From the Department of Neurobiology, Care Sciences and Society,
Division of Nursing
Karolinska Institutet, Stockholm, Sweden

CHILDHOOD CANCER AND SCHOOL

Margareta af Sandeberg

Karolinska Institutet

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"En droppe droppad i livets älv
har ingen kraft till att flyta själv
Det ställs ett krav på varenda droppe:
Hjälp till att hålla de andra oppe!"
Tage Danielsson

ABSTRACT

The school situation is one area identified as being affected during and after treatment for childhood cancer and only studied to a limited extent. A contributing factor to that school absence is not always recommended is uncertainty about whether it increases the risk of infection. Furthermore, there is a lack of valid instruments for the measurement of HRQOL in this population. The overall aim of this thesis was therefore to investigate the school situation and HRQOL of school-aged children (7-16 years) during initial cancer treatment and 4 to 6 years after diagnosis.

The thesis includes four studies with a longitudinal design following a cohort of school-aged children (n=126) diagnosed with cancer and starting chemotherapy and/or radiation therapy, response rate 87%. Data during initial cancer treatment were collected one month (T1), 2.5 months (T2) and 5 months (T3) after the start of initial treatment using a study-specific questionnaire to examine school attendance and a standardized instrument for the measurement of HRQOL: the Disabkids chronic generic module (DCGM-37). Study I reports on data quality and psychometric properties of the DCGM-37. Study II followed school attendance and HRQOL over three different weeks during the first 5 months of cancer treatment. Study III included children who were free from infection the day before the start of two observation periods (19 days) during initial cancer treatment. Demographic and clinical data as well as school attendance were analysed regarding the association to the start of antimicrobial treatment. A median of 5 years after diagnosis 63 of the former patients agreed to participate in a follow-up study of school situation and self-rated independence in survivors of childhood cancer (study IV). In study IV data were collected using telephone interviews with open-ended and structured questions. The survivors' responses from the structured questions were compared with those from age-matched comparison group drawn from the general population (n=257).

The evaluation of data quality and psychometric properties of the DCGM-37 (study I) indicates that it is a feasible instrument for children with cancer though dimensionality was not entirely supported. Furthermore, the results of study II-III revealed that school attendance significantly increased over the first 5 months of initial cancer treatment while self-reported HRQOL diminished, especially among the girls, which did not change throughout the first five months of treatment. Furthermore, HRQOL was positively related to school attendance. Hospital visits and fatigue were the two most common given reasons for school absence. Children who attended school did not appear to develop more infections than children not attending school. The results of study IV, conducted a median of 5 years after diagnosis, showed that despite that 62% of the survivors considered their school situation to be more or less the same as their peers' situation, a significant proportion reported difficulties in school because of physical and cognitive limitations. At follow-up, the survivors scored significantly higher on the independence dimension (i.e. on HRQOL) than they did during initial treatment and their scores were significantly higher than the controls.

The present findings underscore the importance of psychosocial care and nursing for children undergoing cancer treatment and continued follow-up of survivors after completion of treatment. Furthermore, given the social benefits of school attendance, our results support the encouragement of school attendance during cancer treatment. Because of the relatively short time of the follow-up, it is not possible to draw conclusions about long-term outcome of the school situation for children with cancer.

Keywords: childhood cancer, health-related quality of life, school, antimicrobial treatments, survivorship

LIST OF PUBLICATIONS

This doctoral thesis is based on four studies, referred to in the text by their Roman numerals.

I. af Sandeberg, M., Johansson, E., Hagell, P. & Wettergren, L. (2010). Psychometric properties of the DISABKIDS Chronic Generic Module (DCGM-37) when used in children undergoing treatment for cancer. *Health and Quality of Life Outcomes, 8:109*

II. af Sandeberg, M., Johansson, E., Björk, O. & Wettergren, L. (2008), Health-related quality of life relates to school attendance in children on treatment for cancer. *Journal of Pediatric Oncology Nursing, Sep-Oct;25(5):265-74*.

III. af Sandeberg, M., Wettergren, L., Björk, O., Arvidson, J. &. Johansson, E. Does school attendance during initial cancer treatment in childhood increase the risk of infection?
(manuscript).

IV. af Sandeberg, M., Jervaeus, A.M., Johansson, E. & Wettergren, L. School situation and self-reported independence in survivors of childhood cancer. *(manuscript).*

CONTENTS

LIST OF ABBREVIATIONS

ALL	Acute lymphoblastic leukaemia
ANC	Neutrophil Blood Count
AML	Acute myeloid leukaemia
CNS	Tumors in the central nervous system
CVC	Central Venous Catheter
DCGM-37	Disabkids Chronic Generic Module
HADS	Hospital Anxiety and Depression scale
HRQOL	Health-related Quality of Life
MSAS	Memorial Symptom Assessment Scale
NHL	Non - Hodgkin's lymphoma
PedsQL	Pediatric Quality of Life Inventory
PEG	Percutaneous Endoscopic Gastrostomy
QOL	Quality of life
SBLG	Childhood Leukaemia Group
SPAR	Statens person och adress register
SPSS	Statistical Package for Social Science
SVP	Subcutaneous Venous Port
TACQOL	TNO-AZL Children's Quality of Life
VCTB	The Swedish Childhood CNS Tumour Group
VSTB	The Swedish Childhood Solid Tumour Group
WHO	World Health Organization

PREFACE

In the late 1970s, as a rather newly registered nurse, I was working at the children's department in a ward with five beds allocated for children and adolescents with cancer. At that time, the main focus of paediatric oncology nursing was palliative care. My initial experience during the time when survival rates were very poor was that children and adolescents who eventually survived their cancer became lonely and were stigmatized by their illness. It seemed as though our society was not prepared to deal with survivors of childhood cancer, probably because of fear and lack of knowledge in the children's surroundings. Since then, childhood cancer treatment, together with the social situation for these children, has developed dramatically. However, many of these children still spend considerable time away from school and friends. Children treated for cancer worry about being away from school and friends, including having concerns about not being able to keep up with school work. In addition, there exists the risk of being forced to repeat a grade as well as the fear of losing their position among peers. A common reason for school absenteeism is fear that school attendance poses risks in terms of infections. Few researchers have investigated the susceptibility to infection among children treated for cancer. The consequence of this lack of knowledge is that health care professionals in paediatric oncology are uncertain as how to guide these children and their families to take part in social activities, including school. As long as it is unclear how the social life of children with cancer should be like in order not to pose risks, it is likely that school absence will remain a problem. The rational for this thesis is based on the fact that little is known about the school situation during and after childhood cancer as well as about the relation between school attendance and infection.

BACKGROUND

DIAGNOSED WITH CANCER IN CHILDHOOD

When a child is diagnosed with cancer the whole life of an entire family changes completely (Collins, Devine et al. 2002; Björk, Wiebe et al. 2005). While parents of children diagnosed with cancer are undergoing an extremely distressing experience, they constitute the most important support of their child (Boman, Lindahl et al. 2003). Furthermore, due to shorter hospital admissions a great responsibility in caring for the child rests on the parents resulting in major demands on a close collaboration and support from health care. Even siblings experience a difficult time with ambivalent feelings concerning the constant worry and of always having to make way for the needs of their sibling (Nolbris, Enskär et al. 2007).

Having cancer during childhood typically implies being bound to hospital and treatments for a long period (Enskär and von Essen 2007). Thus, it is difficult to make plans for more than one day at a time. It also means that the young patient is highly dependent on others, particularly parents and health care professionals (Landolt, Vollrath et al. 2006). Children with cancer are living with uncertainty not only from the unknown outcome of the cancer but also in the context of treatment, adverse events and procedures and their effects (Stewart 2003).

Living with uncertainty has been described by children with cancer and their parents (Stewart 2003; Al-Gamal and Long 2010). Such uncertainty is known to cause the children emotional distress, such as worry and fear, and makes it impossible to prepare themselves for negative events (e.g., painful procedures and side effects of treatment). Children and adolescents (8 to 19 years) undergoing treatment for cancer were asked to indicate whether they had experienced any distressing event in relation to disease and treatment (Hedström, Haglund et al. 2003). The most frequent examples of experiencing distressing events given by children 8 to 12 years of age were nausea, oral medication, worrying about death, confinement and feelings of alienation. For children between 13 and 19 years, the distressing events most frequently mentioned were nausea, pain from diagnostic procedures and treatments and a changed appearance.

During recent decades, paediatric cancer care has undergone a major change in the form of a shorter length of time admitted to hospital and significantly extended outpatient care. However, the children still spend a great deal of time at hospital. In addition to the treatment of the primary disease and of adverse events, almost all medical treatment protocols include time-consuming examinations that have to be done between each treatment. Consequently, contact with school and friends are periodically limited. During this time, most children with cancer experience changes in appearance and may therefore be concerned about how friends will react and of not being accepted when they return to school (Stewart 2003). Erik Homburger Eriksson (1986) suggested that development of self-identity is dependent on the identity of the group (e.g., school class and friends) (Homburger Eriksson 2004). Eriksson describes the personality

development in terms of eight stages with unique age-specific psychosocial characteristics. The development in one stage influences the progress in the stages that follow. The stage of latency (6-12 years) is primarily characterized by activity and action. Neighbourhood and school are important factors during this stage. However, a chronic illness often leads to inactivity and to changes in appearance, which may result in the child perceiving that he or she is different from others. Adolescence (12-18 years) covers puberty and is largely characterized by searching for a meaning and ego identity. Appearance and socialization with peers are of great importance while parents are considered to show less understanding (Homburger Eriksson 2004). A chronic illness during adolescence may also interfere with the development of autonomy and emancipation from the parents.

DIAGNOSES AND TREATMENT

The annual incidence of cancer in children and adolescents in Sweden is approximately 300, with very little change over the years (Gustafsson, Heyman et al. 2007): the survival rate is today estimated to 80% (Gatta, Corazziari et al. 2003). The majority of cancers that affect children do not occur in adults and the aetiology of childhood cancers is largely unknown. Childhood cancer is most prevalent in preschool age, whereas about one sixth occurs in children of school age. Children with leukaemia represent the largest group of childhood cancers, of which acute lymphoblastic leukaemia (ALL) is the most common. The diagnoses most common in children of school age are ALL, Ewing sarcoma, soft tissue sarcoma and non-Hodgkin's lymphoma (NHL). Osteosarcoma, acute myeloid leukaemia (AML) and Hodgkin lymphoma occur more frequently during puberty. Tumours of the central nervous system (CNS) are evenly distributed across all ages (Gustafsson, Heyman et al. 2007).

At time of diagnosis, children with cancer often exhibit a wide variety of diffuse symptoms. Children with leukaemia, for example, often present with a short history of fatigue, infection, mucosal bleeding and hematoma. The most common symptom of a solid tumour is pain in the affected area. However, before diagnosis, children diagnosed with tumours of the CNS often have a long anamnesis with straining symptoms of headache, energy loss, lost appetite and difficulties with balance and coordination (Rasco Baggott 2001). Consequently, some children may perceive that they were healthy prior to receiving treatment, whereas others may feel a great relief because of the good treatment response.

