Resilience in pediatric oncology

Family risk and resilience factors and child behavioral adjustment

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CHAPTER 1

General introduction

PEDIATRIC CANCER

Cancer during childhood is rare. In the Netherlands, approximately 550 children are diagnosed with cancer each year[1]. Most common diagnoses are leukemias (30%) and brain tumors (25%), followed by lymphomas and solid tumors. Treatment takes place at one of the six pediatric oncology centers in the Netherlands (Beatrix Children's Hospital, Groningen; Amalia Children's Hospital, Nijmegen; Emma Children's Hospital, Amsterdam; VU medical center, Amsterdam; Sophia Children's Hospital, Rotterdam; Princess Máxima Center for pediatric oncology, Utrecht) according to national or international protocols, and consists of chemotherapy, radiation, surgery, or a combination. Treatment intensity and duration is highly dependent on diagnosis and staging of the disease; treatment duration can vary from a few months to two years. Recently, a first step has been made to centralize Dutch pediatric oncology in Utrecht and this will be expanded in the upcoming years, with shared-care centers all over the Netherlands.

Survival of pediatric cancer has improved tremendously during the last decades. Five-year survival rates have increased to approximately 75%[1,2]. With the recent trend of centralizing care for pediatric cancer patients, survival rates are expected to further increase in the near future[3]. Despite these improvements, subgroups of patients with poor prognosis can still be identified, e.g. survival of stage-IV neuroblastoma patients is approximately 50% despite intensive therapy[2].

Cancer treatment is known for its severe side effects, and this is also the case for children treated for cancer. Common side effects of chemotherapy are nausea, hair loss, diarrhea, skin rashes, neutropenic fever, and oral mucositis[4]. Due to neutropenia, children are highly susceptible to bacterial infections and might have to live with restrictions, for example limiting contacts or avoiding crowded places such as public transportation. Children with a solid tumor might also need surgery as part of treatment. In some cases this involves the amputation of a limb or rotationplasty, after which an intensive revalidation process is needed. Children with a brain tumor might need to undergo neurosurgery, which can cause severe neurological, endocrine, and psychological effects. On long-term, children who survived cancer may have a higher risk of second cancers, fertility problems, heart and lung damage, and other effects depending on tumor, treatment, and patient factors[5]. Not only severe side effects are a consequence of pediatric cancer treatment, it has also major psychosocial impact on the entire family, including parents, siblings, and grandparents. Next to this, intensive cancer treatment puts the overall development of children under pressure.

From previous research we learned that childhood cancer and its treatment have also impact on psychosocial outcomes, such as quality of life (qol) problems[6]. When staying in the hospital, children may experience anxiety during medical procedures and may have problems with their separation from familiar surroundings such as their siblings, pets, and peers[7,8]. Nowadays, children are no longer hospitalized during entire treatment, but only

when necessary. Some part of medical care has shifted to the responsibility of the parents, and this challenges their adaptive abilities[9,10]. Parents have to fulfill a great amount of new tasks when caring for their child with cancer as a consequence of both the treatment and the side effects, such as providing medication to the child and meeting hygiene guidelines. Parents can experience the fear of doing something wrong or missing important signs, which might be indicative for a health status change in their child, and puts a great burden on them. Next to this, parents could have less leisure time and might have to reduce their working time or give up working completely[10].

Side effects do not only occur during active treatment, but can become apparent years after end of successful treatment, the so-called late effects. Late effects can be defined as physical effects, such as secondary malignancies and fertility issues, cognitive effects, such as fatigue and impaired memory, and psychosocial effects, such as post-traumatic distress, anxiety and depression. Research showed that up to two-third of all long-term childhood cancer survivors may experience one or more adverse late effects[11]. Families of a child with cancer thus face several major challenges, not only because of the life-threatening and potential traumatic nature, but also regarding the physical and psychosocial functioning of the child on short-term and consequences for the child's health in the long-term, as well as practical issues and the family well-being[6,12]. Psychosocial support is therefore recognized of indispensible value[6,13]. Psychosocial support involves the culturally sensitive provision of psychological, social, and spiritual care[14]. In the Netherlands, psychosocial care is an important part and well integrated in the multidisciplinary treatment of children with cancer. In every pediatric oncology center in the Netherlands, child life specialists, social workers, and psychologists are available.

PSYCHOSOCIAL ADJUSTMENT

Psychosocial reactions to childhood cancer have been the focus of extensive research in the past decades[6]. Being diagnosed with cancer marks the beginning of an intensive process of adjusting to the consequences of the illness and its treatment. Children have to adjust to undergoing invasive medical procedures, coping with the side-effects of chemotherapy, and being hospitalized for longer periods. Adjustment is the most frequently used terminology in pediatric psychology research, because it refers to a broad level of functioning, including social and emotional functioning, and it suggests changeability[15]. Adequate adjustment is not only the absence of problems but can also refer to a resilient response, i.e. initial reactions at diagnosis that are transient and turn back to normal[16].

From recent studies we have learned that most children with cancer show normal to somewhat elevated levels of overall psychosocial adjustment problems[17-24]. However, there is a consistently small but significant group of children and their family members, estimated at 25-30%, at increased risk for experiencing more than average psychosocial

adjustment problems. These include difficulties in specific areas such as personal, social, and family functioning. Behavioral problems, mental health disorders and parenting stress may be observed[6,25,26].

On the longer term, children diagnosed with cancer are at risk for behavioral and neuropsychological difficulties, partly due to their intensive therapy[17,22]. Retrospective studies have shown that up to 60 % of the patients treated for childhood ALL report impairments in various neurocognitive domains[27]. These impairments are often ongoing and significantly impact qol in childhood cancer survivors[22,28].

Given the potentially traumatic nature of a cancer diagnosis, research has also focused on the occurrence of Post-Traumatic Stress Symptoms (PTSS) in children and their families. It was hypothesized for a long time that children would report PTSS. Despite the invasive character of cancer diagnosis and treatment, children with cancer reported lower levels of PTSS compared to peers who experiences other stressful events during childhood, such as an accident or the death of a loved one[29-31]. PTSS is more common in parents, especially shortly after diagnosis[32]. During this initial period, parents are exposed to multiple potentially traumatic events such as seeing their child in pain, frequent hospitalizations, and death of other patients. In most parents, anxiety is elevated at diagnosis and declines over time as the family adapts to the new "routines" in their lives. Depression has not been reported to be significantly elevated in parents[33].

Thus, multiple stress reactions can be seen in patients and their families, ranging from a normal adaptive response to symptoms of anxiety and depression, sometimes reaching the level of psychopathology[34]. This reaction has been described as Pediatric Medical Traumatic Stress (PMTS), which has been defined as "a set of psychological and physiological responses of children and their families to pain, injury, serious illness, medical procedures, and invasive or frightening treatment experiences"[35]. PMTS is not conceptualized as a traumatic stress disorder, but rather as posttraumatic stress symptoms (PTSS), a continuum of key symptoms of PTSD (e.g., arousal, reexperiencing, avoidance) which may be present without meeting criteria for a full diagnosis of PTSD or ASD. Although there is variability, consistent evidence demonstrates that pathological levels of distress are not the normative response, either during or after treatment[35,36]. Overall, children and their families show resiliency[8,37], and it is therefore important to early detect those families at risk for psychosocial problems.

MODEL OF PSYCHOSOCIAL ADJUSTMENT

In order to explain individual differences in adjusting to childhood cancer, it is important to investigate risk and protective factors associated with adjustment. Wallander and Varni's (*1998*) disease-stress-coping (DSC) model of child adjustment to pediatric chronic somatic disorders has proven to be useful for studying families dealing with childhood

disabilities or chronic illnesses[15,38]. The DSC model identifies several illness related (e.g. severity, brain damage), stress-processing (e.g. coping strategies), intrapersonal (e.g. temperament, competence), and social ecological (e.g. family environment, parental functioning, social support) factors, see p. 11 for model. The model fits in the assumption that the psychosocial adjustment of children with cancer is expected to be influenced not only by disease related factors, but also by other personal and family factors. In this model, the child is viewed in context of the family. This is important to do so, because pediatric cancer impacts all parts of the daily life of the child and his or her family, and in most cases the child with cancer is dependent of his parents. Many of the children, typically under the age of twelve, are not yet able to understand and consent with medical treatment[39].

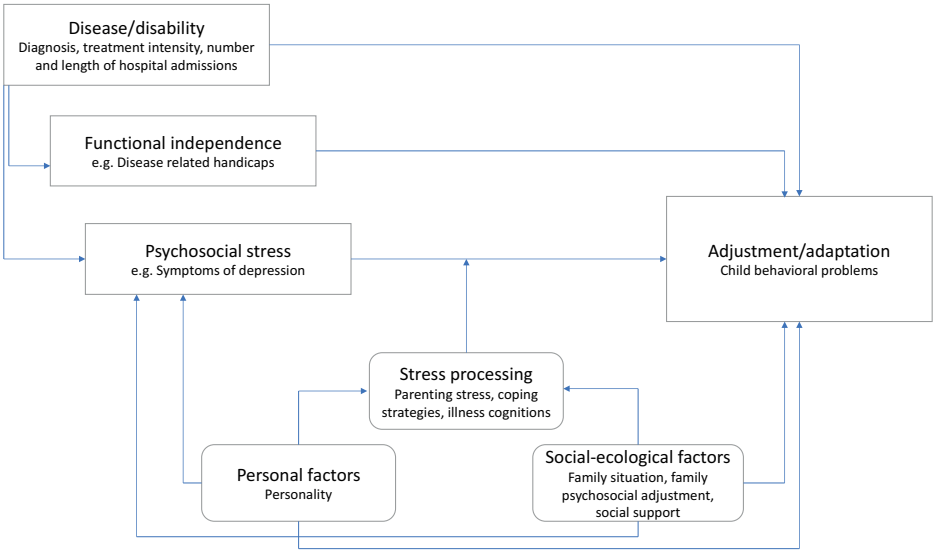

Figure 1. Disease-Stress-Coping model

RISK FACTORS FOR MALADJUSTMENT

Several studies in children with cancer have already taken into account factors, which have been outlined in the DSC model. First, **disease related risk factors**, such as severity, treatment intensity, and number and length of hospital admissions are found to influence family adaptation[15,23,40,41]. However, findings are inconsistent and most studies including both illness- and psychosocial factors in a multivariate regression model show that disease related risk factors account for little of the variability in adjustment.

Second, **psychosocial stress factors** play a substantial role in adapting to disease. Children with worse initial adaptation[42,43] are at risk for psychological maladjustment after a cancer diagnosis.

Stress-processing factors such as disengaged or passive coping is related to poor adjustment to chronic or a life-threatening illness. For instance depressive attributional style, avoidance, and social withdrawal are related to depressive symptoms and anxiety in children with cancer[44]. Next to this, parents with less optimistic cognitions about the child's future[45], higher levels of parenting stress[46-48], and more symptoms of anxiety and depression[49-51] are related to more children experiencing adjustment difficulties after diagnosis.

Personal factors, such as self-confidence and temperament, also affect adjustment but research in this area is scarce. Children in active treatment showed levels of self-esteem, depression, and anxiety comparable to healthy peers, but children off treatment reported lower physical self-esteem and higher levels of depression and anxiety than healthy children[52].

Social-ecological factors play a role in psychosocial adjustment of children with cancer after diagnosis. Literature shows that parents of children newly diagnosed with cancer report significantly higher distress than comparison subjects[53] and a growing body of evidence supports the association between parental functioning and child outcomes in childhood chronic disease[54]. Parents experiencing significant distress or poor family functioning can directly or indirectly affect child adjustment[55,56]. Parents can also have a positive effect on child adjustment to chronic illness[57]. Supportive, non-distressed parents do a better job of making their child feel safe and serve as a model to adapt adequate coping strategies[58]. Other confirmed socio-ecological risk factors for poor adjustment are single-parent household, less parental reliance on social support, financial problems, and prior stressful life events[40,46,59].

SCREENING FOR PSYCHOSOCIAL RISKS AND DISTRESS

Assessing risk factors makes it possible to predict future psychosocial distress and to intervene accordingly. Therefore, screening could be applied to early identify those children who are at risk for a maladaptive trajectory of behavioral adjustment after cancer diagnosis. The aim of screening is to detect patients with risk for psychosocial adjustment problems in an early phase[60]. With this information it is possible to distinguish between the patients who needs additional support the most. While screening seems promising, there has been discussion about the scientific evidence for the effect of screening. Some researchers have the opinion that the positive effect of screening in adult cancer survivors has been proven[60,61], others say that there is no evidence of benefit for patients[62,63]. The poor operationalization of distress has been mentioned as the possible explanation for the lack of effect[60]. Distress corresponds only moderately to known psychiatric disorders and is multifaceted[60,64]. Therefore it seems to be important to screen not only for distress in patients, but also for the determinants of distress[65]. As is previously outlined, family

facors play an important role in child distress and it is therefore important to focus not only on the child, but on the family when screening for distress or determinants of distress in pediatric populations.

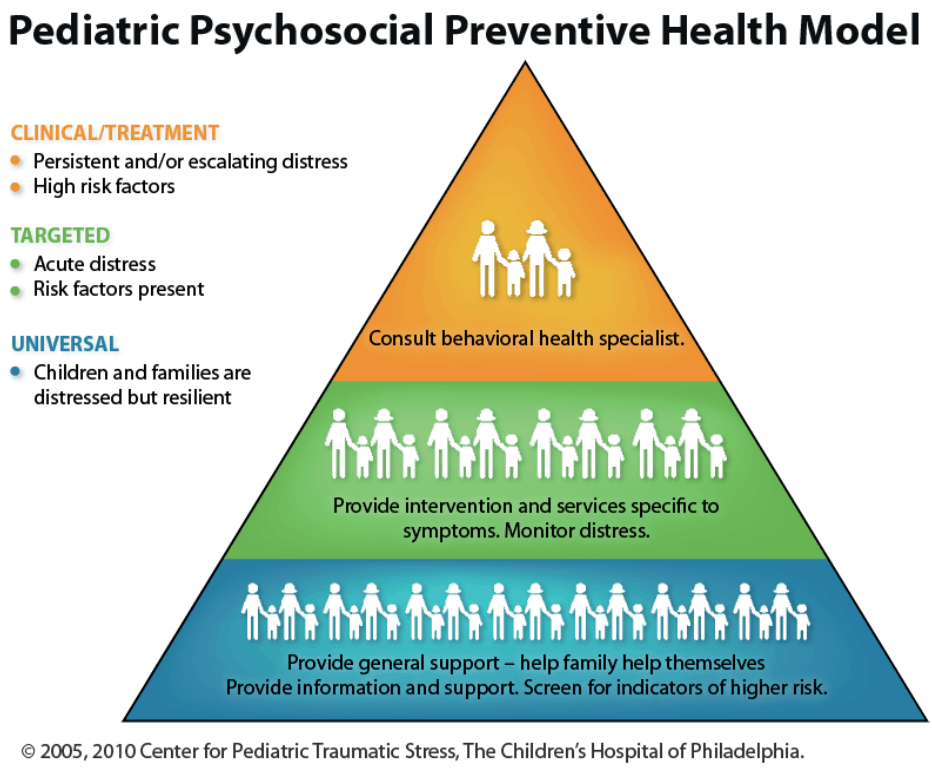

Figure 2. Pediatric Psychosocial Preventive Health Model

PSYCHOSOCIAL SCREENING AND PSYCHOSOCIAL CARE

The Psychosocial Assessment Tool (PAT) is a screening tool, which identifies family risk for developing psychosocial problems after the child's diagnosis of cancer. It covers a broad range of risk and resource factors including family structure and resources, social support, child emotional and behavioral concerns, sibling emotional and behavioral concerns, marital/family problems, family beliefs, and stress reaction[66].

The PAT is based on the Pediatric Psychosocial Preventative Health Model (PPPHM), which provides a conceptual model to guide screening and services entering the pediatric health care system[67]. This model conceptualizes the adjustment of children with PMTS, such as the diagnosis of childhood cancer, and their families.

The base of the pyramid represents the majority of patients and families, which are resilient and able to adapt adequately, in terms of keeping distress levels in the normal range or returning to normal levels within considerable time, when confronted with health-related stressors (Universal group). The assumption is that these are normally functioning families, who experience distress related to the medical circumstances that is within the normal range. A smaller group of families is at risk for developing psychosocial distress (Targeted group). This group of families shows factors that predispose them for ongoing distress. As mentioned before, these predisposing factors might be at different levels, such as child factors (e.g. preexisting child problems), social-ecological factors (e.g. poverty or single-parent households), or parental factors (e.g. parental illness or disability). Coping of these families is challenged, particularly if there occur medical complications. The small group at the top of the pyramid represents the families that show multiple risk factors for serious ongoing and escalating psychosocial distress (Clinical group). For example, these families show problems that were already present before the diagnosis, such as histories of persistent anxiety and depression symptoms or substance abuse in the parent. This classification, and additional information on the risk and protective factors, is intended to inform practice so as to provide personalized, family-based, and cost-effective psychosocial care[67]. In terms of psychosocial care, recently published standards propose that all families in the pediatric oncology setting should be offered at least minimal psychosocial services to support adaptive responses[68,69]. However, it is important to focus especially on the families who are at highest risk for maladjustment, as they can benefit most from tailored psychosocial interventions[67].

Assessment of risk factors can help in identifying the source of distress. In this way, screening could guide tailoring psychosocial care at an early phase for those families who who could benefit most of psychosocial care.

Previous research on the PAT confirmed its reliability and content validity. The PAT showed to be feasible in pediatric oncology both during acute phase[70-72] and in survivorship[73]. Distribution of scores into the three risk classifications was somewhat similar across different studies and countries: between 50% and 70% fell within the universal group, between 18% and 36% in the targeted group, and between 3% and 16% in the clinical group[70-75]. Previous research also indicated that a PAT score at diagnosis predicts the use of psychosocial services during treatment[36,54].

CONCLUSION

Although important knowledge has been collected about behavioral problems and its risk factors in children with cancer and survivors in the last years, most studies have methodological limitations, such as a heterogeneous research sample concerning diagnosis and time since diagnosis, lack of a longitudinal design, absence of information on behavior

problems in detail, and lack of information on the effect of demographic variables on behavioral adjustment such as gender and age[17-23,51,76]. In addition, most longitudinal studies on child adjustment in pediatric oncology have investigated adaptation over time at group level, which might mask individual differences. It is likely that children with cancer do not show a single uniform pattern of adjustment over time and therefore the investigation of individual trajectories is important[77,78].

Next to this, risk factors have been studied in detail, but the exact mechanisms showing how child adjustment is influenced are still largely unclear. When specific factors and pathways can be found, professionals could screen for and intervene on these factors. For efficient intervention it is important to clarify the exact mechanisms that are involved. Aiming at finding clues for intervention, it is important to focus on factors that might affect the adaptation of the child. If clinical significant effects are found, it is assumed that interventions focused on these factors have the power to change the adjustment of the child to illness.

At last, the PAT has been studied in North America and Australia[70-72], but not validated before in a European country. As mentioned before, results confirmed its reliability and content validity[70-72]. Recently the use of the PAT has also been extended to other disease groups[79]. Previous research indicated that a PAT score at diagnosis predicts the use of psychosocial services during treatment[36,54].

AIMS OF THIS THESIS

Aims of the present thesis are to describe psychosocial adjustment of children during cancer treatment and to investigate risk and protective factors for adjustment problems in order to be able to identify children at-risk for adjustment problems in time, and to provide timely interventions. In addition, this thesis aims to support focus of psychosocial care for children with cancer and their parents to those who need it most. Not only families at-risk should be identified, but also families adjusting adequately to cancer diagnosis and treatment for whom current psychosocial care sufficiently matches need for help. This thesis adds to the current literature focusing on three domains of pediatric psycho-oncology research. First, it describes child behavioral adjustment during treatment in a homogeneous group of patient with ALL. Next, it describes family risk and resilience factors for child behavioral adjustment. In addition, early identification of families at-risk using the PAT was investigated.

Two theoretical models form the basis of this thesis, namely Wallander and Varni's (*1998*) disease-stress-coping (DSC) model of child adjustment to pediatric chronic physical disorders and Kazak's Pediatric Psychosocial Preventative Health Model (PPPHM), which conceptualizes the adjustment of children with medical traumatic stress, such as the diagnosis of childhood cancer, and their families[15,67].

1) Describing child psychosocial adjustment over time (chapter 2)
Aims:
- To distinct subgroups of patients diagnosed with ALL showing different psychosocial adjustment trajectories during active treatment, rather than studying on group level.

2) Family risk factors (chapter 3,4)
Aims:
- To investigate the specific mechanism in which parental distress (stress of the parents themselves, which is a social-ecologcial factor) and parenting stress (stress of parenting an ill child, which is a stress-processing factor) are related to psychosocial adjustment in children diagnosed with ALL.
- To study the psychometric properties of the Illness Cognition Questionnaire (ICQ), adapted for use in parents of an ill child.
- To assess illness cognitions in parents of a child diagnosed with cancer and to determine whether illness cognitions are associated with parental distress.

3) Early detection of families at-risk for psychosocial maladjustment (chapter 5,6)
Aims:
- To cross-culturally adapt the Psychosocial Assessment Tool (PAT) for usage in the Netherlands.
- To investigate the reliability and validity of the PAT in a Dutch pediatric oncology sample.
- To explore the feasibility of the Dutch version of the PAT in terms of acceptability, demand, and practicality, as rated by the parents[79].
- To investigate the match between Dutch families' psychosocial risk profiles, as measured with the PAT, and psychosocial care provided to the families.

The thesis is based on two larger studies: QoL add-ALL (Quality of life add-on study in children treated by ALL-10 protocol) and IMPROVE (IMplementation of Patient Reported Outcomes Via Electronics in pediatric oncology). The QoL add-ALL study was performed to describe the behavioral adjustment of children diagnosed with Acute Lymphoblastic Leukemia (ALL) and to investigate the specific mechanisms by which parental psychological factors are related to the behavioral adjustment in their children with ALL. This first sample comprised the parents of children with acute lymphoblastic leukemia (ALL) recruited from six of the seven Dutch pediatric oncology centers, namely the Radboud University Medical Center/Amalia Children's Hospital in Nijmegen, the Academic Medical Center/Emma Children's Hospital in Amsterdam, the VU University Medical Center in Amsterdam, the Erasmus Medical Center/Sophia Children's Hospital in Rotterdam, the Leiden University Medical Center in Leiden, and the University Medical Center/Beatrix Children's Hopital in

Groningen (response rate 82 %)[81]. Inclusion criteria were age 1.5–18 years, recent diagnosis of ALL, treatment according to the Dutch Childhood Oncology Group (DCOG) ALL 10 protocol, and parental fluency in Dutch. The study was approved by the medical ethics review boards of the participating institutions. The second study, IMPROVE, was aimed to validate the Dutch version of the Psychosocial Assessment Tool and to investigate the effects of psychosocial screening in pediatric oncology. The IMPROVE study also aimed to implement Patient Reported Outcomes in Dutch pediatric oncology (not described in this thesis) using a so-called 'KLIK"method (Dutch for Quality of Life in Children)[82]. The KLIK method is an online system (www.hetklikt.nu) to enable monitoring and discussion of PROs for children with a chronic health condition[83]. This multicenter study was a collaboration between the Radboud University Medical Center/Amalia Children's Hospital in Nijmegen and the Academic Medical Center/Emma Children's Hospital in Amsterdam. This sample comprised the parents of children (0-18 years) recently diagnosed with cancer from four of seven Dutch pediatric oncology centers, namely the Radboud University Medical Center/ Amalia Children's Hospital in Nijmegen, the Academic Medical Center/Emma Children's Hospital in Amsterdam, the VU University Medical Center in Amsterdam, and the Erasmus Medical Center/Sophia Children's Hospital in Rotterdam (response rate 74 %). Inclusion criteria were recent diagnosis of cancer and parental fluency in Dutch; children with a life expectancy < 6 months or a relapse were excluded. The study was approved by the medical ethics review boards of the participating institutions.

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CHAPTER 2

Predicting Trajectories of Behavioral Adjustment in Children diagnosed with Acute Lymphoblastic Leukemia

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ABSTRACT

Background: Previous research showed that children with cancer are at risk for developing behavioral adjustment problems after successful treatment, however course of adjustment remains unclear. This study focuses on adjustment trajectories of children during treatment for Acute Lymphoblastic Leukemia (ALL) and aims to distinguish subgroups of patients showing different trajectories during active treatment, and to identify sociodemographic, medical, and psychosocial predictors of the distinct adjustment trajectories.

Methods: In a multicenter longitudinal study 108 parents of a child (response rate 80%) diagnosed with ALL were assessed during induction treatment (T0), after induction/consolidation treatment (T1), and after end of treatment (T2). Trajectories of child behavioral adjustment (Child Behavior Checklist; CBCL) were tested with Latent Class Growth Modeling (LCGM) analyses.

Results: For internalizing behavior a three-trajectory model was found: a group that experienced no problems (60%), a group that experienced only initial problems (30%), and a group that experienced chronic problems (10%). For externalizing behavior a three-trajectory model was also found: a group that experienced no problems (83%), a group that experienced chronic problems (12%), and a group that experienced increasing problems (5%). Only parenting stress and baseline qol (cancer-related) were found to contribute uniquely to adjustment trajectories.

Conclusion: The majority of the children (77%) showed no or transient behavioral problems during the entire treatment as reported by parents. A substantial group (23%) shows maladaptive trajectories of internalizing behavioral problems and/or externalizing behavioral problems. Screening for risk factors for developing problems might be helpful in early identification of these children.

INTRODUCTION

Acute lymphoblastic leukemia (ALL) is the most common form of childhood cancer and is characterized by a mainly young age at diagnosis, long duration of treatment, and severe family burden[1]. In the long-term, children diagnosed with leukemia are at particularly high risk for behavioral and neuropsychological difficulties, partly due to their intensive therapy[2,3]. Retrospective studies have shown that up to 60% of the patients treated for childhood ALL report impairments in various neurocognitive domains[4]. As these impairments are often ongoing and significantly impact qol in cancer survivors, long-term monitoring of psychological functioning is needed[3,5].

Although it seems clear that childhood cancer survivors are at risk for psychological problems, the link between adaptation during treatment and long term difficulties is not clear yet. Previous studies showed that children in treatment adapt adequately when analyzed as a group: some studies found increased levels of problems shortly after diagnosis, which normalized during treatment[6,7], while other studies report no behavioral problems in children with cancer[8]. Most longitudinal studies have investigated adaptation over time at group level, which might mask individual differences. It is likely that children with cancer do not show a single pattern of adjustment over time and therefore the investigation of individual trajectories is important[9,10]. Studies describing the longitudinal trajectories of adaptation are scarce. It is possible that the adaptation in children diagnosed with ALL can also be classified into different trajectories, such as documented before in adult care[9-11]. No research has yet distinguished the trajectories of behavioral adjustment in pediatric oncology. It is important to start investigating behavioral adjustment problems in an early phase of treatment, because we know that this has substantial impact on adaptation on the long term[12]. Therefore, it is important to identify the trajectories of adjustment through the illness trajectory into long term survivorship[9]. When distinct adjustment trajectories are found, predictors of these trajectories can be investigated. This information is relevant in early identification of children showing a maladaptive adjustment trajectory, and this is informative for how and when to target psychosocial services.

Previous research suggests that there are sociodemographic, medical, and psychosocial factors which are predictive of child maladjustment after cancer diagnosis. Studies showed that younger child age[13], lower parental education level[14], single-parent household[15], and hospitalizations[7] are all risk factors for child maladjustment. Next to this, a consistent link has been found between low levels of child adaptation response immediately after diagnosis and later adjustment[14,15]. At last, parental psychosocial factors, including distress[16], low social support[17], helpless cognitions[18], avoidant/passive coping[19], and parenting stress[20,21] were consistently found to be risk factors for child maladjustment.

