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Children and Adolescents Surviving Cancer

Psychosocial Health, Quality of Life and Social Support

Thesis for the degree of Philosophiae Doctor

Trondheim, November 2011

Norwegian University of Science and Technology
Faculty of Medicine
Department of Laboratory Medicine,
Children's and Women's Health



NTNU – Trondheim
Norwegian University of
Science and Technology



SØR-TRØNDELAG
UNIVERSITY COLLEGE

NTNU

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ISBN 978-82-471-3125-1 (printed ver.)

ISBN 978-82-471-3126-8 (electronic ver.)

ISSN 1503-8181

Doctoral theses at NTNU, 2011:278

Printed by NTNU-trykk

Barn og ungdom som overlever kreft: psykososial helse, livskvalitet og sosial støtte

Bakgrunn: Å få kreft som barn innebærer en krise for både barnet og dets familie med mange utfordringer for å oppnå normalitet etter diagnose, selv etter vellykket behandling. En faglig samarbeidsmodell (PCM) var utviklet ved Barneklubben, St. Olavs Hospital, Trondheim i 1985, der målet var å tilby optimal oppfølging til barn med kreft og deres familier.

Mål: Hensikten med denne studien (del 1 og 2) var å utforske sosial støtte, psykososial helse og livskvalitet for barn og ungdom som overlever kreft. Målet med del 1 var å utforske og beskrive sosial støtte sett ut i fra fagpersoners oppfatning av samarbeidet. Målet var også å evaluere PCM i Midt-Norge, dette for å videreutvikle og sikre kvaliteten av tiltak som er nødvendig for rehabilitering til barn som overlever kreft. I del 2 var målet å utforske og beskrive psykososial helse og livskvalitet til barn og ungdom som overlever kreft tre år eller mer etter diagnose, sammenlignet med en frisk kontrollgruppe.

Materiale og metode: Fagpersoner (både helse- og ikke helsefaglig) fra familiens hjemmemiljø som hadde omsorg for barn behandlet ved Barneklubben, St. Olavs Hospital i Trondheim, Norge mellom 1990 og 1996, ble invitert til å delta i del 1 av denne studien. Nitti-en av 142 fagpersoner (64%) svarte på et spørreskjema og 17 av disse deltok i fokusgruppeintervjuer. Del 2 var en case-kontroll studie som omfattet 50 barn og unge diagnostisert med kreft mellom 01. januar 1993 – 01. januar 2003. Data ble samlet inn ved bruk av Strengths and Difficulties Questionnaire (SDQ) (selvrapport, foreldre- og lærer rapport), kompetanse skalaer av Achenbach System of Empirically Based Assessment questionnaire (ASEBA) (lærer rapport), Inventory of Life Quality in Children and Adolescents (ILC) og KINDL livskvalitet spørreskjemaer (selv-rapport og foreldre rapport), samt ved å samle inn data om eventuelle somatiske senskader og psykiske problemer fra medisinske journaler til barn og ungdom som hadde overlevd kreft.

Resultater: Fagpersoner i del 1 rapporterte at det å samarbeide gjør det mulig for fagpersoner å bruke hverandres kunnskaper og ressurser, og dermed gi bedre oppfølging til barna og deres familier. Samtidig understreket fagpersoner at samarbeid er avhengig av veletablerte rutiner og struktur. Videre, presiserte fagpersoner at PCM er en verdifull metode for å gi oppfølging til barn med kreft og deres familier. I del 2 av denne studien hadde barn og ungdommer som overlevde kreft mer emosjonelle problemer sammenlignet med sine jevnaldrende kontrollere. Som gruppe vurderte ungdom som overlevde kreft imidlertid sin egen livskvalitet som like god som deres venner gjorde. Likevel rapporterte de ungdommene som var behandlet for hjernesvulst og de som hadde senskader mer emosjonelle problemer og lavere livskvalitet, samt flere livskvalitets områder som problematiske, selv mange år etter diagnose og behandling, sammenlignet med kontrollgruppen. Generelt rapporterte foreldre til barn som overlevde kreft mer emosjonelle problemer og dårligere livskvalitet for barna sine, samt at flere livskvalitets områder var problematiske enn foreldre til kontrollbarn.

Diskusjon og konklusjon: For å forbedre barnets psykososiale helse og livskvalitet tyder våre resultater på at det er behov for å utvikle målrettet og tilpasset tiltak og programmer ved planlegging av langsiktig oppfølging og rehabilitering av barn og ungdom som overlever kreft, spesielt for barn som har vært behandlet for hjernesvulst, eller som har fått senskader. Våre resultater viser også behov for å ta hensyn til både subjektivt opplevd og proxy rapporterte psykososial helse og livskvalitet for barn som overlever kreft. For å kunne gi den nødvendige veiledning, støtte og hjelp er forståelsen av hvordan kreft oppleves av både barn og deres familier viktig for sykepleiere, leger og andre fagpersoner som har omsorg for disse barna.

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Finansieringskilder: Norges Forskningsråd og Høgskolen i Sør-Trøndelag.

Ovennevnte avhandling er funnet verdig til å forsvares offentlig
for graden Doktor Philosophiae

Disputasen finner sted i Auditorium, Medisinsk teknisk forskningssenter, NTNU, Trondheim Fredag, den 18. nov.
2011, kl 10.30



Great is he who knows,
but greater
is he who knows
where to ask
Piet Hein

To Sigbjørn, Daniel, Andreas and Michelle

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1 ACKNOWLEDGEMENTS

The work in this thesis has been carried out at Sør-Trøndelag University College (HiST), Faculty of Nursing, Trondheim in collaboration with The Research Centre for Health Promotion and Resources, HiST/NTNU; Faculty of Medicine, Norwegian University of Science and Technology; Department of Pediatrics, Oncology Unit, St. Olavs University Hospital. This study was funded by The Research Council of Norway (NFR) and the University College, Faculty of Nursing, Trondheim.

I would like to express my sincere appreciation to everyone who has contributed to the completion of this thesis. I would especially like to thank and acknowledge:

- All the children, adolescents and their families who used their time to share their experiences in helping to provide a greater understanding and insight into psychosocial health, quality of life and social support in the lives of childhood cancer survivors. I am sincerely grateful.
- All professionals caring for children with cancer and participated in this study that gave of their time, experiences and knowledge.
- My main supervisor, Professor Torstein Vik, for believing in me, your endless enthusiasm, encouragement, constructive criticism, knowledge and for never giving up on me. I have learnt a great deal from you, not just as supervisor in the field of pediatrics and research, but also as a human being.
- My co-supervisor, Associate Professor Toril Rannestad for your enthusiasm, encouragement, professional help, criticism and support. I would also like to thank you for your warmth and support as a human being and colleague. Your unconditional support has helped me emotionally and professionally.
- My co-supervisor, Associate Professor Marit S. Indredavik for your professional help and support. Your knowledge has been invaluable. Thank you also for your emotional support when “things got a little rough”.
- Associate Professor Thomas Jozefiak for your professional help and support. Your knowledge in the field of Quality of Life has inspired me.
- Associate Professor Kristjana Kristiansen and Associate Professor John-Arne Skolbekken for your help, knowledge and advice in part one of this study.
- Dekan Anne Tveit for your interest in my work, and for giving me the opportunity to complete this thesis, I am grateful for this.

- I would also like to thank my colleagues at the University College, Faculty of Nursing in Trondheim for their interest, support and professional collaboration.
- My colleagues at the Department of Pediatrics, Oncology Unit for their collaboration and support over the years and with this study, especially Professor Svein Kolmannskog, Consultant pediatric oncologist Randi Nygaard, Head nurse Ellen Woldseth and her nursing staff.
- In memory of Professor Peter Johan Moe who introduced me to the professional world of childhood cancer. His encouragement was an inspiration for me as a young nurse.
- My colleagues at the Research Centre for Health Promotion and Resources as well as the Department of Social Work and Health Science (ISH) for their support during the final stage of my thesis, especially Professor Geir Arild Espnes and Professor Borgunn Ytterhus, as well as my research colleagues.
- My earlier colleagues at the Norwegian Cancer Society in Trondheim, Eva Faanes and my close colleagues that I worked with for over 24 years. It was “here it all started”, without your professional and personal warmth, help, support and friendship I would not be in the final stage of my thesis.
- A special thank you to Trude Reinjfjell for your professional collaboration and enthusiasm in childhood cancer. Also a special thank you to Heidi Killingberg for your professional collaboration and support in the first stage of part 2 of this thesis.
- A warm thank you to all my girlfriends and friends in Canada and Norway, I am indebted to each and every one of you, thank you for your support and friendship.
- A warm thank you to my siblings, siblings-in-law and family in Canada and Norway who have always been there for me and give me a true quality of life.
- My 93 year old father, Walter Bradley who gave me the love and care when growing up and in the memory of my mother, Irene Bradley who gave me love and taught me to never give up when I believe in something; in memory of my parents-in-law, Mary and Jørulv Eilertsen who whole-heartedly accepted me as a young woman into their family in Norway.
- My loving husband Sigbjørn, who has always supported, encouraged and believed in me as a woman and as a professional. Sharing this path with you in life gives me the best quality of life I could ever wish for.
- Finally to the dearest gift in my life, my children; Daniel, Andreas and Michelle, in your own very unique way make my life worth living, you make me proud to be your mom.

2 ABBREVIATIONS

| | |
|-------|---|
| ASEBA | Achenbach System of Empirically Based Assessment |
| ALL | Acute Lymphoblastic Leukaemia |
| BHIM | Biopsychosocial health and illness model |
| CNS | Central Nervous System |
| HiST | Høgskolen i Sør-Trøndelag (Sør-Trøndelag University College) |
| ILC | Das Inventar zur Erfassung der Lebensqualität bei Kindern und Jugendlichen (ILK) (Inventory of Life Quality for Children and Adolescents – ILC) |
| HOD | Helse- og omsorgsdepartementet (Ministry of Health and Care Services) |
| KINDL | Kinder Lebensqualität Fragebogen |
| NOBOS | Nordic Society of Pediatric Oncology Nurse |
| NOPHO | Nordic Society for Pediatric Hematology and Oncology |
| NFR | Norges Forskningsråd (The Research Council of Norway) |
| NOU | Norges offentlig utredning (Official Norwegian Reports) |
| PCM | Professional Collaborative Model |
| QoL | Quality of Life |
| SD | Standard Deviation |
| SDQ | Strength and Difficulties Questionnaire |
| SES | Socioeconomic status |
| SIOP | International Society of Paediatric Oncology |
| WHO | World Health Organization |

3 ABSTRACT

Children and Adolescents Surviving Cancer: Psychosocial Health, Quality of Life and Social Support

Background: Childhood cancer involves a crisis for the child and their family where they face many challenges to achieve normality after diagnosis, even after successful treatment. In 1985, a professional collaboration model (PCM) was developed at the Department of Pediatrics, St. Olavs University Hospital, Trondheim where the goal was to offer optimal follow-up care to children with cancer and their families.

Aim: The aim of this two part study (part 1 and 2) was to explore social support, psychosocial health and quality of life (QoL) for children and adolescents surviving cancer. The specific aim of part 1 was to explore and describe social support in view of professionals' perception of collaboration. An additional aim was to evaluate the PCM in Central Norway taken into consideration the need to further develop and ensure the quality of supportive interventions necessary for rehabilitation for childhood cancer survivors. In part 2 the specific aim was to explore and describe psychosocial health and QoL of children and adolescents surviving cancer at least 3 years after their cancer diagnosis, compared with a healthy control group.

Material and Methods: Health and non-health professionals from the families' home communities caring for children treated at the Department of Pediatrics, St. Olavs University Hospital in Trondheim, Norway between 1990 and 1996 were invited to participate in part 1 of this study. Ninety-one of 142 eligible professionals (64%) responded to a questionnaire and 17 of these professionals participated in focus group interviews. Part 2 was a case-control study including 50 children and adolescents diagnosed with cancer between January 1, 1993 – January 1, 2003. Data was collected by using the Strengths and Difficulties Questionnaire (SDQ) (self-report, parent report and teacher report), the competence scales of Achenbach System of Empirically Based Assessment questionnaire (ASEBA) (teacher report), the Inventory of Life Quality in Children and Adolescents (ILC) and the KINDL QoL questionnaires (self-report and

parent report), as well as by collecting data for any somatic late effects and psychological problems from the medical records of children surviving cancer.

Results: Professionals in part 1 stated that collaboration enables professionals to make use of each other's knowledge and resources thus, giving better follow-up care for children and their families. However, professionals also stated that collaboration is dependent on well-established routines and structure. Moreover, professionals stated that the PCM is a valuable method for follow-up care for children with cancer and their families. In part 2 of our study, children and adolescents surviving cancer had generally more emotional problems when compared to their peers. However, adolescents surviving cancer as a group assessed their QoL as similar to that of their peers. Yet, adolescents surviving brain tumours or those with late effects reported more emotional problems and lower QoL and an increased number of QoL domains perceived as problematic, even many years after diagnosis and treatment. Parents generally reported more emotional problems and a poorer QoL for their children surviving cancer, as well as an increased number of QoL domains experienced as problematic compared with parent controls.

Discussion and Conclusion: To improve the child's psychosocial health and QoL our results indicate the need to develop pertinent and adequate supportive interventions and programs when planning and implementing long-term follow-up care and rehabilitation of children and adolescents surviving cancer, especially for survivors with brain tumours, and those with late effects. Our results also indicate the need to take into account subjectively perceived and proxy reported psychosocial health and QoL for children surviving cancer. To offer the necessary guidance, support, and assistance, is the understanding of how cancer is experienced by both children and their families important in the practice of pediatric oncology; for nurses, medical doctors and other professionals in the collaborative team.

Keywords: Children, Adolescents, Cancer, Survivors, Quality of Life, Psychosocial health, Mental health, Psychosocial functioning, emotions, behaviour, support, professional collaboration, follow-up care.

4 LIST OF PAPERS

- Paper I: Eilertsen M.E., Reinfjell T., Vik T., 2004. Value of professional collaboration in the care of children with cancer and their families. *European Journal of Cancer Care*, 13, 349-55.
- Paper II: Eilertsen M.E., Kristiansen K., Reinfjell T., Rannestad T., Indredavik M.S., Vik T., 2009. Professional collaboration – support for children with cancer and their families – focus group interview – a source of information and knowledge – professionals’ perspectives. *Journal of Interprofessional Care*, 23 (4), 355-68.
- Paper III: Eilertsen M.E., Rannestad T., Indredavik M.S., Vik T., 2011. Psychosocial Health in Children and Adolescents Surviving Cancer. *Scandinavian Journal of Caring Sciences*, In press.
doi:10.1111/j.1471-6712.2011.00883.x
- Paper IV: Eilertsen M.E., Jozefiak T., Rannestad T., Indredavik M.S., Vik T. Quality of Life in Children and Adolescents Surviving Cancer. *European Journal of Oncology Nursing*, In press.
doi:10.1016/j.ejon.2011.08.001

5 PREFACE

5.1 Clinical background: personal reflection

For over 25 years I worked in the field of pediatric oncology, employed as a nursing advisor in the Norwegian Cancer Society (1980-2004), and collaborated with the Department of Pediatrics, St. Olavs University Hospital, Trondheim, Norway. As a nursing advisor I worked in close contact with children with cancer and their families, and collaborated with both health and non-health professionals in Central Norway. I was privileged to follow these children through the different phases of their illness and treatment, as well as after completion of treatment. As a result, I had the opportunity to view the extent of how children themselves, as well as their parents and siblings were able to adapt back to their normal life with family, friends, school and work (parents). I also had the opportunity to be a part of a team which built up a professional collaborative model (PCM) for children with and surviving cancer, essential for follow-up care and rehabilitation of children with a chronic, life-threatening illness.

Children with cancer were subjected to intense and long-term treatment with a diagnosis that was fatal without the required treatment. In my experience, most families had an enormous burden to carry over many years. Even though the strain of the cancer illness and treatment was difficult and the sick child's future was uncertain, many families appeared to function well and adapted back to their "normal" life, coping well in their daily living. However, other children and their families often seemed to struggle "alone" back to their normal daily living at home, as well as at school or work (parents).