The high survival rate in childhood cancer is mainly due to chemotherapy that constitutes the majority of the treatment protocols, either exclusively or in combination with surgery or radiotherapy. Chemotherapy in children is often more aggressive than in adults, partly because of a better tolerance of the medication in children (Smith and Ho 1996). The treatment of ALL, AML and NHL is mainly chemotherapy of varying intensity and in treatment of Hodgkin’s lymphoma and Ewing's sarcoma often in combination with radiation therapy. Children with CNS tumours are the only childhood tumours that primarily undergo surgery, usually followed by radiotherapy and

chemotherapy (Rasco Baggott 2001). Because of the risk of irreversible injuries, efforts are made to minimize radiation therapy in the treatment of children. However, radiotherapy is often required in the treatment of children with CNS tumours (Wallace 2004). Children with solid tumours other than CNS tumours and who require surgery are normally treated with chemotherapy pre-operatively and most often postoperatively. Osteosarcoma is a primary skeletal tumour arising from bone-forming cells. The treatment consists of intensive chemotherapy, both pre- and postoperatively. The surgically removed part of the bone is usually replaced by prosthesis and total amputations are nowadays rare (Lietman and Joyce 2010). Additionally, many of the medical treatment protocols used in childhood cancer include treatment with corticosteroids.

In Sweden, all children and adolescents (i.e. newborns to 18 years of age) with cancer are diagnosed at one of six Paediatric Oncology Centres (Umeå, Uppsala, Stockholm, Linköping, Gothenburg and Lund). Most of the treatment is provided at the centre and occasionally at the patients' local hospital in consultation with the centre. The type of cancer is classified according to the International Classification of Childhood Cancer and the treatment is given according to national and international treatment protocols sanctioned by the Swedish Childhood Leukaemia Group (SBLG), the Swedish Childhood Solid Tumour Group (VSTB) and the Swedish Childhood CNS Tumour Group (VCTB).

Early and late complications of treatment

Complications of treatment, both acute and later in life, differ from patient to patient and depend on type of cancer and treatment (Collins, Devine et al. 2002; Oeffinger, Mertens et al. 2006). Chemotherapy primarily affects fast growing cells, and consequently, side effects of treatment arise in the normal cells that divide frequently (Rasco Baggott 2001). The acute symptoms include nausea and vomiting, loss of appetite, constipation, oral mucositis, infections with fever, fatigue and loss of strength, pain, leg weakness and psychological distress (Collins, Devine et al. 2002; Sala, Pencharz et al. 2004; Christensen, Nielsen et al. 2005; Hedström, Ljungman et al. 2005; Selwood 2006; Wicki, Keisker et al. 2008; Gomber, Dewan et al. 2010). Shortly after the start of cancer treatment, most of the children experience a changed appearance. One of the most visible and at first most distressing side effects from treatment is hair loss (Hedström, Ljungman et al. 2005). Practically all children treated with chemotherapy lose their hair as well as those treated with radiotherapy of the scull, with the only difference that the hair starts to grow back after chemotherapy but not always after radiotherapy (Rasco Baggott 2001; Oeffinger, Mertens et al. 2006). Children with certain cancer diagnoses often experience nutrition problems with either gained or lost weight. A frequent complaint is not being able to enjoy food due to chemotherapy effects with changed taste perception and increased sensitivity to smells (Moody 2006). Corticosteroids, periodically included in several childhood cancer treatment protocols, are often associated with a constant demand for food. Furthermore, during treatment with corticosteroids, many children experience frequent mood swings from euphoria to severe dysphoria.

Neutropenia is one of the most frequently reported side effects of cancer therapy and therefore, children undergoing treatment for cancer may be particularly vulnerable to infections. Depending on the dose intensity of the chemotherapy regimen, bone marrow function is suppressed, resulting in a low absolute neutrophil count (ANC) that poses a high risk of infection. An ANC of $<0.5 \times 10^9$/l is considered as severe neutropenia (WHO grade IV). The risk of infections increases with the depth and duration of neutropenia. Children with neutropenia who develop fever may be at risk of significant complications and even death from infection (Santolaya, Alvarez et al. 2007). Increased susceptibility to infections in children with cancer has been suggested to be associated with higher intensity of chemotherapy and central venous catheters (CVC) (Haupt, Romanengo et al. 2001; Wicki, Keisker et al. 2008), less time since diagnosis, bone marrow involvement, prior episodes of febrile neutropenia (Wicki, Keisker et al. 2008), nutritional state (Israels, van de Wetering et al. 2009) and genetically determined variations of the immune system (Neth, Bajaj-Elliott et al. 2005).

Social aspects of susceptibility to infections, such as school attendance, are rarely mentioned and recommendations during childhood cancer treatment vary, usually being based on diagnosis, laboratory results or the child's general condition (Christensen, Nielsen et al. 2005). An increased risk for infections has been reported among healthy children in kindergarten and pre-school (Nafstad, Hagen et al. 1999) but little is known about the risk of infections for school-aged children and children undergoing treatment for cancer.

Traditionally, standard care of children with febrile neutropenia is immediate hospitalization and the collection of blood cultures, followed by treatment with intravenous broad-spectrum antibiotic agents for at least 24 hours. Research has focused on identifying those children at low-risk for severe complications during febrile neutropenia in order to limit time of hospitalization and use of antimicrobial treatment (Hakim, Flynn et al. 2010; Macher, Dubos et al. 2010; Agyeman, Aebi et al. 2011). The results, however, are not conclusive and consequently the management of children with febrile neutropenia in clinical practice vary (Boragina, Patel et al. 2007).

In a longer perspective childhood cancer survivors have been reported to be three times more likely to experience at least one chronic health condition and five times more likely to experience two chronic health conditions compared with sibling controls (Oeffinger, Mertens et al. 2006). Furthermore, almost 30% of the survivors are reported to have severe or life-threatening conditions. Survivors of bone tumours are most likely to experience physical limitations; survivors of CNS tumours are most likely to experience cognitive, visual and auditory impairments; and survivors of Hodgkin's lymphoma are most at risk for secondary cancers and heart failure. Radiotherapy for growing children, especially of the brain, is always associated with risk of significant long-term effects, such as endocrine (growth and thyroid) and neurological abnormalities (Mitby, Robison et al. 2003; Barrera, Shaw et al. 2005).

CARE

When a child is diagnosed with cancer, a long period of intensive nursing contact begins, where a trustful relationship between the nurses and the child and family is crucial. Caring for a child with cancer will involve the care and support of a whole family, e.g. parents and siblings (Nolbris, Enskär et al. 2007; Norberg and Boman 2007; Björk, Wiebe et al. 2009). The nurses should provide the family with information and education concerning childhood cancer, treatment and treatment-related complications (Rasco Baggott, 2002). The families are taught to prevent side effects from treatment, how to alleviate the side effects and how to know when it is urgent to contact the treating hospital. Fever during treatment may, for example, be an emergency and it is important that the child and family are made aware of this. The paediatric oncology nurses have an important role in the prevention of acute side effects from treatment and must make sure they are properly treated if side effects do occur (Rasco Baggott, 2002).

One of the most important and challenging tasks for paediatric oncology nurses is to ensure the child's right to receive information. Considering the large variation in ages among treated children, good knowledge of child development is required. Information to children is not given at a certain time but continuously at moments when the child indicates being receptive and it is not possible to use general routines. Nurses caring for children with cancer have an excellent opportunity to establish close contact with the child while carrying out treatment and other procedures. By carefully listening to the child and by posing counter questions, it is possible for the nurse to identify the concerns of the individual child. Moreover, it makes it possible to respect those children that do not want to have certain information. Information to children needs to be frequently repeated, not only to make sure that it has been correctly understood but also because children are undergoing constant development and so does their focus of concern. All children need to be well prepared before procedures are introduced and the way the nurse performs painful procedures and responds to the child is crucial to how the child manages these procedures in the future (Stephens, Barkey 1999; Heden, von Essen 2009).

Missing school is considered a major concern for children when undergoing treatment for cancer (Hedström, Ljungman et al. 2005; Moody 2006). Poor communication among nurses, school personnel and parents has been identified as a major barrier in facilitating the cancer patient's return to school (Moore, Kaffenberger et al. 2009). All paediatric oncology nurses have the responsibility to facilitate and support contact with the child's school and friends. Moreover, in Sweden the national network of consultant nurses in paediatric oncology, financed by the Foundation of Märta and Gunnar V Philipson and the Swedish Childhood Cancer Foundation, is especially focused on issues concerning the social life of children with cancer. The consultant nurses offer visits to the patients' schools at the time of diagnosis, at relapsed disease, in case of no hope for cure and on request. In close collaboration with the family general information about childhood cancer and the individual child's treatment are provided to school

personnel and classmates. The aim is to prevent children diagnosed with cancer to become separated from a normal social life. The importance of an early, constantly evaluated individualized study plan for the child, defined actions to maintaining close contact between school and the child and his or her family and to minimize absence from school are emphasized.

SCHOOL SITUATION

The Swedish school system

The Swedish public school system consists of compulsory and non-compulsory schooling. Compulsory education includes a 9-year regular comprehensive school. Non-compulsory education comprises the preschool class, upper secondary school and adult education. Compulsory school entry is normally at the age of 7 years and finishes at the age of 16 years. Education throughout the public school system is free. Approximately 12% of compulsory school students attend one of the country's approved independent schools (The Swedish National Agency for Education, 2010).

Social life including school situation

To investigate the impact of social life from health conditions measures are used in which individuals are asked to estimate their role in relation to social function and well-being. The term social life includes different aspects of social life, aspects that are often assessed in different combinations, referring to different, often overlapping concepts. One dimension of health-related quality of life (HRQOL) is social functioning, which focuses on measurement of inter-personal functioning in peer relations (Varni, Seid et al. 1999; Eiser 2007). Psychosocial function, according to Bullinger et al (2002), coping, social support, perceptions of care and socio-economic factors (Bullinger 2002). Social outcome, another concept frequently used in connection with measurements of Quality of life (QOL), includes variables such as having and using friends as confidants (Barrera, 2005) and marital, educational and employment status (Ishida, Honda et al. 2011). Johannisdottir et al. (2010) add items related to parenthood and independent living, a combination of variables sometimes referred to as social adjustment (Boman and Bodegård 2004; Johannsdottir, Hjermstad et al. 2010). Studies evaluating children undergoing cancer treatment have reported that social life, including the school situation, may be negatively affected by disease and treatment (Lähteenmäki, Huostila et al. 2002; Hedström, Ljungman et al. 2005; Moody 2006). Few studies, however, have investigated school attendance and its relation to HRQOL during childhood cancer treatment. While absent from the community, school children may be provided schooling at hospital and at home by the community school. In two qualitative studies one of children undergoing treatment for cancer and one of cancer survivors, homebound schooling was found to be inadequate and isolating (Bessel 2001; Searle, Askins et al. 2003).