The first aim of the present study was to identify distinct subgroups of patients diagnosed with ALL showing different adjustment trajectories during active treatment. The second aim of this study was to explore demographic, medical, and psychosocial predictors of

these adjustment trajectories. In line with previous literature, we hypothesized that worse child baseline response, parental negative affect, parental helpless cognitions, parenting stress, low parental social support, and low parental acceptance would be associated with maladaptive adjustment trajectories. Medical factors such as hospitalizations and ICU admissions were also expected to be related to adjustment trajectories.

METHODS

Sample

Parents of children with ALL from six of seven Dutch pediatric oncology centers were enrolled. Inclusion criteria were: 1) child age between 1,5-18 years, 2) newly diagnosed with ALL, and 3) treated according to the Dutch Childhood Oncology Group (DCOG) ALL 10 protocol[22]. In addition, parents had to be fluent in Dutch and children with an important pre-existing condition (e.g. Down syndrome), potentially affecting baseline measurement, were excluded.

Procedure

From October 2006 till October 2009 parents of newly ALL-diagnosed patients were invited to participate in this study. Parents who were willing to participate received verbal and written information on the study within the first weeks after diagnosis by one of the principal researchers. Families were instructed to choose one parent respondent for all assessments. Informed consent was obtained from all participants in this study. Parent-proxy measurements were performed three times for the children treated according to the Standard Risk (SR) or Medium Risk (MR) ALL-10 protocol: during induction treatment, after ending induction/consolidation treatment and during maintenance, and shortly after finishing treatment. For children treated according to the High Risk (HR) ALL-10 protocol measurements were performed only two times due to higher intensity and shorter duration of treatment: during induction treatment, and shortly after finishing treatment. The study was approved by each of the medical ethical review boards of the participating institutions.

Measures

Sociodemographic information (gender, date of birth, socioeconomic status, family situation, treatment protocol, number of hospitalizations, and number of ICU admissions) was collected with a self-developed questionnaire.

Parental subjective well-being was assessed with the Dutch shortened version of the Profile of Mood States (POMS)[23,24]. The shortened POMS consists of 32 items and is designed to measure mood in five different domains. The answers are graded on a 5-point scale

ranging from 'not at all' (0) to 'extremely' (4). Norm scores are available[23]. In the current study, internal consistency for the different domains ranged from α=.79 to α=.91.

Parental illness cognitions were assessed with the Illness Cognitions Questionnaire - parent version (adapted from the ICQ)[25,26]. The ICQ-p measures illness cognitions that reflect different ways of evaluating the aversive character of a chronic condition of the child. In the current study, internal consistency for the subscales ranged from α=.75 to α=.87.

Parental coping strategies were assessed with the Utrecht Coping List (UCL)[27]. Two of the seven scales were used in the current study, namely the less adaptive coping strategies avoidance/awaiting (8 items) and passive reaction pattern (7 items). Items are scored on a 4-point scale. Internal consistency for the current sample was α=.47 for the avoidance/awaiting subscale (this subscale was excluded from analyses due to limited reliability) and α=.64 for the passive reaction pattern subscale.

Parental parenting stress was assessed with the Parenting Stress Index-short form (PSI)[28]. The PSI measures the level of stress parents experience in raising their child and it consists of 25 statements on a 6-point Likert scale. In the current study, the total stress score was used as a measure of parenting stress. In the current sample internal consistency was α=.92.

Parental perceived social support was assessed with the Inventory for Social Reliance (ISR)[29]. The subscale potential emotional support was used in the current study, which consists of 5 items measuring perceived social support. Internal consistency for the current sample was α=.92.

Child generic Quality of Life was assessed with the Child Health Questionnaire (CHQ)[30]. The CHQ is a 50-item parent-reported questionnaire, covering the physical, emotional, and social well-being of children. Items are scored on a 4- to 6-item Likert scale and converted to a 0-100 score, with higher scores indicating higher qol. Two summary scores are available (physical and psychosocial). Internal consistency for the total questionnaire in this sample was α=.69.

Child disease-specific qol was assessed with the PedsQL cancer module[31]. This is a 27-item multidimensional cancer-specific questionnaire. Items are scored on a 4-point Likert scale with a higher score indicative for better qol. Internal consistency was α=.82 for the total scale in the current sample.

Parent-rated child behavioral adjustment was collected using the Dutch translation of the Child Behavior Checklist[32,33]. The CBCL is a parent-reported questionnaire that provides scores on global, internalizing and externalizing behavioral problems. In this study two distinct versions were used, one for children aged 1,5-5 years (101 items), and one for 6-18 years (113 items). Items are scored on a 3-point Likert scale; a total problem score is obtained by summing item scores. Available norms provide age and gender-standardized T-scores (mean=50; SD=10)[32]. For analyses on trajectories, T-scores could not be used because they differed between the two ages versions. Therefore, only items that appear on both age versions of the CBCL were used to include all in the same analysis[34,35]. For the internalizing

scale, 6 items were used ("Too fearful or anxious", "Self-conscious or easily embarrassed", "Shy or timid", "Unhappy, sad, or depressed", "Withdrawn, doesn't get involved with others", and "Worries"). These items correlated highly with the T-score of the internalizing scale (r= 78-.80) and showed acceptable reliability (α=.77 for CBCL version 1,5-5 years and α=.74 for CBCL version 6-18 years). Possible range for this scale was 0-12 and mean score varied between 1.77-2.18 (SD=2.15-2.36). Based on a norm population of 2119 Dutch children, a cut-off score of 3 (M+1SD; M=1.29, SD=1.61) was defined to distinguish between children with and without clinically significant behavioral problems. For the externalizing scale, nine items were used ("Can't sit still, restless, or hyperactive", "Cruel to animals", "Destroys own things", "Destroys things belonging to family or others", "Disobedient", "Doesn't seem to feel guilty after misbehaving", "Gets in many fights", "Physically attacks people", and "Temper tantrums or hot tempered"). These items correlated highly with the T-score of the externalizing scale (r=78-.82) and showed acceptable reliability (α=.81 for CBCL version 1,5-5 years and α=.78 for CBCL version 6-18 years). Possible range for this scale was 0-18 and mean score varied between 2.35-2.81 (SD=2.57-2.79). Based on the Dutch norm population, a cut-off score of 5 (M+1SD; M=2.22, SD=2.35) was defined to distinguish between children with and without clinically significant behavioral problems. During the study period, a total of 28 families switched from the CBCL 1,5-5 years to CBCL6-18 years because aging of the child. When 50% or more of the items on a subscale were missing, the subscale score could not be computed and was handled as missing data. The CBCL has well-established reliability and validity[32].

Statistical methods

The Statistical Package for Social Sciences (SPSS) for Windows version 20.0 was used for descriptive analyses. Normal distribution of continuous data was assessed using skewness and kurtosis scores. All data showed a normal distribution. Trajectories of child behavioral adjustment were tested with Latent Class Growth Mixed Modeling (LCGM) with maximum likelihood estimation using the R package LCMM[36].

We tested linear and quadratic models ranging from 1 to 4 trajectory groups. Multiple criteria were used for deciding which model (number and type of trajectories) better fit the data[37,38]. First, we examined the Bayesian Information Criterion (BIC) and the Akaike Information Criterion (AIC). The closer the values are to 0, the better the fit of the model[37]. Then, we looked at the size of each trajectory group. Each group should contain at least 5% of children[38]. At last, we inspected the posterior probabilities, which indicate the reliability of each trajectory classification, minimum threshold of 0.7[38]. Visual exploration of the data was used to judge the adequacy of the final predicted trajectories against the actual data. To take into account the uncertainty of class trajectory assignment, the posterior classification probabilities of class membership were used as weights (same procedure as in Henselmans et al., 2010[10]). Then we explored the relation between adjustment trajectories

and demographic, medical, and psychosocial factors. For categorical variables chi-square tests were used, and continuous variables were tested with analyses of variance. Variables that were significantly related ($p<.05$) to adjustment trajectories were entered in a final multinomial regression analysis. Post-hoc power analysis showed that with the study sample (N = 108, power = .80, alpha = .05) we were able to detect medium effect sizes (fsquared = 0.15). P-values (two-sided tests) ≤0.05 were considered statistically significant. Cohen's d was calculated as a measure for effect size. Effect sizes .20 were considered small, .50 medium, and .80 large[39].

RESULTS

Sample characteristics

During the study period, a total of 164 families were eligible and could be invited to take part in the study of which 159 agreed (reason for rejection was feeling too overwhelmed *n*=5). 131 parents returned completed questionnaires at baseline (response rate 80%). One patient was excluded from analyses because the questionnaire was returned long after the induction phase. Only families with complete data at two out of the three assessment moments were included in analyses (*n*=108) of which 84 families completed all assessments. No differences were found between participants (N=108) and drop-outs (N=23) with respect to age (p=.52) and treatment protocol (p=.10). Drop-outs were more often boys (p=.00). See Table 1 for demographic information. Parent-proxy measurements were performed three times for the children treated according to the Standard Risk (SR) or Medium Risk (MR) ALL-10 protocol: during induction treatment (**T0**: *n*=95, *M*=42.1 days, *range*=5-131 days), after ending induction/consolidation treatment and during maintenance treatment (**T1**: *n*=91, *M*=397.4 days, *range*=348-687 days), and shortly after finishing treatment (**T2**: *n*=87, *M*=781.2 days, *range*=651-1000 days). For children treated according to the High Risk (HR) ALL-10 protocol measurements were performed only two times due to higher intensity and shorter duration of treatment: during induction treatment (**T0** *n*=12, *M*=46.0 days, *range*=12-96), and shortly after finishing treatment (**T2** *n*=12, *M*=379.0 days, *range*=259-487 days).

Trajectories of behavioral problems

Internalizing behavioral problems

Latent Class Growth Modeling (LCGM) revealed that the linear three-trajectory model fitted best (see Table 2). The average posterior probabilities all exceeded .70 (.95, .86, and .96) and each trajectory was composed of at least 5% (60%, 30%, and 10% respectively). The three different behavioral adjustment trajectories will now be described. Children in the Resilience trajectory (60%) did not experience any internalizing behavioral adjustment problems after diagnosis. Children in the Recovery trajectory (30%) started out with

Table 1. Demographic information

Variable	
Age child	
M (SD)	6.3 (4.2)
Range	1-17
Gender child	
Male	51 (47%)
Female	57 (53%)
ALL risk stratification	
SR	27 (25%)
MR	69 (64%)
HR	12 (11%)
Age parent	
M (SD)	38.2 (5.6)
Range	25-52
Gender respondent	
Male	15 (14%)
Female	93 (86%)
Education level	
Low	13 (12%)
Medium	51 (47%)
High	44 (41%)
Single parent household	11 (10%)

sub-clinical levels of internalizing behavioral adjustment problems, but showed recovery. Children in the Chronic trajectory (10%) started out with high levels (above cut-off of 3) of internalizing behavioral adjustment problems, which stayed at stable heightened levels halfway through treatment. There was no recovery at the end of treatment (Figure 1).

Externalizing behavioral problems

Table 2 shows the BIC, AIC, and estimated probabilities of the tested models. The BIC indicated that the linear two-trajectory model fitted best, whereas the AIC favored the linear three-trajectory model or the quadratic four-group model. We chose to maintain the linear three-trajectory model for several reasons. The additional third group was clearly different from the pattern showed by the two-trajectory model. It showed a chronic problems trajectory. The four-group model was not chosen, due to the significant difference in BIC of 10. The average posterior probabilities of the linear three-trajectory model all exceeded .70 (.97, .78, and .96) and each trajectory was composed of at least 5% (83%, 12%, and 5% respectively). Children in the Resilience trajectory (83%) did not experience any externalizing behavioral adjustment problems after diagnosis. Children in the Chronic trajectory (12%) started out with clinical levels of externalizing behavioral adjustment

Table 2. Model (linear) selection results

No. of groups	BIC	AIC	Estimated probabilities (% in each group)			
			1	2	3	4
1 INT	1280.67	1267.26	100			
2 INT	1267.72	1246.27	86	14		
3 INT	1260.80	1231.30	60	30	10	
4 INT	1274.85	1237.30	56	33	10	0
1 EXT	1368.35	1354.94	100			
2 EXT	1346.48	1325.02	90	10		
3 EXT	1348.01	1318.51	83	12	5	
4 EXT	1362.06	1324.51	83	12	5	0

Note. BIC = Bayesian information criterion; AIC = Akaike information criterion.

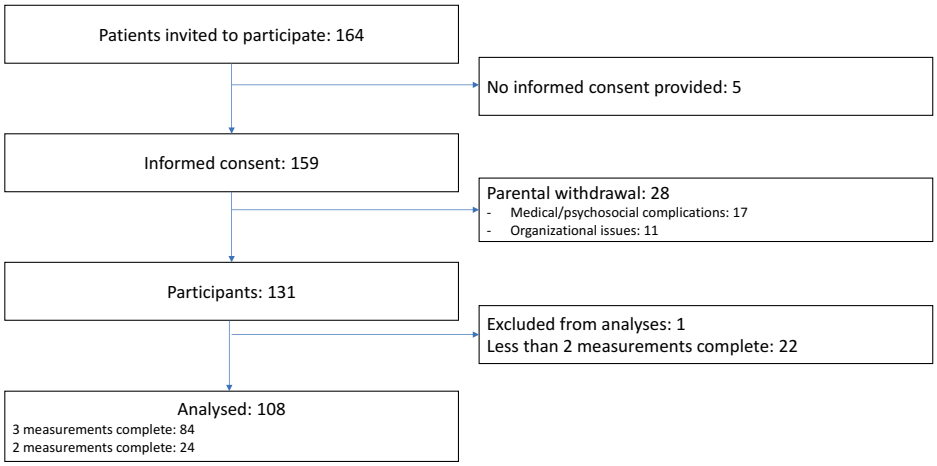

Figure 1. Flowchart of study participants

problems, which stayed stable. Children in the Increasing trajectory (5%) started out with clinical levels of externalizing behavioral problems, and showed no recovery but increasing problems during treatment (Figure 2).

Demographic, medical, and psychosocial predictors of trajectories

Internalizing behavior problems

Table 3 shows the results of continuous and categorical predictor variables for each trajectory. Only significant predictors were entered in the final multivariate analysis. Demographic and medical characteristics were not found to be of significant influence on the trajectories. Of the personal characteristics of the parents, coping and parenting stress had a significant impact on adjustment trajectory of the child. Compared with Resilience, children in the Chronic trajectory had parents who showed higher levels of parenting

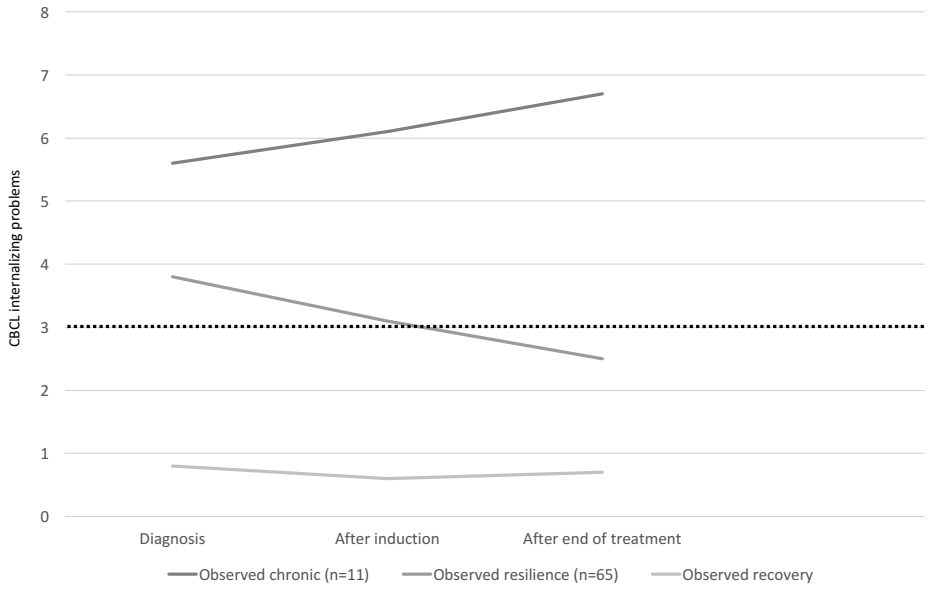

Figure 2. Trajectories of internalizing problems

stress (p<.001; d=1.20) after the cancer diagnosis. At last, child physical and psychological qol at diagnosis were significantly associated with trajectory membership. Compared with the Resilience trajectory, children in the Chronic trajectory experienced lower physical qol (p<.01; d=.94), psychosocial qol (p<.001; d=1.53), and cancer-related qol (p<.001; d=1.51) at diagnosis.

Externalizing behavior problems

Only parenting stress had a significant impact on adjustment trajectory of the child. Compared with Resilience, children in the Increasing trajectory had parents who showed a higher levels of parenting stress (p<.001; d=2.30) after the cancer diagnosis. Also children in the Chronic trajectory had parents experiencing more parenting stress (p<.01; d=.91).

Multivariate Regression analyses

For internalizing problems, the personal characteristics of the parents (parenting stress) and baseline adaptation of the child (physical, psychosocial, and cancer-related qol) were entered simultaneously in a multinomial logistic regression analysis with the Resilience trajectory as the reference group (Table 4). The final model was statistically significant (X^2 = 58.906, df = 8, p < .001, Cox & Snell R^2 = 0.45, Nagelkerke = 0.54, McFadden = 0.34). Only parenting stress (X^2=11.02, p<.01) and baseline cancer-related qol of the child (X^2X^2=18.08, p<.001) were still a significant predictor of behavioral adjustment trajectory. Children with parents experiencing higher levels of parenting stress (Recovery odds ratio=1.01; Chronic

Table 3. Demographic, Medical, and Psychosocial Characteristics of the Total Sample and Each Trajectory: Analysis of Variance (ANOVA) and Chi Square Test Results

		Trajectory groups Internalizing problems (M[SD])					Trajectory groups Externalizing problems (M[SD])				
Predictor	**Total M (sd)**	**Resilience N=65 Weighted N=61.75**	**Recovery N=32 Weighted N=27.52**	**Chronic N=11 Weighted N=10.56**	***F***	***p***	**Resilience N=90 Weighted N=87.30**	**Chronic N=13 Weighted N=10.14**	**Increasing N=5 Weighted N=4.80**	***F***	***p***
Child demographic											
Age at diagnosis	6.4 (4.3)	6.4 (4.4)	5.6 (3.3)	8.0 (5.3)	1.27	.29	6.7 (4.2)	3.8 (2.7)	7.2 (5.7)	2.24	.11
Child medical											
Hospitalisations	12.6 (34.7)	13.5 (35.8)	11.1 (38.4)	10.7 (13.4)	.06	.94	12.3 (37.5)	10.3 (13.4)	21.8 (20.1)	.19	.83
ICU admissions	1.7 (9.5)	2.2 (11.7)	1.0 (4.6)	0.0 (0.0)	.33	.72	2.0 (10.3)	0.0 (0.0)	0.0 (0.0)	.27	.77
Child psychosocial											
QoI-physical	21.2 (14.1)	25.0 (13.6)	15.0 (14.1)	14.7 (8.1)	**6.49**	**.00**	21.2 (14.1)	20.4 (16.5)	19.9 (10.9)	.03	.97
QoI-psychosocial	40.6 (8.9)	43.9 (7.8)	36.1 (7.5)	31.5 (8.4)	**16.68**	**.00**	40.8 (8.9)	39.4 (7.7)	36.2 (12.5)	.69	.50
QoI-cancer related	66.9 (13.8)	72.7 (11.9)	59.1 (12.1)	53.2 (13.8)	**21.35**	**.00**	67.0 (14.1)	66.0 (13.3)	63.0 (13.8)	.21	.81
Parent psychosocial											
Helplessness	13.1 (3.1)	13.4 (3.3)	12.6 (2.9)	12.3 (2.3)	1.03	.36	13.0 (3.2)	13.7 (3.0)	13.0 (2.9)	.21	.81
Acceptance	16.2 (3.6)	16.6 (3.7)	16.0 (3.7)	14.2 (2.0)	2.15	.12	16.2 (3.5)	16.7 (4.5)	14.2 (1.8)	.84	.44
Perceived benefits	16.2 (3.7)	16.0 (3.8)	15.9 (3.6)	18.0 (3.7)	1.44	.24	15.9 (3.5)	17.8 (4.9)	17.0 (2.9)	1.46	.24
Positive affect	8.4 (4.1)	8.7 (4.2)	8.0 (3.9)	7.7 (4.6)	.43	.65	8.2 (4.1)	9.8 (3.8)	7.0 (4.8)	.95	.39
Negative affect	31.7 (18.4)	31.8 (19.2)	29.5 (17.2)	36.1 (17.3)	.48	.62	31.0 (18.8)	36.3 (17.6)	30.0 (10.9)	.39	.68
Avoidant coping	14.9 (2.9)	14.9 (2.9)	15.1 (3.2)	15.1 (1.6)	.06	.94	15.0 (2.9)	15.0 (3.5)	13.6 (1.5)	.54	.59
Passive coping	10.8 (2.7)	10.7 (2.6)	10.4 (2.6)	12.7 (3.0)	**3.24**	**.04**	10.6 (2.6)	11.7 (3.7)	11.4 (0.9)	.83	.44
Social support	17.1 (3.4)	17.4 (3.4)	16.5 (3.7)	16.7 (2.8)	.64	.53	17.0 (3.6)	18.4 (2.1)	15.4 (2.1)	1.36	.26
Parenting stress	52.8 (19.2)	49.1 (17.5)	53.4 (17.6)	72.6 (21.7)	**7.64**	**.00**	49.1 (17.1)	64.8 (17.4)	86.2 (15.0)	**13.65**	**.00**
	N	**N**	**N**	**N**	**X^2**	***p***				**X^2**	***p***
Child demographic											
Gender child					4.32	.12				1.27	.53
Education level parent					5.93	.21				3.05	.55
Family situation					6.68	.35				10.83	.09
Child medical											
Treatment protocol					8.80	.07				.53	.97

odds ratio=1.10) and lower baseline cancer-related qol (Recovery odds ratio=.93; Chronic odds ratio=.83) were more likely to belong to the Recovery or Chronic trajectory than to the Resilience trajectory. For externalizing problems, only parenting stress was entered into the regression analyses (Table 4). The final model was statistically significant (X^2 = 21.289, df = 2, p < .001, Cox & Snell R^2 = 0.19, Nagelkerke = 0.30, McFadden = 0.21). Children with a parent who experienced higher levels of parenting stress were more likely to belong to the Increasing (odds ratio=1.12) or Chronic trajectory (odds ratio=1.05) than to the Resilience trajectory.

Table 4. Multinomial regression analyses results for internalizing (chronic versus resilience trajectory) and externalizing (increasing and chronic versus resilience trajectory) behavior problems

	X^2	*p*	*B*	*Wald*	*Exp (B)*
Predictor internalizing					
Passive reaction pattern	1.32	.52	.07	0.19	1.08
Parenting stress	8.86	.01	.09	6.70	1.09
Qol-physical	3.57	.17	-.06	1.66	.95
Qol-psychosocial	3.77	.15	-.08	1.16	.93
Qol-cancer related	17.14	.00	-.17	7.51	.84
Predictor externalizing					
Parenting stress	21.29	.00			
Increasing			.11	9.64	1.12
Chronic			.05	6.30	1.05

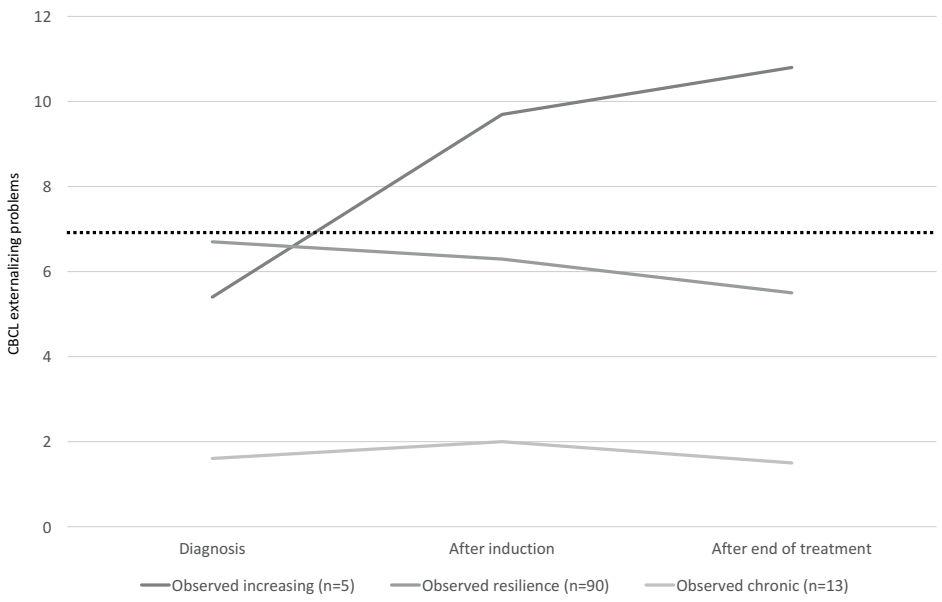

Figure 3. Trajectories of externalizing problems

DISCUSSION

This study identified three distinctive trajectories of both internalizing and externalizing behavioral adjustment, comparable to previous research[10]. The majority of the children (53%) showed no behavioral problems during the entire treatment as reported by parents. A smaller group of children (24%) showed adjustment problems at diagnosis, but recovered at end of treatment to normal. Adjustment problems that not returned to normal were present in a substantial group of children (19%). Severe maladjustment was present in a small but substantial group of the patients (4%), experiencing high levels of both internalizing and externalizing behavioral problems. Thus, most children diagnosed with ALL seem to adjust relatively well regarding their psychosocial well-being.

The categorization into these groups is in concordance with the Psychosocial Preventative Health Model (PPPHM) as described by Kazak, 2006[40]. Although this model is focused on family adjustment, it might also be applied to child adaptation due to the important influence of the family on the ill child. Compared to research in adults, children seem to have a more resilient trajectory of adjustment[10]. However, we know that a substantial amount of the survivors of childhood cancer experience ongoing problems even long time after the ending of treatment, apparently more than children during active treatment. The adequate adjustment of children during treatment seems therefore treacherous: during the structured period of treatment children are adapting quite well, but after the end of treatment, a period in which the number of hospital visits declines, a growing number of children experience late effects. Psychosocial care is important for these groups of patients, to support the process of getting back to life as usual.

This study also showed that not medical factors, such as diagnosis and number of hospitalizations, of the child puts them at risk for psychosocial difficulties, but mainly the psychological reaction of the parents after diagnosis. Children with chronic high scores regarding internalizing behavior could be distinguished from the group that showed recovery by more passive coping by the parents, and higher levels of parenting stress. Children with growing externalizing problems could be distinguished from the stable group by higher levels of parenting stress. A link between passive coping style and adverse psychological reactions has been reported repeatedly before in both pediatric and adult care[19,41]. Therefore, it can be seen as a substantial risk factor for maladjustment after diagnosis and should be paid attention to. At last, an effect for parenting stress has also been previously reported, with higher levels of stress being indicative for family adjustment difficulties[21]. Attention is needed for families experiencing parenting stress while raising a child with a chronic and life-threatening illness. Interventions focused on reducing stress, for example by improving problem solving skills would be helpful for this specific vulnerable population.

As mentioned before, this study did not find an effect for demographic and medical variables of the patient and on behavioral adjustment problems. This lack of effect of

gender[7] and age at diagnosis[42] on behavioral problems has been previously reported. An effect for medical risk stratification has been previously reported, with higher treatment intensity being indicative for behavioral problems[2]. However, differences in time since diagnosis and treatment protocol limit comparisons. Also illness cognitions, parental affect, and social support were not found to be of significant influence. It might be that these factors are mainly associated with parental distress and not directly influence behavior of the child after diagnosis[19,25].

