3–4-årsalderen kan barn spontant bruke avledning og rapportere at å leke kan hjelpe dem å føle seg bedre.

Skolebarn

Barn i 7–11-årsalderen er i stand til å tenke om årsak til sykdommen, selv om deres forklaringer er begrensede. Sykdom blir forstått å være oppstått gjennom at kroppen er i fysisk kontakt med noe, og internalisering. Ved det sistnevnte aksepterer barn at sykdommen er lokalisert inni kroppen selv om de tror at årsaken er ekstern. På den måten kan de ikke helt forstå at sykdommen er et resultat av en feil i en kroppsfunksjon.

Li og Stone rapporterte (1976 i Eiser, 1995) at bare 4 av 142 som hadde overlevd sin kreftsykdom, hadde blitt fortalt at de hadde kreft. Koocher og O'Malley (1981) rapporterte at 42 % av utvalget hadde blitt informert innen ett år etter diagnostiseringen, og 38 % senere. I alt 20 % hadde aldri blitt gitt noen formell forklaring på sin sykdom av legene eller foreldrene. I dag er man som nevnt mer oppmerksom på at barn har behov for detaljert informasjon om sykdommen og behandlingen.

I den senere førskolealderen har barn fått et større ordforråd når det gjelder emosjonsord, og språket får stor betydning for emosjonshåndteringen. Det gjør det lettere for barn å formidle sin egen emosjonelle tilstand til andre, og å forstå og regulere sine egne følelser.

Skolebarn bruker i økende grad kognitive strategier som å si til seg selv at de klarer det, eller å prøve å tenke på noe annet. Tiåringer tar spontant i bruk kognitive strategier, mens femåringer må ha hjelp til det (Brenner & Salovey, 1997). Barn i den tidlige skolealderen henviser mest til foreldre som kilde til emosjonell støtte, mens eldre barn oftere sier at de vil søke hjelp hos venner.

Ungdom

Gjennom ungdomstiden har ungdommene fått økt forståelse for forholdet mellom sykdom, behandling og helseforebygging. Fra 14-årsalderen utvikles en gradvis forståelse for den gjensidige avhengigheten mellom fysisk og psykisk helse, med en forståelse for hvordan sykdom kan være påvirket av psykologiske faktorer.

Deling av følelser og emosjonell støtte er sentrale elementer i ungdommers beskrivelser av vennskap, og de vender seg til venner i større grad etter støtte til å håndtere emosjonelt vanskelige situasjoner. Dette er også en alder preget av større svingninger i emosjonalitet. En kreftdiagnose kan derfor være spesielt traumatisk når den framtrer i løpet av ungdomstiden (Eiser, 1995). De fleste ungdommer har noe viten om kreft, og vil lett innse at de er alvorlig syke. Samtidig er de ofte mindre i stand til å dele denne viten enn unge voksne. Informasjonen er kompleks og vanskelig å forstå. I tillegg kan mange ha liten sosial støtte. De kan ha blitt uavhengige av familien, men har ikke selv etablert nære mellommenneskelige relasjoner. Kreft kan da oppleves å bli en krise som de må håndtere alene.

Rosenberg (1979) fant at den utviklingsmessig viktigste endringen i denne aldersperioden var at ungdommene begynte å oppfatte seg selv som objekt for andres oppfatninger. Denne egosentriske forvirringen bidrar til at ungdommer tror at alle andre ser på dem, og derfor blir overbekymret om sin egen framtreden. Erikson (1959 i Eiser, 1995) hevdet at selvsentrering eller selvopptatthet er et kjennetegn for personer i ungdomsalderen. Betydningen av venner er stor, og kontakt med jevnaldrende kan være vanskelig å opprettholde i faser av sykdommen. I forbindelse med sykdom kan ungdommens eventuelle negative tanker og følelser om seg selv bidra til å vanskeliggjøre relasjonen med andre ungdommer, og skape isolasjon, noe som videre kan bidra til depresjon. Ungdommer har også et perspektiv på fremtiden når det gjelder utdanning, reiser, familie. En kreftsykdom kan oppleves som en trussel mot planer og drømmer i ungdommenes liv, og derfor bidra til å forsterke sorg og frustrasjon over å ha blitt rammet.