Few researchers have studied the implications of childhood cancer survivorship on the school situation (Sheinfeld Gorin 2009). In a Canadian retrospective mail survey parents of survivors of childhood cancer (aged 17 years or less) reported 10 years or

more after diagnosis (n=800) that their child had repeated a grade significantly more often than a group of matched controls (21% vs. 9%). These same children attended a learning disability programme more often (19% vs. 7%) or attended a special education programme more often than the matched controls (20% vs. 8%). In addition, more parents of survivors of childhood cancer reported that their child had educational or other school problems (46% vs. 23%) (Barrera, Shaw et al. 2005). In an American study using self-reports from participants aged 18 years or over and from parents of participants aged younger than 18 years (n=12430) long-term survivors were compared with a sibling control group 5 years or more after diagnosis. The authors found that 23% of the long-term survivors versus 8% of the siblings attended special education programmes and that those diagnosed before the age of 6 years (mostly associated with females), treated for tumours in CNS and treated with intracranial methotrexate and/or cranial radiation were more likely to attend special education programmes. Long-term childhood cancer survivors of leukaemia, CNS tumours, NHL and neuroblastoma were significantly less likely to complete high school and college than siblings. However, among those attending special education programmes only long-term survivors of CNS and kidney tumours were less likely than siblings to complete high school and only those who had received cranial radiation therapy were less likely to have completed college (Mitby, Robison et al. 2003). Other studies have shown that survivors of rhabdomyosarcoma (Punyko, Gurney et al. 2007) and sarcoma of the lower extremities (Nagarajan, Neglia et al. 2003) have good high school graduation rates when compared with siblings. When long-term survivors and parents were asked to respond to a question about reasons for the need to attend a special education programme, the response alternative 'due to missed school' was more frequently chosen among survivors of all diagnoses compared with siblings and were most associated with survivors diagnosed before the age of 16 years and with sarcoma (bone and soft tissue). The response alternative 'low test scores' was most associated with leukaemia, CNS, Wilms and neuroblastoma (Mitby, Robison et al. 2003). Knowledge about the survivors' experiences of how the school situation is affected by them having had cancer is still limited, however. Feelings of being different (Prouty, Ward-Smith et al. 2006; Enskär and Bertero 2010), the importance of support from others and that school attendance is associated to living a normal life (Prouty, Ward-Smith et al. 2006) have all been noted by adult survivors after childhood cancer.

HEALTH-RELATED QUALITY OF LIFE

In this thesis HRQOL is viewed as a multidimensional construct with physical, emotional, mental, social and behavioural aspects of well-being and function as perceived by patients, as defined by the Disabkids group (Bullinger 2002).

Measurement of health and quality of life in children

Because of a general lack of valid instruments for self-reports, assessment of HRQOL in children and adolescents with cancer is often based on proxy reports (Eiser, Eiser et al. 2005; Upton and Eiser 2006; Fluchel, Horsman et al. 2008). One of the instruments most frequently used in children with cancer is the Paediatric Quality of Life Inventory

(PedsQL) for children aged 5-18 years. The PedsQL, which is a self-report questionnaire, includes a generic scale and a disease-specific cancer module (Varni, Seid et al. 2001). Another instrument used in children with cancer is the revised Memorial Symptom Assessment Scale (MSAS) for children aged 7 to 12 years (Collins, Devine et al. 2002). The MSAS is a self-report questionnaire that assesses established cancer-related symptoms (Collins, Devine et al. 2002). Follow-up studies after cancer treatment have commonly used generic and domain-specific instruments developed for an adult population, such as the Short Form Survey (SF-36) (Jörngården, Mattsson et al. 2007; Sundberg, Doukkali et al. 2010), the TNO-AZL Children's Quality of Life (TACQOL) questionnaire (Landolt, Vollrath et al. 2006) and the Hospital Anxiety and Depression scale (HADS) (Jörngården, Mattsson et al. 2007). These instruments also provide validated normative data for adolescents and young adults in the general population (Jörngarden, Wettergren et al. 2006). The above-mentioned instruments contain no items or only a limited number of items concerning school. Kidscreen is a generic self-report HRQOL instrument. The instrument contains school items designed for children 8-18 years and has recently been used to measure HRQOL in childhood cancer survivors close to completion of treatment (Engelen, Koopman et al. 2011).

HRQOL during and after treatment

Childhood cancer and its treatment often cause physical, social, emotional and cognitive concerns and may thus affect HRQOL (Doward and McKenna 2004; Rajmil, Herdman et al. 2004). Studies that have followed HRQOL in children diagnosed and treated for cancer the first year after diagnosis have reported emotional distress (Eiser, Eiser et al. 2005; Hedström, Ljungman et al. 2005; Landolt, Vollrath et al. 2006; Jörngården, Mattsson et al. 2007), diminished physical and functional status (Landolt, Vollrath et al. 2006; Engelen, Koopman et al. 2011) and lack of vitality among the young cancer patients (Eiser, Eiser et al. 2005; Jörngården, Mattsson et al. 2007). Female adolescents in the general population have reported poorer HRQOL than males (Bisegger, Cloetta et al. 2005; Jörngarden, Wettergren et al. 2006) and the same gender difference has been demonstrated in children treated for cancer (Landolt, Vollrath et al. 2006). Results from a recent study showed that, in comparison with norms, physical well-being was worse among children aged 8-18 years who had completed childhood cancer treatment 2 months earlier (Engelen, Koopman et al. 2011). However adolescents aged 12-18 years scored significantly better than norms on the following dimensions of HRQOL: parent relation and home life, school environment, bullying and financial resources.

In a longer perspective findings of HRQOL among childhood cancer survivors are not conclusive in the sense that some studies have shown that survivors reported equal or even better HRQOL controls without cancer experience (De Clercq, De Fruyt et al. 2004; Jörngården, Mattsson et al. 2007), whereas others reported considerable impact on HRQOL (Armstrong, Stovall et al. 2010; Dowling, Yabroff et al. 2010). A study of long-term survivors of childhood cancer found that 68% reported at least one negative consequence and 50% at least one positive consequence after the cancer experience

(Sundberg, Lampic et al. 2009). Some studies have shown that childhood cancer survivors who reach adulthood do not manage as well as controls regarding employment (Johannsdottir, Hjermstad et al. 2010), marriage (Dieluweit, Debatin et al. 2010; _ENREF_67Pivetta, Maule et al. 2011) and parenthood (Dieluweit, Debatin et al. 2010; Johannsdottir, Hjermstad et al. 2010; Pivetta, Maule et al. 2011_ENREF_67).

AIMS

The overall aim of this Swedish nationwide longitudinal study was to investigate the school situation and HRQOL among children during and after treatment for cancer.

The specific aims of the present thesis were:

- To evaluate data quality and psychometric properties of an instrument for the measurement of HRQOL using the DISABKIDS Chronic Generic Module (DCGM-37) among school-aged children with cancer (Study I).

- To follow HRQOL, school attendance and social interaction with friends in children with cancer and explore the potential relation between HRQOL and school attendance. Furthermore, the study investigated self-reported reasons for not attending school and not meeting friends (Study II).

- To investigate the relation between school attendance and infection in children undergoing treatment for cancer (Study III).

- To investigate the school situation and self-rated independence in survivors of childhood cancer (Study IV).

METHODS

DESIGN

A longitudinal design was used in this nationwide cohort study. Study I-III are descriptive and comparative and have a quantitative approach. Study IV includes both quantitative and qualitative data.

STUDY SUBJECTS

All children in Sweden attending compulsory school (aged 7 to 16 years) and who were diagnosed with cancer and starting chemotherapy and/or radiation therapy from January 2004 to May 2006 were eligible for inclusion in the studies. Children treated with stem cell transplantation or surgery as single treatment and those that did not understand Swedish were excluded. One hundred and forty-five children and adolescents were eligible for participation, of which 126 (87%) consented.

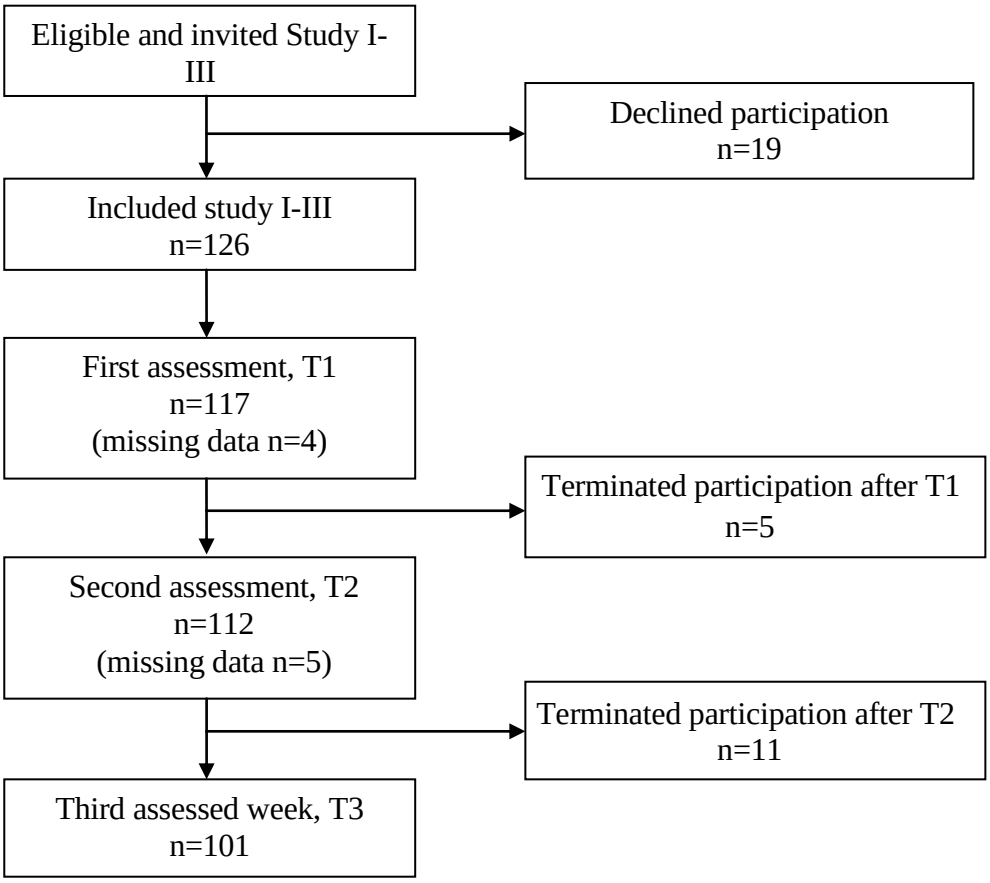

Figure 1. Overview of the inclusion of participants in study I-III

Study I

In study I 83 of the 126 children that consented to participate completed the DCGM-37 at 2.5 months after the start of treatment (T2) and 87 five months after start of treatment (T3).

Study II

Of the 126 children, 101 (70%) participated in all three assessment weeks (T1, T2, T3) and were included in study II (Figure1). The median age of the participants was 12 years (range 7 to 16 years). The participants from study I are included in the 101 participants in study II.