Through these years of clinical work I was fortunate to experience that many children survived their cancer diagnosis, something which gave me a desire and a need to document the effect the cancer illness and its treatment had on the child, even several years after their diagnosis. It was both the families that functioned well, as well as the families that struggled back to a "normal" life that inspired me to evaluate the PCM and further explore psychosocial health and quality of life (QoL) for children and adolescents surviving cancer. Obtaining more information and new knowledge of what

children themselves experience, as well as their parents was an important goal in improving follow-up care through the PCM, thus giving the necessary social support and rehabilitation essential for the individual child surviving cancer and their family. My goal and dream started after evaluating the PCM in 1997 and became a total reality in 2006 after receiving a grant from NFR and HiST enabling the possibility to achieve more knowledge about children and adolescents surviving cancer.

5.2 Evidence-based nursing

The practice of nursing is a complex profession, mainly because the field of nursing demands a great deal of flexibility in the use of different types of knowledge in different situations (Nortvedt et al. 2007). The nursing practice needs both knowledge that research can give, as well as knowledge based on experience. In collaboration between the nurse, patient and their family it is important that different interventions are based on high quality research in helping the patient in a best possible way. Nortvedt et al. (2007) states however, that knowledge based only on research is not sufficient to support nursing procedures or actions when caring for human beings. The nursing practice needs also knowledge based on the nurse's clinical experience, reflections and ethical assessment showing consideration and respect for the individual's (patient) wishes and needs. Evidence-based nursing has been defined as: "the process by which nurses make clinical decisions using valid and relevant research-based evidence, their clinical expertise and patient preferences, in the context of available resources" (Nortvedt et al. 2007; Cullum et al. 2008).

In the context of this thesis, knowledge is thus achieved through research to document knowledge achieved through experience, thereby increasing knowledge in the profession and practice of nursing in "evidence-based nursing".

6 INTRODUCTION AND CONCEPTUAL FRAMEWORK

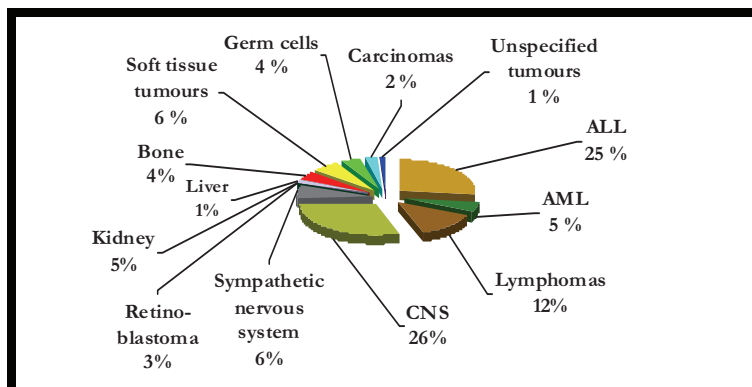
"Great is he who knows, but greater is he who knows where to ask" *Piet Hein*.

"Knowing when you know something and knowing when you do not know something – that is knowledge" *Confucius*.

6.1 General Introduction

In Norway, approximately 120-150 children and adolescents under the age of 15 are diagnosed with cancer each year (annual incidence 16.2/100,000) and approximately 40 children die yearly of their cancer illness (Cancer Registry 2009). The most common type of malignancy in children is leukaemia, accounting for approximately 1/3 of childhood cancers. The second most frequent malignancy in children is tumours of the central nervous system (CNS) (figure 1).

Figure 1: Distribution of childhood cancer in the Nordic countries (NOPHO Annual Report 2009) (Used with kind permission from the author, B. Lund from a lecture 14.12.2010)



Generally, cancer is one of the most common diseases in both genders and in all age groups in the Western world (Baider et al. 1996). Nevertheless, childhood cancer is rare and accounts for less than one percent of all cancer in industrialized countries (Stiller et al. 2005). Children have most often other cancer diagnoses than adults and several types of cancer are unique to childhood, whereas the most frequently seen carcinomas in

adults are extremely rare among children. Children have types of cancer where malignant cells are derived from immature cells originating in fetal life which divide rapidly and grow fast (Bringager et al. 2003). Nonetheless, a major advance in the understanding of the genetic etiology of cancer generally has arisen from the investigation of childhood tumours (Stiller et al. 2005).

Since childhood cancer is uncommon, professionals are dependent upon collaboration both nationally and internationally to gain the necessary knowledge for diagnosis, treatment and rehabilitation (Bringager et al. 2003). Through NOPHO (established in 1982) pediatricians collaborate and register all children with cancer in the Nordic countries. The nursing organization collaborates through a corresponding group in the Nordic countries (NOBOS), as well as internationally (SIOP) (Bringager et al. 2003).

6.1.1 Survivorship

For two or three decades ago cancer was associated with death and dying in the general population. Recent advances in diagnosis and treatment, as well as international collaboration in pediatric oncology have shifted the focus from coping with dying from cancer, to coping with life with cancer, where cancer is seen as a treatable disease for the majority, with high probability of living beyond a diagnosis of childhood cancer (Baider et al. 1996; Stiller et al. 2005, Shepherd et al. 2010). As a result of improvements in therapy, most children and adolescents are living for years after the completion of treatment and are now survivors of childhood cancer.

The concept “survivorship” has been in use in the English language from approximately the year 1625 (Shepherd et al. 2010). The literature reveals a diversity of uses of survivorship in the different fields of biological sciences, finance, law and health (Shepherd et al. 2010). In the field of cancer research there has been much discussion about the use of the term survivorship, specifically about when a person enters into survivorship (Lewis 2006). The National Coalition for Cancer Survivorship (NCCS 1996) in USA defined cancer survivorship as “the experience of living with, through, and beyond a diagnosis of cancer” (Shepherd 2010). The Office of Cancer Survivorship (Shepherd 2010) adopted the revised definition of survivorship to be: “An individual is

considered to be a cancer survivor from the time of diagnosis, through the balance of his or her life. Family members, friends, and care-givers are also impacted by the survivorship experience and are therefore included in this definition,” National cancer Institute 2004 (Shepherd 2010).

6.1.2 Childhood cancer survivors

Survival rates for childhood cancer have improved dramatically through the past years, resulting in a growing population of childhood cancer survivors. With the help of cancer treatment such as chemotherapy, radiation, surgery and improved supportive care (both somatic and psychosocial) nearly 80 % of children currently treated for cancer will become long-term survivors (Meadows 2006; Oeffinger et al. 2006; Landier 2007; Shepherd 2010).

Even though childhood cancer today is no longer considered a terminal illness, but viewed as a chronic, life-threatening illness (Hoekstra-Weebers 1996; Stiller & Eatock 1999; Last et al. 2005; Robinson et al. 2007), the diagnosis of childhood cancer is still a crisis for both the child and its family (Hagedoorn et al. 2011). Intensive medical treatment together with its side effects and prolonged periods of uncertainty about the outcome can result in psychosocial problems for parents and child, and affect their QoL several years after diagnosis and treatment (Koocher & O’Malley 1981; Spinetta 1984; Van Dongen-Melman et al. 1995; Dyregrov & Raundalen 1996; NOU 1997:20 (§ 8.10.4.2.); Eiser 1998; Eiser et al. 2000; Koot & Wallander 2001; Patenaude & Kupst 2005). As survival rates for childhood cancer have increased, research has therefore focused on QoL issues (Koot & Wallander 2001) as well as on psychological adjustment and late effects (Patenaude & Kupst 2005) among survivors. The degree to how children surviving cancer and their families are able to deal with challenges of cancer diagnosis and treatment appears to be partly dependent on the support available from others (Lazarus 1984; Bloom 1996; Taylor 2007). Social support has been associated with better adjustment and has been regarded as an important stress-buffering factor (Taylor 2007).

A review of the literature on children and adolescents surviving cancer shows that psychosocial health and QoL are often proxy reported, although in the last decade studies are also reported by children themselves. However, to our knowledge no studies have particularly addressed the adolescents' psychological functioning as assessed by themselves, parents and teachers. Moreover, a review of the literature shows only a few studies that explore or discuss the association between social support, psychosocial health, QoL and late effects. Attention has often been given to the child's cognitive understanding and not to a great extent to the emotional and social consequences of the cancer illness (Eiser 1998). In addition, there are few studies that use mixed methodologies to provide a more comprehensive understanding of psychosocial health and QoL in survivors of childhood cancer. Furthermore, the reported physical late effects and psychological problems in children surviving cancer suggest a need for follow-up care, social support and rehabilitation comprising collaboration between healthcare professions (HOD 2004).

6.2 Childhood cancer

6.2.1 Leukaemia

The leukemias, cancer of the white blood cells, are the dominating malignancy of childhood. They account for approximately 1/3 of all childhood malignancies and have a peak incidence at 2–7 years of age (Schmiegelow & Gustafsson 2005). Leukaemia is divided into acute and chronic lymphocytic leukaemia. In children, acute leukaemia is more common than chronic (Schmiegelow & Gustafsson 2005). Acute lymphoblastic leukaemia (ALL) comprises 85% and acute myeloid leukaemia comprises 10-15%, while a few sporadic cases (< 5%) have chronic myeloid leukaemia (Bringager et al. 2003).

In Europe and the USA the annual incidence of ALL, is 3.5-4.0 per 100.000 children <15 years of age (Schmiegelow & Gustafsson 2005). In the Nordic countries ALL accounts for approximately 1/4 of all childhood malignancies (NOPHO annual report 2009) (figure 1). While nearly all patients with ALL died 40 years ago, cure is now realistic in 75 – 80 % (Gustafsson et al. 2000; Bringager et al. 2003; Rubnitz & Pui

2003; NOPHO annual report 2011). The improved understanding of the biology with risk-group adapted therapy, pharmacology, medical supportive care, and randomized clinical trials, as well as a close international collaboration has made an impressive difference in the cure of childhood ALL (Gadner et al. 2003).

ALL is a malignant disorder of the immature lymphoid cells (lymphoblasts) found in the bone marrow and is interchangeably referred to as lymphocytic or lymphoblastic leukaemia, referring to the cells involved which if normal would have developed into mature lymphocytes (Bringager et al. 2003). *Acute* refers to the relatively short time course of the disease, being fatal in as little as a few weeks if untreated.

The excess of malignant lymphoblasts crowd out normal blood cell production in the bone marrow and infiltrate other organs. The signs and symptoms of ALL vary and are both due to lack of normal functioning blood cells, as well as to damage of other tissues. Generally typical symptoms are fatigue, anemia, fever, infections, weight loss and/or loss of appetite, excessive and unexplained bruising, petechiae, bone and joint pain, enlarged lymph nodes, liver and/or spleen (Schmiegelow & Gustafsson 2005). The clinical picture may be confused with other conditions such as idiopathic thrombocytopenic purpura or rheumatoid arthritis and hence a bone marrow examination is warranted in children with prolonged monocytopenia (Schmiegelow & Gustafsson 2005).

Diagnosis is obtained through a physical examination, blood count and other blood tests, bone marrow biopsy with histologic, immunologic and molecular biological examination of the involved cells. Lumbar puncture is also performed to examine the cerebrospinal fluid for malignant cells (Bringager et al. 2003), since leukemia can also involve the central nervous system. The main treatment is chemotherapy- intravenous, intrathecal, as well as oral administration. Primary treatment protocols include intensive induction and consolidation phases, as well as a less intensive maintenance phase, over a 2 to 2 ½ year total time period (Bringager et al. 2003). In special high risk cases and at relapse, bone marrow transplantation is also done.

6.2.2 Tumours of the central nervous system (CNS): Brain tumour

Tumours of the CNS constitute the most common solid tumour in children (2.7 per 100.000 children annually) representing the second most frequent malignancy in children <16 years of age (Pötter et al. 2005) (figure 1). Tumours of the CNS include both brain tumours and tumours in the spinal cord, accounting for approximately 1/3 of all childhood malignancies (Cancer Registry 2009). Primary tumours in the spinal cord in children are rare and will therefore not be discussed further in this study.

Every year approximately 35 children are diagnosed with a brain tumour in Norway (Bringager et al. 2003). These tumours are very diverse regarding histology, malignancy grade, location, pattern of spread, clinical picture, natural history and age of occurrence. Some “benign”, lowgrade tumours may grow slowly over many years, other more aggressive anaplastic tumours may be fastgrowing and have a large potential for invasion and metastasis (Bringager et al. 2003; Pötter et al. 2005). Although a tumour may be histologically benign, the location may cause it to be unavailable for surgery and therefore clinically “malignant”. Most CNS tumour types occur preferentially in specific age-groups and at specific sites in the brain (Pötter et al. 2005). Compared with tumours in adults, the posterior fossa site is over-represented in children (approx. 50%). In the younger age group, CNS tumours occur near the midline, suggesting a developmental aspect to their origin (Pötter et al. 2005). The histology, as well as the localization is of importance for cure. Surgical intervention remains the basis of the diagnostic and therapeutic management of most primary brain tumours and completeness of surgical excision is then the most important prognostic factor (Bringager et al. 2003; Pötter et al. 2005). Unfortunately, many brain tumours infiltrate the normal brain tissue even though they have a benign histology. Radical excision can therefore be difficult without causing serious damage. The most usual brain tumours are medulloblastoma (malignant), pilocytic astrocytoma (“benign”), ependymoma (malignant/”benign”) and craniopharyngioma (“benign”).

As significant progress has been achieved and is developing in the different areas of diagnosis and treatment, adequate clinical management and follow-up today involves professional collaboration between many specialities. The goal of therapy is to achieve

cure while minimizing late effects and obtaining optimal QoL (Pötter et al. 2005; Wallace & Green 2004; Oeffinger et al. 2008).

Signs and symptoms of neurological dysfunction in a child with a brain tumour are various and depend on the tumours' location and the child's age (Bringager et al. 2003; Pötter et al. 2005). General symptoms from increased intracranial pressure are common, such as headaches and vomiting (especially in the morning) (Bringager et al. 2003). Increased intracranial pressure may also result in declining academic performance, fatigue, personality and behaviour changes (Pötter et al. 2005). Localized symptoms may occur depending on the tumour site involved, including balance problems, seizures and paralyses, vision disturbances such as squinting, double vision and nystagmus. In small children the head circumference may increase, caused by tumour expansion inside a cranium with sutures still open (Bringager et al. 2003).

Brain tumours are diagnosed by imaging techniques, MRI (Magnetic resonance imaging) being the most important. Both the head and spine are examined, as several pediatric brain tumours may seed malignant cells in the cerebrospinal fluid causing "drop metastases" down the spinal canal. Histological classification of the tumour tissue is important, and molecular biological profile is of increasing interest for risk stratification (Pötter et al. 2005). Additional tests such as tumour markers in blood and spinal fluid may also be of value (Triche & Sorensen 2002).

Many types of brain tumours require combination therapy; with chemotherapy and/or radiotherapy, in addition to surgery (Bringager et al. 2003; Pötter et al. 2005). Radiation is preferably reserved for older children in order to avoid late effects. There have been technical improvements both within surgery and radiotherapy in order to minimize damage to the surrounding normal brain tissue.

6.2.3 Other cancer tumours

Carcinomas are very infrequent in children, as opposed to adults. But several other types of malignant solid tumours can occur in children and adolescents (figure 1), many of them typically being of immature/embryonic origin, and often disseminated. Since these diagnoses are few and seldom, the diverse types of childhood cancer will not be

elaborated any further in this study. For further details Bringager et al. (2003) and Vôte et al. (2005) are suggested references.

6.2.4 Late effects

Medical advances in the diagnosis, treatment and management of childhood cancer have resulted in an increasing number of long-term survivors. The majority of children with cancer can now be cured from their malignancy. It has been estimated that by the year 2010, 1:250 of the adult population will be a long-term survivor of childhood cancer (Wallace & Green 2004). As survival rates improve, it has become evident that cure also has a price. Research documents that survivors are at risk for a multitude of chronic or late-occurring health problems caused by their cancer or its treatment, often referred to as “late effects” (Shannon 2007). Bradwell (2009) defines late effects as any physical, psychological or social consequence of the disease or treatment, appearing after months or years following treatment.