This study with its longitudinal design and a homogenous population made it possible to investigate patterns of behavioral adjustment after the diagnosis of childhood cancer. Instead of examining this at group level, we looked at individual differences in trajectories of behavioral adaptation. By aggregating these individual differences, we found three distinctive patterns of behavioral adjustment problems over time, for both internalizing and externalizing symptoms. This approach provided us with more advanced knowledge about the course of adjustment in children diagnosed with cancer. However, there are also some limitations. This study included child behavior problems and parenting stress as important variables. Parenting stress was treated as predictor and behavior problems as the outcome, based on previous findings. However, they also might influence each other the other way around: child behavior might lead to parenting stress. The longitudinal nature of this study provided evidence for the framework we tested, however the effect of behavior problems on parenting stress could not be delineated with the current study. Next to this, the power to detect differences between groups was limited due to little N in the smallest internalizing and eternalizing classes. Furthermore, we focused on the behavioral adjustment during treatment, which might limit the ability to draw conclusions on long-term behavioral adjustment. Further studies need to be performed with a longer follow-up period and broader patient sample to evaluate the course of behavioral adjustment of children with cancer in general into long-term survivorship. In addition, we only used parent proxy reports in this study due to the young median age of children diagnosed with ALL. Parent reports were used to assess both parent and child functioning, and from previous research it is known that child behavior judged by parents is difficult to interpret[43]. At last, selection bias might be present in this study sample. It could be that the parents who dropped out of the study were more stressed or had children with greater problems compared to those who completed all assessment time points.

The results of this study show the importance of early identification of patients at risk for ongoing or escalating problems. Screening would facilitate this, assessing a broad range of risk factors, such as child baseline adaptation, parental stress, and coping. Information on such risk and protective factors is helpful to provide personalized, family-based, and cost-effective psychosocial care[40].

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CHAPTER 3

Family adjustment in Children with Acute Lymphoblastic Leukemia: the mediating role of parenting stress

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ABSTRACT

Background: Although knowledge has been gathered about risk factors for child maladjustment to cancer diagnosis and treatment, the exact mechanism of how factors influence child adjustment is still largely unclear. This study investigated parenting stress as a mediator between various parent factors and child behavioral adjustment in families of a child recently diagnosed with ALL.

Methods: In a multicenter longitudinal study, 108 parents of children aged 1-17 (response rate 80%) diagnosed with ALL, completed questionnaires on child behavioral problems (CBCL), parental well-being (POMS), illness cognitions (ICQ-P), parenting stress (PSI), social support (ISR), coping (UCL), at time of diagnosis (T=0) and at end of treatment (T=1). Structural Equation Modeling (SEM) was performed to test the hypothesized models.

Results: This study showed important indirect effects of perceived disease benefits, positive affect, and social support on child behavioral problems via parenting stress. Parenting stress seemed to a stronger predictor for externalizing behavior, than for internalizing behavior. The tested models showed an excellent fit to the data.

Conclusion: This study showed that parenting stress is a key factor in explaining psychosocial adjustment in children during treatment for ALL. Screening focused on predictors of parenting stress such as cognitions, coping, and social support would facilitate early detection of families at-risk. Timely interventions, focused on parenting capacities, can provide family-based psychosocial care to prevent escalation of problems and support adequate child and family adjustment after diagnosis.

INTRODUCTION

The diagnosis of childhood cancer and its treatment causes various emotional reactions and requires a certain adaptation process for the families to keep fulfilling the daily demands. Parents must learn to cope with the intense demands of the child's treatment, the uncertainty of the child's prognosis, and fear/threat of the child's death. After the diagnosis of Acute Lymphoblastic Leukemia (ALL) families experience frequent hospital appointments, hospitalizations, medical complications, invasive medical procedures, and child behavioral problems due to dexamethasone administration for a total period of 2 years[1].

Although the majority of the families of children with cancer show no psychosocial maladjustment[2,3] previous studies reveal that still a considerable group of the children does develop problems with their emotional and social adjustment[4,5]. Parents as well might experience symptoms of depression and anxiety as a reaction to illness of their child[6]. The disability-stress-coping (DSC) model of Wallander and Varni (1998) describes by what factors and which pathways child adjustment to pediatric chronic illness might be influenced[7]. Increased risk for psychosocial adjustment difficulties in pediatric cancer is associated with different factors including demographic factors (such as age[8], gender[8], ethnic background[9,10], and socio-economic status[8,11]), disease-related factors (such as treatment intensity[8,12]), and parental psychosocial factors (such as cognitions[13], parental affect[14,15], and social support[16]). From previous research in other pediatric populations, it is known that associations between parent and child functioning tend to be in the direction of parent to child[17]. Parenting stress is an important factor in influencing family psychosocial adjustment and is suggested to directly influence child behavior[18-22]. Parenting stress can be experienced by parents while raising their child and trying to meet parenting role demands[23,24]. Parenting a child with a prolonged and/or serious adverse health condition is complex and can be stressful[25]. Most parents experience parenting stress to some extent, but various studies indicate that parenting stress increases in children with health problems[23,24]. Parents have to fulfill a great amount of new tasks when caring for their ill child as consequence of both the treatment and the side effects. Combining this with general parenting tasks, such as setting boundaries and rules while raising a child, can be difficult[26]. Moderate to severe parenting stress is common in the first year of childhood cancer treatment[27]. Previous research suggests that parenting stress especially influence externalizing behavior in children[17].

Although much knowledge has been gathered about risk factors for family psychosocial maladjustment in pediatric oncology, the exact mechanism of how parent factors influence child adjustment is still largely unclear. When specific factors and pathways are found, one could screen for and intervene on these factors. For efficient intervention it is important to clarify the exact mechanisms that are involved. Aiming at finding clues/ingredients for intervention, this study aimed to point out on whom such an intervention should be focused: on the child, the parent, or the child-parent interaction. This study

aimed to investigate parenting stress as a mediator between various parent factors and child behavioral adjustment in families of a child recently diagnosed with ALL. First, it was hypothesized that parent factors, such as coping, cognitions, affect, and social support would significantly predict child behavioral adjustment. Second, it was expected that parenting stress would function as a mediator between parent and child factors. At last, it was hypothesized that results were particularly strong for externalizing behavior.

METHOD

Participants

Parents of children with ALL from six Dutch pediatric oncology centers were enrolled. Inclusion criteria were: 1) child age between 1,5-18 years, 2) newly diagnosed with ALL, and 3) treated according to the Dutch Childhood Oncology Group (DCOG) ALL-10 protocol[28]. In addition, parents had to be fluent in Dutch and children with an important pre-existing condition (e.g. Down syndrome), potentially affecting baseline measurement, were excluded.

Therapy according to ALL-10 protocol was provided to children with ALL in the Netherlands between 2004 and 2012. In this protocol, three risk groups are identified, mainly based on response to therapy: standard risk (SR), medium risk (MR) and high risk (HR). Treatment is risk-adjusted with a reduction in treatment intensity for SR-ALL (good response to therapy, low risk of relapse) and higher treatment intensity for MR-ALL and HR-ALL (higher risk of relapse)[28].

Procedure

From October 2006 till October 2009 parents of newly ALL-diagnosed patients were invited to participate in this study. Parents who were willing to participate received verbal and written information on the study within the first weeks after diagnosis by one of the principal researchers. Parent-proxy measurements were performed two times for children treated according to the SR or MR ALL-10 protocol: during induction treatment (T0 *Mean completion time post-diagnosis*=42.1 days, *range*=5-131 days), and shortly after finishing treatment (T1 *Mean completion time post-diagnosis*=781.2 days, *rang*e=651-1000 days). For children treated according to the HR ALL-10 protocol, measurements were also performed two times. These children received more intense treatment followed by maintenance therapy, so T0 and T1 slightly differed from those in SR and MR groups: during induction treatment (T0 *Mean completion time post-diagnosis* =46.0 days, *range*=12-96), and shortly after finishing treatment (T1 *Mean completion time post-diagnosis* =379.0 days, *range*=259-487 days).

A set of questionnaires was distributed together with a stamped return envelope to the participating families. Families were instructed to choose one parent respondent for

all assessments. Parents were contacted by one of the researchers if the booklet was not returned within two or three weeks. Information on risk-adapted treatment regime was available through Dutch Childhood Oncology Group (DCOG) databases. The study was approved by each of the medical ethical review boards of the participating institutions.

Measures

Parental subjective well-being was assessed with the Dutch shortened version of the Profile of Mood States (POMS)[29,30]. The POMS is a self-report questionnaire concerning changeable mood states, that are supposed to represent subjective well-being. The shortened POMS consists of 32 items and is designed to measure mood in five different domains: fatigue (6 items), irritation (7 items), vigor (5 items), tension (6 items), and depression (8 items). The answers are graded on a 5-point scale ranging from 'not at all' (0) to 'extremely' (4). The subscales fatigue, irritation, tension, and depression form the POMS negative affect score. Items on vigor form the POMS positive affect score. In the current study, internal consistency for the different domains ranged from α=.79 to α=.91.

Parental illness cognitions were assessed with the Illness Cognitions Questionnaire - parent version (adapted from the ICQ)[31,32]. The ICQ-p measures illness cognitions that reflect different ways of evaluating the aversive character of a chronic condition of the child. The questionnaire consists of three subscales: helplessness (6 items), acceptation (6 items), and disease benefits (6 items). In the current study, internal consistency for the three scales ranged from α=.75 to α=.87.

Parental coping strategies were assessed with the Utrecht Coping List (UCL)[33]. This inventory consists of 47 items and measures the characteristic ways in which a person reacts when confronted with circumstances that require adjustment on a 4-point scale. Seven scale scores can be assessed, of which two scales were used in the current study, namely the less adaptive coping strategies avoidance/awaiting (8 items) and passive reaction pattern (7 items). Internal consistency for the current sample was α=.47 for the avoidance/awaiting subscale and α=.64 for the passive reaction pattern subscale.

Parental perceived social support was assessed with the Inventory for Social Reliance (ISR)[34]. The ISR is a self-report inventory for the measurement of social support. The subscale potential emotional support was used in the current study, which consists of 5 items measuring perceived social support. Internal consistency for the current sample was α=.92.

Parenting stress was assessed with the Parenting Stress Index-short form (PSI)[35]. The PSI measures the level of stress parents experience in raising their child and it consists of 25 statements on a 6-point Likert scale. In the current study, the total stress score was used as a measure of parenting stress. In the current sample internal consistency was α=.92.

Parent-rated child behavioral adjustment was collected using the Dutch translation of the Child Behavior Checklist[36,37]. The CBCL is a parent-reported questionnaire that provides scores on global, internalizing and externalizing behavioral problems. In this study two

distinct versions were used, one for children aged 1,5-5 years (101 items), and one for 6-18 years (113 items). The subscales anxious/depressed, withdrawn, somatic problems, attention problems and aggressive behavior syndromes are suitable to compare the different age versions. In addition, the CBCL 1,5-5 includes sleep problems and emotional reactions, while the CBCL 6-18 includes social behavior, thought problems and rule breaking behavior. Parents are requested to circle a 0 if the item is not true for the child, a 1 if the item is somewhat or sometimes true, and a 2 if it is very true or often true. A total problem score is obtained by summing item scores. Available norms provide age and gender-standardized T-scores (mean=50; SD=10)[36]. T-scores were used for descriptive analyses because they make it possible to analyze the two different age versions of the CBCL as one group. Total, internalizing and externalizing problems T-scores of 60-63 (percentile 84-90) represent the borderline clinical range and T-scores above 63 represent the clinical range in the general population. During the study period, a total of 28 families switched from the CBCL 1,5-5 years to CBCL6-18 years because aging of the child. When 50% or more of the items on a subscale were missing, the subscale score could not be computed and was handled as missing data. The CBCL has well-established reliability and validity[36].

Statistical methods

The Statistical Package for Social Sciences (SPSS) for Windows version 20.0 was used for descriptive analyses. All data showed a normal distribution. Relations between child behavioral problems (CBCL), dichotomized demographic variables (gender, age, education), and parental variables (cognitions, coping, affect, social support, parenting stress) were assessed with Pearson correlations. Structural Equation Modeling (SEM) was performed to test the hypothesized mediation models. Predictor variables were selected based on findings in the literature. The sample size did not allow for the inclusion of all predictors observed in this study. Therefore, we had to make a post hoc selection of the observed predictors for inclusion in the mediation model. Selection was based on the significance of the correlations; we are aware this in not the most elegant way to select variables to include in the analyses. We estimated two mediation models, one with child behavior problems as the outcome and one with internalizing behavior and externalizing behavior as outcomes. Testing mediation on cross-sectional data is usually seen as problematic because of the temporal order of the variables in the model. In order to overcome this problem, the mediator and the predictors were measured at the start of the treatment (T0) and the outcome variables were measured after the treatment (T1). P-values (two-sided tests) ≤ 0.05 were considered statistically significant. All models were estimated with LISREL8.8[38] using the full information maximum likelihood (FIML) procedure. Enders & Bandalos (2001) have shown that FIML has a superior performance compared to listwise deletion if missing data is present[39]. All models were evaluated with the CHI2 and the RM-

SEA. A model with an RMSEA smaller than .05 and a p-value larger than .05 is considered a fitting model, although the exact cut-offs are subject of debate[40].

RESULTS

Descriptives

During the study period, a total of 164 families were invited to take part in the study of which 159 agreed (reason for rejection was feeling too overwhelmed *N*=5). 131 parents returned completed questionnaires at baseline (response rate 80%). One patient was excluded from analyses because the questionnaire was returned long after the induction phase. Only families with complete data at T0 and T1 were included in analyses (*N*=108). See Table 1 for demographic information.

Table 1. Demographic information of the sample

Variable	*Mean (SD)*	*Range*
Age child	6.3 (4.2)	1-17
Age parent	38.2 (5.6)	25-52
	Frequency (%)	
Gender child (female)	57 (53%)	
ALL risk stratification		
Standard risk	27 (25%)	
Medium risk	69 (64%	
High risk	12 (11%)	
Gender respondent (female)	93 (86%)	
Education level		
Low	13 (12%)	
Medium	51 (47%)	
High	44 (41%)	
Household (single parent)	11 (10%)	

Small significant correlations (Table 2) were found between child behavioral problems and parent education level (total CBCL*edu low *r*=-.28; internalizing*edu low *r*=-.23, externalizing*edu low *r*=-.25), indicating that child behavior problems were related to a higher level of parent education. Another small significant correlation was found between internalizing behavioral problems and parental gender (*r*=-.21), indicating that more internalizing behavioral problems were related to the parent filling in the questionnaires being the father.

None of the assumed predictor variables (parental subjective wellbeing, parental illness cognitions, parental coping strategies, parental perceived social support) correlated with child behavioral problems. The assumed mediator 'parenting stress' correlated significantly with the outcome variable 'child behavioral problems' (total CBCL *r*=.54, internalizing *r*=.43, externalizing *r*=.61), indicating that a higher level of stress of the parents was related to more child behavioral problems. Most of the parental predictor variables showed a significant association with the assumed mediator 'parenting stress'. A higher level of parenting stress was related to more helpless cognitions (*r*=.29), a lower level of acceptance (*r*=-.20), less positive affect (*r*=-.34), more negative affect (*r*=.46), adopting a passive coping style (*r*=.37), and less social support (*r*=-.27). All associations between demographic variables and parenting stress were not significant.

Table 2. Pearson correlations between the variables in the study (n=97).

	PSI	CBCL	CBCL_I	CBCL_E	Help	Accept	Benef	PosA	NegA	NegAF	Avoid	Pass	SocS	Gender	Age	Fam	Sibling	GenderP	AgeP	EduL	EduM	EduH
PSI	1.00																					
CBCL	.54**	1.00																				
CBCL_I	.43**	.88**	1.00																			
CBCL_E	.61**	.87**	.62**	1.00																		
Help	.29**	.06	.01	.14	1.00																	
Accept	-.20*	-.12	-.18	-.12	-.33**	1.00																
Benef	.18	.07	.00	.08	-.03	.31**	1.00															
PosA	-.34**	-.07	-.09	-.11	-.38**	.30**	.13	1.00														
NegA	.46**	.14	.17	.15	.62**	-.41**	.05	-.47**	1.00													
NegAF	.46**	.10	.13	.12	.65**	-.38**	.02	-.55**	.97**	1.00												
Avoid	.00	-.04	.10	-.12	.09	.09	-.07	-.08	.08	.12	1.00											
Pass	.37**	.10	.19	.07	.48**	-.31**	.00	-.41**	.62**	.63**	.24*	1.00										
SocS	-.27**	-.09	-.04	-.16	-.11	.16	.16	.13	-.10	-.08	.04	-.22*	1.00									
Gender	.11	.05	.02	.00	.08	.06	.13	-.04	.07	.05	-.05	.01	-.10	1.00								
Age	-.16	-.04	-.02	-.09	-.21*	.00	.04	.19	-.27**	-.28**	-.05	-.19	.01	-.07	1.00							
Family	.06	.07	.11	.01	-.02	.05	.07	.00	.02	.04	.04	.16	-.08	-.02	.20*	1.00						
Sibling	-.08	-.13	-.06	-.09	-.10	.04	.04	.24*	-.11	-.12	-.03	-.19	.07	-.14	.14	-.26**	1.00					
GenderP	.06	-.15	-.21*	-.03	.09	.01	.03	.05	.01	.02	-.06	.02	.00	-.10	.00	.15	.13	1.00				
AgeP	-.17	.11	.17	-.03	-.22*	-.03	-.06	.29**	-.27**	-.31**	-.11	-.15	-.05	-.03	.64**	.06	.15	-.26**	1.00			
EduL	-.06	-.28**	-.23*	-.25*	.18	-.06	.07	-.10	.08	.08	.10	.00	.04	-.02	.03	-.05	.04	.07	-.19	1.00		
EduM	.06	.01	-.01	.00	-.07	-.04	.05	-.07	.05	.04	.19	.16	-.21*	.10	.16	.30**	-.14	.13	.08	-.34**	1.00	
EduH	-.02	.17	.17	.16	-.05	.08	-.10	.13	-.10	-.10	-.26*	-.16	.18	-.09	-.18	-.27**	.12	-.17	.05	-.33**	-.78**	1.00

** p<.01; * p<.05

Note: PSI=Parental Stress Index; CBCL=Child Behavior CheckList; CBCL_I= Internalizing scale of the Child Behavior CheckList; CBCL_E=Externalizing scale of the Child Behavior CheckList; Help=Helplessness scale of the Illness Cognition Questionnaire; Accept=Acceptance scale of the Illness Cognition Questionnaire; Benef=Perceived benefits of disease scale of the Illness Cognition Questionnaire; PosA=Vigor scale of the Profile of Mood States; NegA=Sumscore of the irritation and tension scales of the Profile of Mood States; NegAF=Sumscore NegA and the fatigue scale of the Profile of Mood States; Avoid=Avoidance/awaiting scale of the Utrecht Coping List; Pass=Passive reaction scale of the Utrecht Coping List; SocS=Inventory for Social Reliance (social support); Gender=Gender of the child; Age=Age of the child; Family=Family situations (0=two parent household, 1=other); Sibling=Siblings of child (0=only child, 1=with siblings); GenderP=Gender of the parent (who completed the questionnnares); AgeP=Age of the parent; EduL=Education of Parent (0=other, 1=low); EduM=Education of Parent (0=other, 1=medium); EduH=Education of Parent (0=other, 1=high).

The mediation model results

The first model we analyzed (Figure 1) is the model with child behavior problems (CBCL) after the end of treatment as the outcome. The variables parental stress, helplessness, acceptance, perceived disease benefits, positive affect, negative affect, passive coping, and social support were all measured at the start of the treatment. The model showed an excellent fit to the data: χ^2(df=7)=3.93, p=.79, and the *RMSEA*=.00. The explained variance

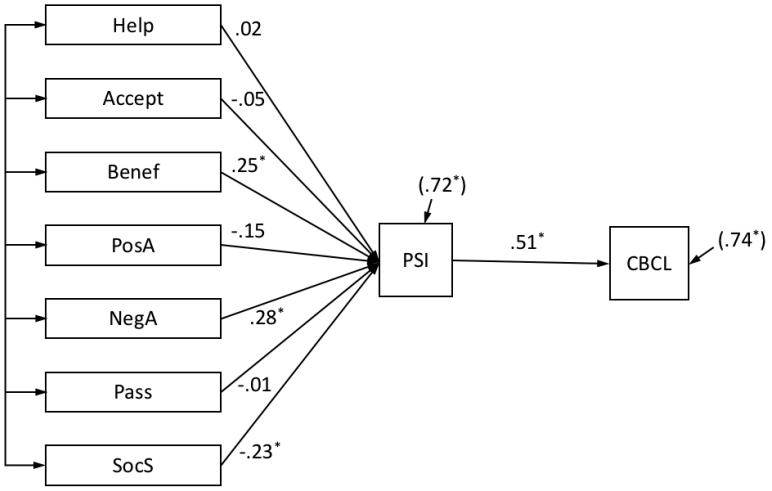

Figure 1. Standardized effects of the mediation model, explaining child behavior problems in children
* p<.05
Note: PSI=Parental Stress Index; CBCL=Child Behavior CheckList; Help=Helplessness scale of the Illness Cognition Questionnaire; Accept=Acceptance scale of the Illness Cognition Questionnaire; Benef=Perceived benefits of disease scale of the Illness Cognition Questionnaire; PosA=Vigor scale of the Profile of Mood States; NegA=Sumscore of the irritation and tension scales of the Profile of Mood States; Pass=Passive reaction scale of the Utrecht Coping List; SocS=Inventory for Social Reliance (social support).
Numbers between brackets are the unexplained variances; the explained variance is 1-unexplained variance.

of the CBCL was 26% (1-unexplained variance). The explained variance of parenting stress was 28% (1-unexplained variance).

The second model we analyzed (Figure 2) is the model with child internalizing and externalizing behavior problems (CBCL) after the treatment as outcome. In the second model, the internalizing and externalizing scores were included as outcome variables (Figure 2). The model showed an excellent fit to the data: χ^2 (df=14)=18.34, p=.19, and the *RMSEA*=.056 The explained variance of the CBCL was 26% (1-unexplained variance). The explained variance of parenting stress was 28% (1-unexplained variance). The explained variance of the CBCL internalizing score was 17% (1-unexplained variance), compared to 36% (1-unexplained variance) for the externalizing score.

DISCUSSION

This study showed that parenting stress is a key factor in explaining psychosocial adjustment in children during treatment for ALL. This study tested a model of factors influencing child behavioral problems during treatment for ALL, in which an indirect effect of parenting stress was assumed. We hypothesized that the relation between parent factors and child behavioral adjustment was indirect via parenting stress. Results of this study showed

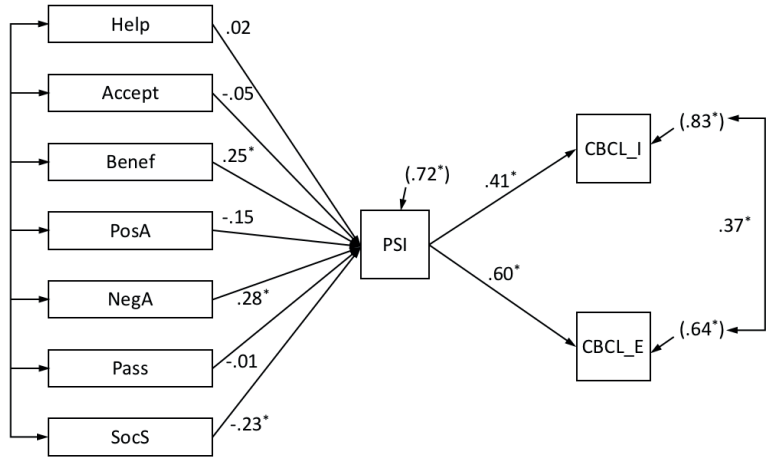

Figure 2. Standardized effects of the mediation model, explaining internalizing and externalizing child behavior problems in children with ALL (n=108) , CHI2(df=14)=18.34, p=.19, and RMSEA=.056.
* p<.05
Note: PSI=Parental Stress Index; CBCL_I= Internalizing scale of the Child Behavior CheckList; CBCL_E=Externalizing scale of the Child Behavior CheckList; Help=Helplessness scale of the Illness Cognition Questionnaire; Accept=Acceptance scale of the Illness Cognition Questionnaire; Benef=Perceived benefits of disease scale of the Illness Cognition Questionnaire; PosA=Vigor scale of the Profile of Mood States; NegA=Sumscore of the irritation and tension scales of the Profile of Mood States; Pass=Passive reaction scale of the Utrecht Coping List; SocS=Inventory for Social Reliance (social support).
Numbers between brackets are the unexplained variances; the explained variance is 1-unexplained variance.

important indirect effects of perceived disease benefits, positive affect, and social support on child behavioral problems via parenting stress.

Since parents who report more positive effects of their child's cancer and sufficient social resources experience less parenting stress and subsequently less child behavioral problems, these positive states variables seem to function as a buffer for family distress.

Parenting stress seemed to be a stronger predictor for externalizing behavior, than for internalizing behavior. To our knowledge, Van der Geest et al (2014)[19] were the first to investigate the mediating effect of parenting stress on the association between parental distress and child adjustment. Our longitudinal study found similar results, and is therefore stronger evidence for the role of parenting stress in adjusting to medical illness. One could screen for important predictors of parenting stress and offer psychological intervention to timely improve child outcome by focusing on the parent-child relationship. A well-known effective intervention that is taking this relationship into account and focuses on improving parenting in order to enhance the development and well-being of both children and their parents is the Triple P-Positive Parenting Program[41,42]. By improving the knowledge, skills, and confidence of parents, Triple P aims to prevent and diminish psychosocial problems in children.

Table 3. Standardized indirect effects of the predictors on CBCL in Figure 1.

	Help	Accept	Benef	PosA	NegA	Pass	SocS
Indirect effect on CBCL	.01	-.03	.13*	-.07	.14*	.00	-.12*

* p<.05

Note: CBCL=Child Behavior CheckList; Help=Helplessness scale of the Illness Cognition Questionnaire; Accept=Acceptance scale of the Illness Cognition Questionnaire; Benef=Perceived benefits of disease scale of the Illness Cognition Questionnaire; PosA=Vigor scale of the Profile of Mood States; NegA=Sumscore of the irritation and tension scales of the Profile of Mood States; NegAF=Sumscore NegA and the fatigue scale of the Profile of Mood States; Pass=Passive reaction scale of the Utrecht Coping List; SocS=Inventory for Social Reliance (social support).

Table 4. Standardized indirect effects of the predictors on CBCL_I and CBCL_E in Figure 2.

	Help	Accept	Benef	PosA	NegA	Pass	SocS
Indirect effect on CBCL_I	.01	-.02	.10*	-.06	.11	-.00	-.10*
Indirect effect on CBCL_E	.01	-.03	.15*	-.09*	.17	-.01	-.14*

* p<.05

Note: CBCL_I= Internalizing scale of the Child Behavior CheckList; CBCL_E=Externalizing scale of the Child Behavior CheckList; Help=Helplessness scale of the Illness Cognition Questionnaire; Accept=Acceptance scale of the Illness Cognition Questionnaire; Benef=Perceived benefits of disease scale of the Illness Cognition Questionnaire; PosA=Vigor scale of the Profile of Mood States; NegA=Sumscore of the irritation and tension scales of the Profile of Mood States; NegAF=Sumscore NegA and the fatigue scale of the Profile of Mood States; Pass=Passive reaction scale of the Utrecht Coping List; SocS=Inventory for Social Reliance (social support).