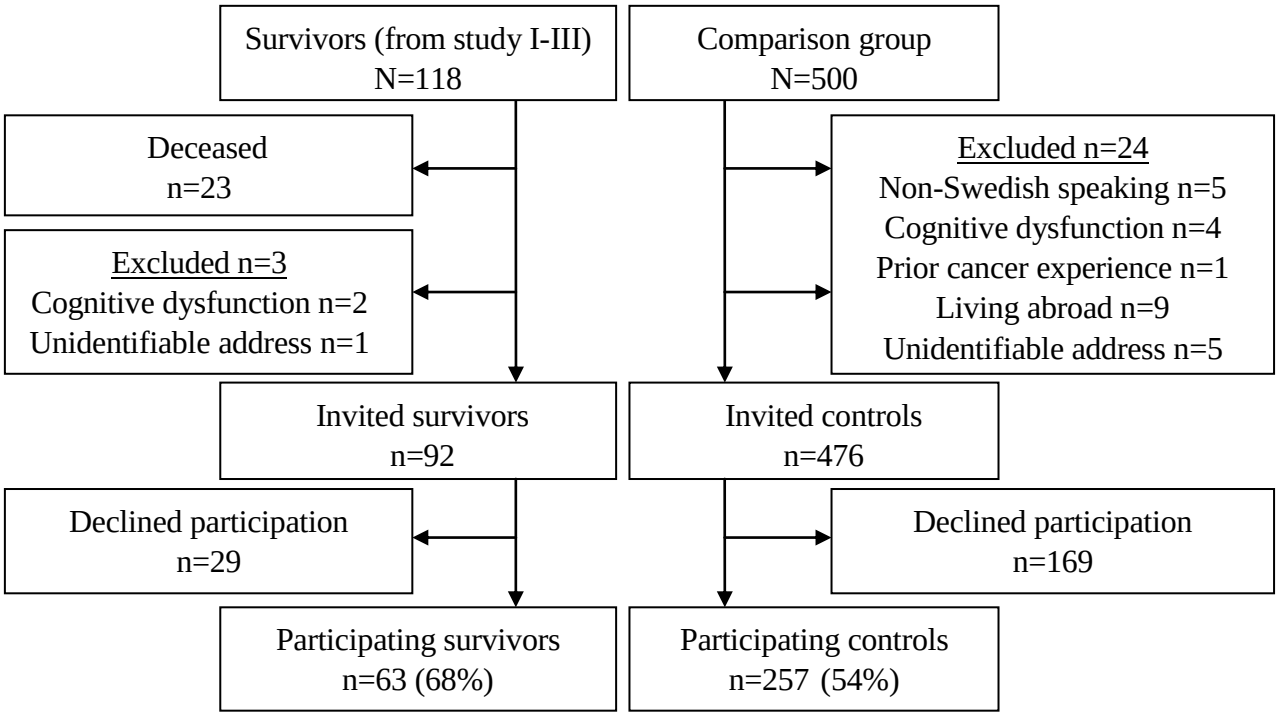

Figure 2. Overview of the inclusion of survivors and controls in study IV

Study III

Of the 101 participants included in study II those who were free from infection the day before the start of two observation periods of 19 days at TI (n=89) and T2 (n=89) were included in study III.

Study IV

Survivors

A median of 63 (range 50 to 74 months) months post-diagnosis, 92 of the former childhood cancer patients were eligible and invited to participate in a follow-up. Sixty-three (68%) of the 92 survivors, now aged from 12 to 22 years (median 17 years, range 12 to 22 years), agreed to participate in Study IV (Figure 2).

Comparison group

A sample of 500 young persons (250 girls and 250 boys) with a median age of 16 (range 11-23 years) years was randomly selected from the Swedish population register (SPAR). Twenty-four persons were excluded and 257 (54%) of the remaining 476 agreed to participate (Figure 2).

DATA COLLECTION

The four studies included in this thesis are presented in Table 1.

During initial treatment, data were collected using two questionnaires, one study-specific questionnaire measuring school attendance and social interaction with friends and one standardized instrument (i.e. the DCGM-37) measuring HRQOL. The time points for data collection are displayed in Figure 3.

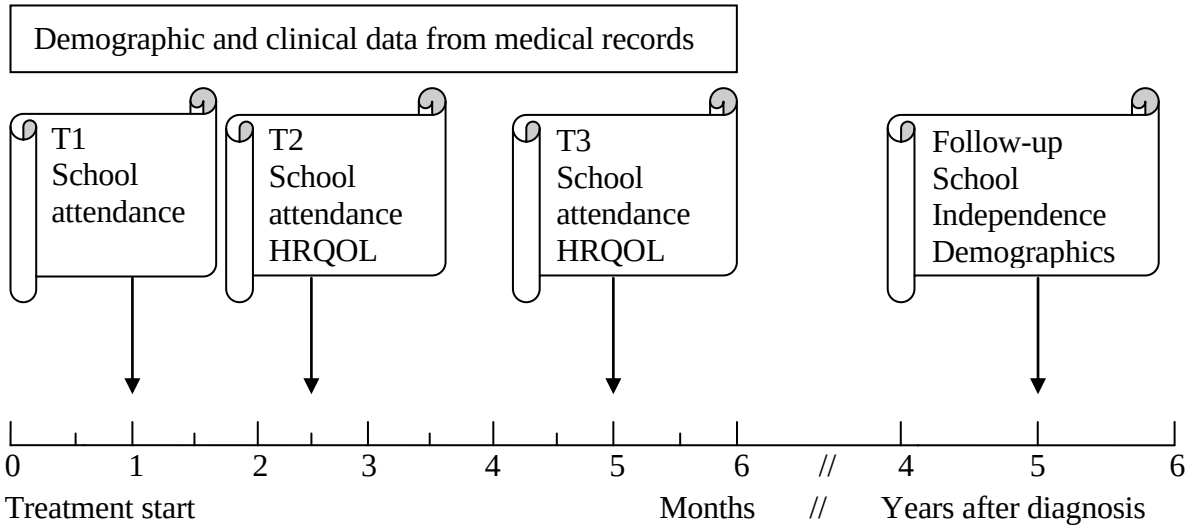

Figure 3. Time points for data collection study I-IV

Data from the survivors of childhood cancer were collected by telephone interviews that included both open-ended and structured questions (study-specific and the DCGM-37 dimension Independence). Two survivors accepted participation provided that the questionnaire was sent home by mail for self-administration. The time points for data collection are presented in Figure 3.

Data from the comparison group were only based on structured questions (study-specific and the DCGM-37 dimension Independence) and in most cases collected via telephone interviews though 27 persons received the questionnaires by mail for self-administration.

Table 1. Summary of the four studies with regard to study outcomes, number of participants, measures and analyses

Study	Study outcomes	Number of participants	Measures	Analyses
I	Data quality and psychometric properties of Disabkids chronic generic module (DCGM-37)	n=170 (pooled data)	DCGM-37 Medical records	Descriptive statistics Multi-trait scaling analyses Cronbach's alpha Student's unpaired t-test Effect sizes
II	School attendance, social interaction with friends and reasons for school absence	n=101	Study-specific questionnaire regarding school attendance Medical records DCGM-37	Descriptive statistics Cronbach`s alpha Chi-square statistics Friedman's test Student's unpaired t-test Pearson's correlation coefficient
	HRQOL	T2, n=83 T3, n=87		
III	Relation between school attendance and infection	n=101	Study-specific questionnaire regarding school attendance Medical records	Chi-square statistics Fisher's exact test Mann-Whitney U test Kaplan-Meier method The log-rank test
IV	School situation and self-rated independence	Survivors, n=63	Study-specific questionnaire with both open-ended and structured questions regarding school situation and perceived susceptibility to infections The DCGM-37 dimension Independence	Content analysis Descriptive statistics Chi-square statistics Mann-Whitney U test Cronbach`s alpha Student's paired t-test Student's unpaired t-test Effect sizes
		Comparison group, n= 257	Study-specific questionnaire with structured questions regarding school situation and perceived susceptibility to infections The DCGM-37 dimension Independence	

Measures

Disabkids Chronic Generic Module (study I, II, IV)

The DCGM-37 was designed to assess HRQOL in children and adolescents with chronic conditions. The instrument was developed within a European collaboration involving seven countries and six languages (Dutch, English, French, German, Greek and Swedish) to measure HRQOL in seven chronic conditions (Asthma, Arthritis, Atopic Dermatitis, Diabetes, Cystic Fibrosis, Cerebral Palsy and Epilepsy). When this project was started, the DCGM-37 had not been used in children with cancer (Bullinger 2002). The instrument consists of 37 items that measure mental, social and physical domains of HRQOL: Independence (autonomy and living without impairments), Physical Limitation (functional limitations, perceived health), Emotions (emotional worries and concerns), Social Exclusion (stigma, feeling left out), Social Inclusion (acceptance of others, positive relationships) and Treatment (perceived emotional impact of treatment). The items refer to the four previous weeks and are answered on a 5-point Likert scale ranging from 1 (never) to 5 (very often). In accordance with the standard scoring algorithms of the instrument, raw scores are coded for each question, summed and transformed into a scale from 0 (worst possible HRQOL) to 100 (best possible HRQOL). In the studies included in this thesis the version from 2004 was used. In study IV the dimension Independence (six items) was included in the assessments of the survivors and controls.

The DISABKIDS Smiley version was developed to assess HRQOL and level of distress in children with chronic conditions aged 4 to 7 years. The participating children that were not considered by the parents and the nurse to be able to manage the DCGM-37 were presented the Smiley version. This version consists of six items with a five-point rating scale of smiley face responses. The happiest face receives the highest score and the unhappiest face the lowest (The European DISABKIDS Group 2006). Eleven children (7-14 years old) fulfilled the Smiley version on either one or both occasions. (Results from the Smiley version are not included in this thesis).

Study-specific questionnaire regarding school attendance (study II, III)

To measure school attendance and socialization with friends during treatment for cancer a study-specific questionnaire was developed. The questionnaire consisted of eight items: two of the eight items measure number of days at school and attended lessons each day; three items assess the number of friends the child played or interacted with and the place and length of the social interaction; two items concern reasons for not attending school and seeing friends; and one item asks who completed the questionnaire. Six response alternatives were presented for not attending school and not seeing friends: “hospital visits”, “infections”, “fear of getting infections”, “fatigue/tiredness”, “fear of other people’s reactions” and “other reasons”. To test the face validity of the questionnaire 10 parents to children undergoing cancer treatment at Astrid Lindgrens Children’s Hospital, Karolinska University Hospital, Stockholm were asked to fill out the questionnaire on two separate occasions. The parents’ comments on the 10 questions resulted in some minor modifications of the questionnaire.

Study-specific questionnaire regarding school situation and the person's perceived susceptibility to infections (study IV)

The telephone interviews conducted with the survivors and the comparison group included study-specific questions. Three of the study-specific questions are presented below: "How important do you consider school to be in your life?" "How much have you been absent from school during the past month?" "If you compare yourself to your peers do you think that you catch colds more easily?" Demographic questions (living situation, siblings, main occupation, education) were also included in this questionnaire.

Open questions regarding the school situation (study IV)

Semi-structured telephone interviews with open-ended questions were conducted with the survivors. The interviews were performed using an interview guide with follow-up questions to clarify the meaning of statements. Two of the posed questions in the telephone interviews are presented here: "Because of your cancer experience, do you think things are different in school for you today compared to your peers?" "When thinking back on life during the time of your cancer treatment, what do you first think about?"