Selv om mange ungdommer er modne nok til å beskrive tanker og følelser når de har kreft, har hjelpeapparatet fremdeles en tendens til å bruke foreldre som informanter. Samtidig er det klart at foreldre ikke er reliable informanter for sine egne barn i alle omstendigheter, blant annet vil foreldrene ha begrenset kunnskap om ungdommenes forhold til venner og skole (Eiser, 1995). For å betrakte hvordan ungdommene selv tenker om sin kreftsykdom og andre forhold, er det viktig å spørre dem direkte.

Kliniske implikasjoner

Barn må få nødvendige informasjoner og fakta omkring sykdommen for å fremme en mest mulig konkret forståelse, gjerne

med bruk av relevante bøker, bildemateriell og hånddukker. Eiser (1998) understreker betydningen av å oppdatere informasjonen når det skjer endringer i behandlingen, som ved tilbakefall, og påpeker at dette ofte blir oversett. Det samme gjelder spørsmål i forhold til bivirkninger av behandlingen. Barn med kreft gjennomgår intensive behandlingsprosedyrer og bivirkninger som følger disse Barn kan i slike sammenhenger lett miste kontroll over sine egne følelser. Emosjonell ubalanse kan være en psykisk konsekvens av sykdom og tøff behandling, men kan også være forårsaket av medisiner som benyttes i behandlingen. Det er viktig ikke å frata barn ansvar i en behandlingsmessig sammenheng og å forklare rasjonalen for behandlingen og diskutere effekter og eventuelt bivirkninger. De voksne rundt barna må forsikre seg om at informasjonen blir tolket og riktig forstått (Dyregrov & Raundalen, 1996). I tillegg er det viktig at barnet blir gitt alternative valg; det kan gi barnet en følelse av at det selv kan påvirke og ha innflytelse over sitt eget liv og sin egen helse.

Barn forstår stadig mer etter hvert som de utvikler seg, derfor er det viktig å ta temaer opp igjen med jevne mellomrom. Et barn som var fem år da det fikk sin diagnose og ble forklart om kreften og behandlingen, vil som niåring ha behov for ny informasjon. Det å i ettertid bli klar over hvilken alvorlig sykdom man har vært igjennom, kan skape usikkerhet og bekymringer for om sykdommen kan komme tilbake. Mange barn har med seg en sorg og et savn etter små medpasienter som døde av sykdommen. Noen barn bærer på skyldfølelse for at de selv overlevde sykdommen, mens kameraten ikke gjorde det. Dyregrov og Raundalen (1996) understreker at skyldfølelse kan oppstå hos førskolebarn som følge av barnas kognitive umodenhet. Magisk og egosentrisk tenkning kan lede dem til å tro at det som skjedde, oppstod på grunn av deres tanker eller handlinger. Hvis ikke dette blir korrigert med forklaringer som kan forhindre unødvendig skyldfølelse, kan barnet fortsette å bære på følelsen av at det burde eller skulle ha gjort noe. Barn på sykehus vil bli kjent med og gjøre erfaringer i kontakt med andre barn som har samme sykdom eller ligger på samme avdeling. I slike sammenhenger har barna behov for informasjon om de andre barnas sykdomssituasjon, og dette er et voksent ansvar.

Informasjon til barn må betraktes som en prosess over tid, også i et kortere perspektiv. Det er fordi barn tar inn komplisert informasjon gradvis, og gjør konkrete erfaringer som gjør dem i stand til å integrere mer avansert informasjon i et kortere perspektiv. Første behandlingsfase preges av krise, hvor kaos, forvirring og overveldende inntrykk tar stor plass i barnets opplevelse. Dette medfører at informasjon må gjentas. Informasjon må være svært enkel og konkret i starten, men kan etter hvert utvikles og utvides også i et kortere perspektiv.