This study showed that psychological factors, such as the parent-child interaction and parental reliance on social support proved to be more relevant concepts than demographic variables in predicting adjustment difficulties in children with cancer. This lack of effect of child gender[43] and child age at diagnosis[44] on behavioral problems has been previously reported. We did find a small but statistically significant effect for parental gender and education level on behavioral adjustment of the child. Mothers reported less internalizing problems in their child as compared to fathers. Research showed that proxy reports of parents are difficult to interpret, especially concerning internalizing behavior in the child[45]. Parents tend to overestimate problems in children with a chronic health condition, and this might be especially the case for fathers. In most families, mothers are still the primary caregiver and spend more time with their child, which makes it easier for them to estimate problem behavior in their child, especially the behavior in which children direct their feelings and emotions inward[45]. In this study, parents with lower education levels reported less child behavioral problems compared to higher educated parents. Previous research on the effect of parental education level on child behavioral problems shows no or small effects[46]. In this study, the group of parents with low education level was small, and results should be interpreted with caution. Due to the small effect of parental gender and education level, the limited theoretical background, and relatively small sample size of this study, these factors were not included in the final model.

This study with its longitudinal design and a homogenous population made it possible to investigate a model of factors influencing child behavioral adjustment after the diagnosis of cancer. The statistical approach used in this study provided us with more advanced knowledge regarding this subject. Due to the relatively small sample size, we tested a model in which variables were included based on observed correlations. Non-significant correlations were excluded from the model, while previous studies have found an effect on some of these excluded variables, such as demographic and disease-related factors. Next to this, in this study we focused only on the behavioral adjustment during treatment, which might limit the ability to draw conclusions on long-term behavioral adjustment. In addition, this study included child behavior problems and parent factors as important variables. Parenting stress was treated as influencing child adjustment, based on previous findings. However, they also might influence each other the other way around: child behavior might lead to parenting stress. The longitudinal nature of this study provided evidence for the framework we tested, however the effect of behavior problems on parenting stress could not be delineated with the current study. Next to this, in this study there was no assessment of variables, such as parenting behaviors, that could directly link parenting stress to child behavioral problems. In addition, we only used parent proxy reports in this study due to the young median age of children diagnosed with ALL. Parent reports were used to assess both parent and child functioning, and from previous research it is known that child behavior judged by parents is difficult to interpret[47]. At last, selection bias might be present in this study sample. It could be that the parents who dropped out of the study were more stressed or had children with greater problems compared to those who completed all assessment time points.

The results of this study show the prominent role of parenting stress in the behavioral adjustment of children diagnosed with cancer. Screening would facilitate early detection of families experiencing distressing levels of parenting stress. For effective intervention, it is important to clarify the exact mechanisms that are involved in child adjustment after being diagnosed with a life-threatening disease. Focusing on early detection of clinical levels of inadequate coping, negative health beliefs, poor reliance on social support, and negative parental affect and intervene on this by focusing on parenting capacities could support the adequate adjustment of children and their families in pediatric oncology. Timely interventions focused on improving the knowledge, skills, and confidence of parents in raising an ill child can prevent escalation of problems and support adequate child and family adjustment after diagnosis.

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CHAPTER 4

Illness cognitions and family adjustment: psychometric properties of the Illness Cognition Questionnaire for parents of a child with cancer

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ABSTRACT

Background: Illness cognitions are an important mediator between disease and psychological adjustment. This study assessed the psychometric properties of the Illness Cognition Questionnaire (ICQ), adjusted for the parents of an ill child.

Methods: Participants were recruited from two multicenter studies: sample 1 included 128 parents of a child diagnosed with acute lymphoblastic leukemia (ALL) (response rate 82%), and sample 2 included 114 parents of a child diagnosed with cancer (response rate 74%). Parents completed an adapted version of the ICQ (ICQ-P), together with the Profile Of Mood States (POMS; sample 1) or the Hospital Anxiety and Depression Scale (HADS; sample 2). The factor structure of the ICQ-P was examined by means of principal component analysis. Cronbach's alpha for each subscale and correlations between the ICQ-P scales and the HADS and POMS were calculated. The illness cognitions of parents with and without psychological distress were compared.

Results: Factor analysis confirmed the hypothesized structure of the ICQ-P in our sample (n=242). The three scales Helplessness, Acceptance, and Perceived Benefits explained 9.8%, 31.4%, and 17.9% of the variance, respectively. Cronbach's alpha showed adequate internal consistency (.80-.88). Concurrent and criterion-related validity were appropriate.

Conclusion: The results confirm that the ICQ-P reliably assesses the illness cognitions of the parents of a child with cancer. Psychologically distressed parents showed less acceptance and more helplessness. The availability of a short and valid illness cognition questionnaire will help clinicians gain insight into parental cognitions regarding the illness of their child, information that might be helpful for targeting interventions.

INTRODUCTION

Patients diagnosed with a chronic illness have their own beliefs about their illness, defined as illness cognitions. Illness cognitions can be described as a patient's perception, interpretation, and understanding of the disease and its treatment[1-3]. Illness cognitions refer to the common-sense model of illness representations from Leventhal[1]. The theory describes beliefs and expectations people have regarding a disease or medical complaints. A patient's beliefs influence their ability to cope with and adjust to illness[4], and illness cognitions may be a significant mediator between the condition and the patient's wellbeing[5-9]. For example, patients who perceive their illness as having serious consequences and as being chronic, experience more physical, emotional, and social problems than do patients who perceive their illness as being curable and controllable[6-8].

Similar findings have been obtained regarding the illness cognitions of the parents of an ill child, particularly a child with cancer. Parental cognitions about how stressful the illness is to the child, how life-threatening the cancer is, the intensity of treatment, and their own ability to cope with their child's disease are significantly associated with parental distress[10-13]. Parents who are optimistic and who see benefits are less distressed than parents who do not have this optimistic frame of mind[14-16]. In turn, parental distress influences the child's distress[17-21], and therefore illness beliefs affect the psychological adjustment of the entire family. Insight into parental cognitions regarding their child's disease may help therapists to understand maladaptive adjustment. While there are some questionnaires to assess parental illness cognitions[12,22], they mainly focus on negative illness cognitions. We used the Illness Cognition Questionnaire (ICQ) in this study because it has been shown to predict adjustment problems in adults with chronic conditions[5,23] and includes both positive and negative cognitions related to disease, namely, helplessness, acceptance, and perceived benefits.

The objectives of this study were to adapt the ICQ, which was originally developed for adults with a chronic condition[5], for use in parents of an ill child (ICQ-P), to assess its psychometric properties, and to determine whether scores are associated with parental distress. We also investigated whether the original three-factor structure (Helplessness, Acceptance, and Perceived Benefits) found in adult patients is equally valid for the parents of children with cancer. We expected that the ICQ-P would have an adequate factor structure and appropriate reliability and validity in our sample. Furthermore, we expected adaptive illness cognitions (Acceptance) to be negatively associated with parental psychological distress and hypothesized that maladaptive illness cognitions (Helplessness) would be associated with parental psychological distress.

METHODS

Sample

Data on the illness cognitions of the parents of a child with cancer were collected in two studies: sample 1 consisted of parents who participated in the period 2006–2009, and sample 2 consisted of parents who participated in the period 2012–2013. The two studies were similar in terms of including the parents of a child diagnosed with cancer and the time since diagnosis (around 1 month, see Table 1). Families in sample 1 completed paper-and-pencil questionnaires, whereas families in sample 2 filled in web-based questionnaires.

The first sample comprised the parents of children with acute lymphoblastic leukemia (ALL) recruited from six of the seven Dutch pediatric oncology centers (response rate 82%)[24]. Reasons for non-response were too overwhelmed or medical complications. This study focused on the adjustment of children with ALL during treatment and predictors of child adjustment. Inclusion criteria were age 1.5–18 years, recent diagnosis of ALL, treatment according to the Dutch Childhood Oncology Group (DCOG) ALL 10 protocol[25], and parental fluency in Dutch. The study was approved by the medical ethics review boards of the participating institutions.

The second sample comprised the parents of children recently diagnosed with cancer from four of seven Dutch pediatric oncology centers (response rate 74%). Reasons for non-response were too overwhelmed, not interested, or medical complications. This study focused on the validation of the Psychosocial Assessment Tool (PAT) and investigated the effects of psychosocial screening in pediatric oncology. Inclusion criteria were age 0–17 years, recent diagnosis of cancer, and parental fluency in Dutch; children with a life expectancy < 6 months or a relapse were excluded. The study was approved by the medical ethics review boards of the participating institutions.

The samples were compared regarding child age and gender, and time since diagnosis. The patients in sample 1 were younger (T=-2.25, p=.03) and their parents completed the questionnaires longer after diagnosis (T=4.30, p=.00) than the patients/parents in sample 2. Patient gender was not significantly different (χ^2=.78, p=.38).

Measures

Sociodemographic information (diagnosis, family structure, socioeconomic status) was collected with a self-developed questionnaire.

Parental illness cognitions about the disease of their child were assessed with the Illness Cognitions Questionnaire - Parent version (ICQ-P, adapted from the ICQ with permission of the developers)[26]. See appendix 1 for the questionnaire. The ICQ measures illness cognitions that reflect different ways of evaluating the aversive character of a chronic condition of a patient, namely, helplessness (e.g. "My illness controls my life"), acceptance (e.g. "I can handle the problems related to my illness"), and disease benefits (e.g. "Dealing with my illness has made me a stronger person"). Items are scored on a 4-point Likert scale (1=not

Table 1. Demographic information of participating families

	Study 1 N=128	Study 2 N=114	Total N=242
Age parent			
M (SD)	38.20 (5.99)	39.86 (6.55)	38.98 (6.30)
Range	25-55	24-55	24-55
Gender parent			
Mother	111 (87%)	74 (65%)	185 (76%)
Father	17 (13%)	40 (35%)	57 (24%)
Education parent			
Low	16 (13%)	9 (8%)	25 (10%)
Medium	62 (48%)	37 (32%)	99 (41%)
High	50 (39%)	68 (60%)	118 (49%)
Marital status parent			
Single	15 (12%)	3 (3%)	18 (7%)
Age child			
M (SD)	6.52 (4.26)	7.87 (5.10)	7.15 (4.71)
Range	1-17	0-17	0-17
Gender child			
Boy	68 (53%)	65 (57%)	133 (55%)
Girl	60 (47%)	49 (43%)	109 (45%)
Diagnosis			
Hematological			
Leukemia	128 (100%)	29 (25.4%)	157 (64.9%)
Hodgkin's lymphoma		8 (7.0%)	8 (3.3%)
Non-Hodgkin lymphoma		13 (11.4%)	13 (5.4%)
Neuro-oncological			
Brain/CNS tumor		19 (16.7%)	19 (7.9%)
Solid			
Ewing's sarcoma		6 (5.3%)	6 (2.5%)
Neuroblastoma		7 (6.1%)	7 (2.9%)
Rhabdomyosarcoma		6 (5.3%)	6 (2.5%)
Wilm's tumor		8 (7.0%)	8 (3.3%)
Osteosarcoma		11 (9.6%)	11 (4.5%)
Other solid tumor		7 (6.2%)	7 (2.9%)
Mean time after diagnosis			
M (SD)	41 days (22.84)	30 days (14.61)	36 days (20.08)
Range	5-131 days	4-80 days	4-131 days

at all, 2=somewhat, 3=to a large extent, 4=completely) and each subscale consists of 6 items. Scale scores are calculated by summing the item scores, resulting in a subscale score ranging from 6 to 24 and a total score ranging from 18 to 72. The text of the questions was adapted to make it appropriate for the parents of ill children. For example, "my illness" in the original questionnaire was changed to "my child's illness". The internal consistency of the three scales of the original ICQ ranged from α=.84 to α=.91[5].

Parental psychological distress (sample 1) was assessed with the Dutch shortened version of the Profile of Mood States (POMS)[27,28]. The POMS is a self-report questionnaire investigating changeable mood states and consists of 32 items. It is designed to measure mood in five different domains: fatigue (6 items), irritation (7 items), vigor (5 items), tension (6 items), and depression (8 items). The answers are scored on a 5-point scale ranging from 'not at all' (0) to 'extremely' (4). The reliability and validity of this scale are good (α=.76-α=.95)[27]. In the current study, internal consistency for the different domains ranged from α=.79 to α=.91.

Parental psychological distress (sample 2) was assessed with the Hospital Anxiety and Depression Scale (HADS)[29,30]. The HADS is a self-report questionnaire assessing the presence of anxious and depressive states in a medical setting. It consists of 14 items in two domains: anxiety (7 items) and depression (7 items). Answers are scored on a 4-point scale, ranging from 0 to 3. The Total score is an indication of overall distress (range 0-42). In this study, a cutoff score of ≥13 for the total scale was used to distinguish clinically distressed parents from normally functioning parents[31]. The reliability and validity of this scale are good (α=.71-α=.90)[30]. In the current study, internal consistency for the different scales ranged from α=.82 to α=.91.

Statistical methods

First, the factor structure of the ICQ-P was examined using principal component analysis (PCA) with oblique rotation with a fixed number of three factors, using Statistical Package for Social Sciences version 20 (SPSS). Analyses were first performed separately for the two samples, but results are reported for the combined sample because of the high levels of agreement. Kaiser-Meyer-Olkin Measure of sampling adequacy (KMO) and Bartlett's Test of Sphericity were checked before interpreting the rotated factor loadings. Kaiser (1974) recommends a minimum KMO of 0.5[32]. Each item was assumed to load on one factor only. Factor loadings of 0.36 or higher were considered significant, based on a sample size of 200[33]. To examine the psychometric properties of the ICQ-P, Cronbach's alpha was calculated for each subscale; a value of 0.60 or higher was considered acceptable[34]. Pearson correlations were calculated between the three subscales to investigate their mutual relationship. A one-way ANOVA was used to compare scores on the ICQ-P between mothers and fathers, and between the different diagnoses (hematological=leukemia and lymphoma; solid=Ewing's sarcoma, neuroblastoma, rhabdomyosarcoma, Wilm's tumor, osteosarcoma,

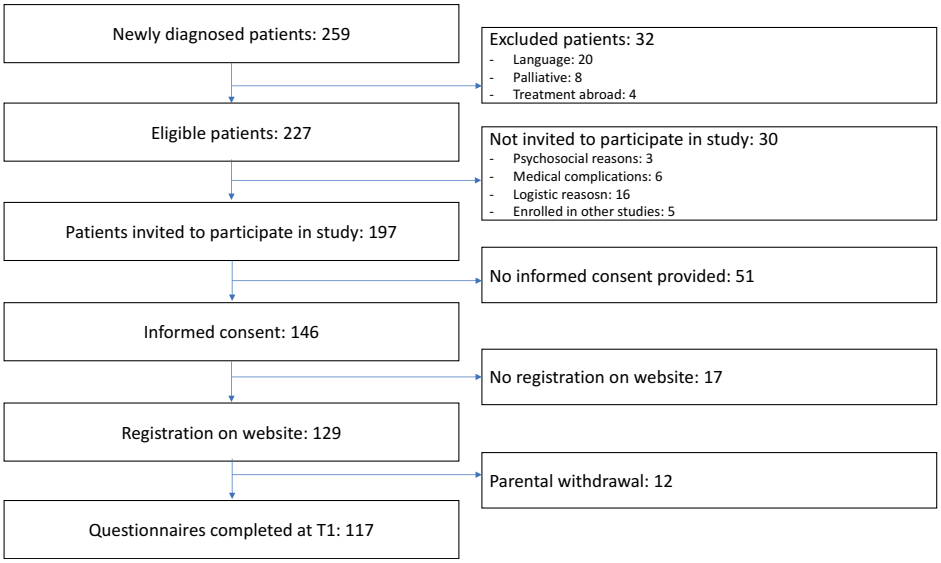

Figure 1. Flowchart of participants

and other solid tumors; neuro-oncological=brain/CNS tumor). To test the concurrent validity of the ICQ-P, Pearson correlations between ICQ-P scores and POMS (sample 1) and HADS (sample 2) scores were calculated. To test criterion-related validity, the ICQ-P scores of distressed parents (HADS total score ≥ 13) and non-distressed parents (HADS total score ≤ 12) were compared, using a one-way ANOVA. This analysis was performed only with the HADS, which has a validated cut-off point, unlike the POMS. Cohen's d was calculated as a measure of effect size. P-values ≤ 0.05 were considered statistically significant. Effect sizes .20 were considered small, .50 medium, and .80 large[35].

RESULTS

Sample characteristics

In total, there were 242 participants (Table 1). The patients were aged 0–17 years (*M*=7.15, *SD*=4.71) years; 133 boys (55.0%) and 109 girls (45.0%). The mean time from diagnosis to completion of the questionnaires was 36 days. Overall, 73.6% children were diagnosed with a hematological tumor, 7.9% with a neuro-oncological tumor, and 18.6% with a solid tumor. Questionnaires were completed by either mothers or fathers: 185 (76.4%) mothers and 57 (23.6%) fathers, aged 24–55 (*M*=38.98, *SD*=6.30) years.

Factor analysis and reliability of the ICQ-P

The suitability of data for factor analysis was established with the Kaiser-Meyer-Olkin test (.87) and Bartlett's Test of Sphericity. The different items loaded on the three original factors (Helplessness, Acceptance, and Perceived Benefits) (Table 2). The three original subscales, each consisting of 6 items, explained 9.8%, 31.4%, and 17.9% variance, respectively. Together, this three-component solution explained 59.1% of the total variance. Cronbach's alpha (.80–.88) showed that the scales had an adequate internal consistency. The mean scores of mothers and fathers on all subscales were not significantly different, and scores did not differ by diagnosis. There was no correlation between the subscales Helplessness and Perceived Benefits (r=-.04), a weak correlation between Acceptance and Perceived Benefits (r=.28), and a moderate negative correlation between Helplessness and Acceptance (r=-.48).

Table 2. Principal Components Analysis with oblique rotation and three fixed factors in parents of a child recently diagnosed with cancer (N=242), and Means and Standard Deviations, Eigenvalues, % variance explained, and Cronbach's Alpha.

	Rotated factor loadings		
Item	**Helplessness**	**Acceptance**	**Perceived benefits**
15. My child's illness frequently makes me feel helpless.	**.37**	-.40	.28
12. My child's illness limits me in everything that is important to me.	**.80**	-.03	-.08
5. My child's illness controls my life.	**.55**	-.28	.07
1. Because of my child's illness, I miss the things I like to do most.	**.86**	.14	-.11
9. My child's illness prevents me from doing what I would really like to do.	**.87**	.04	-.08
7. My child's illness makes me feel useless at times.	**.48**	-.05	.18
10. I have learned to accept the limitations imposed by my child's illness.	-.07	**.65**	.24
3. I have learned to live with my child's illness.	.00	**.83**	-.02
13. I can accept my child's illness well.	-.02	**.78**	-.04
17. I can cope effectively with my child's illness.	.05	**.85**	.10
2. I can handle the problems related to my child's illness.	-.06	**.76**	-.02
14. I think I can handle the problems related to my child's illness, even if the illness gets worse.	.03	**.81**	-.08
4. Dealing with my child's illness has made me a stronger person.	-.03	.47	**.55**
6. I have learned a great deal from my child's illness.	.14	.16	**.65**
18. My child's illness has taught me to enjoy the moment more.	-.03	-.01	**.79**
8. My child's illness has made life more precious to me.	.06	-.08	**.82**
16. My child's illness has helped me realize what is important in life.	-.04	-.19	**.84**
11. Looking back, I can see that my child's illness has also brought about some positive changes in my life.	-.18	.16	**.63**
M (SD)	12.45 (3.31)	16.60 (3.93)	15.88 (4.04)
Eigenvalues	1.77	5.65	3.22
% of variance	9.83	31.38	17.90
α	.80	.88	.83

Predicting parental psychological distress

Concurrent validity was measured with Pearson's correlation coefficients between the ICQ-P and the measures of parental psychological wellbeing (Table 3). As expected, cognitions of Helplessness were moderately to relatively highly (*r*=.42-.59) associated with a worse psychological wellbeing, that is, with higher levels of overall distress, depression, anxiety, tension, irritation, and fatigue, as assessed with the HADS and POMS. The opposite was seen for cognitions of Acceptance. Higher levels of Acceptance were moderately to relatively highly associated with a better psychological wellbeing, namely, higher levels of vigor and lower levels of overall distress, depression, anxiety, tension, irritation, and fatigue. No statistically significant correlations were found between the subscale Perceived Benefits and levels of psychological distress.

To test criterion-related validity, we compared the illness cognitions of parents who were clinically distressed (HADS total score ≥ 13, *N*=57) with those of non-distressed parents (HADS total score ≤ 12, *N*=56). One month after diagnosis, clinically distressed parents had more cognitions of Helplessness (*M*=13.05 vs. *M*=10.41, *F*=19.96, *p*<.001, *d*=0.78) and fewer cognitions of Acceptance (*M*=15.23 vs. *M*=18.91, *F*=28.04, *p*<.001, *d*=0.89) than non-distressed parents. No significant results were found for Perceived Benefits.

Table 3. Correlations between the Illness Cognition Questionnaire-parent version scales and measures of psychological distress

	Helplessness *r*	Acceptance *r*	Perceived benefits *r*
Parental psychological well-being			
HADS Total[a]	.46***	-.53***	-.06
HADS Depression[a]	.42***	-.49***	-.10
HADS Anxiety[a]	.45***	-.52***	-.02
POMS Tension[b]	.42***	-.39***	.03
POMS Depression[b]	.59***	-.54***	.02
POMS Irritation[b]	.54***	-.33***	.09
POMS Fatique[b]	.53***	-.29**	-.06
POMS Vigor[b]	-.41***	.40***	.12

[a] Note: N=113

[b] Note: N=126

[c] Note: HADS=Hospital Anxiety and Depression Scale, POMS=Profiles Of Mood States

[d] HADS Total M=13.7, SD=7.5, range=0-33; HADS Depression M=6.3, SD=4.0, range=0-17; HADS Anxiety M=7.4, SD=3.9, range=0-18; POMS Tension M=7.5, SD=5.2, range=0-23; POMS Depression M=8.9, SD=6.3, range=0-26; POMS Irritation M=6.7, SD=5.4, range=0-22; POMS Fatigue M=8.8, SD=5.7, range=0-24; POMS Vigor M=8.5, SD=4.3, range=0-19.

*p<.05, **p<.01, ***p<.001

DISCUSSION

The results of this study confirm that the ICQ-P, which was originally developed for adult patients with a chronic disease, is suitable for assessing the cognitions of the parents of a child recently diagnosed with cancer. The same three-factor (each with six items) structure of the original ICQ (Helplessness, Acceptance, Perceived Benefits) was also found in two samples of parents of children recently diagnosed with cancer. Factor loadings were adequate and exceeded previously determined factor loadings, showing that the adapted ICQ (ICQ-P) had an adequate factor structure. All subscales showed high reliability (α=.80-.88), comparable to that of the original questionnaire[5]. Correlation analysis of the subscales of the ICQ-P demonstrated no association between Helplessness and Perceived Benefits, a small association between Acceptance and Perceived Benefits, and a moderate association between Helplessness and Acceptance, indicating that these factors are distinct constructs of illness cognitions.

The scores of mothers and fathers were not significantly different, consistent with an earlier study using the ICQ[5], but not with an earlier study of the parents of a child with cancer in which the Control Strategy Scale (CSS) was used[22]. Grootenhuis et al. (1996) investigated differences in control strategies in dyadic couples, and this might explain the absence of an effect in the present study. We used data obtained from one parent per child and therefore compared the scores of mothers and fathers of different families. Parental ICQ scores were not significantly different by cancer diagnosis – the parents of children with hematological, solid, or neuro-oncological tumors had similar beliefs of Helplessness, Acceptance, and Perceived Benefits. This suggests that illness cognitions are not determined by diagnosis, which was also found in a previous study[12]. Treatment intensity or survival perspective might be of influence, as suggested by previous research[36], but we were not able to investigate this in the present study.

We found that parental illness cognitions were significantly correlated with psychological distress, with parents with beliefs of helplessness and little acceptance having a worse psychological wellbeing, in terms of overall distress, depression, anxiety, tension, irritation, and fatigue, than parents without these beliefs. In addition, clinically distressed parents had more helplessness cognitions and fewer acceptance cognitions than did their non-distressed counterparts. Although the data were not suitable for causal analyses, these results are in line with earlier reports on the effect of parental illness beliefs on adaptation[5,10-12]. Perceived Benefits were not significantly associated with parental psychological distress. This lack of correlation has been reported in other studies, in which benefit was found to be associated with positive constructs, such as trait optimism, positive mood, higher quality of life, and positive reframing as coping mechanism[37-38], and not with distress. Another possible explanation for this lack of correlation is that we included only families in which the child had recently been diagnosed with cancer, so that survival would be of key importance; finding benefit might occur later[39]. Thus while all subscales

of the ICQ-P were reliable and valid in the acute phase after the diagnosis of childhood cancer, the subscale Perceived Benefits might be more relevant in a later stage of cancer treatment. Changes in illness cognitions during long-term adjustment to disease and their predictive contribution to adjustment processes might be a topic for future research in these patient and parent groups.

The study had a number of strong points. It had a large sample, a broad range of children ages, a heterogeneous group of childhood cancer diagnoses, and mothers and fathers as respondents. However, it also had a number of limitations. First, we included the parents of children with cancer from two different studies; however, both samples completed questionnaires in the period shortly after diagnosis. While different questionnaires were used in the two studies, which reduced the sample size for analyses, similar results were obtained for both samples, which strengthened our conclusions. Although we intended to recruit both mothers and fathers, mothers were overrepresented in both samples; however, there were sufficient fathers to compare the scores of mothers with fathers. Secondly, this questionnaire was designed for the parents of sick children, and this is the only study to validate it in this population. In adults, the ICQ has proven to be reliable and valid in diverse patient groups[5], and therefore this can be expected to be the case for pediatric populations as well. Illness cognitions are generic and unrelated to medical factors, and therefore the ICQ-P should be applicable for children with chronic or life-threatening illnesses[5]. Future research should confirm the utility of this questionnaire in other pediatric populations. Thirdly, patients with a neuro-oncological diagnosis were under-represented and patients with hematological diseases, especially ALL, were overrepresented in our sample. This is because study 1 consisted solely of ALL patients and their parents. However, we found that cancer diagnosis did not affect parental ICQ-P scores. Our cross-sectional design limits our ability to assess causal relations and the long-term effects of illness cognitions on family adjustment.

Overall, this study showed that this version of the ICQ adapted for the parents of children with a chronic illness, specifically cancer, is a reliable and valid tool to evaluate illness cognitions. Assessment of the illness cognitions of the parents of children diagnosed with cancer is clinically relevant, because it may be a predictor of psychological distress, as suggested by our findings. The availability of a short and valid parent illness cognition assessment tool makes it possible to target interventions for parents at risk of maladaptive cognitions regarding their child's illness. Such interventions have been found to improve parental outcomes and to diminish child adjustment problems[40,41].

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Illness Cognition Questionnaire - Parent version

Instructions

On the next page is a list of statements by parents of a chronically ill child. Please indicate the extent to which you agree with them by circling one of the answers following the statement. Do not spend too much time considering your answer. Your first impression is usually the best.

To what extent do you agree with the following statements?