The child’s cancer diagnosis, age at diagnosis, tumour location, type of treatment received and complications during treatment are factors of major importance for which late effects occur. Children treated for a brain tumour with radiation therapy are at special risk for late effects that contribute to academic problems in school. The young brain is especially vulnerable for radiation damage during growth and development the first 3-5 years of life, with cognitive and neuro-psychological late effects as a result (Nygaard 1999; Reinfjell et al. 2007). But chemotherapy has also been seen to give diffuse cognitive problems (Mennes et al. 2005; Reinfjell et al. 2007).

Monitoring the long-term effects of treatment on children and adolescents is now an essential part of follow-up care of survivors. A major challenge within pediatric oncology is to sustain the high survival rates while striving to achieve optimal QoL (Wallace and Green 2004; Oeffinger et al. 2008; Bradwell 2009). Cure remains the most important goal, even where concerns of adverse late effects exist. But the increasing understanding of the biology of tumours and the risks associated with the different treatment forms is leading to strategies that aim to decrease late effects to a minimum (Jenney 2005). Chemotherapy, surgery and radiotherapy are increasingly better

better “tailored and timed” for the individual patient and tumour according to risk factors. However, some children will inevitably require therapy with predictable physical late effects. For these children the early identification of problems, prompt intervention, and optimal coordination of ongoing care, will be important in preventing and minimizing the results of this damage, as well as giving best possible follow-up care through multidisciplinary support (interdisciplinary professional collaboration) (Jenney 2005; Pemberger et al. 2005). Long-term monitoring of adult survivors of childhood cancer in a follow-up clinic may offer care of both somatic and psychological cancer-related problems, as well as providing a forum for research on late effects.

The literature states that approximately two-thirds of childhood cancer survivors experience physical late effects (Hudson et al. 2003; Wallace & Green 2004; Eiser 2007) and/or psychosocial problems (Hobbie et al. 2000; Glover et al. 2003; Eiser 2007). It is also documented that childhood cancer survivors are more likely to have mental health disorders, chronic pain or fatigue than the general population (Hudson et al. 2003; Oeffinger et al. 2008). Eiser (2007) emphasizes the challenge survivors have in their balance between obtaining “normalcy” while recognizing and living with the consequences of the cancer disease after treatment.

6.2.4.1 Somatic late effects

Somatic (physical) late effects include specific organ dysfunctions, due to for instance cardiomyopathy, kidney dysfunction and after certain cancer drugs or radiation fields. Several factors can contribute to endocrine impairment, growth and developmental problems, fertility and gonadal dysfunction, dental problems, obesity, hearing loss, cutaneous and musculoskeletal complications. Neuropsychological and cognitive dysfunctions are especially associated with treatment of brain tumours. Survivors of childhood cancer also have an increased risk for second malignancies, the degree depending mainly on the kind of treatment given (Wallace & Green 2004; Eiser et al. 2007; Oeffinger et al. 2008). A second primary cancer is defined as a histological distinct second neoplasm that develops after the first neoplasm (Wallace & Green 2004).

6.2.4.2 *Psychological problems*

Being diagnosed and treated for a cancer illness during childhood can have a considerable psychological strain on both the child and their family. Living with an uncertainty about their future health, concerns about relapse, restrictions associated with possible late effects and changes in physical and psychosocial functioning may have an influence on the survivors' psychosocial health and QoL (Wallace & Green 2004; Eiser et al. 2007). Reports of long-term psychological or adjustment problems in survivors of childhood cancer are however, conflicting (Jenney 2005). Many survivors adapt extremely well to normal life following therapy, and report normal mental health, adjusting well both psychologically and socially (Jenney 2005). However, it is well recognized that some survivors are at risk of anxiety and depression (Hudson et al. 2003), behavioural problems (Nathan et al. 2009; Gurney et al. 2009), concentration problems, fatigue, learning disabilities (Eiser et al. 2007; Upton & Eiser 2006), difficulties in making friends and therefore being often socially isolated (Noll et al. 1997; Florin & Hinkle 2005; Patenaude & Kupst 2005). There is also evidence of post-traumatic stress in some survivors (Lansky et al. 1978; Fife et al. 1987; Mott 1990; Jankovic et al. 1999; Hobbie et al. 2000; Meeske et al. 2001; Jenney 2005; Eiser et al. 2007), as well as reduced QoL among childhood cancer survivors with late effects (Pemberger et al., 2005; Calaminus et al. 2007; Eiser et al. 2007; Ishida et al. 2010, 2010).

6.3 Conceptual framework

The concepts psychosocial health, QoL and experiencing social support are interrelated, especially psychosocial health and QoL. Furthermore, being satisfied with social support can have a direct effect on a person's well-being, serving as a buffer between negative consequences of stress and grief (Hoekstra-Weebers 1996; Woodgate 1999, 1999; Earle et. al 2005). Consequently, social support through professional collaboration may contribute to promote optimal psychosocial health and QoL for children surviving cancer and their families. As a basis for understanding the concepts of psychosocial health and QoL, as well as social support, the concept of health will first be clarified.

6.3.1 Health – an introduction

The concept of health has been a focus of interest, dating as far back to the Greek philosopher Plato. Plato described health as a natural and moral ideal, which every human being should attempt to achieve (The Norwegian Medical Association 2001). The World Health Organization defines health (1948) as a state of complete physical, mental and social well-being, and not merely the absence of disease and infirmity.

The general understanding of health is often linked to the disease concept and in the previous two centuries has health been regarded as the opposite of disease. This narrow understanding of health is often shared by the general public, as well as professionals of medicine, social science and psychology (Lindström 1994). The clinical focus has mainly been on biological causes, where treatment and rehabilitation have focused on biological healing models. Consequently, health is often measured in terms of ill-health such as death, disease, disability and often directly related to the biomedical health concept (Lindström 1994; Mæland 2010). This narrow vision of health has been exposed to a great deal of criticism since it presumes individuals with disease or injury as being unable to attain good health (Lindström 1994; Espnes & Smedslund 2009; Mæland 2010). Thus, the broader understanding of health as a source of well-being is not often considered a possibility (Lindström 1994).

In this study the definition of the concept of psychosocial health and QoL, as well as social support is based on the biopsychosocial health and illness model (BHIM) (Espnes & Smedslund 2009). The BHIM was developed through the recognition that the biomedical model was inadequate, in cases where diagnosis and cure were not the main focus. The BHIM also recognizes the preventive aspect; to avoid the development of unnecessary illnesses or problems based on biological, social, psychological, spiritual and environmental factors. The *biological factor* is based on genetic predisposition, physiological reactivity, pathogens and immune response; the *social factor* on social support, health education, hygiene, availability of health resources; the *psychological factor* on stress, cognitive resources, health expectations, personality, response to disease, mental health resources; the *spiritual factor* on living according to your own philosophy of life, coherence of life and hope; the *environmental aspect* is based on

pollution and the working environment. The holistic basis for the BHIM has its main focus therefore on health promotion and in this study, in relation to childhood cancer survivors.

6.3.2 Psychosocial health

6.3.2.1 The concept of psychosocial health

The concept *psychosocial* may be defined as psychological development and interaction within the context of an individual's social environment (Oxford English Dictionary 2010). Psychosocial health can further be seen as the relationship between coping with a chronic illness and psychological adaptation (Manne 2004). In some cases, the concept of psychosocial health may combine traditional medical definitions of disease and disability with measures that recognize individuals' experiences and psychological functioning and well-being, a dimension that is becoming increasingly recognized in clinical trials (Martikainen et al. 2002).

6.3.2.2 Definition of Psychosocial health used for this study

The empirical work in this thesis has been based on the following definition of psychosocial health in the child: "Assessment of the child's emotional, behavioral and social health and functioning in a multi-informant perspective". This definition is therefore in agreement with Espnes & Smedslund (2009) psychological and social factors of the BHIM, in relation to health and illness.

6.3.2.3 Psychosocial health in children and adolescents surviving cancer

The improved survival rates for childhood cancer have lead to an increasing focus on psychological adjustment (Gray et al. 1992; Elkin et al. 1997; Noll et al. 1997; Patenaude & Kupst 2005; Meyerowitz et al. 2008). Research on psychosocial outcome for cancer survivors has shown varying and contradictory results (Baider et al. 1996; Zebrack & Zeltzer 2003; Sundberg et al. 2009; Zeltzer et al. 2009). Some studies report negative outcomes and an increased degree of maladjustment such as behavioural problems (Nathan et al. 2009; Gurney et al. 2009), learning problems (Upton & Eiser 2006) and post-traumatic stress disorder (PTSD) (Fife et al. 1987; Lansky et al. 1978;

Mott 1990; Jankovic et al. 1999; Hobbie et al. 2000; Meeske et al 2001). Many studies found that children surviving cancer had emotional problems with anxiety, depression, low self-esteem, fluctuations in mood, social isolation and most often, problems in social adjustment (Koocher & O'Malley 1981; Zeltzer et al. 1997; Richardson 1999; Van Dongen-Melman 2000; Hudson et al. 2003; Mulhern et al. 2004; Florin & Hinkle 2005; Patenaude & Kupst 2005; Sands et al. 2005; Oeffinger et al. 2008).

However, other studies show that rates of depression are similar in childhood cancer survivors and healthy controls (Gray et al. 1992; Kupst et al. 1995; Zebrack & Zeltzer 2003). Many studies have also demonstrated that cancer survivors, including children, fare the same or even better than those who have not had cancer (Langeveld et al. 2002; Langeveld et al. 2004) in view of psychological well-being (Eiser et al. 2000; Gray et al. 1992; Elkin et al. 1997; Noll et al. 1997), resilience (Haase 1997; Haase 2004; Woodgate 1999a,b; Borge 2010), and appreciation for life and relationships (Zebrack & Chesler 2002; Florin & Hinkle 2005; Patenaude & Kupst 2005; Zeltzer et al. 2008; Sundberg et al. 2009; Zeltzer et al. 2009). Studies have included children and parent responses or parent and teacher responses in relation to psychosocial health (Elkin et al. 1997; Noll et al. 1997; Zebrack & Chesler 2002; Upton & Eiser 2006; Zeltzer et al. 2008) whereas, other studies (Zeltzer et al. 2009; Reinfjell et al. 2009; Gray et al. 1992; Langeveld et al. 2002; Langeveld et al. 2004; Shankar et al. 2005) have included a matched healthy control group. However, as stated earlier in 6.1.2., none of these studies particularly addressed the adolescents' psychological functioning as assessed by themselves, their parents as well as teachers.

6.3.3 Quality of Life (QoL)

6.3.3.1 The concept of QoL

QoL is a fairly new concept in health research. However, reflections on happiness and "the good life" date back to ancient philosophy where a definition of QoL appears in the Greek word "eudaimonia" which was translated to happiness, a state of well-being (Fayers & Machin 2007), to characterize a person who lived a good life (Jozefiak et al. 2009b). By the end of the last century living standards in developed countries became

better and there was a major progress in medical diagnostics, together with improved treatment for many illnesses resulting in an increased longevity. After World War II, QoL in the Western world became an important priority and was gradually recognized as a valuable outcome in the fields of medicine and nursing (Padilla et al. 1992; Rannestad 2001; Mæland 2010).

There are close associations between the health and QoL concepts. Lindström (1994) states that the health concept has developed primarily from a single discipline (medicine), as an expression of negative life conditions (disease), and developed towards a multidisciplinary concept expressing positive life values. The basis of the QoL concept is multidisciplinary, expressing positive values based on subjectively perceived or objectively evaluated well-being close to the contemporary health concept. The WHO describes QoL as “the individual’s perception of their position in life in the context of culture and value systems in which they live and in relation to their goals, expectations, standards and concerns” (WHOQOL 1997). The QoL concept has therefore emerged to cover the individual’s well-being, happiness and satisfaction (Bowling 1999; Koot & Wallander 2001; Fayers & Machin 2007).

Koot & Wallander (2001) define QoL of children and adolescents with chronic health conditions as “QoL is the combination of objectively and subjectively indicated well-being in multiple domains of life considered salient in one’s culture and time, while adhering to universal standards of human rights.” Koot & Wallander (2001) emphasize the change that has occurred in the last century to how children and adolescents are viewed and how society has come to put a value on each individual’s life. In recent years and because of the advancement in medical treatment, emphasis has changed from maintaining life to enhancing QoL. Efforts have been made to assess the impact of disease on QoL in children and adolescents from the viewpoint of pediatrics, psychology, and public health administration (Newachek & Taylor 1992; Spieth & Harris 1996).

Mattejat & Remschmidt (1998) present an overview of the basic aspects of QoL in children and adolescents, stating that QoL can be viewed in a narrow or a broad sense. QoL in a narrow sense can be divided into *the ability to act and function* on the one

hand, and *well-being and satisfaction* experienced by children themselves on the other. QoL can also be seen in a broad sense including also *objective preconditions for QoL* such as material and psychosocial factors (figure 2).

Figure 2: Basic aspects of Quality of Life (*Adapted from Jozefiak (2009b) and Mattejat & Remschmidt (1998)*)

A. QoL in a broad sense (1, 2 and 3) and **B.** QoL in a narrow sense (2 and 3)

1. *Objective preconditions for QoL*

e.g., material preconditions, somatic or mental disease, psychosocial factors, medical treatment etc. that may increase or decrease QoL.

2. *The ability to act and function*

e.g., achievements provide an “objective” QoL that can best be evaluated from an external perspective.

3. *Well-being and satisfaction*

“Inner QoL is a subjective QoL that can best be evaluated by the child report, according to his/her own experience”.

The term “QoL” is a broader concept than the term “Health-related quality of Life” (HRQoL) and includes aspects of life such as family and school, as well as being independent of the symptoms impact (Varni et al. 2007; Rosenbaum 2009). The different concepts such as QoL, HRQoL, and well-being, as well as life satisfaction are often used in similar ways (Mattejat & Remschmidt 1998; Jozefiak et al. 2009b). Koot & Wallander (2001), state that an important differentiation in the concept of QoL has been the subjective and objective perspectives where the use has been the cause for discussions and is still an ongoing debate in QoL research.

Although there does not appear to be agreement on a single definition of QoL - “no gold standard”, there does appear to be a consensus that QoL is a multidimensional construct. There also appears to be a consensus of the importance of including the perspectives of both children and their parents’ evaluation when assessing the child’s QoL with respect to physical, psychological and social dimensions (Bowling 1999; Koot & Wallander 2001; Jozefiak et al. 2009b).

6.3.3.2 *Definition of QoL used for this study*

The empirical work in this thesis has been based primarily on the following definition of QoL in the child: “the subjective perceived well-being on the child’s physical and mental health, self-esteem, and on the different life domains such as school, family,

friends, hobbies and activities, as well as a global evaluation of QoL”. This definition is in agreement with the subjective component of Koot & Wallander’s (2001) definition of QoL as well as Matthejat & Renschmidt’s (1998) component of well-being and satisfaction experienced by children themselves. In accordance to the recommendations mentioned above, we also included the parents’ perspective, i.e. how parents evaluated the perceived well-being on behalf of their children on the life domains mentioned above.

6.3.3.3 QoL for children and adolescents surviving cancer

Since the improvement of cancer treatment and the survival of children with cancer, there has been an increased interest for QoL research in pediatric oncology (Koot & Wallander 2001). QoL is mainly considered as a result of an interaction between the individuals’ physical and psychological health, degree of independence and social relations. This type of research is rather new with several methodological challenges, in terms of assessment, methods and in the use of proxy informants (Baider et al 1996; Koot & Wallander 2001).

Since the QoL concept has developed to cover the individual’s well-being, happiness and satisfaction, a number of instruments aiming to assess the QoL of children with different chronic diseases, including cancer have consequently been developed (Ravens-Sieberer & Bullinger 2000; Varni et al. 2001; Matthejat & Renschmidt 1998, 2006; Upton et al. 2008). These instruments have different psychometric properties, which may explain why research on QoL for cancer survivors have shown conflicting results (Eiser et al. 2000; Baider et al. 1996; Zebrack & Zeltzer 2003; Packer 2008; Foster et al. 2009; McDougall et al., 2009; Sundberg et al. 2009; Zeltzer et al. 2009). A number of studies and reviews have reported adverse outcomes in QoL compared with healthy controls (Grant et al. 2006; Speechley et al. 2006; Stam et al. 2006).