Eiser (1995) påpeker at det er utført lite arbeid med å beskrive hvordan barn lærer om diagnosen, og viser til studier som har funnet at barn plukker opp informasjon underveis, mer enn å lære om sykdommen i formelle situasjoner. Barn legger merke til endringer i nære personers følelser, eller forandringer i sykehusrutiner og behandlingsforløp. Van Dongen-Melman et al. (1995) viser til en rekke studier som har dokumentert at innhenting av nøyaktig informasjon er av stor betydning for å redusere usikkerhetsfølelse og tendenser til depresjon. Barn registrerer atmosfæren og foreldrenes bekymringer, men unngår å spørre fordi de vil beskytte foreldrene sine. En syv år gammel jente fortalte om første gangen hun kom til sykehuset, og beskrev følgende:

«Jeg husker veldig godt at foreldrene mine var så triste og lei seg, mamma gråt. Jeg skjønte at noe var galt, men jeg var så redd og torde ikke å spørre.»

Spinetta og Spinetta (1981) viste at barn som ikke hadde muligheten til å diskutere sine bekymringer, ble tilbaketrukne og bekymrede. Claflin og Barbarin (1991) konkluderte med at effekten av å holde tilbake informasjon var å få barna til å føle seg ensomme og isolerte. En studie av Ellis og Leventhal (1993) viser at barna ønsket informasjon om alle aspekter ved sykdommen. Selv om 78 % av barna ønsket informasjon om prognosen, følte bare 38 % av foreldrene at dette var nødvendig. Slavin, O'Malley, Koocher og Foster (1982) rapporterte at barn som ble fortalt om sin diagnose innen ett år, viste en bedre tilpasning til sykdommen enn de som hadde blitt informert først etter en lengre tidsperiode. Holen (1999) påpeker at mangel på informasjon reduserer barnets muligheter til å forberede seg på fremtidige hendelser, og dette skaper mye usikkerhet hos barnet.

Den emosjonelle ivaretagelsen

Dyregrov og Raundalen (1996) påpeker at barn ofte føler seg ensomme med sine følelser, og at dette kan ha en sammenheng med at voksne generelt undervurderer barnas reaksjoner, samtidig som den voksne kan ha vanskeligheter med å gå inn i barnas følelsesmessige verden på grunn av sin egen sterke sorg og sitt ønske om å beskytte barnet. Barn trenger å få både konkret og detaljert informasjon for å kunne forstå, og samtidig bli møtt på sine følelser.

Det vil være en stor utfordring å ivareta barnets emosjonelle behov når en som forelder selv overveldes av bekymring og angst. Når foreldre selv er i stand til å erkjenne at situasjonen er vond og vanskelig, kan dette åpne opp for lignende følelser hos barnet (Dyregrov, 1996). En viktig psykologisk intervensjon vil derfor være å hjelpe foreldrene til å tørre å kjenne etter på egne følelser, og å finne en balanse med hensyn til å åpne opp for noen av disse overfor barnet.

I barnets hverdag på sykehuset vil det være betydningsfullt å sette av tid til å få tak i hvordan barnet har det følelsesmessig. Både foreldre og pedagoger som omgås barna mellom de intensive behandlingsperiodene, er betydningsfulle når det gjelder å observere barnas allmenntilstand og følelsesmessige reaksjoner. Sykehusbarnehagen er et mer ufarlig sted hvor barnet i større grad får bruke det friske i seg selv, leke og utfolde seg. Den er et viktig fristed som kan gi barn trygghet til å leve ut følelsesmessige aspekter. Barnehagen og skolen er bemannet med personell som har kunnskap om barns situasjon og behov, voksne som barna kjenner og har et tillitsforhold til.

Et nært tverrfaglig samarbeid mellom yrkesgruppene, blant annet sykepleiere, leger, pedagoger, psykologer og sosionomer, er vesentlig for å kunne gi helhetlig

Ingen av de 147 foreldrene som oppga at de hadde snakket med barnet om døden, angret på dette

og adekvat hjelp til barn med kreft og deres pårørende. Man må kjenne til barnets medisinske situasjon, hvilken type informasjon barnet har fått, hvordan barnet synes å tolke og forstå informasjonen, og hvordan barnet reagerte følelsesmessig. Det vil være betydningsfullt å kjenne til barnets familiesituasjon og tidligere erfaringer, for eksempel om barnet har opplevd dødsfall og ulykker i familien. Dette kan medføre at barnet vil ha behov for enda grundigere informasjon og ivaretagelse. Den aktuelle krisen som barnet opplever, kan aktivere tidligere kriser som barnet og familien har opplevd.