Medical records

Disease- and treatment-related data were collected from the participants' medical records. The information collected included demographic data (gender, date of birth, siblings in pre-school age) and information on diagnosis and cancer treatment (type, date of diagnosis, treatment protocol and date of treatment start). Furthermore, antimicrobial treatment (number, type, duration and, if applicable results from microbiological cultures), prophylaxis (antimicrobial or granulocyte colony-stimulating factor), laboratory reports (absolute neutrophil cell count, ANC) and invasive devices (number, type) were retrieved for each observation period of 19 days.

DATA ANALYSIS

The data analyses performed in the different studies are summarized in Table I (page 15). All statistical calculations were conducted using the Statistical Package for Social Sciences (SPSS Inc, Chicago, IL, USA) for windows, version 18.0 and StatView 5.0.1 software (© 1992-98 SAS Institute, Inc. Cary, NC, USA).

Descriptive statistics (frequencies, percentages, medians and ranges, means and standard deviations) were used to characterize measured variables. To determine differences in categorical variables chi-square statistics were performed or, in cases of small numbers, Fisher's exact test was applied. Differences in medians were determined by the Mann-Whitney U test and Friedman's test (over time). Cronbach's alpha values were calculated to estimate the internal consistency reliability of the DCGM-37. Alpha values $\geq$0.70 are considered acceptable though $\geq$0.80 are preferred (Nunnally JC 1994). Mean value differences in variables normally distributed were analyzed with Student's unpaired and paired t-test. Effect sizes (ES) were calculated to underscore the clinical importance of potential mean value differences. ES is calculated

by dividing the mean value difference between two groups with the standard deviation. According to Cohen, an ES=0.20-0.50 indicates a small difference, ES=0.51-0.80 a medium difference and ES>0.80 a large difference (Cohen 1988). Associations between variables were analyzed with Pearson's correlation coefficient, and when appropriate, Spearman's rank correlation coefficient. P-values <0.05 were considered statistically significant.

Study I

Descriptive and psychometric analyses in study I are based on pooled data from T2 (n=83) and T3 (n=87). When sample sizes are small, pooling of data is recommended to increase precision of the estimates (Ware and Gandek 1998; Westen and Weinberger 2004).

Feasibility of the DCGM-37 was examined through the nurses' comments on the items, as well as by oral and written comments given by the participants and their parents.

Data quality of the DCGM-37 was evaluated by examining the number of missing item responses (Ware and Gandek 1998). Missing responses of up to 10% have been suggested as acceptable (Saris-Baglama 2004.). Simple summation of item scores into a total score is supported by similar item means and standard deviations within each dimension and corrected item-total correlation coefficients exceeding 0.3 (Ware and Gandek 1998). Furthermore, items within each dimension are considered to represent the same latent variable if corrected item-total correlations are ≥0.40 (Ware and Gandek 1998). The distribution of dimension scores is considered supported with floor and ceiling effects <15% (McHorney and Tarlov 1995) and alpha values ≥0.70 (Nunnally 1994). The internal construct validity of the DCGM- 37 was examined by multi-trait scaling analysis with correction for overlap. An item's corrected item-total correlation ≥0.40 with the dimension it is hypothesized to belong to and a weaker correlation with all other dimensions support the internal construct validity of the instrument (Ware 1997; Fayers 2007). Items within each dimension that met these criteria were referred to as the scaling success rate. An alpha value of a dimension that is higher than the dimension's correlation to the other dimensions indicates that the dimension scores represent different aspects of HRQOL (Ware and Gandek 1998). The criterion-based validity, i.e. the instrument's capacity to discriminate between patients differing in symptom burden, was evaluated by comparing data from children diagnosed with ALL to those diagnosed with sarcoma.

Study II

Demographic and clinical characteristics of children undergoing treatment for cancer were analysed with regard to self-reported school attendance, HRQOL and reasons for school absence.

Study III

Children undergoing cancer treatment were compared with respect to clinical and demographic characteristics and start of antimicrobial treatment during two observation periods of 19 days.

Time to start of antimicrobial treatment was estimated by the Kaplan-Meier method (Kaplan 1958). Children not starting antimicrobial treatment during the observation period of 19 days were censored on the last day of the investigated period. Differences in time to start of antimicrobial treatment between children attending school and those not attending school were analyzed using the log-rank test (Kaplan 1958).

Study IV

The recorded telephone interviews were transcribed verbatim. The answers to the two open-ended questions were analyzed using content analysis (Graneheim and Lundman 2004). Content analysis is a suitible instrument for analyzing and handling large and relatively unstructured data in view of meaning, symbolic qualities and expressive contents. To gain a sense of the whole the data analysis started with repeated readings of all the responses to each of the two open-ended questions. The process continued in an effort to search for sentences capturing key thoughts or concepts. These key thoughts or concepts were subsequently transformed into meaning units. The answers to the question "Because of your cancer experience, do you think things are different in school for you today compared to your peers?" were sorted into categories. The identified meaning units of the answers to the question "When thinking back on life during the time of your cancer treatment, what do you first think about?" were first divided into subcategories and then sorted into categories (Graneheim and Lundman 2004).

Table 2. Examples of categorization of statements

Example of meaning units	Subcategory	Central characteristic of the subcategories	Category
"The worse time of my life and it was bad all the time"	Emotionally distressing	Statements describing the experience as troublesome	A straining experience
"The first treatment was hard. I felt sick and vomited and could not eat at all; it was really hard"	Distressing adverse effects from treatment	Descriptions of side effects from treatment, including fatigue, hair loss, nausea and vomiting, lack of appetite, mucositis and body changes	

PROCEDURES

During initial cancer treatment (study I-III)

Data were collected from January 2004 to November 2006 with the assistance of the national network of consultant nurses in paediatric oncology. Approximately 3 weeks after diagnosis, the consultant nurses contacted possible participants at the hospital and

presented both oral and written information about the study. Those who accepted participation received the first questionnaires at time for the first assessed week (T1). At the second (T2) and third assessment (T3), the questionnaire were either submitted to the participants at a scheduled hospital visit or sent home by mail. If the questionnaires were not returned within a week, families were reminded by telephone or by mail. The consultant nurses also collected additional data from the participants' medical records, both at the centre and in case of a co-operating local hospital.

Follow-up 5 years after diagnosis (study IV)

Survivors

An information letter was sent to all eligible participants. The letter was addressed to a parent for participants aged 11-15 years, to the possible participant including a letter to the parent/parents for those aged 16 to 17 years and directly to participants aged 18 years and above. Potential participants or parents were contacted by telephone within 2 weeks after the letter was mailed; for those who accepted participation, a suitable time for the telephone-administered interview was agreed upon. Written reminders were sent when participants were difficult to reach. Written informed consent was obtained from participants and parents for participants <18 years of age and from participants aged ≥18 years. The interviews were tape-recorded and responses to the structured questions (study-specific and for the dimension Independence in the DCGM-37) were written down.

Comparison group

The comparison group basically underwent the same procedure as the survivors. The interviews with structured questions were tape-recorded and responses were written down. Written consent for participants <18 years of age was obtained from the participants and parents; oral consent for participants aged ≥18 years was tape-recorded before the start of the interview.

An episode of infection was defined as the individual period of use of oral or intravenous antimicrobial treatment with one or more antibiotic, antifungal or antiviral agents prescribed because of symptoms of infection. Any prescribed adjustment or shift in antimicrobial therapy during the period was not considered as a new episode. Antimicrobial treatment prescribed without symptoms of infection was considered as prophylaxis. Neutropenia was defined as one day or more with an ANC $<0.5 \times 10^9$/L.

ETHICAL CONSIDERATIONS

Ethical approval was obtained from the Regional Ethical Review Boards in Umeå, Uppsala, Stockholm, Linköping, Göteborg and Lund for the study conducted during initial cancer treatment (2004-2006) and by the Regional Ethical Review Board in Stockholm for the follow-up study.

Approaching families in a vulnerable position where a child is recently diagnosed with cancer requires extreme caution and wise discernment. The risk of causing harm to the children and their parents was weighed against the benefit of possible improvement in future care of children and adolescents with cancer. All children and their parents who were invited to participate were reassured that their decision regarding participation would not affect the child's care in any way.

Furthermore, when approaching persons at follow-up (a median of 5 years after diagnosis), there is a risk that the interviews could evoke thoughts and feelings that the participants may find distressing. Before ending the interview, the researcher pointed out the possibility that troubling thoughts could emerge and in that case the respondent was invited to contact the researcher for advice where he or she could turn to for help. However, to be interviewed may also be perceived as an opportunity to talk about their former experiences. All participants were informed about confidentiality and the possibility to withdraw from the study at any time.

RESULTS

STUDY I-IV

Demographic and clinical characteristics of the participants in study I-IV are presented in Table 3. One difference was found between participants and non-participants in study I-III. Children diagnosed with Non-Hodgkin lymphoma were more likely not to attend the study. In Study IV no statistically significant differences were found between participating and non-participating survivors (Table 3), or between the survivors and the controls.

Table 3. Demographic and clinical characteristics of participants and non-participants in study I-IV

	Study I-III		**Study IV**	
	Participants undergoing treatment n=101	Non-Participants n=44	Survivors 5 years after diagnosis n=63	Non-Participants n=29
Gender, n (%)				
Female	42 (42)	16 (36)	26 (41)	10 (34)
Male	59 (58)	28 (64)	37 (59)	19 (66)
Age groups, n (%)				
7-12 years	56 (55)	20 (46)		
13-16 years	45 (45)	24 (54)		
12-17 years			37 (59)	
18-22 years			26 (41)	
School grade at diagnosis, median (range)	6 (1-9)	6 (1-9)		
Siblings living at home, n (%)	91 (90)			
Siblings			59 (94)	
Diagnosis, n (%)				
Acute lymphoblastic leukaemia	33 (33)	13 (30)	21 (32)	10 (34)
Acute myeloid leukaemia	5 (5)	3 (7)	3 (5)	1 (3)
CNS tumours	16 (16)	5 (11)	10 (16)	2 (7)
Non-Hodgkin's lymphoma	12 (12)	11 (25)*	6 (10)	6 (22)
Hodgkin's lymphoma	9 (9)	3 (7)	6 (10)	4 (14)
Sarcoma	17 (17)	4 (9)	10 (16)	3 (10)
Rhabdomyosarcoma	5 (5)	2 (5)	3 (5)	2 (7)
Other [c]	4 (4)	3 (7)	4 (6)	1 (3)

[a] Tested for difference in proportions by Chi-square test or Fisher's exact test.
*<0.05, **<0.01, ***<0.001

[c] Neuroblastoma, Germ cells tumour, Soft tissue sarcoma (nerve), Sertoli leydig cell tumour, Synovial sarcoma, Teratoma and a mixed tumour.

SCHOOL SITUATION

During initial cancer treatment

School attendance significantly increased over the first 5 months of cancer treatment, with 47 (47%) of the 101 participating children attending school at least once during the first assessed week (T1) 1 week after the start of treatment and 71 (70%) 4 months later (T3). The median number of attended school days per child and week significantly increased during the first 5 months (Table 4). The most commonly reported reasons for absence from school and not meeting friends were hospital visits and fatigue (Table 4). A median number of 14 (T1), 17 (T2) and 8 (T3) children were on scheduled holiday during the three assessment periods.