		Not at all	*Somewhat*	*To a large*	*Completelyextent*
1.	Because of my child's illness, I miss the things I like to do most.	1	2	3	4
2.	I can handle the problems related to my child's illness.	1	2	3	4
3.	I have learned to live with my child's illness.	1	2	3	4
4.	Dealing with my child's illness has made me a stronger person.	1	2	3	4
5.	My child's illness controls my life.	1	2	3	4
6.	I have learned a great deal from my child's illness.	1	2	3	4
7.	My child's illness makes me feel useless at times.	1	2	3	4
8.	My child's illness has made life more precious to me.	1	2	3	4
9.	My child's illness prevents me from doing what I wouldeally like to do.	1	2	3	4
10.	I have learned to accept the limitations imposed by my child's illness.	1	2	3	4
11.	Looking back, I can see that my child's illness has also brought about some positive changes in my life.	1	2	3	4
12.	My child's illness limits me in everything that is important to me.	1	2	3	4
13.	I can accept my child's illness well.	1	2	3	4
14.	I think I can handle the problems related to my child's illness, even if the illness get worse.	1	2	3	4
15.	My child's illness frequently makes me feel helpless.	1	2	3	4
16.	My child's illness has helped me realize what is important in life.	1	2	3	4
17.	I can cope effectively with my child's illness.	1	2	3	4
18.	My child's illness has taught me to enjoy the moment more.	1	2	3	4

CHAPTER 5

Screening for Psychosocial Risk in Dutch Families of a Child With Cancer: Reliability, Validity, and Usability of the Psychosocial Assessment Tool

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ABSTRACT

Background: The Psychosocial Assessment Tool (PAT) was developed to screen for psychosocial risk in families of a child-diagnosed with cancer. The current study is the first describing the cross-cultural adaptation, reliability, validity, and usability of the PAT in an European country (Dutch translation).

Methods: 117 families (response-rate 59%) of newly diagnosed children with cancer completed the PAT2.0 and validation measures.

Results: Acceptable reliability was obtained for the PAT total score (α = .72) and majority of subscales (.50 - .82). Two subscales showed inadequate internal consistency (Social Support α = .19; Family Beliefs α = .20). Validity and usability were adequate. Of the families, 66% scored low (Universal), 29% medium (Targeted), and 5% high (Clinical) risk.

Conclusion: This study confirms the cross-cultural applicability, reliability, and validity of the PAT total score. Reliability left room for improvement on subscale level. Future research should indicate if the PAT can be used to provide cost-effective care.

INTRODUCTION

The diagnosis of cancer is a particularly severe threat and a potentially traumatic event[1,2]. Multiple stress reactions can be seen in patients and their families, ranging from a normal adaptive response to symptoms of anxiety and depression, sometimes reaching the level of psychopathology[3]. Although there is variability, consistent evidence demonstrates that pathological levels of distress are not the normative response in children or their parents, either during or after treatment[3,4]. A small, but substantial number of families show problems in adapting to the new circumstances or present risk factors for developing psychological difficulties[5]. The way people react after a diagnosis varies and is dependent on many factors[6]. First, disease related risk factors, such as severity, treatment intensity, and number and length of hospital admissions can influence family adaptation[6,7]. Second, socio-ecological factors play a role in adjustment, such as family functioning, parental cognitions and coping, social support, financial problems, and prior stressful life events[8-11]. Finally, child factors, such as behavioral problems and temperament, also affect family adjustment[6,12]. Assessing risk factors across these levels makes it possible to predict future psychosocial distress and to intervene accordingly.

In terms of psychosocial treatment, all families should be offered at least minimal psychosocial services to support adaptive responses, but it is important to focus especially on the families who are at greatest risk for problems, as they can benefit most from tailored psychosocial intervention[5]. Tailoring such care at an early phase for those families who need it most, might prevent escalation of distress. Given current economic constraints and limited availability of psychosocial services, it is particularly important to allocate resources in a cost-effective way and incorporate this into standards of care.

The Psychosocial Assessment Tool (PAT) is a brief parent-reported screening tool aimed at detecting families at risk for psychosocial difficulties in pediatric oncology. It assesses both child and family distress, and evidence-based risk and protective factors for developing distress[13]. The PAT is a unique screener of family stress. Most screening approaches are directed towards psychopathology rather than normative distress and are not intended to identify people with less severe problems who might benefit from psychosocial interventions[14]. Available screening instruments, such as the distress thermometer[15], are focused on the individual, either child or parent, instead of the family system as a whole. An advantage of the PAT is that the content is based on both scientific research and clinical experience. The PAT maps on to the Pediatric Psychosocial Preventative Health Model (PPPHM), which conceptualize three levels of risk[5]. The majority of families are resilient and able to adapt adequately when confronted with health-related stressors (Universal group). A smaller group of families is at risk for developing psychosocial distress (Targeted group). Another small group of families shows multiple risk factors for serious ongoing and escalating psychosocial distress (Clinical group). This classification, and additional

information on the risk and protective factors, are intended to inform practice so as to provide personalized, family-based, and cost-effective psychosocial care[5].

Research in the United States, Canada, and Australia showed the PAT to be a reliable and valid screening instrument, adequate for use shortly after the diagnosis of childhood cancer[13,16,17]. Use has proven to be feasible both during the acute phase[13,16,17] and in survivorship[18]. Recently the use of the PAT has also been extended to other disease groups[19]. All studies showed somewhat similar distribution of scores into the three PPPHM categories: between 50% and 70% fell within the universal group, between 18% and 36% in the targeted group, and between 3% and 16% in the clinical group[13,16-18,20,21]. Concerning the reliability of the PAT, the alpha of the total score is consistently acceptable, however moderate to low alpha's have been reported on three of the seven subscales, namely 'Structure and Resources', 'Social Support', and 'Family Beliefs'[13,16,18,20,21]. Previous research also indicated that a PAT score at diagnosis predicts the use of psychosocial services during treatment[4,22].

The present study is the first to culturally validate the PAT in a European country. The first aim is to cross-culturally adapt the PAT for usage in the Netherlands using the methods outlined by Beaton et al.[23]. In their view, cross-cultural adaptation contains both the process of translation and adaptation of a questionnaire for use in another setting and is completed in six stages: 1) initial translation, 2) synthesis of translations, 3) back translation, 4) expert committee, 5) pilot testing, 6) submission of documentation. Then, this study aims to investigate the reliability and validity of the total PAT score and its subscales in a Dutch pediatric oncology sample. Finally, the usability of the Dutch version of the PAT, as rated by the parents, will be explored. Minor cultural differences in the PAT were expected. In the Netherlands distances to the hospital are relatively short and all families have obligatory public health insurance. We expect that after minor textual adjustments, the PAT will found to be valid, reliable, and usable. We also expect to find similar risk classification as was found in previous research on the PAT.

METHODS

Procedure

Families of newly diagnosed patients were asked to participate in this study in four pediatric oncology centers in the Netherlands: Emma Children's Hospital/AMC Amsterdam, Radboud University Medical Center Nijmegen, Sophia Children's Hospital/Erasmus MC Rotterdam, VU University Medical Center Amsterdam. During a 19-month period between June 2012 and December 2013 pediatric oncologists identified newly diagnosed patients. Inclusion criteria were (1) a confirmed first diagnosis of a pediatric cancer in a child to the age of 19 years, (2) speaking fluently Dutch, and (3) receiving curative treatment. Eligible families were approached by the investigators during the first weeks after diagnosis either during inpatient hospitalization, outpatient clinic visit, or by phone and were given both

written and oral information about the study. After both parents and patient (when 12 years or older) provided written informed consent, they were asked to register on the website (www.hetklikt.nu) to complete the PAT and validation questionnaires digitally around 1 month post-diagnosis. In the Netherlands, it is obligatory for children over 12 years of age to also give consent. All Medical Ethical Committees of the participating hospitals approved this study.

Participants

A total of 259 children were diagnosed with cancer from June 2012 to December 2013, of which 227 families were eligible for participation according to our inclusion criteria (Figure 1). Of those, 197 could be invited to participate of which 117 families (59% final response rate completed the questionnaires at baseline (*M* = 33.9 days post-diagnosis; *SD* = 9.24; *Range* = 16 – 59). To avoid selective overrepresentation of families and to minimize family burden, only one parent per family was asked to complete the measures. No differences were found between responders (*N* = 117) and non-responders (*N* = 80) with respect to age, gender, and diagnostic subcategory (hematological, neuro-oncological, or solid tumor). Details about the socio demographic characteristics of the sample are listed in Table 1.

Measures

Psychosocial Assessment Tool (PAT 2.0): The PAT[13] is comprised of 7 subscales: Family Structure and Resources, Family Social Support, Family Problems, Parent Stress Reactions, Family Beliefs, Child Problems, and Sibling Problems. Each subscale includes 3-15 items, which are scored dichotomously (risk = 1 / no risk = 0). Scores on the 7 subscales were calculated by dividing the number of high-risk items by the total number of items in the respective domain, yielding a subscale score from 0.00 to 1.00. The subscale scores were summed to create a total score of 0.00 to 7.00. PAT total scores ranging from 0.00 - 0.99 were considered universal, 1.00 - 1.95 targeted, and 2.0 and higher clinical. Internal consistency of total PAT score was good (α = .81), and subscales ranged from acceptable to good (α = .59-.81)[13]. Minor cultural differences were expected compared to the US PAT. For example, in the Netherlands all families have public health insurance, which covers most treatment costs, and live within two hours of an academic medical center. Parents also get a minimum of 2 weeks paid leave to care for their ill child[24] (Government of the Netherlands). The item on health insurance coverage was therefore not included. Omission of this item on health insurance did not affect scoring. PAT-NL usability questionnaire: To assess the usability of the PAT in the Dutch population, a 5-item questionnaire was developed. Parents rated each item on a visual analogue scale (VAS) scale ranging from 0 (totally disagree) to 100 (totally agree). (Example of questions: "Did you think the questions in the PAT were clear?")

Table 1. Demographic and Illness information of sample (N = 117)

Variables	*N / M*	*% / SD*
Patient characteristics		
Gender		
Female	51	43.6
Male	66	56.4
Age		
< 2 years	15	11.9
2-5 years	34	29.9
6-10 years	25	21.4
>10 years	43	36.8
Diagnosis		
Hematological		
Leukemia	30	25.6
Hodgkin's lymphoma	8	6.8
Non-Hodgkin lymphoma	13	11.1
Neuro-oncological		
Brain/CNS tumor	19	16.2
Solid		
Ewing's sarcoma	7	6.0
Neuroblastoma	8	6.8
Rhabdomyosarcoma	6	5.1
Wilm's tumor	8	6.8
Osteosarcoma	11	9.4
Other solid tumor	7	6.0
Time since diagnosis (days)	33.9	9.24
Parent characteristics		
Gender		
Female	77	65.8
Male	40	34.2
Age		
20-29 years	7	6.0
30-39 years	53	45.3
40-49 years	47	40.2
≥50 years	10	8.5
Ethnicity		
Dutch	113	96.5
Other	4	3.5
Marital status		
Married/partnered	114	97.4
Separated/divorced	2	1.7
Single	1	0.9
Education		
Low	9	7.7
Medium	38	32.5
High	70	59.8

Note. Education level of the parent was classified according to the International Standard Classification of Education: low = level 0 - 2, medium = level 3 - 5, high = level 6 – 8[42].

Validation Measures

Each PAT subscale, except for the Structure and Resources subscale, was validated using parent-report standardized instruments to measure the similar construct (see Table 3).

Inventory Social Reliance (ISR): The ISR[25] is an inventory designed to identify the social network of a person. The 5 items measuring perceived social support were used. Items are scored on a 4-point Likert scale. Internal consistency for the ISR in the current sample was excellent (α = .94).

Strengths and Difficulties Questionnaire (SDQ): The SDQ[26] is a valid and reliable instrument to assess parental report of psychosocial problems and strengths of the patient. There are 25 items on 5 subscales: hyperactivity/attention deficit, emotional problems, problems with peers, behavioral problems, and prosocial behavior. All items are scored on a 3-point scale to the extent of agreement (not true, somewhat true, certainly true). For the current study we used the SDQ to assess problems in the patient as well as in the siblings using two versions, one for 3-year-old children, and one for 4 - 16 year old children. Because we only used it for validation, parents also completed the SDQ for patients and siblings aged 17 - 18 years. Internal consistency for the SDQ in the current sample was good (α = .71) for the 3 - year patient version, 3 - year sibling version (α = .75), and for both the 4 - 16 year patient and sibling version (α = .66).

Hospital Anxiety and Depressions Scale (HADS): The HADS[27] is a valid and reliable self-report 14-item instrument to assess symptoms of anxiety and depression. Items are scored on a 4-point Likert-type rating scale. Internal consistency for the HADS in the current sample was excellent (α = .91).

Parenting Stress Index (PSI-short version): The PSI-short version[28] is comprised of 25 items, rated on a 6-point Likert scale, assessing perceived parental stress in the nurturing of their child. Parents of patients aged 2 to 18 years completed the PSI Internal consistency for the PSI in the current sample was excellent (α = .92).

Illness Cognitions Questionnaire-parent version (ICQ-P): The ICQ-parent version[10,29] consists of three subscales, i.e. helplessness, acceptance, and perceived benefits to assess parental cognitions regarding the child's illness. Each of the three subscales compromises 6 items rated on a 4-point Likert scale. Internal consistency for the ICQ-parent version in the current sample was excellent (helplessness α = .83, acceptance α = .89, perceived benefits α = .87).

Statistical analyses

In the process of culturally adapting the PAT, guidelines of Beaton et al. (2000) were followed[23]. First, the PAT was professionally translated into Dutch (forward translation) by two independent translators (Bureau Bothof). Both translations were compared and synthesized into one version. This version was then translated back to English by an independent native English speaker. This back-translated English version was reviewed

and approved by the developer of the PAT. Then, a pilot study was performed to test this version. A total of 25 parents completed the PAT before the start of this study. Internal consistencies between α = .40 (Family Beliefs) and α = .85 (Sibling Problems) were found. Given this preliminary evidence of success in adaptation, the Dutch PAT was approved for usage in the present study. First, reliability was calculated for the PAT2.0 total and subscale scores[13] using Cronbach's alpha. Due to the diversity of items within one scale, the small number of items in some subscales, and previous results on the internal consistency of the different subscales of the PAT a Cronbach's alpha of ≥ .50 was considered acceptable[30]. For scales where the initial internal consistency was inadequate (α < .50), individual items were further examined with respect to variability and inter-item correlations. When an item was not normally distributed and/or had zero variance, the scoring of the item was adapted or the item was removed from the calculation of the PAT total score as described below. Second, descriptive statistics were calculated for PAT total and subscale scores. Third, content validity and criterion-related validity were examined using Pearson Correlations between each PAT Subscale, except for the Structure and Resources subscale, and the standardized validation instrument corresponding to that scale. Criterion validity was tested by correlating the PAT total score with standardized measures of parent distress, family functioning, child functioning, and sibling functioning (HADS, PSI, ISR, ICQ-P, SDQ, and SDQ-sibling) version using Pearson Correlations. Medium correlations (r = .30) will be interpreted as meaningful. To identify a medium correlation, a sample of 111 analyzable participants will provide 95% power to differentiate a statistical significant correlation from no correlation at the 0.05 significance level[31]. With a sample size of N = 117 this study provides adequate power.

The distribution of PAT total scores into the three risk categories was calculated. This distribution of total scores for mothers and fathers separately, was then compared with the distribution found in previous studies with the PAT using cross-tabs. Fisher's exact test was interpreted, due to small N in one cell (N < 5). Finally, descriptive statistics for the usability questionnaire were used to evaluate parents' opinion regarding the PAT. All statistical analyses were conducted using the Statistical Package for Social Sciences (SPSS) version 20. In this study, no missing data were possible because of our electronic test environment. P-values (two-sided tests) ≤ .05 were considered statistically significant. Pearson correlations > .1 were considered small, > .3 medium, and > .5 large[30].

RESULTS

Reliability

Internal consistency for the PAT total score was acceptable (α = .69, Table 2). For four of the seven subscales an acceptable alpha coefficient was obtained (α = .50 - .82). For the subscales Structure and Resources, Social Support, and Family Beliefs initial internal

Table 2. Descriptive Statistics and Reliability of the PAT2.0 (Dutch translation)

				Family respondent N=117			
PAT 2.0 scale	Scale range	M	SD	Range	95% CI	Internal consistency	Internal consistency *(cultural adaptation)*
PAT Total	0-7	.80	.62	.00-3.10	.69 - .91	.69	.72
1. Structure/resources	0-5	.41	.87	0-4	.25 - .57	.31	.65
2. Social support	0-4	.20	.46	0-2	.12 - .28	.19	.19
3. Child problems							
< 2 years age (*N* = 15)	0-8	2.27	1.83	0-6	1.94 - 2.60	.67	.67
≥ 2 years age (*N* = 102)	0-15	3.31	3.11	0-12	2.75 - 3.87	.82	.82
4. Sibling problems							
< 2 years age (*N* = 11)	0-8	.56	.73	0-2	.43 - 69	.36	.36
≥ 2 years age (*N* = 86)	0-15	1.46	1.92	0-8	1.11 - 1.81	.69	.69
5. Family problems	0-8	.75	1.02	0-4	.56 - .94	.50	.50
6. Stress reaction	0-3	.36	.68	0-3	.24 - 48	.55	.55
7. Family beliefs	0-4	.59	.71	0-3	.46 - 72	.20	.20

consistencies were unacceptable (α = .31, α = .19, α = .20 respectively). After further examination of these subscales, in agreement with the developer of the PAT, some cultural adaptations in the subscale Structure and Resources were made. The items 'age person of completing form', 'number of children', and 'transport to hospital' were removed due to limited spread. In the Netherlands none of the families scored at risk on these items. For the item 'financial problems', also the option 'minor problems' was considered as a risk factor in the Netherlands. As a result, for the Dutch population only the items 'number of adults', 'marital status', 'education level', 'financial problems', and 'areas financial problems' were used for calculating the Structure and Resources subscale and the total score. After these cultural adaptations the internal consistency of the Structure and Resources subscale was acceptable, α = .65, and the PAT total score increased to α = .72.

Mean PAT scores

Descriptive statistics were calculated for the PAT total and subscale scores (Table 2). After minor cultural adaptations, the mean score on the Dutch PAT was *M* = .80 with a standard deviation of *SD* = .62. Total scores ranged from 0.00 to 3.10 and median score was *Med* = .65.

Criterion-related validity

The correlations of the PAT total score with validation measures can be found in Table 3. The total PAT score was significantly related to all of the validation measures (*r* = .23 - .61), with the exception of the ICQ-P perceived benefits (*r* = -.07). All correlations were medium to large, except for the ICQ-P helplessness (*r* = .23).

Table 3. Correlations of PAT Total Score (Criterion-Related Validity) and Subscale Scores(Content Validity) with Validation instruments

PAT 2.0 scale	Validation instrument	Correlation	P-values
PAT Total	ISR	-.38	.00
	SDQ	.61	.00
	SDQ-sibling version	.49	.00
	HADS-total	.46	.00
	HADS-anxiety	.47	.00
	HADS-depression	.41	.00
	PSI	.56	.00
	ICQ-P helplessness	.23	.02
	ICQ-P acceptation	-.35	.00
	ICQ-P perceived benefits	-.07	.45
1. Structure/resources	-	-	
2. Social support	ISR	-.26	.01
3. Child problems	SDQ	.80	.00
4. Sibling problems	SDQ-sibling version	.70	.00
5. Family problems	HADS-total	.30	.00
	HADS-anxiety	.34	.00
	HADS depression	.23	.01
	PSI	.20	.05
6. Stress reaction	HADS-total	.54	.00
	HADS-anxiety	.58	.00
	HADS-depression	.45	.00
7. Family beliefs	ICQ-P helplessness	.14	.15
	ICQ-P acceptation	-.21	.03
	ICQ-P perceived benefits	-.21	.02

Note. ISR = Inventory Social Reliance, SDQ = Strengths and Difficulties Questionnaire, HADS = Hospital Anxiety and Depression Scale, PSI = Parenting Stress Index, ICQ-P = Illness Cognitions Questionnaire-parent version.
N = 117

Content validity

With respect to content validity, each subscale of the PAT was significantly associated with the corresponding validating measure (r = .20 - .80), with the exception of Family Beliefs and ICQ-P helplessness (r = .14; see Table 3). For the subscales Child Problems, Sibling Problems, and Stress Reaction correlations were large; for the subscale Family Problems correlation was medium; and for the subscales Social Support and Family Beliefs correlations were small.

Classification by PPPHM Universal, Targeted, and Clinical groups

The 117 families were distributed as follows based on PAT total scores; 66% (n = 77) Universal, 29% (n = 34) Targeted, and 5% (n = 6) Clinical. Table 4 shows the breakdown by parent

Table 4. Percentage of Mothers and Fathers in respectively Universal, Targeted, and Clinical Group

	Universal		Targeted		Clinical	
	Mothers (%)	Fathers (%)	Mothers (%)	Fathers (%)	Mothers (%)	Fathers (%)
Pai et al. [10]	55	67	32	32	13	1
McCarthy et al. [13]	62	75	27	19	12	6
Barrera et al. [14]	60	60	35	24	5	16
Sint Nicolaas et al., this study	68	63	27	33	5	5

Note.
United States completion time *M* = 7 days, mothers *N* = 132, fathers *N* = 73
Australia completion time *M* = 18 days, mothers *N* = 135, fathers *N* = 85
Canada completion time *M* = 14-28 days, mothers *N* = 42, fathers *N* = 25
Netherlands completion time *M* = 34 days, mothers *N* = 77, fathers *N* = 40

gender. The classification of mothers in the Universal, Targeted, and Clinical group in the Netherlands was comparable to the United States, Canada, and Australia (Table 4) (Fisher's Exact Test p-values ranging $p = .10 - 1.00$). Regarding the classification of the fathers' PAT scores, no differences were found with the United States, Canada, and Australia (Fisher's Exact Test p-values ranging $p = .11 - 1.00$).

Usability of the PAT

On a VAS-scale ranging from 0-100 (0 = totally disagree, 100 = totally agree), parents rated the comprehensibility (*M* = 79.72, *SD* = 18.55), clarity (*M* = 79.72, *SD* = 19.50), and appropriateness (*M* = 61.72, *SD* = 21.23) of the PAT positively. In addition, parents did not find it unpleasant to complete the PAT(*M* = 19.82, *SD* = 23.49). The length of the questionnaire was considered acceptable (*M* = 68.18, *SD* = 23.47).

DISCUSSION

Conducting family risk assessment in pediatric oncology is an important and helpful step in providing comprehensive care to patients and their families. This study is to our knowledge the first to describe the validation of the PAT in a European country. New aspects of this study compared to previous published research are the online administration of the PAT and the parental assessment of the usability of the PAT. In general, the Dutch version of the PAT is reliable, valid, and applicable for use in a pediatric oncology setting. Importantly, the families themselves reported that the PAT was acceptable to them. This makes systematic screening for risk and resilience factors possible to facilitate the provision of cost effective targeted and family based care for those families in the Netherlands who need it most[32].

The PAT has been validated in several countries around the world[13,16-18,20,21]. Similar findings have been reported regarding its generalizability. However, questions remain

regarding the applicability of the PAT in a European country. Dutch health care is structured differently compared to other countries in which the PAT has already been validated. Given the small size of the country, distances are relatively small and healthcare is easy to reach for anybody[33]. Also, all Dutch citizens are obliged to have health insurance that covers most of the medical costs. Hospitalization is mainly restricted to the time required for treatment or management of complications[34]. Many medical treatments are offered in an outpatient manner and travel distances are no more than 1,5 hour. In most cases, children are thus not separated from their home and relatives for a long period of time and are close to their home situation. For families in financial need, transportation can be arranged by social workers. Furthermore, Dutch parents are able to have a paid sick leave for a certain period of time[35]. Nonetheless, there are still families with risk factors placing them in the Targeted and Clinical levels in the Netherlands. This implies that the risk factors identified by the PAT are universal, and that the PAT is applicable, also in a Western European country like the Netherlands.

The reliability on total scale level was good but lower than expected: the initial study on the PAT in the United States reported somewhat higher levels of internal consistency[13]. The PAT score seems to be applicable in Western European countries, such as the Netherlands, and the majority of the subscales confirmed adequate reliability and validity, however, the content of some subscales lacks adequate internal consistency and content validity. It is difficult to interpret these findings, since we know that there is great diversity of items within the subscale Structure and Resources and Social Support, which made it difficult to reach optimal internal consistency[36]. It is also known that internal consistency increases with the number of items per scale[36], while the subscales Social Support and Family Beliefs include only 4 items. Since inadequate internal consistencies were found consistently for the subscale Family Beliefs[13,18,20,21], and in this study also for Social Support, a more detailed look is necessary. Confirmatory factor analysis in a larger sample also could be helpful in examining whether all subscales represent themselves as theoretically hypothesized.

This study used an online version of the PAT. This might have contributed to diminishing burden for the families, because they can complete the questionnaire any time; in the hospital, at home, or in the waiting room of the outpatient clinic. Web-based measures have advantages compared to paper-and-pencil data collection, with regards to completeness of data, less proneness for social desirability answering, and higher cost-effectiveness[37]. It is likely that parents of children with cancer will have the same preference. However, there may be some families for whom paper forms are more feasible or acceptable.

There are some limitations of this study. Although our sample size is sufficiently large to conduct reliability and validity analyses, it was not adequate for conducting a confirmatory factor analysis. Another limitation is the possible underestimation of families with high levels of distress. The exclusion of families of a child who already had entered end-of-life care at diagnosis together with the families who were not invited by the medical doctor

to participate due to psychosocial reasons/medical complications, which might be the most distressed and at-risk families, possibly reflect an under-estimation. Next to this, we excluded families with insufficient knowledge of the Dutch language. The parents in our study were quite highly educated compared to the Dutch general population (25% low, 40% medium, 35% high)[38], and almost all parents were married, which raises questions about the representativeness of our sample group. However, we did not find differences in the number of 'high risk' families compared to the United States, Australia, and Canada.

This study can be regarded as an additional step in the overall international, multi-cultural validation of the PAT. Some important questions have been answered with this study, however future research is needed to address some issues, which still remain unknown. In a next study, the applicability of the PAT to other ethnic groups in the Netherlands should be tested using interpreters or translated versions of the Dutch PAT. Future studies also need to assess the best moment to assess the PAT in acute pediatric oncology care. Findings on the test-retest reliability of the PAT showed very good correlation, indicating that there was no difference in score between the measurement 1 week and 3 weeks after diagnosis[13]. It seems reasonable and recommendable to ask parents to complete the PAT around two weeks after diagnosis, a period in which stress reactions are normalizing, but this need to be studied. A prospective study is needed to confirm the PAT cut-off scores to differentiate between low (Universal), medium (Targeted), and high (Clinical) risk families in the Netherlands. This prospective study can also be used to define which risk factors contribute most to psychological distress. It is possible that there are also additional risk factors which are not measured by the PAT at this moment, such as personality, which is proven to be an important predictor of distress[39]. Another future direction for research is whether families with risk factors at one or multiple domains are equally at risk for developing problems[40]. An important next step is to extend the applicability of the PAT to other patient groups. With the Dutch translation available, it is possible to investigate the usability of the PAT in other patient groups after only minor adjustments in the cancer-specific questions. Finally, we can enhance the applicability of the PAT by investigating its cost-effectiveness.

Increasing attention is being paid to the psychosocial well being of patients and their families in pediatric care, however it is often hard to estimate the risk for developing problems[41] and to select families at risk. The PAT can be used as a valid instrument to identify psychosocial risk in a systematic and identical manner for all new families, supporting the clinical estimation of the healthcare team.

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CHAPTER 6

Match of psychosocial risk and psychosocial care in families of a child with cancer

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ABSTRACT

Background: The Psychosocial Assessment Tool (PAT) was developed to screen for psychosocial risk, aimed to be supportive in directing psychosocial care to families of a child with cancer. This study aimed to determine (1) the match between PAT risk score and provided psychosocial care with healthcare professionals blind to outcome of PAT assessment, and (2) the match between PAT risk score and team risk estimation.

Methods: 83 families of children with cancer from four pediatric oncology centers in the Netherlands participated (59% response rate). The PAT and team risk estimation was assessed at diagnosis (*Mean*=40.2 days, *sd*=14.1 days), and the content of provided psychosocial care in the five months' period thereafter resulting in basic or specialized care.

Results: According to the PAT, 65% of families were defined as having low (universal), 30% medium (targeted), and 5% high (clinical) risk for developing psychosocial problems. 30% of patients from universal group got basic psychosocial care, 63% got specialized care and 7% did not get any care. 14% of the families at risk got basic care, 86% got specialized care. Team risk estimations and PAT risk scores matched with 58% of the families.