Som hjelpere må vi tørre å spørre barna om de gruer seg, gi bekreftelse på at vi skjønner at dette er vanskelig, og normalisere de naturlige følelsene i slike sammenhenger. Vi må vise at vi ser at barnet for eksempel er sint, og bekrefte at det er lov. Det handler også her om å skape et felles fokus, en god samhandling mellom barnet og den voksne, hvor barnet blir bekreftet og gyldiggjort i sin situasjon.

Avhengig av alder kan det være vanskelig for barnet å forstå sine følelser og reaksjoner. For ungdom kan det oppleves flaut å ha oppført seg «barnslig» i en spesiell situasjon, noe som kan være en helt normal reaksjon når de er redde og følelsene tar helt overhånd. Forholdet mellom egen framtreden og forestillingen om hva andre tenker om dem, kan komme i konflikt. Åpenhet kan bidra til å få normalisert slike forhold, ungdommene trenger bekreftelse på at deres atferd ikke er unormal, og få hjelp til å mestre sin reaksjon.

Når åpenhet blir en utfordring

Når barn får tilbakefall av sykdommen, er prognosen dårligere, og det er særlig utfordrende å kunne være åpen overfor barnet selv og deres søsken og venner. I denne sammenhengen blir barnets utviklingsstadier og modenhet viktig å ta i betraktning: Hva trenger barnet å vite for å kunne forstå den endringen som har inntruffet? Hvor mye informasjon har barnet mental kapasitet til å ta innover seg? Følgende utsagn fra en jente i tenårene hvor det nettopp var startet opp strålebehandling etter tilbakefall viser utfordringene i dette: «Hva kommer til å skje hvis ikke strålingen virker?»

Det kan være at denne jenta har mottatt konkret informasjon om hva som skal skje videre behandlingsmessig, men hennes direkte spørsmål viser at hun opplever uforutsigbarhet. Dyregrov og Raundalen (1996) påpeker viktigheten av å få tak i det som kan ligge bak barnets spørsmål, den skjulte meningen. Kanskje er det redselen for å dø som ligger bak jentas spørsmål. Det er vanlig å ha tanker om at man kan dø av kreft, og spesielt ved tilbakefall av sykdommen kommer slike tanker tilbake. Det er av stor betydning å formidle til barnet at man som fagperson tar imot dette spørsmålet, og ikke snakker det bort grunnet egen redsel og usikkerhet. I forhold til jentas spørsmål blir det betydningsfullt å skape en meningsfull dialog ut fra hennes oppmerksomhetsfokus. Svendsen (i trykk) påpeker at barnet vil oppleve det meningsfullt å fortsette med å formidle seg når den voksne retter sin oppmerksomhet mot det barnet formidler, er en god lytter og blir med på å utforske nærmere hva barnet formidler. Deling av referansepunkt er som nevnt en forutsetning for et intersubjektivt fellesskap og selve utgangspunktet for en meningsskapende dialog (Hansen, 1991a; Stern, 1985; Trevarthen, 1980).

Affektinntoning er en ikke-verbal empatisk formidling som innebærer å tone seg inn på den andres opplevelsestilstand (Stern, 1985). Dette forutsetter en gjensidig bekreftelse gjennom deling av den affektive tilstanden som jenta i eksemplet opplever. Denne inntoningsprosessen spiller en avgjørende rolle for barns opplevelse av gjensidighet og mulighet for å dele følelser. En viktig tilnærmingsmåte overfor jenta blir i første omgang å vise at man som hjelper ser henne og hennes situasjon, stoppe opp og formidle forståelse for hennes spørsmål, få frem at man forstår at dette er vanskelig for henne, og forhøre seg om hun tenker mye på det, og om hun er redd.

Å snakke åpent om døden er for mange vanskelig og tabubelagt; det ligger ofte en stor gjensidig beskyttertrang mellom barn og voksne, spesielt i den nærmeste familie. Dette gir utfordringer til helsepersonell i forhold til å bringe døden inn som et naturlig tema, normalisere og ufarliggjøre det å ha tanker om døden. Selv svært unge barn kan ha en forståelse av døden og hva den innebærer, og barns holdning til døden gjennomgår ofte en endring gjennom sykdomsforløpet. En jente formidlet følgende: «Jeg kommer til å dø, men mamma og pappa vet ikke at jeg vet.»