Yet different studies began to focus on the “healthy” adaptation of families (Goggin et al. 1976; Kellerman et al. 1980; Elkin et al 1997; Humpl et al 2001). Apajasalo et al. (1996) showed a significantly better rating of QoL in childhood cancer survivors treated between 1961 and 1993 than a comparable group of the general population. The authors assumed that persons having survived a life-threatening disease presume their present

life more satisfying and regard possible lacking aspects of QoL less important. Other studies also concluded that QoL was satisfactory for the majority of long-term childhood cancer survivors (Langeveld et al. 2002; Zebrack & Chesler 2002; Langeveld et al. 2004; Shankar et al. 2005; Zeltzer et al. 2008; Servitzoglou et al. 2009; Sundberg et al. 2009; Zeltzer et al. 2009). Focus went from all obstacles to all possibilities where many studies reported a general positive coping among parents (Kupst & Schulman 1988; Greenberg et al. 1989; Speechly & Noh 1992; Dolgin et al. 1999; Patenaude & Kupst 2005).

Since there is no gold standard on how to obtain a comprehensive assessment of QoL for all children surviving cancer, more research is needed. Assessment of QoL in children with specific disorders should in all probability use different QoL instruments validated for children, as well as assessing QoL both from the child's subjective perception and from a proxy perspective. Comprehensive assessment of QoL for children surviving cancer is necessary to guide interventions and improve strategies to enhance the child's total functioning and well-being.

6.3.4 Social support

6.3.4.1 The concept of social support

In times of intense stress and as a means of coping to a threatening event, the tendency to come together and support each other is immense. The support of others can protect against adverse changes in mental and physical health that may otherwise occur in response to stress (Taylor 2007). Moreover, Taylor (2007) states that social support is now widely acknowledged in the scientific research field as a critical resource for managing stressful occurrences. Research demonstrates that social support effectively reduces psychological distress, such as depression or anxiety, during times of stress (Fleming et al. 1982; Sarason et al. 1997; Lin et al. 1999; Taylor 2007). Social support has been found to promote psychological adjustment to chronically stressful conditions, such as childhood leukaemia (Magni et al. 1986), among other disorders. Conversely, lack of social support during times of intense stress can increase psychological strain (Dunkel-Schetter et al. 1987; Taylor 2007).

In addition to providing psychosocial benefits, social support is also seen to contribute to physical health and survival. Social support appears to lower the likelihood of illness, as well as speed recovery from illness when it does occur (Kulik & Mahler 1993; Taylor 2007) and reduce psychological complications, problems or the risk of mortality due to serious disease (Taylor 2007).

Social support is typically measured in terms of either the structure of socially supportive networks or the functions that network members may provide (Wills 1998). Structural social support often includes social integration and involves the number and quality of social relationships in which an individual is involved. Functional social support is typically assessed in terms of the specific functions another person may serve (i.e. informational or emotional support) for an individual and the individual's coping strategies with a particular stressor.

Definitions of social support differ in their precision as well as their generality (Bloom 1996). Social support has been defined as the perception or experience that one is loved and cared for by others, esteemed and valued, and part of a social network of mutual assistance and obligations (Cobb 1976; Wills 1991; Taylor 2007). Others define social support as the individual's needs for affection, approval, belonging, and security being met by significant others (Kaplan et al. 1977). In any case, social support may come from a partner, relatives, friends, coworkers, social and community ties, and in some cases from a pet. Moreover, social support can be referred to the function and quality of social relationships, such as perceived availability of help or support actually received. Social support occurs through an interactive process and with a sense of obligation and perception of reciprocity (Wills 1991; Brown et al. 2003; Schwarzer & Knoll 2007; Taylor 2007).

6.3.4.2 Definition of Social Support used for this study

The empirical work in this thesis has been mainly based on the following definition of social support: "the function and quality of social relationships, such as perceived availability of help or support actually received." In this context, social support is given through professional collaboration in and between the hospital, home and school. This

definition of social support is in agreement with the components of perceived support and mutual obligations as defined by Taylor (2007).

6.3.4.3 Social Support for children and adolescents surviving cancer

Childhood cancer is considered one of the greatest challenges a family can face (Hoekstra-Weebers 1996) and families experiencing childhood cancer are confronted with many stressors throughout the course of illness. Some families cope well with the different stressors, others do not. The extent to which children and their families are able to deal with such challenges appears to be partly contingent on the support available from others (Lazarus 1984; Bloom 1996). The selection and implementation of coping strategies for the individual child is dependent on how much support they have in their family and their network around them (Reinfjell et al. 2007).

Studies have shown that satisfaction with social support can have a direct effect on well-being and serve as a buffer between the negative health consequences of a stressor and distress (or grief) (Hoekstra-Weebers 1996; Woodgate 1999a,b; Earle et al. 2005; Taylor 2007). One study (Miller 2002) even found a clear buffering effect of social support on individual's inflammatory process in chronic stress, also in parents of children with cancer. The presence of social support, both perceived and actual, may determine how well a family copes (Magni 1986; Kupst & Schulman 1988; Kupst et al. 1995) and how they assess their psychosocial health and QoL.

In the literature, social support and support systems, also in the form of collaboration and supervision are seen to help in preventing psychosocial problems (Morrow 1984; Fyrand 1994; Taylor 2007) thus, promoting psychosocial adjustment. Possible physical late effects and psychological problems in children surviving cancer suggest a need for follow-up care, social support and rehabilitation of these children and their families, as well as a need for collaboration between healthcare and other services (HOD 2004).

6.3.4.4 The Professional Collaborative Model (PCM)

From 1980 to 1986, a professional collaboration model was developed at the Department of Pediatrics, St. Olavs University Hospital, Trondheim as a means for

social support through professional collaboration for children with cancer and their families. In the development of the PCM, it was regarded important to have a method for social support giving long-term follow-up care and promoting optimal psychosocial health and QoL for children with cancer and their families. The PCM was therefore established as a relatively uncomplicated and low cost model for collaboration between the pediatric oncology unit (Department of Pediatrics, St. Olavs University Hospital) and the family's home community aiming to meet the needs of the individual child and its family. The main goal was to provide social support by securing a functional social network through the utilization of professional resources in the child's home community. Social support was provided to the child with cancer and its family by increasing professionals' knowledge of the individual family's needs and reactions through collaboration with the pediatric oncology unit and the family's home community. The PCM has two main components – the collaborative meeting (arranged and carried through at the pediatric oncology unit) and the support group (arranged and carried through in the child's home community).

The *collaborative meeting* was organized so the child, its parents, teachers and health professionals from the home community could meet with professionals at the pediatric oncology unit. This meeting was held while the child was admitted in the hospital, approximately one to two months after the child was diagnosed with cancer. The collaborative meeting was meant as a onetime meeting between professionals from the pediatric unit and professionals from the child's home community. This meeting was established in order to plan and coordinate further follow-up care as well as giving professionals from the child's home community the opportunity to visit the pediatric unit, its schooling facilities, and experience the child's everyday life at the hospital. Moreover, relevant information about the actual type of cancer, its treatment and prognosis was given. At the meeting a comprehensive overview of the family's situation was discussed and a plan acknowledged where the professionals' mutual responsibilities were identified. These discussions created the basis and goals for the support group, the next part of the model.

A *support group* was established and its main objective was to help, disburden and support affected families in their daily life in their home community. Parents of the

child with cancer and relevant professionals from the home community were members of this group. How often the support group meetings were organized was dependent upon the child's cancer diagnosis and treatment as well as the family's individual needs, but primarily extending until a year after completing treatment.

The PCM was systematically in use in Central Norway from 1990 to 1996 and was still actively in use in 2008, with only slight modifications. An evaluation of the model was undertaken in 1997, which included focus group interviews of professionals. Based upon the results of the focus group interviews, a questionnaire was developed and sent to eligible professionals as a supplement and further evaluation.

7 AIMS OF THE THESIS

This thesis comprises a two part study "part 1 and 2" where the aim was to explore social support, psychosocial health and QoL for children and adolescents surviving cancer.

The specific aim of **part 1** was to explore and describe social support in view of professionals' perception of collaboration. An additional aim was to evaluate the PCM in Central Norway taken into consideration the need to further develop and ensure the quality of supportive interventions necessary for rehabilitation for childhood cancer survivors.

In **part 2** the specific aim was to explore and describe psychosocial health and QoL of children and adolescents surviving cancer at least three years after their cancer diagnosis, compared with a healthy control group.

8 MATERIAL AND METHODS

8.1 Study Design

In **part 1** of this study both *quantitative and qualitative* research methods were applied. Eligible for participation were health and non-health professionals working with children diagnosed and treated with cancer at the Department of Pediatrics, St. Olavs University Hospital, Trondheim between 1.1.1990 and 31.12.1996. In this period, 130 children were diagnosed with cancer in Central Norway and of these were 46 excluded from the study due to: rare haematological diseases, histiocytosis and benign brain tumours treated only by surgery (n=10), families that had moved or did not wish to participate (n=11) and death (n=25). In total, 84 families with a surviving child were eligible and professionals caring for these children were identified on the basis of a letter sent to these families, asking the parents to indicate the names of the local hospital and of their general practitioner, public health nurse, teachers and other professionals in the community involved in the care of their child during and after their cancer diagnosis. They were also asked to give written consent so that their child could be registered in this study. Specifically concerning the qualitative approach in part one of this study, professionals caring for the child at St. Olavs University Hospital in Trondheim were identified from hospital records.

In **part 2** of this study a population-based, case-control study was carried out between April 2007 and May 2008 and included children and adolescents in Central Norway from the ages of six to 20 years who were diagnosed with cancer between 1.1.1993 and 1.1.2003. Eligible for participation were children who had completed their cancer treatment at the Department of Pediatrics, St. Olavs University Hospital, Trondheim, and survived at least three years after diagnosis. Data was collected by using questionnaires mailed to the respective families and the invited child's teacher, and by reviewing the child's medical records. A control group was recruited by asking children and adolescents in the study group to invite one friend of the same gender and age (\pm one year) to participate, as well as one of the friend's parents and teacher.

Questionnaires were sent to these invited families and teachers. A reminder was sent once to those who did not answer the first invitation.

8.2 Study population

In **part 1** of the *quantitative approach*, 56 families (67%) responded to the form sent to the 84 eligible families, which resulted in 142 eligible professionals from the families' home communities. A questionnaire addressing interdisciplinary collaboration was sent to these 142 eligible professionals from the child's home community, where 91 (64%) responded. Among non-health professionals 28 (of 40) schoolteachers and 4 (of 8) daycare teachers responded. Among health professionals 33 (of 40) public health nurses and 9 (of 33) general practitioners responded. In addition, 12 (of 13) registered nurses and 5 (of 8) medical doctors from the local hospitals responded (paper I).

In the *qualitative approach* of part 1, eligible participants were recruited for the focus group interviews among both professionals working in the Department of Pediatrics, St. Olavs University Hospital, Trondheim and in the child's home community. Due to practical and economical reasons, only professionals caring for children living in the immediate area around the city of Trondheim were invited to participate in the focus group interviews. Among the identified professionals from the child's home community, were nine participants from the child's home community invited to partake in the focus group interviews. In addition, 14 professionals caring for the child on the pediatric oncology unit were also invited to participate. Thus, a total of 23 professionals were asked to participate in focus group interviews. These 23 professionals were further divided into three focus groups which included participants representing the different professional categories in each group. There was an absence of five professionals because of illness, resulting in a total of 18 participants. The focus group interviews were arranged and took place on premises outside the hospital grounds. Each group interview met once and lasted approximately two hours or until there was no more relevant and forthcoming information (paper II).

Part 2 was based on children surviving cancer and a control group of children. For *children surviving cancer* there were a total of 50 (46%) children (of 109 eligible

children) who participated, as well as one of their parents. Of these 50 children, 29 (58%) were males and 21 (42%) females, aged 6-20 years and born in the period of 1987 to 2001. The median age was 12.5 years (interquartile range: 10.0-16.0), with 29 (58%) being adolescents (12-20 years). The children took part in this study 4-16 years (median: 7.5; interquartile range: 6.0-10.2) after their cancer diagnosis and 1-13 years (median: 6.0; interquartile range: 4.0-7.2) after completion of treatment. The group included children with leukaemia (n=20), malignant brain tumours (n=13), lymphoma (n=5) and other cancer tumours (n=12) (paper III and IV). Of the 50 parents, 45 consented to further contact the child's teacher, whereof 36 teachers responded (paper III).

Control children were recruited by asking the 50 families in the study group to give written consent to contact one friend to participate as a control in the study, 40 families gave written consent, and 29 (73%) peers (friend) and one of their parents agreed to participate. Of these 29 peers, were 15 (52%) males and 14 (48%) females, aged 6-20 years and born in the period between 1987 to 2001. The median age was 12.0 years (10-14.5), with 21 of the 29 (73 %) being adolescents. Of the 29 parents, 24 gave written consent to further contact the child's teacher and 19 teachers responded.

When comparing the control group with an extensive representative sample of children and parents from the general population in the same geographical area (paper IV) there were no significant differences shown in the total sum scores of the parent report for either the ILC (N=1777) or KINDL (N=1742). Furthermore, no significant differences were shown in the adolescent report for the ILC questionnaire (N=1032). However, a significant difference was found in the child report for the KINDL *Total quality of life* (N=1966), when comparing our control group with the general population (Mean (SD): 75.3 (8.2) and 70.6 (12.4) respectively; $p=0.011$).

There were no significant differences between children surviving cancer and the control group regarding the children's age and gender or in the parents' educational and economical status (Table 1). Mean socioeconomic status (SES) score was 3.8 (SD: 1.1) for parents of children with cancer, compared to 3.7 (SD: 1.2) in the control group ($p =$

0.8) (data not shown). Twelve (24%) children with cancer lived with single parents compared to two (7%) children in the control group ($p= 0.07$).

8.3 Methods

8.3.1 Part 1: Social Support – Quantitative and Qualitative approach

8.3.1.1 Quantitative approach – questionnaire (paper I)

A questionnaire was developed in two steps and based on the following: a) unstructured personal interviews with 18 professionals from the pediatric oncology unit and primary healthcare services and b) a pilot questionnaire tested among 10 professionals. The final version of the questionnaire included questions in the following areas:

1) How professionals' conceive and define collaboration; 2) Factors professionals considered characteristic as well as important for professional collaboration to function well; 3) Questions related to professionals' experience of the PCM's significance for the family as well as professionals' experience of the collaborative meeting and support group; 4) They were also asked to indicate the three most essential collaborating partners as well as being asked if they had received systematic supervision and 5) Questions related to collaboration between the pediatric oncology unit, Department of Pediatrics, St. Olavs University hospital and the family's home community.

8.3.1.2 Qualitative approach – focus group interviews (paper II)

Focus group, as a qualitative research method uses guided group discussions to generate a rich understanding of participants' experiences and beliefs (Kreuger 1998; Morgan 1998). Malterud (1996) emphasizes that focus group interviews function especially well if the researcher will learn of experiences, attitudes or meanings in a situation where many people collaborate.

Focus group interview was used as a method in this part of the study to evaluate the existing PCM. An interview guide was designed including topics of how professionals' perceived collaboration and what they considered important in collaborative care of

children with cancer and their families. Furthermore, the interview guide included questions about the value of the collaborative meeting and support groups, the two main components of the existing model. The discussions in the focus group interview were tape-recorded. One external and experienced moderator, recruited from the Norwegian Cancer Society, was used in all three groups and utilized the same interview guide.

8.3.2 Part 2: Psychosocial health, academic performance and QoL – Standardized questionnaires

Standardized questionnaires for data collection were used and administered to children and adolescents, their parents, and teachers. In addition, diverse background data was recorded, parents were asked to give information about demographic data (where and whom they lived with, number of children and marital status), and for children surviving cancer, their child's diagnosis, as well as their child's health status and late effects at the time of this study. Based upon these questions we defined a variable called late effects which included somatic health problems that could probably be related to the cancer diagnosis or its treatment. Somatic diagnoses and any psychological problems were collected from the child's medical records. Parents' socioeconomic status (SES) were calculated according to Hollingshead's two factor index of social position scaled one (low) to five (high), based on a combination of parents' education and occupation (Hollingshead 1958). Parents also evaluated their economical situation as "poor", "average" or "good".