Conclusion: This study showed that families at risk, based on standardized risk assessment with the PAT, received more specialized care than families without risk. However, still 14% of the families with high risks only received basic care, and 63% of the families with standard risk got specialized care. Standardized risk assessment can be used as part of comprehensive care delivery, complementing the team.

INTRODUCTION

Families of a child diagnosed with cancer face several major challenges, not only because of the life-threatening and potential traumatic nature of the diagnosis, but also regarding the impact on the physical and psychosocial functioning of the child and on daily family life[1,2]. Children encounter difficulties coping with the intense medical treatment and frequent hospitalizations, while parents and siblings experience their own difficulties[2]. Psychosocial care is therefore of indispensible value.

Psychosocial care is currently seen as a valuable and well integrated part of the multidisciplinary treatment of children with cancer in developed countries. It involves the culturally sensitive provision of psychological, social, and spiritual care[3]. In most pediatric cancer centers in developed countries, a psychosocial team works in collaboration with the medical team. Child life specialists support children during their treatment in an age appropriate manner, for example by preparing them for medical procedures and teaching them adequate coping strategies[4]. Social workers can provide practical help and therapeutic interventions to families, for example when the child or parent experiences adjustment issueor financial problems due to the illness of their child[5]. The child psychologists are present to advise and support members of the multidisciplinary team, and could meet families based on specific indication. Possible reasons for referral are medical traumatic stress, severe adjustment problems, post-traumatic stress symptoms, or psychiatric disorders in the child or family members[6]. Psychosocial care is not standardized yet. Provision is highly dependent on available resources. A next step is to investigate the provision of psychosocial care and how we can best spend our available resources.

Recently, a first step has been made to outline pediatric oncology psychosocial standards of care[7]. In this extensive document standards have been recognized as essential for psychosocial care. One of these standards is that children with cancer and their families should routinely receive systematic assessment of their psychosocial health care needs[8]. Implementation of this standard enables psychosocial teams to detect patients at risk for adjustment difficulties and helps to direct the use of specific psychosocial interventions[8,9]. However, standards on specific content of care and criteria for allocation of patients to different disciplines are still lacking.

In pediatric oncology, the Psychosocial Assessment Tool (PAT) is such an instrument, aimed at detecting risk and protective factors for developing distress[10]. Based on this information, families are classified into a low (Universal), medium (Targeted), or high (Clinical) risk group according to the Pediatric Psychosocial Preventative Health Model (PPPHM) model[11]. This broad classification into universal, targeted or clinical, and additional information on the risk and protective factors, intend to inform the multidisciplinary team and to provide personalized, family-based, and cost-effective psychosocial care given current economic constraints and limited availability of psychosocial services[11]. The PAT is sometimes used in a multidisciplinary medical and psychosocial team, and sometimes only

in psychosocial team. This is depending on standards for psychosocial care which vary across countries. Families with low risk for psychosocial problems could be offered basic psychosocial care, supporting the competence of these families. Families with higher risk for developing problems could be offered additional psychosocial interventions matched to their risk profile, to support optimal use of the healthcare team's resources[11,12]. Previous research supported the validity of the PAT in different countries around the world[13-18] and indicated that the PAT correlates with psychosocial risk[10,18] and psychosocial services were provided more frequently to higher risk families[19,20]. Using the PAT reduced family psychosocial risk in the first six months of treatment and improved quality of life related to pain in children[21]. However, recent research of McCarthy et al (2016) showed no differences in psychosocial care provision to families with low versus elevated risk[22].

Potential users need to be convinced of the additional value of innovations for their patients and their own practice before implementation[23]. Information about possible additional value of PAT next to clinical judgment, is therefore mandatory. In order to know the possible additional value of introducing the PAT in the Dutch setting, it is important to know how the relation is between psychosocial care and potential psychosocial risk, in a situation when risk was not assessed systematically. It is unclear whether systematic risk assessment with questionnaires adds to team risk estimations, which are generally used in routine care[24]. With a standardized instrument, it is possible to analyze the same risk factors in the exact same manner for all new families of a child with cancer. Risk estimations made by clinical staff are less standardized, however not less valuable. For this reason, this study aims to determine the match between Dutch families' psychosocial risk scores (universal, targeted, clinical), as measured with the PAT, and psychosocial care provided to the families during the first, half year of treatment. Furthermore, PAT risk scores (universal, targeted, clinical) will be compared to team risk estimations (standard, above average, high). This match will give insight into the potential added value of implementing standardized risk assessment and differentiation of care based on these risk profiles.

METHODS

Procedure

As part of a larger study[18,23], families of patients with newly diagnosed cancer were asked to participate in this study in four pediatric oncology centers in the Netherlands: the Amalia Children's Hospital/ Radboud University Medical Center Nijmegen, the Emma Children's Hospital/AMC Amsterdam, the Sophia Children's Hospital/Erasmus MC Rotterdam, and the VU University Medical Center Amsterdam. During a 19-month period between June 2012 and December 2013 newly diagnosed patients were identified. Inclusion criteria were (1) a confirmed first diagnosis of a pediatric cancer in a child up to the age of 18 years, (2) being able to complete a questionnaire in Dutch, and (3) receiving treatment with curative

intent. Eligible families were approached by the investigators during the first weeks after diagnosis either during inpatient hospitalization, outpatient clinic visit, or by phone and were given both written and oral information about the study. After both parents and patient (when 12 years or older) provided written informed consent, one of the parents was asked to register on the website (www.hetklikt.nu) to complete the electronic PAT around 1 (*M*=40.2, *sd*=14.1 days) and 6 (*M*=190.3, *sd*=16.0 days) month post-diagnosis. The psychosocial team members estimated the risk for psychosocial problems (standard, above average, high) in the first week after families had completed the PAT. All Medical Ethical Committees of the participating hospitals approved this study.

Measures

Parent report

Psychosocial Assessment Tool (PAT 2.0): The PAT[10,18] is comprised of 7 subscales: Family Structure and Resources, Family Social Support, Family Problems, Parent Stress Reactions, Family Beliefs, Child Problems, and Sibling Problems. Each subscale includes 3-15 items, which are scored dichotomously (risk = 1 / no risk = 0). Scores on the 7 subscales were calculated by dividing the number of high-risk items by the total number of items in the respective domain, yielding a subscale score from 0.00 to 1.00. The subscale scores were summed to create a total score of 0.00 to 7.00. PAT total scores ranging from 0.00 - 0.99 were considered universal, 1.00 - 1.99 targeted, and 2.0 and higher clinical. Internal consistency of total PAT score was acceptable ($\alpha = .72$)[18].

Provided Psychosocial Care: Around 6 months post-diagnosis, families were asked to complete a questionnaire that was developed specifically for this study by the research team, in which families rated the amount of psychosocial support they had received during the first six months after diagnosis. Parents rated the amount as following: no contacts, 1 contact, 2-4 contacts, 5 or more contacts. Also contact was assessed in terms of different disciplines for the family, namely psychologist, child life specialist, and social worker. Examples of questions were: 'Has a psychologist provided your child with support relating to your child's cancer?' and 'Has a social worker provided you or your partner with support relating to your child's cancer?'. Basic care was defined as receiving support from 1 psychosocial discipline, and specialized care as support from 2 or more disciplines. More detailed information could not be given due to the multicenter nature of the study and differences in local policies.

Due to the subjectivity of self-reported retrospective data, a random sample of N=15 self-reports regarding provided psychosocial care were compared to the medical record. This random sample was selected by a third person that was not involved in the study. Agreement was moderate to good (k=.87 for social work and k=.60 for psychologist). In 14 of the 15 selected families, data (contact yes/no for each discipline) from the medical record was comparable to self-reported data of the parents regarding care from social

worker. This ratio was 13/15 for care from a psychologist. Exact reasons for discrepancy was unknown. As this was a multicenter study, medical record data were not available for all patients.

Psychosocial team report

Team Risk Estimation: This single question was adapted from the Staff PAT[10]. The psychosocial teams, including a psychologist, social worker, and /or child life specialist, of the participating centers were asked to make a risk estimation of the family based on their clinical experience. Risk estimations were made in a multidisciplinary meeting of psychologists, social workers, and child life specialists. Providers who were responsible for the psychosocial care of the family made a joint estimation during this meeting. If the team thought that the family would adapt adequately to the child's diagnosis and treatment and did not expect to be offering additional care to the family, then the family's risk would be estimated as 'standard'. If the team expected minor risks within the family that would require additional care from the team, then risk would be estimated as 'above average'. If the team expected major difficulties regarding adjustment to the child's disease within the family that required a significant input of the team, then risk would be estimated as 'high'. These categories 'standard', 'above average', and 'high risk' compares to the categories of the total PAT score (universal, targeted, clinical).

Statistical analyses

All statistical analyses were conducted using the Statistical Package for Social Sciences (SPSS) version 20. Families were categorized into low (PAT≤0.99), versus medium (PAT1.00-1.99) or high risk (PAT≥2.00) for developing psychosocial problems following general instructions for scoring the PAT[10]. Frequencies (%) of received psychosocial care from a child life specialist, social worker, and psychologist were computed for families with universal versus targeted and clinical PAT score in terms of basic and specialized care. The team risk estimation was compared to the PAT risk score using kappa level of agreement. P-values (two-sided tests) ≤ .05 were considered statistically significant.

RESULTS

Participants

A total of 197 children were invited to participate in this study, of which 117 parents (59% response rate) completed the questionnaires at baseline. No differences were found between responders (*N*=117) and non-responders (*N*=80) with respect to age (p=.94), gender (p=.39), and diagnostic subcategory (hematological, neuro-oncological, or solid tumor; p=.46). A total of 83 families (29% drop out) completed the questionnaires also at follow-up (6 months post-diagnosis) and could be analyzed. From the total sample of 83

families, 40 children were diagnosed and treated in the Emma Children's Hospital in Amsterdam, 28 in the Radboudumc in Nijmegen, 10 in the VU medical center in Amsterdam, and 5 in the Sophia Children's Hospital in Rotterdam. Response rate per center was: 63% in the Emma Children's Hospital in Amsterdam, 60% in the Radboudumc in Nijmegen, 52% in the VU medical center in Amsterdam, and 47% in the Sophia Children's Hospital in Rotterdam. Between centers, no differences were found in child's age (F=.557, p=.645), child's gender (X^2=.901, p=.825), and diagnostic subgroup ((X^2=11.797, p=.067). No differences were found between responders (*N*=83) and drop-outs (*N*=34) with respect to age (p=.94), gender (p=.94), and diagnostic subcategory (hematological, neuro-oncological, or solid tumor; p=.58). Of 60 families a team risk estimation could be completed. Main reason for not completing the risk estimation was patient was not yet known (due to diagnostic trajectory or second opinion of other hospital). No differences were found between families with a team risk estimation (*N*=60) and without a team risk estimation (*N*=23) in PAT score at diagnosis (p=.76). Details about the socio demographic characteristics of the sample are listed in Table 1.

PAT risk score and provided psychosocial care

In this sample, 65% of families had low (universal), 30% medium (targeted), and 5% high (clinical) risk for developing psychosocial problems according to the PAT. As shown in Table 2, almost all families (95%) received some amount of psychosocial care. Thirty percent of patients from the universal group received basic care, 63% got specialized care, and 7% did not receive any care. Fourteen percent of the families at risk (i.e. targeted or clinical score on the PAT) received basic care, 86% received specialized care. There was a strong trend indicating that families at risk received more specialized care than families with universal scores (χ^2=5.546, p=.06). However, still 14% of the families at risk received basic care, and 63% of the families with standard risk received additional specialized care.

Team risk estimation and PAT risk score

The team estimated the score of 62% of families as standard risk, 27% above average, and 11% high risk for developing psychosocial problems (Table 3).

Match between the team risk estimation and the PAT risk score was low (k=.18). In 58% of the families, team risk estimation and PAT risk score was in agreement (standard-universal; above average-targeted; high-clinical). Seventeen percent of the families was estimated by the team to be at lower psychosocial risk than indicated by the PAT risk score (standard-targeted; above average-clinical), while 25% was estimated to be at higher risk compared to the PAT risk score (above average-universal; high-universal; high-targeted).

Table 1. Demographic and Illness information of sample (N = 117)

Variables	*N / M*	*% / SD*
Patient characteristics		
Gender		
Female	36	43.4
Male	47	56.6
Age		
< 2 years	10	12.0
2-5 years	25	30.1
6-10 years	17	20.5
>10 years	31	37.3
Diagnosis		
Hematological		
Leukemia	21	25.3
Hodgkin's lymphoma	5	6.0
Non-Hodgkin lymphoma	8	9.6
Neuro-oncological		
Brain/CNS tumor	17	20.5
Solid		
Ewing's sarcoma	5	6.0
Neuroblastoma	4	4.8
Rhabdomyosarcoma	4	4.8
Wilm's tumor	5	6.0
Osteosarcoma	9	10.8
Other solid tumor	5	6.0
Hospital		
Emma Children's Hospital	40	48.2
Radboudumc	28	33.7
VU medical center	10	12.0
Sophia Children's Hospital	5	6.0
Parent characteristics		
Gender		
Female	57	68.7
Male	26	31.3
Age		
20-29 years	5	6.0
30-39 years	37	44.6
40-49 years	34	41.0
≥50 years	7	8.4
Ethnicity		
Dutch	80	96.4
Other	3	3.6
Marital status		
Married/partnered	80	96.4
Separated/divorced	2	2.4
Single	1	1.2
Education		
Low	6	7.2
Medium	28	33.7
High	49	59.0

Note. Education level of the parent was classified according to the International Standard Classification of Education: low = level 0 - 2, medium = level 3 - 5, high = level 6 - 8 (International Standard Classification of Education [ISCED], 2012).

Table 2. Comparison of PAT risk scores and actual provision of psychosocial care

	No psychosocial care	Basic care	Specialized care	Total
Universal PAT score	4	16	34	54 (65%)
Targeted/Clinical PAT score	-	4	25	29 (35%)
Total	4 (5%)	20 (24%)	59 (71%)	83

Note.
Basic care=1 discipline
Specialized care=2 or 3 disciplines

Table 3. Agreement between PAT risk scores and team risk estimation

	Team Risk Estimation			
	Standard	Above average	High	Total
Universal PAT score	28	9	3	40 (67%)
Targeted Pat score	9	6	3	18 (30%)
Clinical PAT score	-	1	1	2 (3%)
Total	37 (62%)	16 (27%)	7 (11%)	60

DISCUSSION

Standardized assessment of psychosocial problems in pediatric oncology could be helpful in focusing family based psychosocial care to the risks and needs of patients and their families[11]. This study investigated the relationship between psychosocial risks (as indicated by the PAT) and provided psychosocial care. Results indicate that differentiating psychosocial care is partly matched to risk scores and that standardized assessment with the PAT could add information to risk estimations, which are generally used in routine care, in 42% of patients. As a golden standard does not exist, the PAT should be used complementary to clinical estimations of the team, not replacing them[11].

The PAT has been studied in several developed countries around the world[10;13-18] and its validity has been well established. Little is known yet about the association of the PAT with subsequent psychosocial resource use. Previous research already indicated that a higher PAT risk score at diagnosis predicted more social work services provided in the first four to five months post-diagnosis[19,20]. Furthermore, Kazak et al. (2011) found that when implementing standardized risk assessment in clinical practice, psychosocial services were provided corresponding to need[25]. On the other hand, a recent study of McCarthy et al (2016) showed no differences in psychosocial care provision to families with low versus elevated risk[21]. Care provision was rather associated with length of hospital stay than the presence of family psychosocial risks and needs. It should be noted that this study took only the first eight weeks post-diagnosis into account.

Before introducing the PAT in the Dutch setting it was important to gain more insight into the relation between psychosocial care and psychosocial risk, in a situation when risk assessment was not systematically used in clinical practice. Our study showed that without the implementation of standardized risk assessment in clinical practice, psychosocial services were provided partly matched to PAT risk scores. There is a fit between allocated care (basic versus specialized) and risk profile according to the risk indication on the PAT in approximately half of the cases. Match was strongest in families identified as high risk by the PAT and all received some amount of psychosocial care. However, in 5% (4/83) of the families, their seemed to be less care than needed. In the other 41% (34/83), allocated care was more than what is recommended based on the PAT risk profile.

Data from this study could not explain the exact reasons behind this discrepancy. It seems reasonable that the PAT adequately recognizes families with relatively stable risk factors, such as problems within the social support of families or financial resources, but that it is not sufficient for focusing care in case of incidents, such as illness of parent or sudden loss of a job. In this case, a family with a universal PAT score at diagnosis might need specialized psychosocial care which might be higher or lower than was expected at the beginning of treatment when families completed the PAT. However, the PAT measures relatively stable risk factors, such as socio-economic circumstances. Although sudden events might occur, families without risks are able to adapt better to such events compared to families with elevated risks[26]. Next to the presence of risk factors, other factors might explain psychosocial care provision. Some families report relatively low levels of distress, while asking high need for support. If resources are available, psychosocial care might support adequate adjustment or prevent problems in these cases. Therefore, it is important to provide basic psychosocial care to all families of a child with cancer and remain monitoring family functioning to be able to act promptly when needed. The psychosocial team plays a crucial role in this process of allocating care. Recent standards of care for pediatric oncology have been developed to support the psychosocial team in delivering care[7]. Standards on specific content of care and criteria for allocation of patients to different disciplines are lacking and require further attention.

Next to this, risk assessment with the PAT seems to provide other information on top of team risk estimations. In a considerable group (42%) of families, risk estimation by the PAT differed from team risk estimations. It is unclear how these differences could be explained and future research is warranted. Assessment with the PAT adds information to team risk estimations, which are generally used in routine care, in approximately 40% of patients and could therefore be used complementary. The PAT is promising, but no studies indicate how to use it next to standard psychosocial care, this is the first study addressing this important issue. Pediatric oncology centers in the Netherlands are currently using the PAT as part of clinical practice, but how the PAT should be implemented as part of new standards of care has not yet been studied. Screening based on information from questionnaires

should never be the only source of risk assessment. The same is true for somatic care when e.g. lab results do not fit with the impression from clinical evaluation. Different sources of information have to be judged always. The same is true for psychosocial risk profiling.

This study can be seen as a next step in integrating risk assessment in daily clinical practice. We investigated the extent to which standardized risk assessment provided by the PAT agrees with risk estimations of the psychosocial team, which are generally used in routine care, but none of them can be seen as a golden standard, i.e. the true value or outcome. Both ways of risk assessment could be used complementary.

A limitation of this study is the relative small sample size, which led to a small group of families with high risk for developing psychosocial problems and limited the power of this study. However, the classification into a Universal, Targeted, and Clinical PAT score was comparable with the PPPHM-model and previous research on the PAT. The response rate of 59% is relatively low and questions the generalizability of our findings. Although we did not find statistic differences between responders and non-responders, and between responders and drop-outs, it might be that our sample is not an accurate reflection of the population. The parents in our study were highly educated and almost all parents were married, which raises questions about the representativeness of our sample group. Self-selection bias might have played a role in this study. Furthermore, this study assessed provided psychosocial care by using a parent-reported questionnaire. This is less objective than using patient registration systems regarding provided care, but this was not possible in this study because of the different registration systems in each center. In a random sample of N=15 families we found moderate to good agreement with medical records and confirmed the reliability of self-reported data. This study used a broad categorization into basic versus specialized care based on the content of psychosocial care. Multiple disciplines caring for a family may be a sign that a family receives more complex care. Each family receives standard psychosocial care, however, who provides the psychosocial care is not standardized. For example, in some cases, it is the social worker who provides standard psychosocial care, in other cases it is the child life specialist. Every family has the opportunity to meet with at least one psychosocial professional as part of standard care. When there is a need for extra care, more specialized care is warranted. The aim of the contact was also not assessed. This information would be helpful in determining if provided care was focused on family needs when using the PAT. Future studies should include this information and should investigate whether standardized risk assessment with the PAT and focusing care to the needs of families result in less distress over time. Self perceived needs and risks could be added to this investigation. The PAT is a parent-reported family risk screener and child self-report is not included. Future studies might also include child self-report regarding the 'child problems' subscale and other questions that children are able to report of the PAT from the age of eight years, complementing the parent view of family functioning and risks.

This study showed that standardized risk assessment with the PAT is promising and complementary to team risk estimations, which are generally used in routine care. It can assist in the process of allocating psychosocial care to those who need it most and can be viewed as a first step in a process of targeted approach to psychosocial care delivery[27]. The PAT can be used as a valid instrument to identify psychosocial risks and needs in a systematic and identical manner for all new families, supporting the clinical estimation of the health care team. This information can be used to promote adaptive functioning in children with cancer and their families.

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CHAPTER 7

General Discussion

Survival of pediatric cancer has improved tremendously during the last decades. Because more children survive cancer, more attention is being paid to quality of life (qol) and long-term effects of the disease and treatment. It is relevant to learn which difficulties children and their families can encounter during treatment and thereafter, and who needs extra support in adjusting to the disease. This thesis focused on children with cancer during treatment and their parents, in particular on their psychosocial adjustment. First, the aim was to describe child psychosocial adjustment in terms of behavioral problems in children during treatment in a homogeneous group of patients with acute lymphoblastic leukemia (ALL). Next, the aim was to describe family related risk factors explaining differences in child adjustment. In addition, early identification of families at-risk for psychosocial problems was studied using the Psychosocial Assessment Tool (PAT), an instrument to identify these family risk factors. At last, integration in daily clinical practice was tested.

In this chapter the results from this thesis are described and discussed in a broader perspective. Implications for future research and for clinical practice are discussed in more detail.

MAIN RESEARCH FINDINGS

In ***Chapter 2*** we identified three distinctive trajectories of both internalizing and externalizing behavior during two year treatment period for ALL. For internalizing problems, we defined a resilient group who did not experience behavioral adjustment problems throughout treatment (60%), a group who showed initial problems but recovered (30%), and a group who experienced chronic problems during the entire treatment trajectory (10%). For externalizing problems, we again defined a group who did not experience behavioral adjustment problems throughout treatment but showed resilience (83%), a group who experienced chronic problems during entire treatment trajectory (12%) and a group who showed increasing problems (5%). These results indicate that most children diagnosed with ALL seem to adjust relatively well in terms of their internalizing as well as externalizing behavior. This study showed that mainly the parent related factors, compared to child and disease related factors, puts children at risk for psychosocial difficulties. Children with chronic high levels of internalizing behavior could be distinguished from those who recovered in terms of more passive coping of the parents, and higher levels of parenting stress. Children with growing externalizing problems could be distinguished from the group with stable externalizing behavior by higher levels of parenting stress. A link between parental passive coping style and adverse psychological reactions has been reported repeatedly before in both pediatric and adult care[1,2]. Therefore, it can be seen as a substantial risk factor for maladjustment after diagnosis and should be paid attention to.

In agreement with current literature and in concordance with the research model of Wallander and Varni (1998)[3], we have found in ***Chapter 3*** that, again, parenting stress is

a key variable in explaining psychosocial adjustment in terms of behavioral problems in children during treatment for ALL. This study tested a model of factors influencing child behavioral problems during treatment for ALL, in which an indirect effect of parenting stress was assumed. Results of this study showed important indirect effects of perceived disease benefits, positive affect, and social support on child behavioral problems via parenting stress. Since parents who were able to perceive also some positive effects of the illness of their child, who report less negative affect and who have sufficient social resources experience less parenting stress and subsequently less child behavioral problems, these positive states variables seem to function as a buffer for family distress. Parenting stress was a stronger predictor for externalizing behavior, than for internalizing behavior. To our knowledge, Van der Geest et al (2014)[4] were the first to investigate the mediating effect of parenting stress on the association between parental distress (stress of the parents themselves) and child adjustment. Our longitudinal study found similar results, and is therefore comfirming the evidence for the role of parenting stress in child psychosocial adjustment to medical illness. One could screen for these important predictors (parental cognitions, parental affect, and social support) of parenting stress and offer a psychological intervention to timely improve child outcome by focusing on the parent-child relationship. Interventions could focus on parenting capacities supporting the adequate adjustment of children with cancer and their families. Timely interventions focused on improving the knowledge, skills, and confidence of parents in raising an ill child may prevent escalation of problems and support adequate child and family psychosocial adjustment after diagnosis. From previous research it is known that effectivity of interventions in a pediatric population increases when parents participate next to the children[5].

As is shown in studies in adult populations, illness cognitions could importantly contribute to adjustment processes to severe medical condition. In line with this, we considered the cognitions of parents of importance. However, for the pediatric population, no valid and reliable instrument is currently available. Therefore we translated the Illness Cognition Quationnaire ICQ- which has been used in adult population withc chronic diseases. In ***Chapter 4*** we showed that the Illness Cognition Questionnaire (ICQ)[6], adapted for parents of children with a chronic illness, specifically cancer, is suitable for assessing the cognitions of the parents of a child recently diagnosed with cancer. The ICQ consists of three subscales: cognitions of helplessness regarding the disease (it controls my life), cognitions of acceptance (irrespective of the outcome, at the end, I think I can deal with it), and cognitions of disease benefits (next to all the negative impact of the disease, I can also identify some positive effects). The same three-factor structure of the original ICQ (Helplessness, Acceptance, Perceived Benefits) was found and all subscales showed good reliability (α=.80-.88). We found that parental illness cognitions were significantly correlated with their psychological distress. Parents who have difficulties in imagining that they can accept, or adjust to the consequences of the disease had a worse psychological

well-being, in terms of overall distress, depression, anxiety, tension, irritation, and fatigue, than parents without these beliefs. In reverse, clinically distressed parents had more cognitions of helplessness regarding the disease and fewer cognitions of acceptance than did their non-distressed counterparts. These results are in line with earlier reports on the effect of parental illness beliefs on their adaptation[7-9]. Perceived benefits were not significantly associated with parental psychological distress. The lack of correlation has been reported in other studies, in which benefit was found to be associated with positive constructs, such as trait optimism, positive mood, higher QoL, and positive reframing as coping mechanism[10,11] and not with distress. Positive and negative adjustment seem to be different constructs, which can co-occur. Assessment of illness cognitions of parents is clinically relevant, because it may be a predictor of psychological distress, as suggested by our findings. The availability of a short and valid parent illness cognition assessment tool makes it possible to target interventions for parents with maladaptive cognitions regarding their child's illness. The questionnaire directly refers to maladaptive cognitions regarding the illness of the child and could as such, help focus cognitive interventions. Interventions, such as cognitive behavioral therapy, have been found to improve parental outcomes and diminish child adjustment problems[12].

While gaining more insight into risk and resilience factors for child behavioral adjustment, there is need for an instrument assessing these factors. Recognition of families at risk for maladaptive functioning using the Psychosocial Assessment Tool (PAT) was the central theme in ***Chapter 5*****.** New aspects of this study compared with previous published research were the online administration of the PAT and the parental assessment of the usability of the PAT. In general, the Dutch version of the PAT was found to be reliable, valid, and applicable for use in a pediatric oncology setting. Importantly, the families themselves reported that the PAT was acceptable to them. This makes systematic screening for risk and resilience factors possible to facilitate the provision of targeted and family-based care for those families in the Netherlands who need it most[13]. The reliability on total scale level was good but lower than expected: the initial study on the PAT in the United States reported somewhat higher levels of internal consistency[14]. The PAT score seems to be applicable in Western European countries, such as the Netherlands, and the majority of the subscales confirmed adequate reliability and validity; however, the content of two subscales 'Social Support' and 'Family Beliefs' lack adequate internal consistency and content validity. Further research could investigate to what extent the integration of the helplessness and acceptance scales of the ICQ-P instead of the 'Family Beliefs' scale could increase the reliability and validity of the PAT. This study can be regarded as an additional step in the overall international, multi-cultural validation of the PAT. Some important questions have been answered with this study; however, future research is needed to address some issues, such as the impact of the integration of the ICQ-p in the PAT and the way of calculating the

overall score that, in the current version, do not differentiate between being at-risk on one risk factor or being at-risk on multiple risk domains.