Table 4. Self-reported school attendance in study II and reasons for being absent from school during 3-week periods in the first 5 months of cancer treatment (N=101)

	T1	T2	T3
Number of children attending school **each day**, median	27	36	52
Number of days attending school, median	1	1	3***
Median number of children absent from school	59	48	42
Reasons for absence from school, median			
Hospital visit	31	27	18
Fatigue	14	11	9
Infection	5	5	4
Fear of being exposed to infections	4	2	3
Pain	1	2	1
Nausea	1	1	1
Other disease and treatment-related causes	0	1	2
School-related reasons[a]	2	2	2
Fear of the reactions of others	2	1	1
Don't want to go to school	0	1	1
Miscellaneous	3	1	3

[a]School-related reasons included the class performing activities outside school and the child having too much home work

Sixteen children (16%) did not attend school at all during the studied weeks. Children with osteosarcoma were more likely not to attend school than children with other diagnoses (31% of the osteosarcoma patients vs. 10% of all other diagnoses combined, $X^2=9.71$, $p<0.01$).

Antimicrobial treatment

Eighty-nine children were free from antimicrobial treatment at start of T1 and T2. Thus, these 89 children were included in the analysis to examine the association between school attendance and start of antimicrobial treatment.

Table 5. Differences in clinical characteristics in children free from antimicrobial treatment at start of potential school weeks, T1 (n=89) and T2 (n=89) in relation to start of antimicrobial treatment

	T1 (19 days)		**T2 (19 days)**	
	Observation	Started antimicrobial treatment	Observation	Started antimicrobial treatment
	n	n (%)	n	n (%)
<13years	50	18 (36)	51	14 (27)
≥13years	39	9 (23)	38	6 (16)
Girl	37	13 (35)	37	11 (30)
Boy	52	14 (27)	52	9 (17)
Preschool-aged siblings	16	2 (13)	17	5 (29)
No preschool- aged sibling	73	25 (34)	72	15 (21)
Children attending school	47	10 (21)	51	9 (18)
Children not attending school	42	17 (40)*	38	11 (29)
Acute lymphoblastic leukaemia (ALL)	30	3 (10)**	30	5 (17)
Not ALL	59	24 (41)	59	15 (25)
Acute myeloid leukaemia (AML)	3	2 (67)	4	4 (100)**
Not AML	86	25 (29)	85	16 (19)
Central nervous system tumours (CNS)	15	0 (0)**	14	1 (7)
No CNS tumours	74	27 (36)	75	19 (25)
Non-Hodgkin's lymphoma (NHL)	9	6 (67)*	10	4 (40)
Not NHL	80	21 (26)	79	16 (20)
Hodgkin's lymphoma	8	2 (25)	9	0 (0)
Not Hodgkin's lymphoma	81	25 (31)	80	20 (25)
Sarcoma	16	12 (75)***	14	5 (36)
Not sarcoma	73	15 (21)	75	15 (20)
Rhabdomyosarcoma	4	1 (25)	4	1 (25)
Not rhabdomyosarcoma	85	26 (31)	85	19 (22)
Other diagnoses[a]	4	1 (25)	4	0 (0)
Not other diagnoses	85	26 (31)	85	20 (24)
Chemotherapy alone	48	12 (25)	50	13 (26)
Not chemotherapy alone	41	15 (37)	39	7 (18)
Chemotherapy and surgery	15	10 (67)**	14	3 (21)
Not chemotherapy and surgery	74	17 (23)	75	17 (23)
Chemotherapy and radiotherapy	4	1 (25)	5	0 (0)
Not chemotherapy and radiotherapy	85	26 (31)	84	20 (24)
Surgery and radiotherapy	2	0 (0)	2	0 (0)
Not surgery and radiotherapy	87	27 (31)	87	20 (23)
Chemotherapy, surgery and radiotherapy	20	4 (20)	18	4 (22)
Not chemo, surgery and radiotherapy	69	23 (33)	71	16 (23)
Children with ANC[b]<0.5 ≥1 day	40	21 (53)***	37	13 (35)***
Not ANC[b]<0.5	49	6 (12)	52	7 (13)
Children with prophylactic oral antibiotics	20	3 (15)	15	3 (20)
No prophylactic oral antibiotics	69	24 (35)	74	17 (23)
Children with G-CSF	5	1 (20)	10	4 (40)
No G-CSF	84	26 (31)	79	16 (20)
SVP[c]	57	17 (30)	62	16 (26)
No SVP	32	10 (31)	27	4 (15)
CVC[d]	29	10 (34)	24	4 (17)
No CVC	60	17 (28)	65	16 (25)
PEG[e]	11	5 (45)	9	1 (11)
No PEG	78	22 (28)	80	19 (24)

Differences in proportions tested by Chi-square statistics or Fisher's exact test: *<0.05, **<0.01, *** <0.001

[a]Neuroblastoma, Germ cells tumour, Sertoli leydig cell tumour, Synovial sarcoma

[b]Absolute neutrophil count

[c]Subcutaneous venous port, [d]Central venous catheter, [e]Percutaneous endoscopic gastrostomy

During the first observation period (T1) of 19 days, 27 (30%) of the 89 children started antimicrobial treatment (Table 5). Children starting antimicrobial treatment during T1 attended school more seldom and their median number of attended days was lower (0, range 0 to 4 vs. 1, range 0 to 5; p-value=0.048) than children not starting antimicrobial treatment (Table 5). Furthermore, variables found to be more strongly associated with children starting antimicrobial treatment were the diagnoses sarcoma and NHL, neutropenia (21 (77%) vs. 19 (31%), p-value<0.001) and treatment with a combination of surgery and chemotherapy. During the second observation period (T2), 20 (22%) of the 89 children started antimicrobial treatment. The median number of attended school days was significantly lower in children starting antimicrobial treatment during T2 compared with those not starting antimicrobial treatment (0, range 0 to 5 vs. 2, range 0 to 5, p-value=0.022). Other variables showing a strong association with children starting antimicrobial treatment were AML and neutropenia (Table 5).

Time to start of antimicrobial treatment was significantly longer among children attending school during T1 than those not attending school. However, no difference in time to start of antimicrobial treatment was observed during T2.

The 47 antimicrobial treatments prescribed to children during T1 and T2 assessment periods were, with very few exceptions, intravenous antibiotics (91%).

At T1 and T2, microbial cultures were obtained during 45 of the 47 episodes of antimicrobial treatment. Positive microbial findings were detected in 12 of the 45 episodes of antimicrobial treatment (four in blood, five in urine, one in both blood and urine, one in both blood and faeces and one in secretion of vesicle). During T1, none of the six microbial blood cultures in children attending school was positive and in 1 of 15 children not attending school. The corresponding number of positive blood cultures during T2 was one of six in children attending school and four of nine in those absent from school.

Follow-up 4-6 years after diagnosis

Fifty-three (84%) of the survivors and 205 (80%) of the controls were currently in education. The male survivors were (p<0.05) more often currently in education than were the male controls. The distribution of type and level of education did not differ between the survivors and controls. Furthermore, the majority of the participants (survivors and controls) considered school to be important in their lives though to a somewhat lower extent in the survivors (47, 89%. vs. 198, 97%, p=0.019). Fifty-one percent of the survivors and 42% of the controls stated that they had not been absent from school during the past month and the majority in both groups reported absence ranging between 0-3 days during the past month.

Fifty of the 53 survivors currently in education answered the question “Because of your cancer experience, do you think things are different in school for you today compared to your peers?” The answers were grouped into seven categories. Sixty-two per cent of

the survivors described the situation in school as basically the same compared to peers, categorized as 'More or less like anyone else'. Twenty percent of the survivors described decreased strength and difficulties to walk and run categorized as 'Difficulties getting around and sporting' and 10% mentioned deficiencies in school work due to problems with memory, concentration and being slow, categorized as 'Difficulties related to cognition dysfunction. A small number of participants cited falling behind, categorized as 'Impact on school results'. Furthermore, statements made by 10% of the survivors described feelings of appreciation and of being more mature compared with their peers and were categorized as 'Different view of life' and a few stated that they had better school results than their peers, characterized as 'good school results'. Some survivors contributed to more than one category in that they reported having more than one difference in school compared with their peers.

Sixty-one (97%) of the 63 survivors answered the question "When thinking back on life during the time of your cancer treatment, what do you first think about?" The content analysis of the answers resulted in meaning units grouped into 15 subcategories that were sorted into six categories. Some survivors expressed thoughts contributing to more than one subcategory.

Table 6. Survivors' (n=61) thoughts when thinking back on life during the time of cancer treatment by subcategories and categories

Subcategory	N	Category
Emotionally distressing Disturbing side effects Extensive and strenuous treatment Realizing that it was cancer	36	A straining experience
School attendance Being away from friends Friends as resource Keeping up with school work Unsupportive friends Fear of being different	16	School and friends
	14	Being in hospital
	7	Few thoughts from time of treatment
Positive aspects/impact Positive memories	6	Positive experiences
	3	Social comparison

Slightly more than 25% of the survivors mentioned issues of how school and relationship to friends was affected by illness and treatment, categorized as 'School and friends'. Statements about school included in this category concerned school attendance and absence, as well as the struggle to keep up with school work during treatment. Statements about friends included descriptions of being away from friends, friends showing concern, friends not knowing about what had happened and fear of being different. Most frequently mentioned statements (60% of the survivors) were

descriptions and memories of the difficult period during treatment, categorized as 'A straining experience'. This category includes descriptions of the emotionally distressing cancer experience, disturbing side effects and the burdens associated with intensive therapy. Almost 25% of the survivors described having to stay at hospital for long periods and pointed out different activities (e.g., treatment, playing computer games and expressing opinions about meals) that they were engaged in during their hospital stay, categorized as 'Being in hospital'. More than 10% declared that they rarely, if ever, thought about the time when they had cancer, categorized as 'Few thoughts from time of treatment'.

No significant difference was found between the survivors and controls in perceived susceptibility to infections compared to peers.

HEALTH-RELATED QUALITY OF LIFE

During initial cancer treatment

Data quality and psychometric properties of the DCGM-37 (study I)
Data quality was acceptable with the percentage of missing items by dimension below 6% (range 0 to 5.3%). The largest number of missing items was found in the dimension Social Exclusion (Table 8). Reasons for not responding to an item were seldom reported. Occasionally, the reason for not answering items in the school dimension was explained by not having been in school while the reason for not answering items in the Treatment dimension was explained in terms of not taking any medication.