8.3.2.1 Psychosocial health and academic performance

8.3.2.1.1 Strengths and Difficulties Questionnaire (SDQ) – Psychosocial health (paper III)

The Strengths and Difficulties Questionnaire (SDQ) (Goodman & Goodman 2009) is a brief behavioural screening questionnaire for children and adolescents aged 4-16 years (may be used up to 20 years). The SDQ was completed by the participants themselves, aged 12 years and older (self-report), while children and adolescents were also assessed by one of their parents (parent report) and teacher (teacher report). It includes 25 items (rated 0-1-2), constituting four problem scales (scored 0-10): Emotional symptoms,

Conduct problems, Hyperactivity, Peer problems, which are added to a Total difficulties score (0-40), and a Pro-social scale (scored 0-10). SDQ is a well-established questionnaire that has been tested for its reliability and validity in the Norwegian population (Heyerdahl 2003; Obel et al. 2004; Goodman & Goodman 2009).

The *Emotional symptoms scale* includes questions about headaches, stomach-aches, worrying, as well as if the child is unhappy, nervous or clingy, or has many fears or easily becomes scared. *Conduct problems scale* covers behavioural problems, “temper tantrums” or problems with lying or fighting. *Hyperactivity scale* includes questions regarding if the child is restless, overactive, fidgeting, being easily distracted or having a poor attention span. The *Peer problems scale* includes questions if the child is rather solitary, has problems with friendship or bullied. The *Pro-social scale* includes questions if the child is considerate of others, sharing with others and is helpful and kind.

8.3.2.1.2 *The Achenbach System of Empirically Based Assessment (ASEBA) - academic performance (paper III)*

The Achenbach System of Empirically Based Assessment (ASEBA) – Teacher Report Form (TRF) is a screening instrument on emotional and behavioural symptoms for ages 6 to 18 years (Achenbach & Rescorla 2001). We used the Academic Performance and Adaptive functioning scales of the ASEBA questionnaire. These items were completed by teachers who were familiar with the child’s functioning in school. The child’s academic performance was evaluated on a scale from 1 – 5 (1: far below grade level, 5: far above grade level). The adaptive characteristic questions were evaluated on a scale from 1 – 7 (1: much less, 7: much more) compared to typical pupils of the same age; covering working habits, learning capacity, behaviour and mood. ASEBA is a well-established questionnaire that has been tested for its reliability and validity in the Norwegian population (Nøvik 1999).

8.3.2.2 *Quality of Life (QoL)*

To gain a comprehensive picture of various aspects of QoL we used two different instruments; the Inventory of Life Quality in Children and Adolescents (ILC) (Mattejat

& Remschmidt 2006) and the Kinder Lebensqualität Fragebogen (KINDL) (Ravens-Sieberer & Bullinger, 2000) questionnaires. These instruments are developed for different research and clinical purposes and differ in items, content and length.

8.3.2.2.1 *The Inventory of Life Quality in Children and Adolescents (ILC) – QoL (paper IV)*

The Inventory of Life Quality in Children and Adolescents (ILC) questionnaire was developed in Germany by Matthejat et al. (1998, 2006) as a short and practical instrument assessing QoL over the past week and used in the field of child mental health issues. The ILC was translated into Norwegian according to international standards and approved by the original authors. The Norwegian version of the ILC for adolescents (aged 12-18 years and may be used up to 20 years) and their parents have shown satisfactory reliability (Jozefiak et al. 2008, Jozefiak et al. 2010). Both adolescent (self report) and parent (proxy report for children and adolescents from 4-20 years) versions were used in the present study. The questionnaire includes six items of life domains addressing the child/adolescent's perception of school performance, family functioning, friends and social integration, activities and hobbies, physical health, and the child's mental health. In addition, it includes one global QoL item ("All these things considered: How are you currently feeling?"). Each of the seven items are rated on a 1-5 scale (1=very good; 5= very bad).

Two types of scores were calculated from the ILC in our study: 1) The problem score (0-7) is computed by dichotomizing each of the seven items such that ratings of 1 or 2 (= 0) signify no problem and ratings of 3, 4, 5 (=1) signify the present problem. This problem score indicates the number of life domains perceived as problematic; 2) The QoL score LQ0-28 is calculated by multiplying the mean of the seven items by seven, and subtracting 35, thereby obtaining absolute values with a range of 0-28 (0= very low QoL and 28= very high QoL). In contrast to the subscale scores (seven life domains), low values for the QoL scale score correspond to a poor QoL, whereas a high QoL scale score indicates a very good QoL. The ILC has shown a moderate convergent validity with the KINDL (Child Self-report, general population, $r = 0.69$; $p < 0.01$; $n = 1961$) (Jozefiak 2008).

8.3.2.2.2 *The Kinder Lebensqualität Fragebogen (KINDL) – QoL (paper IV)*

The Kinder Lebensqualität Fragebogen (KINDL) (Ravens-Sieberer & Bullinger 2000) was developed for epidemiological use in healthy and clinical groups of children and adolescents aged 4 to 16 years. This questionnaire includes generic forms for several age groups (4-7, 8-12, and 13-16 years) as well as a proxy report for parents. In the present study we used the KINDL for children from 8 years to adolescents up to 20 years. The forms consist of 24 items equally distributed into the following six subscales: physical well-being, emotional well-being, self-esteem, family, friends and school. Each item addresses the child's experiences over the past week and is rated on a 5-point scale (1=never; 5=always). Mean scores are calculated for each of the six subscales as well as the total quality of life scale, which again are transformed to 0-100 scale (0=very low and 100=very high QoL). The KINDL questionnaire was completed by the participants themselves (self-report) as well as one of their parents (parent proxy report). The original KINDL showed satisfactory validity and reliability (www.Kindl.org). The Norwegian version, which had been translated according to international standards (Helseth & Jozefiak 2004) showed also satisfactory reliability (Jozefiak et al. 2008).

In all, the questionnaires in this study included 100 questions to be answered by one parent, 60 to be answered by the child/adolescent (or child by proxy/parent), 25 by the pre-school teacher and 36 questions by the school teacher. The number of questions equals that of a study successfully conducted in the same geographical area on QoL and mental health among low birth weight adolescents, their parents and their teachers (Indredavik et al. 2005).

8.4 Ethical considerations

In **part 1** the study was approved by the Regional Committee for Medical and Health Research Ethics in Central Norway for addressing parents and including professionals as participants (Ref. nr. 122-97). Parents gave written consent to contact professionals who were involved in the care of their child in their home community. It was emphasized that participating in the study was voluntary and that all information given would be treated confidentially and made anonymous.

In **part 2** ethical approval was obtained from the Regional Committee for Medical and Health Research Ethics in Central Norway (Ref.nr. 4.2006.2610), ensuring that the project did not violate the UN Convention of the Rights of the Child (CRC) (1991). Approval was given for a single written reminder, whereas permission was not given to get in touch with the individual families by telephone. Written consent to participate in the study, as well as access to the medical records of children surviving cancer, was given by the participant or by one of the child's parents, if the child was younger than 16 years of age. Families also gave written consent to contact the child's teacher and a friend of the same gender and age. Approval by the Norwegian Social Science Data Services (Ref.nr. 15372/JE) was obtained for a license to maintain a register containing personal data.

8.5 Statistical analyses

In the *quantitative approach* of **part 1**, SPSS for Windows version 11.0 (SPSS Inc, Chicago, IL) was used for data analysis. The raw data from the questionnaires were coded and divided into relevant themes based upon the study's purpose. All items were treated as categorical variables in the analyses. To compare differences in proportions between groups the chi-square test was used (Rosner 2000). P-values ≤ 0.05 were seen as statistically significant. Due to missing data, there are different "n" for the different questions (paper I).

In the *qualitative approach* the taped interviews were fully transcribed by an independent professional working in the field of computer sciences and information technology. To identify important themes from the focus group interviews, a thematic analysis from the raw material to the central findings was done independently by two of the authors (Eilertsen & Reinfjell) (Eilertsen et al. 2009) and an analysis model was designed (Kvale 1996; Thagaard 2002). Main themes in the material were arranged systematically to give meaning to the questions raised in the study (Kvale 1996; Krueger 1998). Analysis involved reading each transcript several times, noting all examples of meaning, comments and views in the context of the participants' discussions (Krueger 1998). These examples were then grouped into main categories based on the individuals' views and further grouped into common themes and sub-

themes giving a general overview (Kvale 1996). In the analysis we endeavoured to be loyal to the participant's original statement and meaning, not including information where there was uncertainty (Malterud 1996). It was important to gather an overview of collaboration generally, independent of the individuals' professions. Consequently, we did not state the professional category of the individual quotations (paper II).

In **part 2**, SPSS for Windows version 17.0 (SPSS Inc, Chicago, IL) was used for data analysis. Pearson correlation coefficient was used to study the association between the "number of years after diagnosis" and the SDQ Symptom Score (paper III). Spearman's correlations coefficient was used to study the correlation between the ILC *Total quality of life* scores on the self-report and on the parent proxy report (paper IV). In accordance with the SDQ (Goodman & Goodman 2009) and KINDL manuals (Ravens-Sieberer & Bullinger, 2000), and in order to compare our results with other studies, we have chosen to present location and distribution of the QoL scores as mean values and standard deviations, even if these were not normally distributed (paper III and IV). Group differences were analyzed using the Mann Whitney *U*-test. Group differences in proportions were analysed using Chi-square statistics. Although, many comparisons may increase the risk for type I error, we did not correct for multiple comparisons since we were primarily interested in comparing children surviving cancer with the control group and not comparing several sub-groups. Our results were coherent and such methods used for adjusting for multiple comparisons (i.e. Bonferroni correction) are conservative as well as likely to detract the results and would eventually increase the risk of making a type II error (Rothman 1990; Altman 1999; Rosner 2000; Bacchetti 2002). When data are not random numbers but actual observations, adjusting for multiple comparisons may lead to missing important findings (Rothman 1990). To compare scores obtained in the control group with a representative sample obtained from the general population we used one-sample T-Test. Two-sided p-values ≤ 0.05 were considered statistically significant.

9 MAIN RESULTS: SYNOPSIS OF PAPERS I-IV

9.1 Part 1

9.1.1 Paper I: Value of professional collaboration in the care of children with cancer and their families

In paper I the aim was to describe health and non-health professional's perception of interdisciplinary collaboration as well as their evaluation of a professional collaborative model for children with cancer and their families in Central Norway. Of professionals participating in this study (n=91) were 77% female, 68% had over 10 years of working experience, 65% were health professionals, consisting mainly of public health nurses and 35% were non-health professionals, consisting mainly of schoolteachers. Results will be given in percentage, for exact numbers see paper I.

9.1.1.1 Significance of Collaboration

Seventy-six percent of professionals that reported collaboration took care of the family's situation as a whole and 77% reported that collaboration broadened their own knowledge and perspectives. In addition, 47% of professionals experienced collaboration as timesaving, whereas 32% considered collaboration to be time-consuming. Health professionals rated doctors and non-health professionals rated teachers as being the most essential collaborating partners. Collectively, both health- and non-health professionals ranged nurses as the most essential collaborating partner. Over 75% of professionals regarded 'the will to collaborate' as the most important factor for a well functioning collaboration, as well as 'putting the necessary time aside' and 'having the knowledge of each professional's area of responsibility'. Eighty-eight percent of professionals considered collaboration between health and non-health professionals as being important for patients and their families. However, only 28% of professionals believed families were confident that involved professionals had the necessary information that was important for follow-up care.

9.1.1.2 Significance of the PCM in Central Norway

In all, 87% of professionals stated that collaboration with the pediatric oncology unit (Department of Pediatrics, St. Olavs University Hospital) functioned well, although there were more health professionals (92%) who emphasized this than non-health professionals (72%). Only 13% health and non-health professionals stated that collaboration did not function well. Overall, 90% of respondents emphasized the PCM for children with cancer as being a valuable method that can be conveyed to other sick children, especially with serious and chronic diseases.

Collaborative meeting

Forty percent of respondents had participated in the pediatric oncology unit's collaborative meeting; 60% of these were public health nurses and 82% believed they had received enough information to take the necessary responsibility for follow-up care in the family's home community.

Professional support group

Ninety-nine percent of respondents considered support groups as being an effective and systematic method for follow-up care. Forty-six percent had participated in a support group and 87% of these professionals considered such groups as helpful and valuable for both the child and their family. However, only 26% of professionals received systematic supervision.

This study concludes that health and non-health professionals regard collaboration as being valuable for follow-up care for children, their families and professionals themselves. The results suggest areas of potential improvement in the existing PCM.

9.1.2 Paper II: Professional collaboration – support for children with cancer and their families – focus group interview – a source of information and knowledge – professionals' perspective

The aim in paper II was to explore professional's perception of collaboration generally, and to evaluate the PCM as a support system for children with cancer and their families

in Central Norway. The main themes and sub-themes emerging from the focus group interviews are described as follows:

9.1.2.1 Professionals' perspectives of collaboration generally

Professionals working together can enhance knowledge

Participants stated that collaboration enabled professionals to make use of each other's knowledge and resources thus, giving better follow-up care.

Well-established routines and structure

To obtain a well-functioning collaboration, professionals emphasized the importance of having well-established routines and structure in their work. Participants also considered collaboration as a dynamic process. Collaboration however, could at times be experienced as time-consuming for professionals, impacting the team's ability to function at an optimal level.

The view of collaboration as experienced as time-consuming was reflected in the case where many diverse meetings were not chaired by a coordinator, ultimately undermining the responsibility of individual professionals.

9.1.2.2 Professionals' perspectives of collaboration through evaluation of the PCM

Valuable method for follow-up care of children with a chronic illness

The PCM was seen as uncomplicated follow-up support care system that could prevent possible psychosocial problems. The PCM was also seen as a follow-up system which could be conveyed to other sick children especially to those with serious and chronic diseases.

Collaborative meeting – Mutual information and responsibility

All involved professionals receiving the same information at an early stage of the child's diagnosis was expressed by participants as being important. Participants also expressed the importance of mutual responsibility for information between the various professionals and between institutions.

Support group – Systematic information and distribution of responsibility

Participants expressed that support groups provide systematic information as well as help and disburdening families of practical problems. They expressed that support groups increased knowledge and understanding to each professional, thus helping in preventing problems that might arise for the child, such as peer harassment. The support group could be helpful to professionals working with families by enabling mutual information, distribution of responsibility and giving a better understanding and insight into other professional occupations.

Supervision

Many professionals in the home community worked by themselves and were responsible for follow-up care of the child with cancer and its family. Supervision could be experienced as an important support system for these professionals. However, only a few of the professionals actually received systematic supervision at their place of work. Professionals expressed the need for more frequent contact with the pediatric oncology unit especially if the child's illness extended over many years.

This study concludes that professionals perceived the PCM as being a valuable support system for long-term planning of follow-up care. Participants emphasized however, the importance of having well-established routines, independent of an individual professional to enhance communication between professionals and to achieve a well-functioning collaboration.

In conclusion of Part 1 of this study it became clear that we needed more knowledge about psychosocial health and QoL in children surviving cancer to further develop the PCM and ensure the quality of supportive interventions necessary for follow-up care, social support and rehabilitation for childhood cancer survivors.

9.2 Part 2

9.2.1 Paper III: Psychosocial health in Children and Adolescents Surviving Cancer

The aim in paper III was to explore and describe psychosocial health of children and adolescents surviving cancer at least three years after their cancer diagnosis, compared with a healthy control group. On psychosocial health, children surviving cancer had significantly higher mean scores on the *SDQ total difficulties score* when assessed by their parents compared to the control group, especially among children surviving brain tumours ($p < 0.001$), but also leukaemia ($p = 0.05$). Teachers reported a higher total difficulties score for children with brain tumours than for control children ($p = 0.003$). There was no difference on the total difficulties score in the adolescent self-report, although the mean score for children with brain tumours was 14.1 (SD: 8.3) compared with 7.9 (SD: 3.8) in the control group ($p = 0.09$).