The next question of this thesis was whether conducting family risk assessment in pediatric oncology could be a helpful step in providing comprehensive care to patients and their families. In ***Chapter 6*** we studied the added value of using the PAT in pediatric oncology practice to psychosocial care allocation. Before introducing the PAT in the Dutch setting we wanted to gain more insight into the relation between psychosocial care and psychosocial risk, in a situation when risk assessment was not systematically used in clinical practice. Our study showed that without the implementation of standardized risk assessment in clinical practice, psychosocial services were provided partly matched to PAT risk scores. There is a fit between allocated care (basic versus specialized) and risk profile according to the risk indication on the PAT in approximately half of the cases. The match was strongest in families identified as high risk by the PAT and all received some amount of psychosocial care. However, still 14% of the families with high risks only received basic care, and 63% of the families with standard risk got specialized care. Next to this, standardized risk assessment with the PAT seems to provide other information than team risk estimations/evaluations. In a considerable group (42%) of families, risk estimation by the PAT differed from team risk estimations. Data from this study could not explain the exact reasons behind this discrepancy. However, it indicated that team estimations and PAT partly point to different families identified as at risk for adjustment problems, meaning that both kind of risk estimations could be used next to each other and additional research has to point out reasons behind different risk estimations. Standardized risk assessment can be used as part of comprehensive care delivery, complementing the team and standardized monitoring of family functioning.

METHODOLOGICAL CONSIDERATIONS

The studies described in this thesis made it possible to investigate patterns of behavioral adjustment and to test a model of factors influencing child behavioral adjustment after the diagnosis of childhood cancer due to its longitudinal design and a homogenous population. Other methodological strengths of this thesis are the use of valid instruments and multiple informants, such as children, fathers, mothers, and psychosocial team members. The studies were conducted from a systemic perspective: a focus rather on the family than only on the patient. There are however two important aspects of our studies, which limit conclusions and need to be discussed in more detail, namely the generalizability of our study data because of sample bias and the questionnaires we used.

1. Limited generalizability of study data due to selection bias

In this thesis, we described data of two different samples of patients diagnosed with cancer. The first sample consisted of parents of children with Acute Lymphoblastic Leukemia (ALL) recruited from six of the seven Dutch pediatric oncology centers, participating in the study in the period 2006-2011. The second sample consisted of parents of children recently diagnosed with cancer from four of seven Dutch pediatric oncology centers who participated in the study in period 2012-2013. Although the inclusion rates of both studies were acceptable (74-82%), we cannot rule out the role of selection bias. We excluded families of a child who already had entered end-of-life care. This selection may have resulted in a not optimally representative sample and an underestimation of families with high levels of distress which is even strengthened by the exclusion of parents with insufficient knowledge of Dutch language. Therefore we do not know whether our results also apply to non-Western families of a child with cancer in the Netherlands. However, this is always the case in scientific research and not different in this thesis. Furthermore, several demographic aspects of our study sample were not representative for the Dutch general population. The education level in our second study sample was high (8% low, 32% medium, 60% high) compared to the Dutch general population (25% low, 40% medium, 35% high)[15], and almost all parents were married. At last, we had an overrepresentation of female caregivers participating in our study. In our first study we included only one of the parents to complete our study measures, and although we intended to recruit both mothers and fathers, in most cases the mother participated. This is not surprising, because nowadays mothers still tend to be the primary caregiver in most families. However, in order to provide family-centered psychosocial care it is important to include reports of both mothers and fathers, because we know that parents show different perspectives on their children, whereby mothers seem to be more sensitive and worried about their child's health status[16]. Next to this, our first sample consisted only of children with an ALL diagnosis, whether the second sample included all pediatric cancer diagnoses. It is questionable whether these samples are comparable regarding behavioral outcomes and parenting stress and whether study results are applicable to all cancer diagnoses. In treatment for ALL dexamethason is an important medicine, which is known for its severe behavioral side effects such as agitation, sleeping problems and aggressive behavior[17]. This puts parenting capacities under pressure during periods in which dexamethasone is administered. Therefore, parenting stress might be higher in this population compared to other pediatric cancer populations. What we do know is that no differences were found between responders and non-responders with respect to age, gender, and diagnostic subcategory (hematological, neuro-oncological, or solid tumor). In terms of these factors the participants can be considered representative, meaning that, importantly, patients were equally represented.

2. Challenges of questionnaires in pediatrics

In our studies we carefully selected instruments to measure distinct aspects of the families psychological reaction to childhood cancer. However, data collection in a pediatric population has several challenges to be considered. For example, parents in our first study sample reported on behavior of their child as noticed by themselves, and from previous research it is known that child behavior judged by parents is difficult to interpret[18]. Perceptions of parents regarding functioning of their child is an important source of information, but parents experiencing for example symptoms of depression or anxiety might report child behavior in light of their own problems[19]. Next to this, family risk assessment in our second study sample was also based on parent report only. It might be questioned if this is the best method to obtain information. Another challenge of doing research in a pediatric population is the fact that it is hard to measure and compare behavior in children of different ages. Children have to face different tasks and challenges regarding their developmental age. For example, preschool children show more often sleeping and eating problems, while children of school age experience more social and anxiety problems[20]. Different questions and/or questionnaires are applicable for each age group. Comparability of behavior in children of different ages and over time is therefore hindered and hard to interpret.

IMPLICATIONS FOR FUTURE RESEARCH

Two theoretical models formed the basis of this thesis, namely Wallander and Varni's (*1998*) disease-stress-coping (DSC) model of child adjustment to pediatric chronic physical disorders and Kazak's Pediatric Psychosocial Preventative Health Model (PPPHM), which conceptualizes the adjustment of children with medical traumatic stress, such as the diagnosis of childhood cancer, and their families[3,21,22]. In chapter 2 of this thesis both models were confirmed. We identified three groups of psychosocial adjustment in terms of behavioral problems. Resilience was shown in majority of the children, minor problems in a smaller but considerable group, and major problems in a select group. Next to this, this chapter showed that not only medical factors, such as diagnosis, puts the child at risk for psychosocial difficulties, but also the psychological reaction of the parents through parent-child interaction. Chapter 3 and 4 confirmed risk factors, namely parental cognitions, parental affect, and social support as described by Wallander & Varni's DSC model, and additionally showed the mechanism of parental factors influencing child psychosocial adjustment. Parenting stress is an important mediating factor between parent and child psychological functioning. Next to this, parental positive states variables such as perceived disease benefits, positive affect, and social support seem to function as a buffer for family distress. Chapter 5 confirmed Kazak's PPPH model in a Dutch pediatric oncology

population, with 66% low, 29% medium, and 5% high risk for experiencing or developing psychosocial problems.

This thesis showed the confirmation of above mentioned theoretical models and showed new insights such as trajectories of child psychosocial adjustment and the mechanism by which parent functioning affects child adjustment after diagnosis. Future research is needed to address some issues, which still remain unknown.

Risk and resilience factors

With this thesis, we were not able to investigate all risk and resilience factors for child adjustment. We confirmed the influence of social-ecological, such as parental distress, and stress-processing factors, such as parenting stress, on child adjustment. Additional factors, which we did not study but might function as a buffer against distress of children, such as family interactions and personal characteristics such as optimism, should be included in future research[23]. Next to this, relationships between parent and child should be included, because in this thesis we were only able to investigate parenting stress, but not the actual parent-child interactions. This might be a key factor and is suitable to measure in multiple ways, such as child report, parent report and observations. At last, current scoring of the PAT does not allow differentiating between families scoring high at one risk domain and families scoring low to medium on multiple domains. Future research should define what contribute most to psychological distress and whether families with risk factors at one or multiple domains are equally at risk for developing problems[24.]

Long-term psychosocial adjustment

The findings of the studies presented in this thesis are a confirmation of previous results and a next step in research regarding child adaptation to cancer. Most children with cancer in our study seem to adjust relatively well. However, we were only able to study children during active treatment. This period is characterized by a focus on the medical treatment and surviving of the chid and the availability of psychosocial care. Although it is important to start investigating psychosocial adjustment problems in an early phase, because we know that this has substantial impact on adaptation on the long term[25], we do not know the long-term adaptation course. It might be possible that adjustment problems do not become manifest until years after completion of treatment, the period in which number of hospital visits decline and children and their parents have to return to 'normal' life, and therefore research into adjustment trajectories requires longer follow-up. A long time into permanent survivorship an increase in symptoms of anxiety was shown in a recent study and approximately a third of the participants who were diagnosed during adolescence reported possible anxiety[26]. Yearly monitoring of psychosocial functioning of the child, including emotional, social and cognitive functioning is warranted.

Use of valid and internationally accepted questionnaires

Reviewing the literature on previous studies on this thesis' subject, it became clear that psychosocial adjustment of children with cancer could be conceptualized in many ways. Some studies referred to adjustment in terms of distress, others of behavior problems. There are many related constructs, such as distress, behavioral problems, Quality of Life (QoL), post-traumatic stress symptoms, anxiety, and depression. As a result, each construct is measured with slightly different questionnaires, limiting comparability of results. Mostly used instruments are the Child Behavior Checklist (CBCL), Behavior Assessment System for Children (BASC), and Vineland Adaptive Behavior Skills (VABS) for measuring child behavior, and the Pediatric Quality of Life Inventory (PedsQL) for measuring QoL. In the first studies described in this thesis, the CBCL was used to measure child behavioral adjustment. Limitation of the CBCL is its focus on psychopathology rather than on symptoms of for example distress, and its two age versions (1-5 years and 6-18 years), with the last one covering a wide age range that limits comparability. Disease-specific questionnaires regarding child functioning are also available, such as the PedsQL cancer module. However, none of these specifically examines changes attributable to steroids, which are important in the treatment of ALL and known for its behavioral side-effects. Recently, the QuEST tool was developed for assessing treatment-specific QoL in ALL patients[27] and might be a good addition to existing questionnaires for this specific population after further confirmation of its validity and reliability.

It would be recommendable for future studies to take into account the comparability of study results across different countries and time periods. Only when some form of uniformity is reached, results can be compared and conclusions can be made. In order to do so, one valid and internationally accepted questionnaire for each individual construct, i.e. child behavior, should be selected for usage in pediatric oncology research. Consensus in core outcomes sets should be leading. Using Computerized Adaptive Testing (CAT) to shorten the list of items and the Patient reported outcomes measurement information system (PROMIS) could decrease burden of completing long questionnaires and offer a solution for repeated assessment of the same questions[28]. By using PROMIS item banks, patients and their parents only have to answer a few questions per construct, decreasing burden and at the same time remaining or increasing reliability.

IMPLICATIONS FOR CLINICAL PRACTICE

Based on our studies we made some recommendations for the clinical care for children and adolescents with cancer.

Focus on resilience in pediatric cancer

Although patients and children are faced with many challenges when diagnosed with cancer, the majority is able to show a resilient response. Pediatric cancer has long been considered a very stressful and possible traumatic event for patients and their families[29]. As described in the introduction of this thesis, children have to face multiple invasive medical procedures, severe side effects of the treatment regimes, and major changes in physical appearance. Next to this, children are separated from their home and school for a significant period of time, and daily family life is disrupted. Therefore, it is reasonable to expect increased levels of psychosocial adjustment problems in these children and their families. Despite the considerable amount of sources of stress, adjustment of children with cancer and their families seems to be generally well[30,31]. Literature showed a merely resilient response in children and their families, and some studies even reported the pediatric cancer population functioning better than their healthy peers[32]. Literature on pediatric cancer hardiness describe different hypotheses why children diagnosed with cancer function relatively well[33]. One of these hypotheses is that children and adolescents focus on the here and now. This might result in an adaptive response when children face challenges such as trauma or disease, which has been reported before in other pediatric population, such as sickle cell disease[34] and hemophilia[35]. Next to this, the proximity to parents and the community may serve as a protective function resulting in better functioning and perhaps less dysfunction. Another possible explanation is that Dutch pediatric oncology care nowadays is well organized and psychosocial services are present for each family. It might be that the relatively good functioning we found in this thesis, is a result of investing in excellent psychosocial pediatric oncology care. Therefore, it is the time to shift towards a more positive psychology approach in pediatric cancer as also mentioned before[32,33]. The importance of positive emotions is being more and more recognized nowadays, and we currently know that positive and negative emotions can occur shortly after each other or even simultaneously[32]. When patients and their families experience positive states, it can undo harmful effects of negative states and serve as buffer against future distress[36,37]. It is important to inform parents on resilience in majority of the children and families after a cancer diagnosis, to increase confidence in their own coping during adverse events.

With the recommendation of taking on a more positive psychology approach in pediatric oncology, it remains of high importance to be careful and alert on recognizing patients and families experiencing problems. Families might be adapting this well because of the quality of psychosocial care in pediatric oncology in western countries. In this thesis we were able to study the resilience of children during active cancer treatment. The adequate psychosocial adjustment of children during treatment might be treacherous: during the structured period of treatment children and their families might adapt quite well, but after the end of treatment a growing number of children might experience psychosocial late effects[38]. The period after end of treatment is crucial, because the number of hospital visits

declines and the provision of psychosocial care diminishes, while there remains the threat and anxiety of relapse and the increased risk of experiencing numerous treatment-related late effects[39,40]. Psychosocial care nowadays is highly focused during the first period after diagnosis, in which the child pays regular visits to the hospital, but might be intensified in the period after end of treatment in order to prevent or act in time in case of psychosocial difficulties.

Conducting standardized family risk assessment

Risk assessment is a helpful step in providing comprehensive care to patients and their families. By making the PAT available in the Netherlands, we made it possible to take an important step towards standardized risk assessment of children and their families in pediatric oncology. The PAT can be used as an instrument to identify psychosocial risk in a systematic and identical manner for all new families. In this section we formulate some recommendations on conducting this risk assessment in pediatric oncology practice in the Netherlands. First, how should one arrange the integration of risk assessment in clinical care? In the Netherlands, when a child is diagnosed with cancer and being hospitalized, a medical doctor and a nurse are being assigned to the family as main contact. All families also meet a social worker. It can be their task to introduce the standardized risk assessment to the families and complete the questions using integrated assessment of qol in daily clinical care, such as the KLIK method, which was developed in the Emma Children's Hopsital in Amsterdam. The KLIK method is an online system (www.hetklikt.nu) to enable routine monitoring and discussing of Patient Reported Outcomed (PROs) for children with cancer or other pediatric conditions[41,42]. Validated and age-approriate sreening questionnaires such as the PAT are available to be completed by children and/or their parents before an outpatient visit. The results from the PROs are being schematically converted into a ePROfile and transferred to members of the psychosocial team, who are responsible for the interpretation of the assessment results. Results on the risk assessment can be discussed within the treatment team, including pediatric oncologist, nurse, child life specialists, a social worker, and a psychologist, while taking into account the estimation of the team in order to define patient or family-centered care. Results can also be discussed with the patient and families by one of the psychosocial team members. Second, what is a recommendable timing for risk assessment? It seems reasonable and recommendable to ask families to complete the PAT around two weeks after diagnosis, a period in which stress reactions are normalizing. During the study described in this thesis, parents completed the PAT at approximately a month after diagnosis, due to study procedures. When you perform screening as standard care, it is possible to perform it earlier in order to discuss it during the introduction of new families and deciding on the provision of psychosocial care. Third, should the risk assessment be web-based or paper-and-pencil? Web-based measures have advantages compared to paper-and-pencil data collection. Web-based measures

tend to result in complete data, are less prone for social desirability answering, and show higher cost-effectiveness[43]. Also, from a recent review[44] it was shown that adult patients in general prefer online assessment above paper-pencil assessment. It is likely that parents of children with cancer will have the same preference and we therefore recommend to use currently existing systems, such as the KLIK method, to assess standardized screening with the PAT. With centralizing pediatric oncology care in the Netherlands, it has become standard care to assess the PAT using KLIK. Fourth, how does standardized risk assessment relate to clinical estimation of the healthcare team? From previous literature, it is known that it is often hard to estimate the risk for developing problems and select families at risk[45]. Our study also showed that there was partial overlap between standardized risk assessment with the PAT and team risk estimations. As a golden standard does not exist, the PAT should be used complimentary to clinical estimations of the team, not replacing them. In the future however, there is need for one golden standard. Team questions might be added to this final standardized risk assessment functioning as golden standard, including multiple informants and multiple outcomes. Fifth, who should complete the PAT? The PAT is a tool to assess family risk, and therefore it should be completed by the parents together or one of the parents representing the family. Sixth, should the PAT be completed one or multiple times? The aim of the PAT is to screen for psychosocial risk in families of children recently diagnosed with cancer, and therefore we recommend that the PAT should only be assessed once around diagnosis. After that, all families should be psychologically monitored in terms of QoL or distress at least each half year. In this monitoring of psychologically family functioning, the adaptive response of both the child, the parent, and even siblings should be the central theme. For children and their siblings the PedsQL aiming to measure QoL, and for parents the Distress Thermometer for Parents (DT-P) is available in the KLIK system[46].

Defining standards of psychosocial care

When risk assessment is being applied in clinical care, one should also define which care is offered to which families. In our multicenter study, we observed major differences in the arrangement of psychosocial care for families of a child with cancer between the centers in the Netherlands. These practices seem to be based on specific policies in different centers lacking an empirical basis. For the future, it is recommendable to define standards of care in pediatric oncology. Recently, a first step has been made to outline pediatric oncology psychosocial standards of care[47]. In this extensive document standards have been recognized as essential for psychosocial care, but concrete recommendations are lacking and should be specified and described into detail. In the current Standards recommendations for basic elements of psychosocial care for all children with cancer are included. These broadly implementable standards are sufficiently general to be tailored to the resources of individual sites that treat childhood cancer and to the needs of individual children and

families[47,48]. With centralizing complex care in the Netherlands in one major pediatric oncology center (Prinses Maxima Center for pediatric oncology) and more routine care in shared care centers in other parts of the country, there is a need for such recommendations. In a consensus document of all psychologists from the DCOG in the Netherlands the following questions could be addressed:"Which care should be offered to each family?", "How to act if a child experiences severe fear of needles?" and "Which intervention should be offered when a parent suffers from Post-Traumatic Stress?" should be answered.

Psychosocial team members are mentioned shortly and their aim is described as following in the current Standards: "Team members collaborate to enhance communication to patients and parents, observe changes in behavior, support decision making, provide empathetic listening, maximize adherence, minimize distress for children and their caregivers related to illness and treatment, and optimize quality of life"[47]. The aim of each psychosocial discipline should be defined, and the role they play in the treatment of children with cancer. However, the Prinses Maxima Center is not yet finalized and it is not clear how care for pediatric cancer patients will be like. It is an unique opportunity to develop guidelines for defining which professional could provide which care for which patient, offering personalized care.

Interventions for parents

Effort should be put into describing effective and evidence-based psychosocial interventions. Based on the results presented in this thesis, an intervention for decreasing parenting stress in parents of a child with cancer could be designed. Interventions should focus on parenting capacities supporting the adequate adjustment of children with cancer and their families. Previous research has already focused on designing evidence-based psychological interventions for parents of children with chronic illness aiming to improve child and family outcomes[49,50]. Multiple psychological treatments are already studied for its effectivity in pediatric populations, such as cognitive behavioral therapy (CBT), family therapy (FT), problem solving therapy (PST), and multsystemic therapy (MST). A recent meta-analysis showed that psychological therapies in general led to improved parenting behavior in families of a child with cancer after end of successful treatment[50]. Next to this, CBT that includes parents had a positive effect in reducing children's primary symptoms, and PST that includes parents improved parent behavior and parent mental health. There is evidence that the beneficial effects can be maintained at follow-up for the mental health of parents of children with cancer and parents who received PST[49,50].

An example of an Dutch existing intervention is 'Op Koers', including elements of CBT and PST[51]. The intervention aims to empower children with adverse health conditions by teaching the use of active coping strategies. Research on the effectivity of the face-to-face intervention for children showed that effectivity increased when parents also participated next to the children[5] and therefore a parent component was included. Primary purpose

of the parental module is to enhance intervention effects of the children's program, by teaching parents to be sensitive to their children's needs, and encourage their children in using the learned skills. The parent intervention fits into the learning goals of the child intervention. Three learning goals are central to the parent training: 1) Learning: to understand what the children learn, 2) Observing: to be sensitive to children's cognitions and feelings, 3) Motivating: to stimulate their children to apply the learned skills in daily life. At this moment, research is is progress for an online version of children with a chronic disease and for parents of children with cancer. Based on the findings in this thesis it is recommended to pay attention to parent-child interaction and parental factors such as illness cognitions, active parental coping, and supporting social networks of families. This thesis showed mainly how important parental factors are in child psychosocial adjustment to disease, and therefore psychological interventions should be designed in supporting the parents in improving child and family outcomes. Another important stressor, specifically for the population of ALL patients, is the use of corticosteroids[52]. There is a need for specific interventions, providing families with information about possible treatment side-effects and supporting adequate parenting skills[53]. Pilot data of such an intervention supported the beneficial effect, but further research is warranted[54]. In general, psycho-education could be helpful in informing parents regarding adequate adjustment in majority of the families, supporting confidence in their own capacities. Next to this, peer support could be helpful in exchanging information and experiences regarding parenting children with health conditions.

Next to this, preventive interventions could be designed, such as interventions supporting parents in parenting a child during challenging circumstances as during cancer treatment. Thus, interventions for families at risk for developing problems but not currently experiencing psychopathology. These families can be recognized by the PAT and offered early interventions, such as anxiety decreasing exercises and psycho-education materials.

At last, parenting stress and parental distress showed to be higher in our study population of parents of a child with cancer compared to the general population but is not unique for this population. The influence of parental factors on child functioning is also true for healthy children[55]. Interventions reducing distress and parents and supporting adequate parenting can also be helpful for other or non-pediatric populations with minor adaptations. General interventions for parents of a child with cancer including elements of psycho-education, CBT and PST can be used for multiple pediatric conditions. Interventions could be easily adapted for specific populations, including psycho-education on a specific subject such as the effects of corticosteroids next to general elements.

Chapter	Purpose	Sample characteristics	Maesures/content	Main findings
2	To distinct subgroups of patients diagnosed with ALL showing different psychosocial adjustment trajectories during treatment and to explore predictors of these trajectories	N=108 parents of a child (1-18 years) diagnosed with ALL	- Socio-demographic questionnaire - Child behavioral adjustment (CBCL 1-18 year) - Child Quality of Life: Generic (CHQ) Disease-specific (PedsQL-cancer module) - Parent reported predictors: Parental distress (POMS) Illness Cognitions (ICQ-P) Coping (UCL) Parenting Stress (PSI) Social support (ISR)	**(1)** For internalizing behavior a three-trajectory model was found: a group that experienced no problems (60%), a group that experienced only initial problems (30%), and a group that experienced chronic problems (10%). **(2)** For externalizing behavior a three-trajectory model was also found: a group that experienced no problems (83%), a group that experienced chronic problems (12%), and a group that experienced increasing problems (5%). **(3)** Only parenting stress and baseline QoL (cancer-related) were found to contribute uniquely to adjustment trajectories.
3	To assess the specific mechanism in which parental distress is related to psychosocial adjustment in children diagnosed with ALL	N=97 parents of a child (1-18 years) diagnosed with ALL	- Socio-demographic questionnaire - Child behavioral adjustment (CBCL 1-18 year) - Mediator: Parenting stress (PSI) - Predictors: Parental distress (POMS) Illness Cognitions (ICQ-P) Coping (UCL) Social support (ISR)	**(1)** This study showed important indirect effects of perceived disease benefits, positive affect, and social support on child behavioral problems via parenting stress. The tested models showed an excellent fit to the data. **(2)** Parenting stress seemed to a stronger predictor for externalizing behavior, than for internalizing behavior.
4	To study the psychometric properties of the Illness Cognition Questionnaire (ICQ) adapted for use in parents of an ill child, and to determine whether illness cognitions are associated with parental distress	N=242 parents of a child (0-18 years) diagnosed with cancer	- Parent illness cognitions (ICQ-P) - Validation measures: Parental distress (POMS, HADS)	**(1)** Factor analysis confirmed the hypothesized structure of the ICQ-P in our sample (n=242). The three scales Helplessness, Acceptance, and Perceived Benefits explained 9.8%, 31.4%, and 17.9% of the variance, respectively. **(2)** Cronbach's alpha showed adequate internal consistency (.80-.88). **(3)** Concurrent and criterion-related validity were appropriate.

Chapter	Purpose	Sample characteristics	Maesures/content	Main findings
5	To assess the reliability, validity, and usability of the PAT in a Dutch pediatric oncology sample	N=117 parents of a child (0-18 years) diagnosed with cancer	- Family risk and resilience (PAT total score and 7 subscales: structure and resources, social support, family problems, parent stress reactions, family beliefs, child problems, sibling problems) - Validation measures: Child/sibling problems (SDQ) Social support (ISR) Parental distress (HADS) Parenting stress (PSI) Parental illness cognitions (ICQ-P) - ePAT usability measure (comprehensibility, clarity, appropriateness, unpleasantness, length)	**(1)** Acceptable reliability was obtained fort the PAT total score (a=.72) and majority of subscales (0.50-0.82). Inadequate internal consistency for Social Support (a=.19) and Family Beliefs (a=.20) were found. **(2)** The total PAT score was significantly related to all of the validation measures (r=.23-.61), with the exception of the ICQ-P perceived benefits (r=.07). **(3)** Of the families, 66% scores low (Universal), 29% medium (Targeted), and 5% high (Clinical) risk. **(4)** Parents were positive about the comprehensibility, clarity, appropriateness and length of the PAT and did not find it unpleasant to complete the PAT around one month post-diagnosis.
6	To determine the match between Dutch families' psychosocial risk profiles and psychosocial care provided to the families	N=83 parents of a child (0-18 years) diagnosed with cancer	- Family risk and resilience (PAT total score) - Team risk estimation (standard risk, above average, high risk) - Provided psychosocial care in the first 6 months post-diagnosis. Basic care was defined as receiving support from 1 psychosocial discipline, and specialized care as support from 2 or more disciplines.	**(1)** 30% of patients from universal group got basic psychosocial care), 63% got specialized care and 7% did not get any care. **(2)** 14% of the families at risk got basic care, 86% got specialized care. **(3)** Team risk estimations and PAT risk scores matched with 58% of the families. Match between the team risk estimation and the PAT risk score was low (k=.18).

CONCLUSION

Most children diagnosed with cancer adjust relatively well regarding their psychosocial functioning. However, still one out of five showed behavioral problems interfering with their daily life. Parenting stress has shown to be an important risk factor for these problems. With the results of this thesis, risk and resilience factors were pointed out, providing opportunities for timely screening and tailored intervention. Psychosocial care could then be provided in an evidence-based efficient way: extra care for those who need it, basic care for families adjusting adequately. It is important to provide special attention on the parents in their role of parenting, as these parenting factors have shown to be relevant in the relationship between wellbeing of the parents and adjustment of the child. Timely interventions focused on improving the knowledge, skills, and confidence of parents in raising an ill child can prevent escalation of problems and support adequate child and family psychosocial adjustment after diagnosis. Results of this thesis can serve as an example for other pediatric populations, in focusing on the family system rather than only on the patient, and for efficient psychosocial care delivery by integrating standardized risk assessment in clinical practice.

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CHAPTER 8

Summary

In this thesis we focused on the psychosocial adjustment of children with cancer and their parents. It comprised three main topics; 1) child adjustment from diagnosis to two years later, 2) family risk factors for child maladjustment, and 3) early detection of families at-risk.