Table 8. Psychometric statistics from study I for the DCGM-37 in Swedish children on cancer treatment (pooled data, i.e. T1 + T2, n=170)

Dimension	n	Missing items, range (%)	Range of item mean (SD)	Floor/ Ceiling effect (%)	Item-to-own dimension correlation (range)	Item-to-other dimension correlation (range)	Scaling success (%) [a]
Independence	170	0-4 (0)	3.03-3.89 (0,96-1,18)	0.6/ 0	0.43-0.68	0.15-0.60	93
Physical Limitation	169	0-2 (0.6)	3.25-3.94 (1,02-1,34)	0/ 0	0.32-0.66	0.19-0.58	87
Emotion	165	3-5 (2.9)	2.88-3.53 (0,97-1,22)	0/ 1.2	0.54-0.70	0.25-0.65	100
Social Exclusion	161	1-13 (5.3)	3.31.4.51 (0,68-1,22)	0/ 2.9	0.35-0.63	0.09-0.60	90
Social Inclusion	168	0-6 (1.2)	3.02-4.35 (0,83-1,16)	0/0.6	0.28-0.66	-0.01-0.65	73
Treatment	164	4-8 (3.5)	3,35-4.02 (1,14-1,60)	2.4/10.0	0.54-0.77	0.14-0.47	100

[a] Number of item-to-other dimension correlations that are stronger than the corrected item-total correlation within a dimension / Total number of discriminant validity tests (i.e. number of items by number of dimensions minus 1) expressed as a percentage.

The legitimacy of adding up items to generate a total score was supported by the data, i.e. item means and standard deviations within the respective dimensions were roughly equivalent (Table 9). However, all but one corrected item-total correlation exceeded 0.30 and the corrected item-total for item 31 in the dimension Social Inclusion was 0.28. Moreover, in all but six instances (items 10, 11, 22, 26, 30, 31) the item-total correlation was $\geq$0.40 (Table 8). The distribution of dimension scores was supported in that floor effects ranged from 0 to 2.4% and ceiling effects from 0 to 2.9%, with the

exception of the Treatment dimension, which had a larger, but still acceptable ceiling effect of 10% (Table 8). Reliability for all dimension scores exceeded the recommended minimum of 0.70 and three dimension scores exceeded the preferred value of 0.80 (Table 9).Multi-trait scaling analyses supported the grouping of items into dimensions for 26 of the 36 items in that their corrected item-total correlations exceeded the correlations with other dimension scores. Scaling success rates ranged from 73 to 100% (Table 8).

Self-reported HRQOL (study I-II)

The DCGM-37 was completed by 83 participants at T2 and by 87 at T3. All scales in the DCGM-37 had Cronbach's alpha coefficients above 0.70 (range 0.72 to 0.87). HRQOL for the total group did not significantly change between T2 and T3 in any of the dimensions (Table 9).

Table 9. Self-reported HRQOL as measured by the DCGM-37 at 2.5 months (T2), 5 months (T3) and the pooled version (T1 + T2) after the start of cancer treatment, (study I-II)

DCGM-37 scales	**T2 n=83**		**T3 n=87**		**Pooled version n=170**	
	Mean[a] (SD)	Reliability (α)	Mean[a] (SD)	Reliability (α)	Mean[a] (SD)	Reliability (α)
Independence	60.3 (19.0)	0.80	60.5 (20.1)	0.83	60.4 (19.5)	0.81
Physical Limitation	51.1 (18.3)	0.72	55.4 (21.3)	0.78	53.1 (19.6)	0.76
Emotion	57.0 (19.9)	0.82	60.3 (19.4)	0.85	58.5 (19.9)	0.84
Social Exclusion	69.4 (17.6)	0.73	68.3 (18.4)	0.76	68.5 (17.7)	0.76
Social Inclusion	61.7 (17.8)	0.72	62.3 (17.0)	0.70	61.9 (17.3)	0.71
Treatment	65.1 (25.2)	0.85	63.7 (26.8)	0.87	64.0 (25.8)	0.87

[a] Scores range from 0 to 100, with higher scores representing a better HRQOL.

Comparing the scores of the boys and girls at T2 and T3 revealed that the Girls scored worse on four of the six DCGM-37 scales (Independence, Physical limitation, Emotion and Social exclusion) at both T2 and T3. Self-reported HRQOL did not differ between the two age groups (7-12 years vs. 13-16 years), with the exception of the Physical Limitation dimension, which was rated significantly higher among the adolescents than among the younger group. All effect sizes were either low or medium. Mean value differences and effect sizes were found between children with ALL and children with sarcoma. The sarcoma patients scored significantly lower in all dimensions than the ALL patients and all effect sizes were large.

The results of the partial correlations after controlling for sex between days of school attendance and the measured HRQOL dimensions revealed positive coefficients in all dimensions. At T2, all but two coefficients were significant and at T3 all coefficients except one were significant. All correlation coefficients but one were of medium or large size at T3: Independence: T1 0.32, T2 0.50; Physical Limitation: T1 0.32, T2 0.50; Emotion: T1 0.03, T2 0.34; Social Exclusion T1 0.27, T2 0.37; Social Inclusion T1 0.30, T2 0.42; Treatment: T1 0.03, T2 0.27.

Follow-up 4-6 years after diagnosis

The results from the DCGM-37 revealed that survivors rated the Independence dimension statistically significantly higher a median of 5 years after diagnosis compared with the corresponding results during treatment (Table 10). Furthermore, at the 5-year follow-up post-diagnosis, the survivors rated their independence as being higher than the controls. No gender difference in mean values of self-rated independence was seen among the survivors.

Mean value differences were observed on each of the six items of the Independence dimension between time of initial treatment and follow-up a median of 5 years after diagnosis. All items, except the first item (Are you confident about your future?) were scored higher at follow-up than at the time of initial treatment. This first item was rated lower at follow-up than at the time of initial treatment (Not presented).

DISCUSSION

The overall results of this thesis show that even though school attendance and HRQOL is diminished in children undergoing initial cancer treatment, survivors 4-6 years later appear to get along well despite physical and cognitive limitations. Furthermore, the findings do not indicate that school attendance is a risk factor for development of infections that require antimicrobial treatment, during initial cancer treatment.

DURING INITIAL CANCER TREATMENT

School attendance was shown to be limited close after starting cancer treatment, mostly due to hospital visits and fatigue. Furthermore approximately 30% were undergoing antimicrobial treatment due to infections. It is well-known that children in addition to start of chemotherapy and/or radiotherapy are affected by symptoms from the illness as well as side effects from treatment (Hedström, Haglund et al. 2003; Hedström, Ljungman et al. 2005; Moody 2006; Wicki, Keisker et al. 2008). Being diagnosed with cancer and in a new unfamiliar situation with different treatments and side effects may affect the desire to go to school. Still, a median of 5 years after diagnosis, more than half of the survivors think back on the time of treatment as a straining experience. Five months after start of cancer treatment (T3) the children appear to somewhat have adjusted to having cancer reflected by an increase in school attendance (Stewart 2003). However, in line with findings from other studies, self-reported HRQOL scores did not increase during initial cancer treatment (Eiser, Eiser et al. 2005; Hedström, Ljungman et al. 2005; Landolt, Vollrath et al. 2006; Engelen, Koopman et al. 2011) and were low compared with norms (The European DISABKIDS Group 2006). Already after a couple of months' treatment (T2 and T3), many of the children and adolescents may be free from initial symptoms of disease because of quick response from treatment (Smiths 31996). This may be one explanation for the observed increase in school attendance at T3 (5 months after start of treatment) and the decrease in number of antimicrobial treatments the first six months (data not presented). Although some form of normalcy may have returned to the lives of these children 5 months after start of cancer treatment, life is still mostly focused on disease and treatment and the reported reasons for school absence were still mainly disease-related.

School attendance did not appear to be a risk factor for start of antimicrobial treatment due to infection, a finding consistent with one of the few studies that have investigated the relation between social interaction and the risk of acquiring an infection among children with cancer (Tabori, Jones et al. 2007). In accordance with other reports (Bodey 1986; Auletta, O'Riordan et al. 1999; Klaassen, Goodman et al. 2000; Haupt, Romanengo et al. 2001; Christensen, Nielsen et al. 2005; Nam, Kim et al. 2010), we identified neutropenia, certain diagnoses (sarcoma, NHL and AML) and type of treatment (chemotherapy combined with surgery) as factors related to the start of antimicrobial treatment. Yet, we did not collect all data on risk factors suggested to be related to infections (e.g. intensity of treatments and nutrition status) (Haupt,

Romanengo et al. 2001; Wicki, Keisker et al. 2008; Israels, van de Wetering et al. 2009) and thus it is difficult to draw firm conclusions from our results.

4-6 YEARS AFTER DIAGNOSIS

At follow-up, four to six years after diagnosis, no major differences were found concerning the school situation between the survivors of childhood cancer and an age matched comparison group drawn from the general population. Furthermore, self-reported independence, a dimension included in the mental domain of HRQOL, was rated statistically significant better than while undergoing treatment as well as compared to the controls. The finding of diminished HRQOL in children on cancer treatment is in line with results from several studies (De Clercq, De Fruyt et al. 2004; Jörngarden, Wettergren et al. 2006; Jörngården, Mattsson et al. 2007; Engelen, Koopman et al. 2011). Although the majority of the survivors remembered the time of treatment as a straining period and several persons described difficulties in school because of the cancer experience, the overall impression is that most of them function quite well in school as well as with regard to perceived autonomy and the possibility to live without impairments approximately 5 years after treatment.

During initial treatment, children diagnosed with osteosarcoma was showed to be more vulnerable with more school absence, poorer HRQOL and more treated infections than children with other diagnoses. These results support the findings of previous research showing that adolescents diagnosed with sarcoma, close to time for diagnosis score their HRQOL significantly lower compared to those with AML (Hinds, Billups et al. 2009). However, there is nothing in the results from the follow-up study to suggest that this difference between diagnoses remains with the passage of time.

METHODOLOGICAL CONSIDERATIONS

There are some threats to internal and external validity of the studies included in this thesis that need to be mentioned.

Internal validity refers to the likelihood that the results of a study may be explained by the independent variable(s) and not by plausible rival variables. The most obvious threat to internal validity is selection bias (Kazdin 2003), which in this study has been controlled by including all children diagnosed with every type of childhood cancer during a certain time span and by subsequently inviting the same group to the follow-up study. Research on childhood cancer often excludes children with tumours of the CNS (Lähteenmäki, Huostila et al. 2002; Mört, Salanterä et al. 2011) which was not the case in this study, children with CNS tumours represented 16% of the sample in all the four studies, which is considered representative of the Swedish child cancer population. A further strength of the follow-up study was the inclusion of an age matched comparison group drawn from the general population which was randomly assigned making it possible to compare findings to young people without cancer experience (Kazdin 2003). Attrition may also affect the possibility to draw valid conclusions in a longitudinal study. With one exception the analysis of attrition did not reveal any

significant differences in age, gender and diagnoses between participants and non-participants during initial treatment and at follow-up. During initial treatment children diagnosed with NHL were more likely to be non-participants. Accepted response rates for investigations concerning special groups have been suggested to be about 75-85% (Trost 2007) and thus our response rate of 70% during initial treatment and 68% at follow-up must be considered relatively low. We do not know whether those who chose not to participate had a better or worse HRQOL and if they perceived school differently than those who participated. Perhaps, those who decided to participate did so because they were more troubled due to the cancer experience, while those who decided not to participate had less problems. On the other hand, one might also expect that those who wanted to move on with life decided not to participate. Answers from general questionnaire surveys however, may vary from 50 to 75% whereas the response rate in the comparison group, 54%, can be considered acceptable.