On the child's academic performance and total adaptive functioning (ASEBA teacher report) children surviving cancer had lower mean scores compared to control children, especially evident for children surviving brain tumours.

In children surviving cancer, twenty (40 %) parents indicated that their child had late effects, which was confirmed by the children's medical records. All 20 children with late effects (40% leukaemia, 45% brain tumours) had diverse physical problems, where of 16 of these 20 children (50% brain tumours and 38% leukaemia) also had various psychological problems. Children with late effects had higher SDQ mean scores than control children on the total difficulties, emotional symptoms, and peer problems scales, as reported by parents ($p < 0.001$), teachers ($p < 0.01$) and the adolescents themselves ($p < 0.05$). In addition, children surviving cancer who had late effects had higher SDQ mean scores than children surviving cancer *without* late effects on total difficulties,

emotional symptoms and peer problems scales, as reported by parents ($p<0.001$) and teachers ($p<0.01$), but only on peer problems scale on self reports ($p<0.05$). Adolescents without late effects showed a trend to higher mean scores on the emotional symptoms scale than adolescents in the control group ($p=0.07$). Academic performance, as well as several adaptive characteristics were scored lower (by teacher) for children surviving cancer who had late effects than for both children surviving cancer with no late effects ($p=0.005$) and control children ($p<0.001$).

Our study shows that children surviving cancer are at higher risk for emotional problems when compared with their friends, even after several years following diagnosis and treatment. Emotional symptoms were not only found among children with brain tumours and with late effects, but also leukaemia. We conclude that when planning long-term follow-up care, rehabilitation of children and adolescents with cancer should take into account their psychological functioning.

9.2.2 Paper IV: Quality of Life in Children and Adolescents Surviving Cancer

The aim for paper IV was to explore and describe QoL of children and adolescents surviving cancer at least three years after their cancer diagnosis, compared with a healthy control group. On QoL, measured by ILC, parents of children (6-20 years) surviving cancer reported a lower mean total score for their children on the *Quality of life scale*, compared to the control group. Moreover parents reported an increased number of domains as being problematic on the *Problem score*, compared to the control group. This finding was evident among parents of survivors as a group but also among survivors of brain tumours ($p<0.001$ for both scales) and leukaemia (*Quality of life scale* and *Problem scale*: $p<0.05$). However, on the adolescent self-report (12-20 years) this was evident for survivors with brain tumours (*Quality of life scale* and *Problem scale*: $p<0.05$), while no differences on the adolescent self-report were found for survivors as a group or with leukaemia, compared to their controls. Parents reported significantly lower global QoL (higher mean scores) for children surviving cancer as a whole ($p=0.005$), with brain tumours ($p<0.001$) as well as leukaemia ($p=0.05$), however no differences were found on the adolescent self-report.

Parents of children (8 to 20 years) surviving cancer with brain tumours, reported a significantly lower QoL (lower mean scores) on the *KINDL total quality of life scale* compared to the control group ($p < 0.01$). No differences were reported by children on the self-report. Parents of children surviving cancer reported lower mean scores (i.e. lower QoL) or a tendency to lower mean scores for their children on the *physical and emotional well-being*, as well as the *friends' subscales*. Parents' scores showed no significant findings on the *self-esteem, family or school subscales*. On the self report, only children surviving brain tumours reported lower mean scores on the *physical well-being* and *family subscales*.

Twenty (40 %) parents indicated that their child had late effects, where all 20 children had diverse physical problems and sixteen of these 20 children also had various psychological problems. Parents of children surviving cancer with late effects reported a significant lower QoL (lower mean scores) on the ILC as well as an increased number of domains perceived as problematic (higher mean scores) on the ILC problem scale, compared to the control group. Similar results were also reported on the adolescent self report. Moreover, children surviving cancer *with* late effects showed corresponding results on both the parent report as well as the adolescent self-report when compared to children *without* late effects. Furthermore, parents reported a significant difference and a lower QoL on the *KINDL total quality of life scale* for children surviving cancer *with* late effects compared to control children, as well as children surviving cancer *without* late effects. However on the self-report, children with late effects showed no significant difference on the *KINDL total quality of life scale* compared to control children, and only a statistical tendency was shown between children surviving cancer *without* and *with* late effects.

To improve the child's QoL we conclude that when planning long-term follow-up care, rehabilitation of children and adolescents with cancer, especially for children with brain tumours and with late effects, should take into account their subjectively perceived and proxy reported QoL, contributing to a richer and more comprehensive understanding from different informant perspectives.

10 DISCUSSION

This thesis comprises a two part study presented in four scientific papers. To enable further improvement of interventions necessary for long-term follow-up care, social support and rehabilitation the overall aim has been to add evidence to clinical experience in the profession and practice of nursing on social support, psychosocial health and QoL for children and adolescents surviving cancer.

In the following, a discussion of methodological strengths and limitations related to the total study, as well as a general discussion of the main findings presented in papers I – IV will be presented. Moreover, clinical implications of the findings, conclusions, and implications for research will also be presented. For more thorough discussions of the specific topics, the discussion sections in the different papers (I-IV) should be consulted.

10.1 Strengths and limitations

Each scientific method implies both strengths and weaknesses. Different methodologies were used to respond to the different aims of the study. Quantitative approaches convey a broad and general view of the phenomena, explaining the consistency (Ringdal 2007; Foss & Ellefsen 2002). On the other hand, qualitative approaches create data that provides a deeper and more comprehensive insight and understanding of the phenomena (Creswell 1998; Ringdal 2007; Foss & Ellefsen 2002). Today it is usual to use both quantitative and qualitative approaches to complement each other (Kvale 1996; Ringdal 2007). Each part of this study will have different strengths and limitations that will be discussed and reflected upon.

10.1.1 Part 1

The work in part 1 of this thesis was conducted using both quantitative and qualitative approaches, by the use of a questionnaire and focus group interviews.

The strength of the *quantitative approach* in part 1 (paper I) of this study is the comprehensive assessment of professional collaboration as a means of social support

and its direct relation in the PCM of follow-up care of children with cancer and their families. However, a potential limitation to our findings was the low response rate (64%), especially among general practitioners (27%). It would appear that the most probable reason to this low response rate was the difficulty of employing doctors over a longer period of time in rural areas in Norway, resulting in professionals moving away from the child's home community (Aarflot 1965; Grytten et al. 2000; Straume & Shaw 2010). Generalization of the results may be limited and must therefore be carefully interpreted, in particular to this group of professionals (general practitioners). Nevertheless, there were an acceptable number of nurses and teachers that responded to this questionnaire. Standardized questionnaires to explore professionals' view of collaboration were not used in this study and therefore may also be a potential limitation. However, the questionnaire (paper I) developed specifically for evaluating the PCM in this study was created and based on focus group interviews (paper II), as well as a pilot questionnaire tested by 10 professionals, and was therefore regarded as appropriate.

We are also aware of the use of professionals as informants and not the families themselves in part 1 of the quantitative approach may be a drawback. However, the focus in the first part of our study was to give a comprehensive assessment of social support through evaluation of the PCM in view of professionals' perception of collaboration, a topic which was related directly to professionals themselves. Children surviving cancer and their families were given a "voice" in part 2 of this study.

Strengths of the *qualitative approach* of part 1 (paper II) are the use of focus group interview giving depth, clarity and a greater understanding of the social context (Robinson 1999). Although focus group interview was the chosen method for gaining knowledge and meaning created in the individual group of participants, we were aware of the difficult balance that is often experienced with this type of method between allowing participants to set the agenda and holding focus on the topic chosen (Morgan 1998). Moreover, the small sample size (n=18), although usual for qualitative research (Earle et al. 2005), may be a limitation since meanings reflected by only a few may not reflect meanings by *all* professionals. Since the task of the moderator can be a contributing factor to researcher bias, the focus group interview was based on different

topics, rather than a structured questionnaire, reducing this type of bias. Moreover, researcher bias was also reduced by having an independent moderator, as well as being fully transcribed by an independent professional working in the field of computer sciences and information technology, with analysis done independently by two of the authors.

10.1.2 Part 2

Part 2 of this study is a cross-sectional, case-control study employing a quantitative approach and using standardized questionnaires. Based on the data obtained, the internal validity of scientific research is to what degree the conclusions drawn, are correct. The internal validity depends on the degree of chance, bias and confounding.

Strengths in part 2 are the comprehensive assessment of psychosocial health and QoL by children and adolescents surviving cancer, their parents (paper III and IV) and school teachers (paper III), as well as the inclusion of different childhood cancer survivor diagnoses and a healthy control group comprising of children and adolescents, parents (paper III and IV) and teachers (paper III). Moreover, SDQ, ASEBA, KINDL and ILC are well-established questionnaires that have shown satisfactory reliability and validity in former studies, also in Norway (Mattejat & Remschmidt 1998, 2006; Nøvik 1999; Ravens-Sieberer & Bullinger 2000; Achenbach & Rescorla 2001; Heyerdahl 2003; Obel et al. 2004; Helseth & Jozefiak 2004; Goodman & Goodman 2009; Jozefiak et al. 2008, 2010).

The observed differences found between children surviving cancer and controls were statistically highly significant, making chance an unlikely cause of the main findings.

A potential limitation is the low response rate (44%), although not uncommon in long term follow-up studies using mailed surveys (Langeveld et al., 2004; Fewtrell et al., 2008). We consider it less likely that the non-responders differed systematically from responders since there were no differences regarding background data such as age, gender or diagnoses. However, the limited number of participants, resulted in low power to demonstrate small differences between the groups, and lack of statistically

significant findings should therefore be interpreted with caution. To demonstrate small differences between children surviving cancer and the control group would require large numbers.

Although the main results were mainly consistent for emotional problems on all reports (paper III) some information bias cannot be ruled out since parents and teachers were aware of the cancer diagnosis and hence, may have overemphasized any problems in the case group. However, studies including diagnostic assessment of mental health in children with other chronic diseases such as cerebral palsy (Goodman & Graham 1996) and children of very low birth weight (Indredavik et al. 2005), found SDQ completed by parents to give reliable information about the children's mental health status, thus making information bias less likely.

Moreover, using friends (peers) as controls in part 2 (Elkin et al. 1997; Buizer et al. 2006) may introduce a methodological bias since peers are likely to share common interests (Eiser et al. 2000) and attitudes with the case group, and therefore may be more similar in terms of their subjective experience of psychosocial health and QoL. This bias would be expected to decrease the differences between groups, making it less likely to significantly affect our results. However, the control children's scores on the SDQ, ILC and KINDL questionnaires did not differ essentially from that of a representative sample from the general population in the same geographical area. Finally, an epidemiological study did not find significant differences between friends as controls or an "ideal" control group with respect to paternal age as well as maternal and paternal education, even if it was not considered an optimal control group (Xiaomei et al. 2004).

Key variables such as age, gender and parents' socioeconomic status did not differ between the group of children surviving cancer and controls, making confounding by these variables less likely. Moreover, multivariable analyses did not essentially change the results, the main results on the parent report of the SDQ emotional and total score persisted for brain tumour survivors and survivors with late effects (paper III).

Furthermore, even though there was a great variation between the years elapsed after the child's diagnosis (4-16 years), there was no significant correlation found between the "number of years after diagnosis" and the SDQ Symptom Score for parents (paper III).

The highly significant differences in mean scores between the case and control group as particularly reported by parents, may support a causal relation between aspects of the cancer diagnosis, its treatment and reduced psychosocial health and QoL. Our findings of lower QoL and higher emotional problem scores reported by parents and adolescents, especially in brain tumour survivors and survivors with late effects, are consistent with a number of previous studies and reviews of psychosocial functioning and QoL studies in childhood cancer survivors (Upton & Eiser 2006; Hudson et al. 2003; Oeffinger et al. 2008; Reinfjell et al. 2009; Grant et al. 2006; Speechley et al. 2006). Our findings are also consistent with studies in older age groups, using other outcome measures as well as other control groups (i.e. siblings) (Stam et al. 2006; Zeltzer et al. 2009). However, most studies found that on the whole, survivors of childhood cancer fare the same as others or even have a better QoL (Langeveld et al. 2002; Zebrack and Chesler 2002; Langeveld et al. 2004; Shankar et al. 2005; Zeltzer et al. 2008; Servitzoglou et al. 2009; Sundberg et al. 2009; Zeltzer et al. 2009) and function well psychologically (Gray et al. 1992; Elkin et al. 1997; Noll et al. 1997; Patenaude & Kupst, 2005; Meyerowitz et al. 2008). Yet, only a few studies had reported results by both parent proxy and adolescent self-report, compared with controls.

Our findings of more emotional problems, poorer academic performance and a lower QoL score with an increased number of domains perceived as problematic, were found among almost all survivors *with* physical late effects and psychological problems, compared with controls. We cannot rule out the consequences of long-term psychological strain on the individual as a result of the effects of the cancer disease and its treatment. Taken into consideration, these findings may support the suggestion of both a biological and a psychological source for emotional problems, poorer academic performance and a poorer QoL experience among children who have survived cancer. We are however unable to state if the cause is the ongoing physical problems, the cancer diagnosis and its treatment or a combination of the two. Somatic late effects can be caused by the child's cancer diagnosis (i.e. brain tumours; leukaemia), type and length of the cancer treatment (i.e. radiation, surgery, neurotoxic side effects of drugs, bone marrow transplant) and its complications (i.e. severe systematic infections, bleeding, scars) (Wallace & Green 2004; Eiser et al. 2007; Oeffinger et al. 2008). Psychological

problems of the cancer illness can be caused by the suffering caused from a life-threatening disease or its long-term, intensive and severe treatment. Long absences from normal social and school activities, which are consistent with cancer treatment, may also lead to more emotional problems, poorer academic performance and poorer QoL for the child (Eiser et al. 2007). Furthermore, inappropriate attitudes or approaches among other children and adults both at school and at home can influence their expectations of the child with cancer and how they treat them, which may contribute to more emotional problems, poorer academic performance and QoL for the child surviving cancer.

10.2 General discussion of the main findings

10.2.1 Social support in view of professional collaboration in the care of children with cancer and their families

Significance of professional collaboration

Results from both the *quantitative and qualitative approach* of this study showed that professionals regarded collaboration as a positive intervention for themselves and the families they cared for.

The professionals' positive attitudes towards the effects of collaboration were independent of any one profession. Moreover these attitudes were not dependent upon whether professionals experienced collaboration as time-consuming or timesaving. Professional's perceived collaboration as both taking care of the family's situation as a whole as well as broadening their own knowledge and perspectives as a professional. Results from this study can suggest that collaboration between professionals enhances working towards a common goal, thus profiting the family. Moreover, collaboration between professionals was highlighted as being important for providing the needed support and help to the individual family of a child with cancer or surviving cancer. Several studies also emphasized the importance of support systems for families in a difficult life situation, as well as for professionals caring for these families (Masera et al. 1998; Last et al. 2005).

In order to obtain a well-functioning collaboration, professionals in the present study emphasized the importance of having a well-structured collaboration such as well-established routines and organization in their work. Therefore, a well-functioning collaboration may suggest its dependence on a well-structured collaboration. Well-structured collaboration can give professionals an understanding and insight into the family's total life situation, consequently profiting the child and the family as a whole. This positive impact on the family can influence the family's perception of the social support they receive, contributing to their resilience and thereby focusing on their positive health (Haase 2004; Robinson et al. 2007). Moreover, well-structured collaboration can give professionals insight into each others professional working fields and thereby serve to broaden their own knowledge and perspectives, (Lauvås & Lauvås 2004; D'Amour et al. 2005; Berendsen et al. 2007; Ødegård 2007). Having well-established routines can contribute to a well-structured collaboration, such as the use of a coordinator in organizing follow-up care for the child and its family. A coordinator, independent of the individual's professional status, can contribute in giving each and every professional the same and necessary information needed for planning follow-up care.