Studier indikerer at det å samtale om døden med sitt døende barn kan hjelpe barnet i den vanskelige sluttfasen av livet og foreldrene i sin sorgbearbeidelse etterpå. Kreicberg et al. (2004) viser at ingen av de 147 foreldrene som oppga at de hadde snakket med barnet om døden, angret på dette. Derimot angret 27 % av de 258 foreldrene som ikke hadde snakket med barnet om døden. En god åpenhet bidrar til at barn blir møtt på sine bekymringer, ikke bare i forhold til døden, men også bekymringer for hvordan det skal gå videre med foreldre og søsken.

Hjelperens rolle og behov

Sykepleiere og leger er nære hjelpere som kan bidra til å gi god og aldersadekvat informasjon rundt den medisinske situasjonen. De bør også være nære støttespillere overfor foreldre når det gjelder å fremme åpenhet og ivaretagelse av barn som kommer til å dø. I tillegg vil pedagogisk og psykologisk kompetanse være vesentlig. Fagpersoner må tørre å være til stede i siste fase når et barn skal dø. Det innebærer å være emosjonelt til stede for barnet og familien. En viktig forutsetning er at helsepersonell våger å gå inn i seg selv, kjenne på og reflektere over egne holdninger til døden. Fagpersoner kan bære med seg ubearbeidede opplevelser fra sin egen barndom. Alle som arbeider med alvorlige syke barn, bør få faglig veiledning.

Kjønnsforskjeller

Forskning tyder på at jenter snakker mer

om følelser enn gutter (Dyregrov, 1994). Jenter i førskolealderen får flere spørsmål og kommentarer om sine emosjonelle forhold fra foreldre og eldre søsken enn jevnaldrende gutter gjør. Slike kjønnsforskjeller viser seg også i den senere barne- og ungdomsalderen. Jenter formidler i større grad enn guttene at de ville snakke med søsken eller andre om følelser hvis de var lei seg. Jenter fokuserer mer på selve følelsen enn gutter gjør, men vil også i større grad enn gutter bruke kognitive strategier for å prøve å undertrykke følelsen. Gutter sier oftere at de bruker anstrengende fysisk utfoldelse til å regulere seg, for eksempel i situasjoner der de føler seg dårlige, nervøse eller bekymrede (Brenner & Salovey, 1997). Dyregrov og Raundalen (1996) påpeker at spesielt for eldre gutter kan guttekulturen forsterke bortskyving og underrapportering av følelser, men selv gutter i førskolealderen kan ha vanskelig med å uttrykke følelser.

Gutters vanlige mestringsstrategier og emosjonsregulering vil i en behandlingsmessig hverdag være vanskelig å gjennomføre. Dette er forhold som det er viktig å være oppmerksom på når barn rammes av kreft. Fysisk utfoldelse vil i stor grad begrenses som følge av aktuelle bivirkninger fra blant annet cellegiftbehandlingen.

Metodiske tilnærminger

Hvordan kan man åpne opp for barns emosjonelle opplevelser og hjelpe barnet med å gjenkjenne følelser i bestemte situasjoner? Barnegrupper kan være en god innfallsvinkel. Barnet får møte andre i en lignende situasjon og får normalisert og bekreftet egne følelser. Det er lov å føle forskjellig, følelser er viktige og sier noe om hvordan vi har det. Noen barn forteller at de holder sinnefølelsen inni seg, mens andre forteller at de bare vil sparke og slå. Barna får også delt tanker om hva som kan hjelpe dem.