Threats to internal validity include the risk that the participant, after having completed a questionnaire on the next occasion recognize the questions and therefore answer without reflecting. This may have been the case when assessing HRQOL with the DCGM-37 and school attendance. However, when planning the initial studies we considered 2.5 months as a plausible period to avoid this threat especially when taking the present intense situation into account. Another possible weakness may be that the data on school attendance is entirely based on self-reports. Furthermore, we used a study-specific questionnaire for collection of data regarding school attendance which had not been psychometric evaluated. Furthermore, data was incomplete with regard to the exact number of days of school attendance because we only asked for number of lessons the child daily attended. One lesson or more of school attendance during 1 of the 5 days of observation was thus considered as being in attendance. However, the results of school attendance were found to be sensitive for change detecting an increase in attendance over time in an expected direction. In study III if possible the most optimal would have been to monitor school attendance and antimicrobial treatments throughout the study period of six months. Furthermore, we have not studied the incidence of new cancer treatments during the 14 days of follow-up which also may have influenced the start of antimicrobial treatment during these days.

The lack of a comparison group consisting of healthy children in study I-III limits the possibility to draw valid conclusions regarding the level of school attendance. However, it is clear that absenteeism in our studies is higher than the average rate for school children in Sweden. Another threat to internal validity is the occurrence of any internal or external events that may affect the outcome. An example of 'history' that may affect the results is relapse of the cancer which some of the survivors described. However, we lack information on how many of the survivors that had experienced a relapse. One way to deal with this possible threat would have been to ask questions at the follow-up interview about major changes in life during the time that had passed since the initial treatment. Still, maturation and response shift may be a problem in the comparison between the scores of self-reported Independence during initial treatment and at follow-up (Kazdin 2003). Although the wording of the questions in the Independence dimension is exactly the same, they may have changed in meaning over time because of the participants' changed values and expectations.

External validity refers to the extent that the results of a study are generalizable to other contexts and circumstances (Kazdin, 2003). The present study is a national cohort study that increases the possibility to generalize the results to other groups of children beyond the same conditions in the Western world provided that accurate analysis of attrition is performed. To increase external validity the follow-up interviews were performed by more than one person.

The possibility to draw valid inferences may be affected by the low statistical power. Small subgroups increases the probability that the results will incorrectly show no differences between groups (Type II error) (Kazdin 2003). Effect sizes were calculated to highlight the clinical importance of potential differences in means. An important factor for statistical conclusion validity is the reliability of the measures. For measurement of HRQOL the standardized DCGM-37 was used (The European DISABKIDS Group 2006) which in results from pilot testing in children with different chronic conditions have denoted satisfactory internal consistency for all dimensions (The European DISABKIDS Group 2006; Simeoni, Schmidt et al. 2007) and construct validity, as well as convergent and discriminant validity (Simeoni, Schmidt et al. 2007). To further examine the validity we evaluated data quality and psychometric properties of the DCGM-37 in children with cancer. Although the results show that the dimensionality is not optimal we consider that the DCGM-37 is a feasible instrument when used in children with cancer. Continued psychometric evaluation with Rasch, item-response theory or confirmatory factor analyses is however recommended.

NURSING IMPLICATIONS

When a child is undergoing treatment for cancer, the risk of a limited contact with school and friends is imminent. The paediatric oncology nurse has an important role in providing guidance and support to promote close contact between the family and school. When it is advisable and no risk for infection is evident, school attendance should be encouraged. To fulfil this task the nurse needs knowledge about the importance of maintaining an active social life, including school attendance during childhood cancer treatment. Our results showing a positive relation between school attendance and HRQOL and the lack of an association between school attendance and antimicrobial treatment may be encouraging for nurses in clinical practice. Hopefully it enables them to dare to recommend school attendance when the children's general condition is good. The results may facilitate understanding of individual aspects of experiences of having cancer is perceived in a longer perspective which may be important for health care professionals involved in the care of children.

One of the response options possible to record as reason for school absence was "fear of others reactions". This option was rarely chosen which also may indicate a benefit from school attendance and visits by the consultant nurses close to time for diagnosis. These results contrasts to earlier findings whereas bullying was retrospectively perceived by children as their main problem during cancer treatment (Lähteenmäki, Huostila et al. 2002) but are more in line with recent findings where adolescents with

cancer were found to score better HRQOL than a control group on an HRQOL dimension including bullying (Engelen, Koopman et al. 2011). Network-focused nursing is another nursing programme with the aim to support adolescents with cancer and their families in order to establish, maintain and make use of their social network. This programme was developed by Danish nurses working in an oncology section with young persons (15-22 years) mostly diagnosed with sarcoma and testicular cancer (Olsen and Harder 2010). The concept was developed in a grounded theory study of nurses, teenagers and young adults and their families and focuses on the teenagers and young adults need for social support. The nursing programme includes network meetings held by nurses where persons in the social environment of the adolescent and family are invited to receive information are included in the concept. The teenagers are supported in taking an active part in the decision as to which persons should be invited to the meeting. In agreement with my own clinical experience adolescents are often described as a special vulnerable group and several reports advocate special youth units for adolescents and young adults (Whelan 2003; Olsen and Harder 2010). By extending the system of consultant nurses to network-focused nursing, preferably in a special youth unit, the situation of children and adolescents with cancer would be greatly improved.

SUMMARY AND CONCLUSIONS

The DCGM-37 is considered to be a feasible and reliable instrument for use among children on cancer treatment, although the dimensionality was not entirely supported. During initial cancer treatment children were frequently absent from school, which was primarily due to hospital visits and fatigue. In addition, self-reported HRQOL was diminished, especially among the girl participants. We found a positive relation between school attendance and HRQOL and furthermore, school attendance did not appear to be a risk factor for start of antimicrobial treatment. Children with osteosarcoma, in comparison with children with other diagnoses, seem to be more vulnerable during initial treatment with regard to school attendance, HRQOL and infections. Furthermore, the majority of the survivors get along well in school in terms of autonomy and the possibility to live without impairments approximately 5 years after diagnosis. However, a significant part of the survivors described present difficulties in school related to having had cancer. Research is recommended, preferably a larger prospective international multicentre study regarding school attendance among children with cancer, including measurement of HRQOL and established protocols for antimicrobial treatment. Furthermore, continued psychometric evaluation of DCGM-37 when used in children with cancer including more conclusive analyses such as Rasch, item-response theory or confirmatory factor analyses are suggested.

The present findings underscore the importance of psychosocial care for children during initial cancer treatment as well as after completed therapy. Furthermore, given the social benefits of school attendance, our findings support that children with cancer are encouraged to attend school. Since the follow-up study is focused on the situation in school we cannot comment on the survivors' total life situation including relations within the family and partnering. Furthermore, as the time of the follow-up was relatively short it is not possible to draw conclusions about long-term outcome of the school situation. Continued follow-up of all of survivors of childhood cancer is therefore essential. Furthermore, continued research, preferably a register-based study that includes a large cohort to investigate school performance, level of education, choice of career and sick leave from work in long-term survivors of childhood cancer, is recommended.

SUMMARY IN SWEDISH

När ett barn behandlas för cancer påverkas ofta skolsituationen både under och efter behandlingen. En bidragande orsak till skolfrånvaro är bristen på kunskap om risken för infektion under pågående behandling för cancer. Skolsituationen, inklusive skolnärvaro och hälsorelaterad livskvalitet bland barn med cancer har dock studerats i begränsad omfattning. Det saknas dessutom valida instrument för mätning av hälsorelaterad livskvalitet för denna grupp av barn. Det övergripande syftet med denna avhandling var därför att undersöka skolsituationen och hälsorelaterad livskvalitet för skolbarn (7-16 år) under den inledande cancerbehandlingen och 4 till 6 år efter diagnos.

Avhandlingen har en longitudinell design och innefattar fyra studier av en kohort skolbarn (n=126) som fått en cancerdiagnos och påbörjat behandling med kemoterapi och/eller strålbehandling. Under den inledande cancerbehandlingen insamlades data en månad (T1), 2,5 månader (T2) och 5 månader (T3) efter påbörjad behandling med ett studie-specifikt frågeformulär för att undersöka skolnärvaro och ett standardiserat instrument för mätning av hälsorelaterad livskvalitet, dvs. the Disabkids chronic generic module (DCGM-37). I studie I utvärderades datakvalitet och de psykometriska egenskaperna hos DCGM-37. Studie II följde skolnärvaron och hälsorelaterad livskvalitet under tre olika veckor de första 5 månaderna av cancerbehandling. I studie III deltog barn som var utan antimikrobiell behandling dagen innan de två observationsperioderna (19 dagar) under den inledande cancerbehandlingen. Demografiska och kliniska data samt skolnärvaro analyserades med avseende på relation till påbörjad antimikrobiell behandling. Cirka 5 år efter diagnos accepterade 63 av de som behandlats för cancer i barndomen att delta i en uppföljande studie av deras skolsituation och självskattad självständighet (studie IV). I studie IV insamlades data via telefonintervjuer med både öppna och strukturerade frågor samt DCGM-37 dimensionen Independence. Svaren på de strukturerade frågorna från de som behandlats för cancer i barndomen jämfördes med svaren från en åldersmatchad kontrollgrupp från den allmänna befolkningen (n=257).

Utvärdering av DCGM-37:s datakvalitet och psykometriska egenskaper (studie I) visar att det är ett användbart instrument för barn med cancer, även om uppdelningen i dimensioner inte är helt optimal. Resultaten från studie II-III visade en signifikant ökning av skolnärvaron under de första 5 månaderna av den initiala cancerbehandling samtidigt som den självrapporterade hälsorelaterad livskvalitet var låg, särskilt bland flickorna, vilket inte förändrades under studietiden. Dessutom påvisades ett positivt samband mellan hälsorelaterad livskvalitet och skolnärvaro. Sjukhusbesök och trötthet var de två viktigaste angivna orsakerna till skolfrånvaro. Barn som gick i skolan rapporterade bättre hälsorelaterad livskvalitet och verkade inte utveckla fler infektioner än barn som inte gick i skolan. Resultaten från studie IV, cirka 5 år efter diagnos, visade att trots att 62% av de unga som behandlats för cancer i barndomen ansåg att deras skolsituation var mer eller mindre densamma som deras kamraters situation så rapporterade en betydande del svårigheter i skolan på grund av fysiska och kognitiva begränsningar. Vid uppföljningen, skattade de som behandlats för cancer i barndomen sin självständighet (dimensionen Independence) betydligt högre än de gjorde under den

inledande behandlingen, cirka 5 år tidigare och deras skattningar var också betydligt högre än kontrollgruppens. De aktuella resultaten understryker vikten av psykosocialt omhändertagande och omsorg av barn som genomgår cancerbehandling och av fortsatt uppföljning efter avslutad behandling. Med tanke på de sociala fördelarna med skolgång stöder våra resultat att skolnärvaro under behandling för cancer uppmuntras. På grund av den relativt korta uppföljningstiden är det inte möjligt att dra slutsatser om hur skolsituationen ser ut på längre sikt efter behandling för cancer i barndomen.

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