Our findings however, show that professional collaboration can also have its limitations. Collaboration could at times be experienced as time-consuming for professionals often impacting the professional and team's ability to function at an optimal level, ultimately undermining the responsibility of the individual professional. This was clearly depicted where diverse meetings were chaired by many individuals, instead of by one coordinator. Not having a designated professional taking the lead to coordinate could result in individual professionals either not taking the necessary responsibility required or being unable to take the necessary responsibility for their own role in the follow-up care plan. Other studies and literature (Masera et al. 1998; Sommerschild 1998) suggest that the feeling of being responsible may promote individuals in obligating themselves, consequently helping professionals in performing better at their job. In order to make professional collaboration function well, it would therefore appear essential to have one professional take the lead and responsibility to coordinate the follow-up care plan for the child with cancer and their family. Moreover, several studies suggest that some

professionals are more interprofessionally orientated than others, affecting the amount of time they spend on collaboration (D'Amour et al. 2005; Last et al. 2005). Ødegaard (2007) emphasizes the difference between professionals' interest and time they spend on collaboration can be explained by their educational background, and often influenced by their organizational cultures or factors on the organizational level. It appears in our study that a well-functioning collaboration is often more dependent upon an individual's personal qualities, rather than their professional background. It would however, appear difficult to function in professional collaboration with unclear goals and a lack of structure.

Significance of the Professional Collaborative Model (PCM)

Professionals perceived the PCM as being a valuable support system for giving the necessary support and long-term follow-up care necessary for rehabilitation for children with cancer and their families. This follow-up care system integrated parents with the care team, allowing them to collaborate with the necessary professionals. Moreover and consistent with the literature (Last et al. 2005), professionals perceived the PCM to have relevance for rehabilitation of other seriously and chronically ill children as well.

Many studies include and highlight the importance of the individual family's participation with the medical staff (Oeffinger & Hudson 2004; Earle et al. 2005; Last et al. 2005). However, relevant studies discussing the organizational structure of such follow-up systems and their impact on the families have not been found. In a literature review by D'Amour et al. (2005), clients were recognized as the ultimate justification for collaborative care. The authors reported however, that none of the studies offered a detailed discussion of how to integrate clients into the care team. The collaborative model, in our study was seen as a relatively uncomplicated follow-up care system that could prevent possible psychosocial problems as well as integrating parents with the professional care team. Organization of collaborative meetings with the pediatric oncology unit and support groups in the home community, were considered significant in enabling parents to collaborate with the necessary professionals thus, giving the necessary support and follow-up care to each and every family.

In order to prevent psychosocial problems and promote a good QoL, our findings support the importance of establishing the collaborative meeting at an early stage of the child's illness and the family's crisis, a phase that is vulnerable for both children and their families (Patenaude & Kupst 2005). The importance of continuity at this early stage and later on in the collaborative process is also stressed for both the child and its family and each individual professional. However, the importance of information and mutual responsibility in collaborative meetings did not always function satisfactory and appear to be an area for improvement in the PCM.

Another aspect and significant component of the PCM is establishing a support group in the family's home community. Participants emphasized the importance of support groups as giving systematic information, preventing problems that could arise and offering support to the child and its family. Professionals emphasized that a well-functioning support group could contribute to better follow-up care allowing the sick child to stay at home as long as possible (without being admitted to the pediatric oncology unit), function on a daily basis and stay in contact with their family, friends and school. Studies emphasize the significance of support systems as being an important component for the family's adjustment and coping (Kupst et al. 1995; Robinson et al. 2007).

Participants in our study also stressed the importance of support groups as a source for professional help and replenishment, as well as giving better insight into other professionals' working fields. Many professionals were alone with the responsibility for follow-up care and only a minority of the professionals received supervision. Professionals experienced working alone as an extra strain and stress factor, possibly contributing to a lack of self-confidence. Professionals from the child's home community emphasized the need for more frequent contact with the pediatric oncology unit, especially when the child's illness extended over many years. The professionals wanted a more active role for the general practitioner, stating the importance of physician's role as a collaborative partner. The need for more frequent contact with the pediatric oncology unit, a more active role for the general practitioner, as well as the need for professional supervision may suggest an area of potential improvement for the PCM.

Nonetheless, after coming to an end in part 1 of this study, it became clear that we needed more knowledge about psychosocial health and QoL in children surviving cancer to further develop the PCM and ensure the quality of supportive interventions necessary for follow-up care, social support and rehabilitation for childhood cancer survivors.

10.2.2 Psychosocial health and quality of life for children and adolescents surviving cancer

Children surviving cancer had more emotional symptoms, higher total problem scores and poorer academic performance, than healthy controls. Emotional problems were consistently reported by parents, teachers and adolescents themselves, in particular for childhood survivors with brain tumours and late effects. Yet we found that adolescents surviving cancer on the whole reported equal QoL compared with healthy controls, while only adolescents surviving brain tumours and survivors with late effects reported a lower QoL and an increased number of QoL domains perceived as problematic, when assessed with the ILC. Parents however, reported an overall lower QoL and a greater number of QoL domains perceived as problematic for their children surviving cancer. Our findings of lower QoL and higher emotional problem scores are consistent with a number of previous studies and reviews of psychosocial functioning and QoL studies in childhood cancer survivors (Upton & Eiser 2006; Hudson et al. 2003; Oeffinger et al. 2008; Reinfjell et al. 2009; Grant et al. 2006; Speechley et al. 2006; Zelter et al. 2009).

Parent proxy and teacher proxy reports on psychosocial health

There were some notable differences in our findings between the parent and teacher report in the SDQ findings. While parents reported no difference in pro-social behaviour for survivors compared with controls, teachers suggested an abnormal pro-social behaviour for all survivors as well as survivors of brain tumours and leukaemia. Parent and teacher ratings in the present study are somewhat in contrast to the study by Upton & Eiser (2006) where parent ratings showed a significant difference in pro-social behaviour, while teacher ratings showed no significant difference. Upton & Eiser (2006) studied children with brain tumours exclusively and used British norms for comparison.

The lower mean score on the pro-social scale may reflect being less helpful and more unwilling to share with others, a possible and understandable consequence following the intense and long-term cancer treatment, which might be emphasized more by teachers than parents. In addition, cancer treatment can contribute to long absences from normal social and school activities, and consequently impair interaction with others. An adverse psychosocial development could have more impact and thus be more evident in a school setting than at home. Psychosocial support is therefore essential to promote optimal adjustment for the child and its family both at home and at school (Eilertsen et al. 2009).

Child, adolescent and parent proxy reports on psychosocial health and QoL

In general, children and adolescents surviving cancer in our study reported fewer psychosocial problems when assessed by the SDQ and compared to healthy controls than their parents did, when compared to control parents. These results are consistent with other studies of childhood cancer comparing parent and child ratings on the same measures (Eiser et al. 2000; Reinfjell et al. 2009).

There was a strong correlation between the ILC (total) QoL scores reported by parents and by their adolescent child, which was also consistent with other studies (Eiser et al. 1995; Sawyer et al. 1999; De Clercq et al. 2004; Russell et al. 2006; Upton et al. 2008), possibly suggesting that in the case of cancer, parents and adolescents share much of the same perspective. Moreover, our finding of lower QoL among children with brain tumours and late effects compared with controls were found for both parent proxy report and adolescent self-report. These results emphasize the need for addressing the issue of diagnosis and presence of late effects in QoL studies in childhood cancer survivors. Our results are consistent with other studies of reduced QoL among children surviving brain tumours (Upton et al. 2005; Cardarelli et al. 2006; Varni et al. 2007; Penn et al. 2009; Yoo et al. 2010), as well as among studies and reviews of late effects and QoL of childhood cancer (Pemberger et al. 2005; Calaminus et al. 2007; Eiser et al. 2007; Ishida et al. 2010, 2010).

Nevertheless, there were some considerable differences between the results obtained from parents and adolescents when compared with healthy controls, especially when assessed by the ILC. In general in this study, and in keeping with other QoL studies of childhood cancer comparing parent and child ratings with controls (Sawyer et al. 1999; Russell et al. 2006; Varni et al. 2007), adolescents as a group reported a QoL similar to controls, while parents reported an overall poorer QoL for both their children and adolescents surviving cancer compared to controls.

As stated earlier in 6.3.3.1. the subjective and objective perspectives of QoL has been the source for discussions, suggesting that parents and other adults can provide relevant and valid information on behalf of their children's emotional and behavioural problems and other aspects such as QoL. Earlier, were younger children seen as unreliable respondents, lacking both cognitive and linguistic skills to answer questionnaires (Jozefiak et al. 2009a; Eiser & Morse 2001) however, the child and adolescent's subjective perception on QoL has been emphasized in the later years (Eiser & Morse 2001).

The discrepancy on psychosocial health and QoL between the child and parent report for children surviving cancer compared with controls is most likely a consequence of the different perspectives about the child's health and well-being and not a question of which perspective is right or wrong (Varni et al. 2005; Upton et al. 2008; Jozefiak et al. 2008). Parents may vary in their awareness, sensitivity and tolerance of children's health concerns (Upton et al. 2008). In addition, the impact of the child's disease and actual problems may have an influence on the total burden of their parents' experience of stress (Angold et al. 1998; Jozefiak 2004; Davies et al. 2008) and thus, their perception of the child's psychosocial health and QoL. On the other hand, children living with a chronic illness may assess their own psychosocial health, QoL and possible problems differently, dependent upon their subjective experience of how they feel mentally and physically. Findings of good QoL in some survivors with late effects could be related to changes in the survivors' outlook on life resulting from the cancer experience (Apajasalo et al., 1996; Gray et al., 1992), a negative coping style resulting in compensating and overcompensating existing late effects (Apajasalo et al., 1996) or the existence of repressive coping in children (Phipps et al., 2001). Furthermore,

younger children have a limited cognitive capacity (Eiser & Morse 2001) and tend to live more in the present on a “here and now” level, not having the same sense of time as adults, consequently effecting their experience of how they feel mentally and physically. Many children may respond to stressors by repressing their own issues as an important defence mechanism for coping and possibly resulting in poorer psychosocial health and QoL, whereas other children and adolescents may show resilience and positive coping strategies (Woodgate 1999a,b; Borge 2010), which can result in increased growth and the potential for enhanced psychosocial health and QoL for children surviving cancer (Haase 1997; Woodgate 1999a,b). Sequentially, can improved psychosocial health and QoL lead to improved resilience to stressors (Woodgate 1999a,b; Haase 2004).

Therefore as stated by both Parsons (1999) and Upton et al. (2008), the main question is not essentially, “who is right?” but rather, “what does the parent proxy and self-report contribute to our further understanding of pediatric QoL?” If we take the latter question a step further, the most important question may be “how then can the information we receive from both the parent proxy and self-report about psychosocial health and QoL be used to guide and improve interventions enhancing the child’s total functioning and well-being?” (Rosenbaum 2009).

Thus, the difference in children and adolescent’s perspectives in this study also support emphasizing the need for obtaining information from both parents and children (Eiser & Morse 2001; Klassen et al. 2006; Wilson-Genderson et al. 2007). Obtaining information about psychosocial health and QoL provided by children and their parents is therefore important in contributing to a comprehensive understanding from different informant perspectives. Our results are in accordance with other studies reporting a discrepancy between the self-report and proxy-report in different clinical and general population studies (Theunissen et al. 1998; Chang & Yeh 2005; Yeh & Chang 2005; Jozefiak et al., 2008, 2010; Jozefiak 2009b). However, our study showed that comparing both psychosocial health and QoL child vs. proxy report *directly* in studies of children surviving cancer could be misleading without including a control group because of the discrepancies found between the different perspectives. With the use of both the child self-report and parent proxy report our results suggest that especially adolescents

surviving brain tumours and survivors of late effects have more psychosocial problems and an overall poorer QoL compared with a healthy control group.

As stated in 10.1.2., more psychosocial problems, poorer academic performance and a lower QoL score and an increased number of domains perceived as problematic, were found among almost all survivors *with* physical late effects than healthy controls. We can therefore not disregard the physical and psychological consequences of the cancer disease and its treatment. In various other studies suggesting that childhood cancer survivors function well psychologically (Zeltzer et al. 2009; Gray et al. 1992; Langeveld et al. 2002) despite a seemingly traumatic childhood experience, it was uncertain if these survivors suffered from late effects or not. The uncertainty to the cause of children's psychosocial problems, their poorer academic performance, as well as a lower QoL appears to be in agreement with Espnes & Smedslund (2009) biological, psychological and social factors of the BHIM, factors that may play a role in the cause and prevention of somatic late effects and psychological problems.

10.3 Implications for clinical practice

The results presented in this thesis document knowledge achieved through experience, thus increasing knowledge in the profession and practice of nursing in “evidence-based nursing,” emphasizing the need for long-term follow-up care for children and adolescents with cancer. Moreover, to improve the child's psychosocial health and QoL our results indicate the need to develop pertinent and adequate supportive interventions and programs when planning and implementing long-term follow-up care and rehabilitation (Rosenbaum 2009) of children and adolescents surviving cancer, especially for survivors with brain tumours, and those with late effects. Our results also indicate the need to take into account subjectively perceived and proxy reported psychosocial health and QoL for children surviving cancer.

The understanding of how cancer is experienced by childhood cancer survivors, as well as by their families is important to the practice of pediatric oncology, for nurses, medical doctors and other professionals in the collaborative team to offer the necessary guidance, support, and assistance in enhancing outcomes (Rosenbaum 2009) for

childhood cancer survivors and their families. In order to prevent maladjustments and promote optimal psychosocial health and QoL for children surviving cancer and their families, it is important that collaboration with children, adolescents and their parents as well as the professional collaborative team (in the hospital and in the child's home community) be established already at diagnosis. Establishing collaboration as early as possible after diagnosis is also vital in order to help teachers and friends of children with cancer cope with possible problems the child or the family may encounter in association with the cancer diagnosis and treatment. Professional collaboration and social support for children with cancer and their families should continue regularly during treatment and as follow-up care over time, since problems can be seen several years after diagnosis and treatment. In addition, support and follow-up care over a longer period of time can help nurses and other professionals to provide the appropriate care and help needed to achieve the common goal of best possible survivorship for each and every child and their family.

In further development of the PCM it will be necessary to focus on reducing the occurrence of late effects, as well as on helping children surviving cancer and their families cope with possible somatic late effects and psychosocial problems. Further development of adequate supportive interventions in the PCM may have some effect on the parent and child's ability to cope with cancer, thus reducing the prevalence of psychosocial problems and increasing each individual's QoL.

Moreover, in planning long-term follow-up care it will be important to emphasize the necessity of having well-structured collaboration, such as well-established routines, as well as establishing a coordinator for the individual families, thus enabling a well-functioning collaboration for professionals. It will also be essential to institute supervision for professionals, especially those working in the child's home community where professionals were often alone with the responsibility for follow-up care.

10.4 Conclusion

To improve the child's psychosocial health and QoL our results indicate that a collaborative approach is an important resource for social support and is essential in

planning and implementing the necessary interventions for long-term follow-up care and rehabilitation for children and adolescents with cancer, especially for survivors with brain tumours, and those with late effects. To gain a comprehensive understanding our results also show the need to particularly take into account subjectively perceived and proxy reported QoL, in addition to children and adolescents' psychological problems and psychosocial functioning.

10.5 Further research

Gaining knowledge leads to the understanding and need for gaining even more knowledge, "the more you learn, the more you realize how little you know" (Socrates, Plato). Further research is needed to obtain an even more comprehensive understanding of psychosocial health and QoL in survivors of childhood cancer, than we have today.

It can be suggested that further research is needed to provide more information about the significance of risk factors involved for children surviving cancer, as well as explore what contributes to long-term survivors' positive adaptation where focus be given to potential factors such as resilience and the significance this has for childhood cancer survivors and their psychosocial health and QoL.

More in-depth studies using self- and proxy reports, as well as studies using both quantitative and qualitative methods can help in the exploration of specific life domains that are important for children surviving cancer, thus improving their psychosocial health and QoL.

More attention should also be given to siblings, as well as parental stress and mental health of parents with a child surviving cancer and how this can influence the psychosocial health and QoL of the child surviving cancer.

A larger scale study is also needed to be able to further determine the influence of age, illness, and treatment variables giving a more comprehensive picture of the needs of the child surviving cancer.