Hvordan ivareta barns utviklingsfaser og behov? Her er det mange innfallsvinkler å benytte, som leketerapi for de minste, historiefortellinger, samtaler og andre uttrykksmåter som tegning, bilder, bøker og kunst. Fagpersonen og barnet kan lage en fortelling sammen om en jente eller gutt som opplever noe lignende som barnet selv. Dette kan oppleves ufarlig for barnet ettersom det har en mer indirekte innfallsvinkel, men samtidig gir barnet mulighet til å identifisere seg med karakterene i historien (Dyregrov & Raundalen, 1996). Rollespill er en spennende innfallsvinkel til å ta opp erfaringer fra livet med behandling på sykehus. Barn kan i rollen som lege, sykepleier eller pasient få levd ut egne opplevelser. De rollespiller kjente situasjoner, men har samtidig nok avstand til at ikke dette blir så farlig. Rollespill er en unik metode for å involvere de helt minste barna i en gruppesammenheng. Gjennom at fagpersonene også deltar i rollespillet, gir det barna en fin mulighet til å spørre om ting de lurer på. Alle de nevnte tilnærmingsmåtene bidrar til å skape et felles fokus, en interaktiv prosess hvor barn og voksne, barn seg imellom som gruppene gir mulighet til, deler et felles referansepunkt.

Vi har sett at alvorlig sykdom hos barn kan forstyrre samspillet og den affektive dialogen mellom barnet og den voksne, og dermed være en risikofaktor for barnets utvikling. Et viktig spørsmål er hva foreldrene selv trenger for å gi barnet en slik relasjon. Individuelle samtaletilbud til foreldrene, så vel som familieterapi, kan være en viktig støtte. Foreldrene kan ha opplevd tidligere kriser som reaktiveres når barnet får kreft. Det kan være tilleggsvansker i familier utover barnets kreftsykdom, for eksempel psykiske lidelser, og enkelte vil i større grad trenge oppfølging. Men kreftsykdom hos et barn er i seg selv en risikofaktor, og kan true samspillet. Enkelte studier indikerer også PTSD hos foreldre til barn med kreft etter at barna er ferdigbehandlet (Stuber, 1996).

Måleinstrumenter

Måleinstrumenter som ivaretar barnets perspektiv, har vært mangelfulle. I begrepet «helserelatert livskvalitet» ligger individets subjektive opplevelse av sin helse, sitt velvære og sin livssituasjon. Det er gjort få systematiske forsøk på å utvikle instrumenter til å måle livskvalitet hos barn ved å bruke barns selvrapportering. Faktorer som modenhet, hukommelse og språkutvikling, skrive- og leseferdigheter blir vesentlig å ta hensyn til i denne sammenhengen. Livskvalitetsintrumenter for barn bør utvikles separat for forskjellige aldersgrupper (Ringdal, 1999).

En rekke mål vedrørende helserelatert livskvalitet for barn under åtte år er utviklet, selv om de fleste omfatter foreldreinformasjon (Goodwin, Boggs & Graham-Pole, 1994). Et relevant instrument er Pediatric Quality of Life Inventory (PedsQL^{TM}) 4.0, utviklet av Varni et al. (1999) og oversatt og validert for norske forhold (Reinfjell, Diseth, Veenstra & Vikan, 2006). PedsQL er et kortfattet og alderstilpasset livskvalitetsskjema, med egne selvrapporteringsskjemaer for aldersgruppene 5–7, 8–12 og 13–18. Foreldreversjonene går fra 2–4, 5–7, 8–12 og 13–18, og omhandler foreldrenes oppfatning av barnets livskvalitet. Dette er et klinisk og forskningsmessig relevant skjema for å kartlegge barns fysiske, emosjonelle, sosiale og skolemessige fungering, alle sentrale faktorer i livskvalitetsbegrepet. I tillegg gir PedsQL mulighet til å fange opp ulike oppfatninger hos foreldre og barn, noe som kan være et nyttig utgangspunkt for intervensjon.

Konklusjon

For å ivareta barns behov for tilrettelegging for å forstå og mestre tilværelsen som syk vil det være avgjørende at ivaretagelse av informasjonsbehov og strategier for å håndtere sykdommen går hånd i hånd med ivaretagelsen av den emosjonelle opplevelsen. Ivaretagelse og normalisering av følelsene i gitte situasjoner vil være av stor betydning. Åpenhet overfor barn er spesielt vanskelig og utfordrende når barn skal dø, til tross for at vi i dag er mer bevisste på betydningen av åpenhet når det gjelder barns tilpasning og mestring av en vanskelig livssituasjon. Dette bør for fremtiden vies større oppmerksomhet både klinisk og forskningsmessig, og helsepersonells rolle og ansvar i denne sammenhengen må diskuteres.

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