Chapter 1, the general introduction, gives a brief overview of the current knowledge in the field of psychosocial adjustment in children with cancer. Two different research models are presented forming the theoretical basis for this thesis. The first model is Wallander and Varni's (*1998*) disease-stress-coping (DSC) model of child adjustment to pediatric chronic somatic disorders. The DSC model identifies several illness related, stress-processing, intrapersonal, and social ecological factors. The second model is the Pediatric Psychosocial Preventative Health Model (PPPHM), which conceptualizes the adjustment of children with Pediatric Medical Traumatic Stress (PMTS) and their families, and provides a conceptual model to guide screening and services entering the pediatric health care system. Finally, the research questions and the aim of this thesis are presented.

In *Chapter 2* we studied adjustment trajectories of children during treatment for Acute Lymphoblastic Leukemia (ALL) and aimed to distinguish subgroups of patients showing different trajectories during active treatment. Furthermore, we explored sociodemographic, medical, and psychosocial predictors of the distinct adjustment trajectories. In a multicenter longitudinal study 108 parents of a child (response rate 80%) diagnosed with ALL were assessed during induction treatment (T0), after induction/consolidation treatment (T1), and after end of treatment (T2). Trajectories of child behavioral adjustment were tested with Latent Class Growth Modeling (LCGM) analyses. For internalizing behavior a three-trajectory model was found: a group experiencing no problems (60%), a group experiencing only initial problems (30%), and a group experiencing chronic problems (10%). For externalizing behavior a three-trajectory model was also found: a group experiencing no problems (83%), a group experiencing chronic problems (12%), and a group experiencing increasing problems (5%). Only parenting stress and baseline QoL (cancer-related) were found to contribute uniquely to adjustment trajectories. From this study we concluded that the majority of the children (77%) shows no behavioral problems during the entire treatment as reported by parents. A small but substantial group (23%) shows maladaptive trajectories of internalizing and/or externalizing behavioral problems. Not medical factors puts the child at risk for psychosocial difficulties, but mainly the psychological reaction of the parents.

In *Chapter 3* we aimed to investigate the specific mechanism in which parenting stress is related to behavioral adjustment in children recently diagnosed with ALL. In a multicenter longitudinal study 97 parents of children aged 1-17 (response rate 80%) diagnosed with ALL, completed questionnaires on child behavioral problems (Child Behavior Check List), parental well-being (Profiles Of Mood States), illness cognitions (Illness Cognition Questionnaire), parenting stress (Parenting Stress Index), social support (Inventory Social Reliance), coping (Utrecht Coping List) at time of diagnosis (T0) and/or at end of treatment

(T2). Structural Equation Modeling (SEM) was performed to test the hypothesized models. Analyses showed that the explained variance of the CBCL was 26%, which was explained completely by parenting stress. Parenting stress was explained for 28% by the following predictor variables: perceived benefits, negative affect, and social support. Parenting stress was a stronger predictor for externalizing behavior (.60), than for internalizing behavior (.41). Results of this study showed that parent psychological factors did not directly influence child adjustment, but that this association was indirect via parenting stress. So parenting stress would be an important factor facilitating early detection of families at risk for adjustment problems during treatment.

The study described in *Chapter 4* assessed the psychometric properties of the Illness Cognition Questionnaire (ICQ), adjusted for the parents of an ill child. Participants were recruited from two multicenter studies: sample 1 included 128 parents of a child diagnosed with acute lymphoblastic leukemia (ALL) (response rate 80%), and sample 2 included 114 parents of a child diagnosed with cancer (response rate 74%). Parents completed an adapted version of the ICQ (ICQ-P), together with the Profile Of Mood States (POMS) or the Hospital Anxiety and Depression Scale (HADS). The factor structure of the ICQ-P was examined by means of principal component analysis (PCA) and cronbach's alpha for each subscale and correlations between the ICQ-P scales and the HADS and POMS were calculated. Factor analysis confirmed the hypothesized structure of the ICQ-P in our sample (n=242). The three scales Helplessness, Acceptance, and Perceived Benefits explained 9.8%, 31.4%, and 17.9% of the variance, respectively. Cronbach's alpha showed adequate internal consistency (.80-.88). Concurrent and criterion-related validity were appropriate. The results confirmed that the ICQ-P reliably assesses the illness cognitions of the parents of a child with cancer. Psychologically distressed parents showed less acceptance and more helplessness. The availability of a short and valid illness cognition questionnaire will help clinicians gain insight into parental cognitions regarding the illness of their child, information that might be helpful for targeting interventions.

In *Chapter 5* we described the cross-cultural adaptation, reliability, validity, and usability of the Psychosocial Assessment Tool (PAT) in a European country (Dutch translation). The PAT was originally developed in the US to screen for psychosocial risk in families of a child diagnosed with cancer. A total of 117 families (response-rate 59%) of newly diagnosed children with cancer completed the PAT and validation measures (ISR, SDQ, HADS, PSI, ICQ).In the process of culturally adapting the PAT, guidelines of Beaton et al. (2000) were followed. Reliability was calculated for the PAT2.0 total and subscale scores using Cronbach's alpha. Content validity and criterion-related validity were examined using Pearson Correlations between each PAT subscale. The distribution of PAT total scores into the three risk categories was calculated and compared with results found in other countries. Results showed acceptable reliability for the PAT total score (α = .72) and majority of subscales (.50 - .82). Two subscales showed inadequate internal consistency (Social Support α = .19;

Family Beliefs α = .20). Validity and usability were adequate. Of the families, 66% scored low (Universal), 29% medium (Targeted), and 5% high (Clinical) risk. This study confirmed the cross-cultural applicability, reliability, and validity of the PAT total score. Reliability left room for improvement on subscale level.

The study described in *Chapter 6* aimed to investigate the added value of the PAT to psychosocial care allocation by (1) assessing the match between PAT scores and provided psychosocial care, (2) the match between PAT scores and team risk estimations, and (3) the match between team risk estimations and provided psychosocial care. 83 families (response-rate 73%) of children with cancer participated. The PAT and team risk estimations (available in 60/83 families) were assessed at diagnosis, and the intensity of provided psychosocial care (universal, targeted, clinical) five months later. Personnel were blind to PAT scores. PAT scores revealed that 65% of families had low (universal), 30% medium (targeted), and 5% high (clinical) risk. 30% of patients from universal group got basic psychosocial care, 63% got specialized care and 7% did not get any care. 14% of the families at risk got basic care, 86% got specialized care. Team risk estimations and PAT risk scores matched with 58% of the families.We concluded that psychosocial care is only partly matched to family risk, both using standardized screening and team estimations. Standardized risk assessment with the PAT leads to other information regarding needs for psychosocial care compared to the manner in which families are perceived in the clinic, and should be used complementary to tailor care to family needs.

In *Chapter 7*, the general discussion, the main findings of this thesis are placed in clinical perspective. Most children diagnosed with cancer adjust relatively well regarding their psychosocial functioning. However, still one out of five showed behavioral problems interfering with their daily life. With the results of this thesis, risk and resilience factors were pointed out, providing opportunities for timely screening and tailored intervention. Psychosocial care could then be provided in an evidence-based efficient way: extra care for those who need it, basic care for families adjusting adequately. It is important to focus care on the parents in their role of parenting, as these parenting factors have shown to be relevant in the relationship between wellbeing of the parents and adjustment of the child. Timely interventions focused on improving the knowledge, skills, and confidence of parents in raising an ill child can prevent escalation of problems and support adequate child and family psychosocial adjustment after diagnosis. Results of this thesis can serve as an example for other pediatric populations, in focusing on the family system rather than only on the patient, and for efficient psychosocial care delivery by integrating standardized risk assessment in clinical practice.

SAMENVATTING

In dit proefschrift hebben we ons gericht op de psychosociale aanpassing van kinderen met kanker en hun ouders. Het omvat drie belangrijke thema's, namelijk 1) psychosociale aanpassing van het kind tijdens de behandeling, van net na diagnose tot 2 jaar later, 2) risicofactoren voor verminderde psychosociale aanpassing van het kind, en 3) vroegtijdige herkenning van gezinnen at-risk voor psychosociale problemen.

Hoofdstuk 1, de algemene inleiding, geeft een kort overzicht van de huidige kennis op het gebied van psychosociale aanpassing bij kinderen met kanker. Twee verschillende onderzoeksmodellen worden gepresenteerd die de theoretische basis vormen voor dit proefschrift. Het eerste model is het disease-stress-coping (DSC) model van Wallander & Varni. Het beschrijft factoren en hun onderlinge relaties voor psychosociale aanpassing van het kind wanneer zij geconfronteerd worden met een somatische aandoening. Het tweede model is het Pediatric Psychosocial Preventative Health Model (PPPHM), die de aanpassing van kinderen en hun gezin in geval van Pediatric Medical Traumatic Stress (PMTS) beschrijft, en biedt aanknopingspunten voor screening en het bieden van psychosociale zorg. Tot slot worden de vraagstellingen en de opbouw van dit proefschrift toegelicht.

In *Hoofdstuk 2* bestudeerden we aanpassingstrajecten van kinderen tijdens de behandeling voor Acute Lymfatische Leukemie (ALL) en wilden we groepen onderscheiden van patiënten met verschillende aanpassingstrajecten tijdens behandeling. Daarnaast onderzochten we of er bepaalde sociodemografische, medische, en psychosociale factoren voorspellend waren voor de verschillende aanpassingstrajecten. In deze multicenter longitudinale studie includeerden we 108 ouders van een kind met ALL (respons rate 80%), die tijdens inductie behandeling (T0), na inductie/consolidatie fase (T1), en na einde behandeling (T2) vragenlijsten invulden over hun kind. Aanpassingstrajecten werden getoetst met behulp van Latent Class Growth Modeling (LCGM) analyses. Voor internaliserend gedrag werd er een model gevonden bestaande uit drie verschillende trajecten/groepen: een groep die geen problemen ondervond tijdens de behandeling (60%), een groep die alleen aan het begin van de behandeling problemen had (30%), en een groep die chronische problemen ondervond (10%). Ook voor externaliserend gedrag werd een model gevonden bestaande uit drie verschillende trajecten/groepen: een groep die geen problemen ondervond tijdens de behandeling (83%), een groep die chronische problemen ondervond (12%), en een groep die steeds meer problemen ontwikkelde (5%). Alleen opvoedingsstress van de ouders en ziektegerelateerde Kwaliteit van Leven van het kind bij diagnose bleken een unieke voorspeller van aanpassingstrajecten. Uit deze studie concludeerden we dat de meeste kinderen (77%) geen gedragsproblemen vertoont tijdens de gehele behandeling. Een kleine maar klinisch relevante groep (23%) vertoont aanpassingsproblemen op het gebied van internaliserende en/of externaliserende gedragsproblemen. Niet de medische factoren, maar voornamelijk de psychologische

factoren van de ouders, in het bijzonder stress die zij ervaren bij de opvoeding van een ziek kind, zijn een risicofactor voor psychosociale problemen van het kind.

In *Hoofdstuk 3* wilden we onderzoeken op welke manier opvoedingstress van de ouders gerelateerd is aan gedragsaanpassing van kinderen met ALL. In deze multicenter longitudinale studie includeerden we 97 ouders van een kind met ALL (respons rate 80%), die tijdens inductie behandeling (T0) en na einde behandeling (T2) vragenlijsten invulden over het gedrag van hun kind, hun eigen functioneren, ziektecognities, opvoedingsstress, sociale steun, en coping. Met behulp van Structural Equation Modeling (SEM) testten we de veronderstelde modellen. Uit de statistische analyses bleek dat de verklaarde variantie van algehele gedragsaanpassing van het kind 26% was, welke volledig verklaard werd door opvoedingsstress van de ouders. Opvoedingsstress werd op zijn beurt voor 28% verklaard door de volgende voorspellende factoren: positieve gevolgen, negatief affect, en sociale steun. Ouders die in staat waren om ook positieve gevolgen van de ziekte van hun kind te ervaren, die minder negatieve affect vertoonden, en die voldoende sociale steun ervaarden, ervaren minder stress tijdens de opvoeding van hun zieke kind en daardoor vertoont het kind minder gedragsproblemen. Deze factoren lijken gezinnen te beschermen tegen het ervaren van psychosociale problemen. Opvoedingsstress bleek een sterkere voorspeller te zijn voor externaliserend gedrag (.60), dan voor internaliserend gedrag (.41). Uit de resultaten van deze studie bleek dat psychologische factoren van de ouders niet direct aanpassingsgedrag van het kind beïnvloeden, maar dat dit verband indirect loopt via opvoedingsstress. Screening zou vroegtijdige herkenning van gezinnen met hoge niveaus van opvoedingsstress vergemakkelijken.

De studie die wordt beschreven in *Hoofdstuk 4* beschreef de psychometrische eigenschappen van de Ziekte Cognitie Lijst (ZCL), aangepast voor ouders van een ziek kind. Gezinnen werden geworven gedurende twee multicenter studies: studie 1 bestaat uit 128 ouders van een kind met ALL (respons rate 80%), en studie 2 bestaat uit 114 ouders van een kind met kanker (respons rate 74%). Ouders vulden de aangepaste versie van de ZCL (ZCL ouder versie), samen met de Profile Of Mood States (POMS) of de Hospital Anxiety and Depression Scale (HADS). De factorstructuur van de nieuwe vragenlijst werd getoetst met behulp van een Principal Component Analysis (PCA) en cronbach's alpha voor iedere subschaal en correlaties tussen de subschalen en de POMS/HADS werden berekend. Factoranalyse bevestigde de originele structuur van de ZCL in onze groep ouders (n=242). De drie schalen 'Hulpeloosheid', 'Acceptatie', en 'Positieve veranderingen' verklaarden respectievelijk 9.8%, 31.4%, en 17.9% van de variantie. De drie schalen waren intern consistent (α=.80-.88). Inhoudsvaliditeit en criteriumvaliditeit werden bevestigd. De resultaten van dit onderzoek bevestigden dat de ZCL ouder versie in staat is om op een betrouwbare manier de ziektecognities van ouders van een kind met kanker in kaart te brengen. Ouders die minder acceptatie en meer hulpeloosheid aangaven, rapporteerden meer emotionele last. De beschikbaarheid van deze korte en valide vragenlijst kan hulpverleners helpen

inzicht te krijgen in de cognities van ouders ten aanzien van de ziekte van hun kind; informatie die kan helpen bij het vormgeven van een psychologische interventie.

In *Hoofdstuk 5* beschreven we de cross-culturele aanpassing, betrouwbaarheid, validiteit, en bruikbaarheid van de Psychosocial Assessment Tool (PAT) in Nederland. De PAT werd ontwikkeld in de Verenigde Staten om gezinnen van een kind met kanker, die at-risk zijn voor psychosociale problemen, vroegtijdig te herkennen. In totaal vulden 117 gezinnen (respons rate 59%) van een kind met kanker de PAT en verschillende validatie vragenlijsten in. Tijdens de culturele aanpassing van de PAT werden de richtlijnen van Beaton et al. (2000) gevolgd. De betrouwbaarheid werd berekend voor de PAT totaal- en subschalen met behulp van Cronbach's alpha. Inhoudsvaliditeit en criteriumvaliditeit werden getoetst met behulp van correlaties. Tot slot werd de verdeling van de PAT scores in de drie risico categorieën berekend en vergeleken met de resultaten die werden gevonden in andere landen. Analyses toonden aan dat de PAT totaal score voldoende betrouwbaar was (α=.72), en de meerderheid van de subschalen ook (.50-.82). Twee subschalen vertoonden onvoldoende interne consistentie (Sociale Steun α=.19; Familie Cognities α=.20). Validiteit en betrouwbaarheid waren voldoende. Van de gezinnen scoorden 66% laag (Universal), 29% midden (Targeted), en 5% hoog (Clinical) risico. Deze studie bevestigde dus de cross-culturele toepasbaarheid, betrouwbaarheid, en validiteit van de PAT totaal score. Hiermee is een vragenlijst beschikbaar die op een gestandaardiseerde wijze families at-risk voor psychosociale problemen kan herkennen. Betrouwbaarheid op subschaal niveau kan verbeterd worden.

De studie die wordt beschreven in *Hoofdstuk 6* had als doel om de toegevoegde waarde van de PAT op de inzet van psychosociale zorg te onderzoeken door middel van onderzoek naar 1) de match tussen PAT scores en verleende psychosociale zorg, 2) de match tussen PAT scores en risico inschattingen van het team, en 3) de match tussen risico inschattingen van het team en verleende psychosociale zorg. In totaal deden 83 gezinnen van een kind met kanker (repons rate 73%) mee. De PAT en de risico inschattingen van het team (beschikbaar in 60/83 gezinnen) werden afgenomen rondom diagnose, en de intensiteit van de verleende zorg (standaard, gespecialiseerd) vijf maanden later. Het personeel had gedurende deze studieperiode geen inzicht in de PAT scores van de gezinnen. PAT scores toonden aan dat 65% van de gezinnen laag (universal), 30% midden (targeted), en 5% hoog (clinical) risico had. 30% van de gezinnen met een 'universal' PAT score ontvingen standaard psychosociale zorg, 63% gespecialiseerde zorg en 7% ontving geen psychosociale zorg. 14% van de gezinnen met een at-risk PAT score ontving standaard zorg, en 86% gespecialiseerde zorg. Risico inschattingen van het team kwamen in 58% van de gezinnen overeen met actuele PAT score. Uit deze resultaten concludeerden we dat de inzet van psychosociale zorg op dit moment slechts deels is afgestemd op het risico van een gezin, zowel wanneer we dit risico in kaart brengen met een gestandaardiseerde vragenlijst als wanneer we de inschatting van het team hanteren. Het in kaart brengen van risico op

een gestandaardiseerde manier (met behulp van de PAT) leidt tot andere informatie wat betreft de zorgbehoefte van gezinnen, dan wanneer we afgaan op de klinische blik van professionals. Daarom zouden deze twee aanvullend op elkaar gebruikt moeten worden.

In *Hoofdstuk 7* worden de belangrijkste bevindingen in klinisch perspectief geplaatst. De meerderheid van de kinderen die gediagnosticeerd worden met kanker passen zich relatief goed aan op psychosociaal vlak. Toch ervaart een substantiële groep van ongeveer 20% gedragsproblemen die zorgen voor belemmeringen in het dagelijks leven. In deze thesis werden risico en beschermende factoren aangetoond, waarbij het mogelijk wordt om hierop te screenen en interventies op in te zetten. Een bestaand screeningsinstrument, de PAT, bleek geschikt voor gebruik in de Nederlandse praktijk. Psychosociale zorg kan op een wetenschappelijke en efficiënte manier ingezet worden: extra zorg voor de gezinnen die dat nodig hebben, standaard zorg voor gezinnen die veerkracht genoeg hebben om zich adequaat aan te passen. De studies maken overduidelijk dat er in de zorg veel aandacht nodig is voor de ouders en voor hun rol als opvoeder, omdat dit een belangrijke rol speelt in de aanpassing van hun kind na behandeling. Interventies die zich focussen op het verbeteren van de kennis, netwerk, vaardigheden en vertrouwen van ouders in het opvoeden van een ziek kind kan psychosociale problemen voorkomen en verminderen. De resultaten uit deze thesis kunnen ook gebruikt worden in andere pediatrische populaties. De focus op het gezin in plaats van de individuele patiënt en het efficiënt inzetten van psychosociale zorg gebaseerd op gestandaardiseerde screening zijn breed toepasbaar.

APPENDIX

LIST OF PUBLICATIONS
PHD PORTFOLIO
DANKWOORD
CURRICULUM VITAE

ORIGINAL ARTICLES

Sint Nicolaas SM, Schepers SA, van den Bergh EMM, Evers AWM, Hoogerbrugge PM, Grootenhuis MA, Verhaak CM. Illness Cognitions and family adjustment: Psychometric properties of the Illness Cognition Questionnaire in parents of a child with cancer. *Supportive Care in Cancer, 2016 Feb; 24(2): 529-37.*

Sint Nicolaas SM, Schepers SA, Hoogerbrugge PM, Caron HN, Van de Heuvel-Eibrink MM, Kaspers GJL, Grootenhuis MA, Verhaak CM. Screening for psychosocial risk in Dutch families of a child with cancer: reliability, validity, and usability of the Psychosocial Assessment Tool (PAT). *Journal of Pediatric Psychology, 2016 Aug; 41(7): 810-9.*

Sint Nicolaas SM, Hoogerbrugge PM, van den Bergh EMM, Schepers SA, Gemke RJBJ, Verhaak CM. Predicting trajectories of behavioral adjustment in children diagnosed with acute lymphoblastic leukemia. *Supportive Care in Cancer, 2016 Nov; 24(11): 4503-13.*

Sint Nicolaas SM, Custers JAE, Hoogerbrugge PM, van den Bergh EMM, Verhaak CM. Parenting stress and behavioral problems in Children with Acute Lymphoblastic Leukemia: a longitudinal prospective study. *Submitted for publication.*

Sint Nicolaas SM, Schepers SA, van den Bergh EMM, de Boer Y, Streng I., van Dijk-Lokkart EM, Grootenhuis MA, Verhaak CM. Match of psychosocial care and psychosocial risk in families of a child with cancer. *Pediatr Blood Cancer, 2017 Dec; 64(12).*

Schepers SA, **Sint Nicolaas SM,** Haverman L, Wensing M, Schouten AYN, Hoogerbrugge PM, Kaspers GJL, Verhaak CM, & Grootenhuis MA. Real-world implementation of electronic patient-reported outcomes in outpatient pediatric cancer care. *Psychooncology. 2017 Jul;26(7):951-959.*

Schepers SA, **Sint Nicolaas SM,** Maurice-Stam H, Verhaak CM, Grootenhuis MA. Parental distress 6 months after pediatric cancer diagnosis in relation to family psychosocial risk at diagnosis. *Cancer. 2017 Sep 13. doi: 10.1002/cncr.31023. [Epub ahead of print]*

Schepers SA, **Sint Nicolaas SM**, Maurice-Stam H, van Dijk-Lokkart EM, van den Bergh EMM, de Boer N, Verhaak CM, Grootenhuis MA. First experience with electronic feedback of the Psychosocial Assessment Tool in pediatric cancer care. *Support Care Cancer. 2017 May 11. doi: 10.1007/s00520-017-3719-3.*

Haverman L, van Oers HA, Limperg PF, Hijmans CT, Schepers SA, **Sint Nicolaas SM,** Verhaak CM, Bouts AHM, Fijnvandraat CJ, Peters M, van Rossum MA, van Goudoever JB, Maurice-

Stam H, & Grootenhuis MA. Implementation of Electronic Patient Reported Outcomes in Pediatric Daily Clinical Practice: The KLIK Experience. *Clinical practice in pediatric psychology, 2(1), 50-67*.

PUBLISHED ABSTRACTS

Sint Nicolaas SM, Meijer-van den Bergh EMM, Schepers SA, Hoogerbrugge PM, Verhaak CM. Predictors of Behavioral Adjustment of Children Diagnosed with Acute Lymphoblastic Leukemia. Psycho-oncology, 2014, 23 (Suppl.3), p11. DOI: 10.1111/j.1099-1611.2014.3693

Sint Nicolaas SM, Schepers SA, Grootenhuis MA, Verhaak CM. Agreement Between Different Coders: Mothers, Fathers, and Psychosocial Team Completing the Psychosocial Assessment Tool (PAT). Psycho-oncology, 2014, 23 (Suppl.3), p115. DOI: 10.1111/j.1099-1611.2014.3694

Sint Nicolaas SM, Meijer-van den Bergh EMM, Hoogerbrugge PM, Prins JB, Gemke RJBJ, Verhaak CM. Behavioral adjustment of children diagnosed with Acute Lymphoblastic Leukemia: from diagnosis until end of treatment. Psycho-oncology, 2013, 22 (Suppl.3), p70. DOI: 10.1111/j.1099-1611.2013.3393

Schepers SA, **Sint Nicolaas SM**, Schouten-van Meeteren AYN, Hoogerbrugge PM, Veening MA, Verhaak CM, Grootenhuis MA. Multicenter implementation of electronic Patient Reported Outcomes (ePROs) during treatment in pediatric oncology practice (KLIK): is it feasible? Psycho-oncology, 2013, 22 (Suppl.3), p72. DOI: 10.1111/j.1099-1611.2013.3393

Sint Nicolaas SM, van den Bergh EMM, Hoogerbrugge PM, Prins JB, Gemke RJBJ, Verhaak CM. Course of behavioral adjustment of children diagnosed with Acute Lymphoblastic Leukemia. Pediatric Blood and Cancer, 2012, 59 (6), p 1125. DOI:10.1002/pbc

OTHER

Haverman L, Schepers SA, **Sint Nicolaas SM** (2012). KLIK brengt kwaliteit van leven in kaart. *Attent, 26, 8-9*.

PHD PORTFOLIO

Institute for Health Sciences
Radboudumc

Name PhD student: S.M. Sint Nicolaas	***PhD period: 01-09-2011 – 31-12-2015***
Department: Medical Psychology	***Promotor(s): Prof. J.B. Prins, Prof. M.A. Grootenhuis, Prof. P.M. Hoogebrugge***
Graduate School: Radboud Institute for Health Sciences	***Co-promotor(s): Dr. C.M. Verhaak***

	Year(s)	ECTS
TRAINING ACTIVITIES		
a) Courses & Workshops		
BROK course	2012	1.75
NCEBP introduction course	2012	1.75
Workshop 'Cancer from a developmental perspective'	2012	0.2
Workshop 'Pediatric Psycho-oncology: building clinical skills'	2013	0.4
Masterclass 'Resilience'	2013	0.2
Course 'Digitale tools'	2013	0.4
Course 'Academic Writing'	2013	3.25
NVVO course 'Introduction Clinical and Fundamental Oncology'	2013	1.75
Workshop 'Getting Published'	2014	0.2
Course 'Systematic review and meta-analysis'	2015	1.75
Workshop 'Ontwikkelingsgerichte zorg'	2015	0.2
b) Seminars & lectures^		
c) Symposia & congresses^		
NVPO congress, Utrecht^	2012	0.5
International Pediatric Psychology Conference, Oxford ^	2012	1.0
SIOP congress, London ^	2012	1.5
IPOS congress, Rotterdam ^	2013	1.75
NVPO congress, Utrecht ^	2014	0.5
International Pediatric Psychology Conference, Amsterdam ^	2014	1.0
IPOS congress, Lisbon ^	2014	1.5
Kracht van Schakels symposium, Nijmegen ^	2015	0.5
SIOP congress, Cape Town ^	2015	1.5
d) Other		
Member of the working group psychosocial research PMCK	2013-2015	1.5
Member Research Board Medical Psychology	2014-2015	1.0
TEACHING ACTIVITIES		
e) Lecturing		
Workshop KLIK pediatric oncologists	2012	4.0
Guest lecture 'Psychosocial care within pediatric oncology' nurses	2012	1.0
Workshop PAT psychosocial team members	2013	4.0
Guest lecture 'Psychosocial care within pediatric oncology', Tilburg	2012-2016	5.0
Course 'Cancer Research', Tutor Biomedical Science students	2013-2014	4.0
TOTAL		**42.1**

^Indicate oral or poster presentation

Radboud University Radboudumc university medical center

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CURRICULUM VITAE

Simone Sint Nicolaas werd op 2 juni 1988 geboren te Dordrecht. In 2006 behaalde zij het Gymnasium diploma aan het Insula College te Dordrecht. Na het afronden van de bachelor Psychologie aan de Universiteit van Tilburg, volgde zij de tweejarige master 'Medische Psychologie' waar zij ook een jaar lang stage liep op de afdeling Medische Psychologie, kind & jeugd van het Jeroen Bosch Ziekenhuis. In 2011 startte ze dit promotieonderzoek, wat leidde tot dit proefschrift. Momenteel werkt zij als psycholoog i.o. tot GZ-psycholoog binnen de basis GGZ waar zij kinderen behandelt met een diversiteit aan problematiek. Simone woont samen met Bob en hun zoon Mats in Dordrecht.