Results gathered from these various studies can be used to promote and guide interventions, as well as improve strategies to enhance the child's psychosocial health and QoL and to provide the necessary social support for both the child and their family.

10.6 Closing comments

I would like to go back to the two quotations written at the beginning of the introduction of this thesis:

"Great is he who knows, but greater is he who knows where to ask" *Piet Hein*

"Knowing when you know something and knowing when you do not know something – that is knowledge" *Confucius*

It is my greatest desire that this research promotes to an increasing knowledge in the profession and practice of nursing in evidence-based nursing, which can contribute to optimal social support and rehabilitation necessary for children and adolescents surviving cancer and their families, as well as the professionals caring for them. In this study we have gained knowledge after asking the ones that could give us this knowledge: children and their families and the professionals working in close contact with them.

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150. Ketil Jarl Holen: THE ROLE OF ULTRASONOGRAPHY IN THE DIAGNOSIS AND TREATMENT OF HIP DYSPLASIA IN NEWBORNS.
151. Irene Hetlevik: THE ROLE OF CLINICAL GUIDELINES IN CARDIOVASCULAR RISK INTERVENTION IN GENERAL PRACTICE.
152. Katarina Tunòn: ULTRASOUND AND PREDICTION OF GESTATIONAL AGE.
153. Johannes Soma: INTERACTION BETWEEN THE LEFT VENTRICLE AND THE SYSTEMIC ARTERIES.
154. Arild Aamodt: DEVELOPMENT AND PRE-CLINICAL EVALUATION OF A CUSTOM-MADE FEMORAL STEM.
155. Agnar Tegnander: DIAGNOSIS AND FOLLOW-UP OF CHILDREN WITH SUSPECTED OR KNOWN HIP DYSPLASIA.
156. Bent Indredavik: STROKE UNIT TREATMENT: SHORT AND LONG-TERM EFFECTS
157. Jolanta Vanagaite Vingen: PHOTOPHOBIA AND PHONOPHOBIA IN PRIMARY HEADACHES

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158. Ola Dalsegg Sæther: PATHOPHYSIOLOGY DURING PROXIMAL AORTIC CROSS-CLAMPING CLINICAL AND EXPERIMENTAL STUDIES
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160. Christina Vogt Isaksen: PRENATAL ULTRASOUND AND POSTMORTEM FINDINGS – A TEN YEAR CORRELATIVE STUDY OF FETUSES AND INFANTS WITH DEVELOPMENTAL ANOMALIES.
161. Holger Seidel: HIGH-DOSE METHOTREXATE THERAPY IN CHILDREN WITH ACUTE LYMPHOCYTIC LEUKEMIA: DOSE, CONCENTRATION, AND EFFECT CONSIDERATIONS.
162. Stein Hallan: IMPLEMENTATION OF MODERN MEDICAL DECISION ANALYSIS INTO CLINICAL DIAGNOSIS AND TREATMENT.
163. Malcolm Sue-Chu: INVASIVE AND NON-INVASIVE STUDIES IN CROSS-COUNTRY SKIERS WITH ASTHMA-LIKE SYMPTOMS.

164. Ole-Lars Brekke: EFFECTS OF ANTIOXIDANTS AND FATTY ACIDS ON TUMOR NECROSIS FACTOR-INDUCED CYTOTOXICITY.
165. Jan Lundbom: AORTOCORONARY BYPASS SURGERY: CLINICAL ASPECTS, COST CONSIDERATIONS AND WORKING ABILITY.
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168. Eirik Skogvoll: CARDIAC ARREST Incidence, Intervention and Outcome.
169. Dalius Bansevicius: SHOULDER-NECK REGION IN CERTAIN HEADACHES AND CHRONIC PAIN SYNDROMES.
170. Bettina Kinge: REFRACTIVE ERRORS AND BIOMETRIC CHANGES AMONG UNIVERSITY STUDENTS IN NORWAY.
171. Gunnar Qvigstad: CONSEQUENCES OF HYPERGASTRINEMIA IN MAN
172. Hanne Ellekjær: EPIDEMIOLOGICAL STUDIES OF STROKE IN A NORWEGIAN POPULATION. INCIDENCE, RISK FACTORS AND PROGNOSIS
173. Hilde Grimstad: VIOLENCE AGAINST WOMEN AND PREGNANCY OUTCOME.
174. Astrid Hjelde: SURFACE TENSION AND COMPLEMENT ACTIVATION: Factors influencing bubble formation and bubble effects after decompression.
175. Kjell A. Kvistad: MR IN BREAST CANCER – A CLINICAL STUDY.
176. Ivar Rossvoll: ELECTIVE ORTHOPAEDIC SURGERY IN A DEFINED POPULATION. Studies on demand, waiting time for treatment and incapacity for work.
177. Carina Seidel: PROGNOSTIC VALUE AND BIOLOGICAL EFFECTS OF HEPATOCYTE GROWTH FACTOR AND SYNDECAN-1 IN MULTIPLE MYELOMA.

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178. Alexander Wahba: THE INFLUENCE OF CARDIOPULMONARY BYPASS ON PLATELET FUNCTION AND BLOOD COAGULATION – DETERMINANTS AND CLINICAL CONSEQUENCES
179. Marcus Schmitt-Egenolf: THE RELEVANCE OF THE MAJOR HISTOCOMPATIBILITY COMPLEX FOR THE GENETICS OF PSORIASIS
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183. Gunnar Morken: SEASONAL VARIATION OF HUMAN MOOD AND BEHAVIOUR
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187. Trude Helen Flo: RESEPTORS INVOLVED IN CELL ACTIVATION BY DEFINED URONIC ACID POLYMERS AND BACTERIAL COMPONENTS
188. Bodil Kavli: HUMAN URACIL-DNA GLYCOSYLASES FROM THE UNG GENE: STRUCTURAL BASIS FOR SUBSTRATE SPECIFICITY AND REPAIR
189. Liv Thommesen: MOLECULAR MECHANISMS INVOLVED IN TNF- AND GASTRIN-MEDIATED GENE REGULATION
190. Turid Lingaas Holmen: SMOKING AND HEALTH IN ADOLESCENCE; THE NORD-TRØNDELAG HEALTH STUDY, 1995-97
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192. Asbjørn Støylen: STRAIN RATE IMAGING OF THE LEFT VENTRICLE BY ULTRASOUND. FEASIBILITY, CLINICAL VALIDATION AND PHYSIOLOGICAL ASPECTS
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194. Guanglin Cui: FUNCTIONAL ASPECTS OF THE ECL CELL IN RODENTS
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198. Nanna Kurtze: THE SIGNIFICANCE OF ANXIETY AND DEPRESSION IN FATIGUE AND PATTERNS OF PAIN AMONG INDIVIDUALS DIAGNOSED WITH FIBROMYALGIA: RELATIONS WITH QUALITY OF LIFE, FUNCTIONAL DISABILITY, LIFESTYLE, EMPLOYMENT STATUS, CO-MORBIDITY AND GENDER
199. Tom Ivar Lund Nilsen: PROSPECTIVE STUDIES OF CANCER RISK IN NORD-TRØNDELAG: THE HUNT STUDY. Associations with anthropometric, socioeconomic, and lifestyle risk factors
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203. Asta Bye: LOW FAT, LOW LACTOSE DIET USED AS PROPHYLACTIC TREATMENT OF ACUTE INTESTINAL REACTIONS DURING PELVIC RADIOTHERAPY. A PROSPECTIVE RANDOMISED STUDY.
204. Sylvester Moyo: STUDIES ON STREPTOCOCCUS AGALACTIAE (GROUP B STREPTOCOCCUS) SURFACE-ANCHORED MARKERS WITH EMPHASIS ON STRAINS AND HUMAN SERA FROM ZIMBABWE.
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206. Li Lixin: ON THE REGULATION AND ROLE OF UNCOUPLING PROTEIN-2 IN INSULIN PRODUCING β -CELLS
207. Anne Hildur Henriksen: SYMPTOMS OF ALLERGY AND ASTHMA VERSUS MARKERS OF LOWER AIRWAY INFLAMMATION AMONG ADOLESCENTS
208. Egil Andreas Fors: NON-MALIGNANT PAIN IN RELATION TO PSYCHOLOGICAL AND ENVIRONMENTAL FACTORS. EXPERIMENTAL AND CLINICAL STUDIES OF PAIN WITH FOCUS ON FIBROMYALGIA
209. Pål Klepstad: MORPHINE FOR CANCER PAIN
210. Ingunn Bakke: MECHANISMS AND CONSEQUENCES OF PEROXISOME PROLIFERATOR-INDUCED HYPERFUNCTION OF THE RAT GASTRIN PRODUCING CELL
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213. Johan Haux: STUDIES ON CYTOTOXICITY INDUCED BY HUMAN NATURAL KILLER CELLS AND DIGITOXIN
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216. Jan Pål Loennechen: HEART FAILURE AFTER MYOCARDIAL INFARCTION. Regional Differences, Myocyte Function, Gene Expression, and Response to Cariporide, Losartan, and Exercise Training.
217. Elisabeth Qvigstad: EFFECTS OF FATTY ACIDS AND OVER-STIMULATION ON INSULIN SECRETION IN MAN
218. Arne Åsberg: EPIDEMIOLOGICAL STUDIES IN HEREDITARY HEMOCHROMATOSIS: PREVALENCE, MORBIDITY AND BENEFIT OF SCREENING.

219. Johan Fredrik Skomsvoll: REPRODUCTIVE OUTCOME IN WOMEN WITH RHEUMATIC DISEASE. A population registry based study of the effects of inflammatory rheumatic disease and connective tissue disease on reproductive outcome in Norwegian women in 1967-1995.
220. Siv Mørkved: URINARY INCONTINENCE DURING PREGNANCY AND AFTER DELIVERY: EFFECT OF PELVIC FLOOR MUSCLE TRAINING IN PREVENTION AND TREATMENT
221. Marit S. Jordhøy: THE IMPACT OF COMPREHENSIVE PALLIATIVE CARE
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223. Solveig Tingulstad: CENTRALIZATION OF PRIMARY SURGERY FOR OVARIAN CANCER. FEASIBILITY AND IMPACT ON SURVIVAL
224. Haytham Eloqayli: METABOLIC CHANGES IN THE BRAIN CAUSED BY EPILEPTIC SEIZURES
225. Torunn Bruland: STUDIES OF EARLY RETROVIRUS-HOST INTERACTIONS – VIRAL DETERMINANTS FOR PATHOGENESIS AND THE INFLUENCE OF SEX ON THE SUSCEPTIBILITY TO FRIEND MURINE LEUKAEMIA VIRUS INFECTION
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227. Vibeke Nossum: THE EFFECT OF VASCULAR BUBBLES ON ENDOTHELIAL FUNCTION
228. Sigurd Fasting: ROUTINE BASED RECORDING OF ADVERSE EVENTS DURING ANAESTHESIA – APPLICATION IN QUALITY IMPROVEMENT AND SAFETY
229. Solfrid Romundstad: EPIDEMIOLOGICAL STUDIES OF MICROALBUMINURIA. THE NORD-TRØNDELAG HEALTH STUDY 1995-97 (HUNT 2)
230. Geir Torheim: PROCESSING OF DYNAMIC DATA SETS IN MAGNETIC RESONANCE IMAGING
231. Catrine Ahlén: SKIN INFECTIONS IN OCCUPATIONAL SATURATION DIVERS IN THE NORTH SEA AND THE IMPACT OF THE ENVIRONMENT
232. Arnulf Langhammer: RESPIRATORY SYMPTOMS, LUNG FUNCTION AND BONE MINERAL DENSITY IN A COMPREHENSIVE POPULATION SURVEY. THE NORD-TRØNDELAG HEALTH STUDY 1995-97. THE BRONCHIAL OBSTRUCTION IN NORD-TRØNDELAG STUDY
233. Einar Kjelsås: EATING DISORDERS AND PHYSICAL ACTIVITY IN NON-CLINICAL SAMPLES
234. Arne Wibe: RECTAL CANCER TREATMENT IN NORWAY – STANDARDISATION OF SURGERY AND QUALITY ASSURANCE

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235. Eivind Witlø: BONE GRAFT AS AN ANTIBIOTIC CARRIER
236. Anne Mari Sund: DEVELOPMENT OF DEPRESSIVE SYMPTOMS IN EARLY ADOLESCENCE
237. Hallvard Lærum: EVALUATION OF ELECTRONIC MEDICAL RECORDS – A CLINICAL TASK PERSPECTIVE
238. Gustav Mikkelsen: ACCESSIBILITY OF INFORMATION IN ELECTRONIC PATIENT RECORDS; AN EVALUATION OF THE ROLE OF DATA QUALITY
239. Steinar Krokstad: SOCIOECONOMIC INEQUALITIES IN HEALTH AND DISABILITY. SOCIAL EPIDEMIOLOGY IN THE NORD-TRØNDELAG HEALTH STUDY (HUNT), NORWAY
240. Arne Kristian Myhre: NORMAL VARIATION IN ANOGENITAL ANATOMY AND MICROBIOLOGY IN NON-ABUSED PRESCHOOL CHILDREN
241. Ingunn Dybedal: NEGATIVE REGULATORS OF HEMATOPOIETIC STEM AND PROGENITOR CELLS
242. Beate Sitter: TISSUE CHARACTERIZATION BY HIGH RESOLUTION MAGIC ANGLE SPINNING MR SPECTROSCOPY
243. Per Arne Aas: MACROMOLECULAR MAINTENANCE IN HUMAN CELLS – REPAIR OF URACIL IN DNA AND METHYLATIONS IN DNA AND RNA
244. Anna Bofin: FINE NEEDLE ASPIRATION CYTOLOGY IN THE PRIMARY INVESTIGATION OF BREAST TUMOURS AND IN THE DETERMINATION OF TREATMENT STRATEGIES
245. Jim Aage Nøttestad: DEINSTITUTIONALIZATION AND MENTAL HEALTH CHANGES AMONG PEOPLE WITH MENTAL RETARDATION
246. Reidar Fossmark: GASTRIC CANCER IN JAPANESE COTTON RATS

247. Wibeke Nordhøy: MANGANESE AND THE HEART, INTRACELLULAR MR RELAXATION AND WATER EXCHANGE ACROSS THE CARDIAC CELL MEMBRANE

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248. Sturla Molden: QUANTITATIVE ANALYSES OF SINGLE UNITS RECORDED FROM THE HIPPOCAMPUS AND ENTORHINAL CORTEX OF BEHAVING RATS

249. Wenche Brenne Drøyvold: EPIDEMIOLOGICAL STUDIES ON WEIGHT CHANGE AND HEALTH IN A LARGE POPULATION. THE NORD-TRØNDELAG HEALTH STUDY (HUNT)

250. Ragnhild Støen: ENDOTHELIUM-DEPENDENT VASODILATION IN THE FEMORAL ARTERY OF DEVELOPING PIGLETS

251. Aslak Steinsbekk: HOMEOPATHY IN THE PREVENTION OF UPPER RESPIRATORY TRACT INFECTIONS IN CHILDREN

252. Hill-Aina Steffenach: MEMORY IN HIPPOCAMPAL AND CORTICO-HIPPOCAMPAL CIRCUITS

253. Eystein Stordal: ASPECTS OF THE EPIDEMIOLOGY OF DEPRESSIONS BASED ON SELF-RATING IN A LARGE GENERAL HEALTH STUDY (THE HUNT-2 STUDY)

254. Viggo Pettersen: FROM MUSCLES TO SINGING: THE ACTIVITY OF ACCESSORY BREATHING MUSCLES AND THORAX MOVEMENT IN CLASSICAL SINGING

255. Marianne Fyhn: SPATIAL MAPS IN THE HIPPOCAMPUS AND ENTORHINAL CORTEX

256. Robert Valderhaug: OBSESSIVE-COMPULSIVE DISORDER AMONG CHILDREN AND ADOLESCENTS: CHARACTERISTICS AND PSYCHOLOGICAL MANAGEMENT OF PATIENTS IN OUTPATIENT PSYCHIATRIC CLINICS

257. Erik Skaaheim Haug: INFRARENAL ABDOMINAL AORTIC ANEURYSMS – COMORBIDITY AND RESULTS FOLLOWING OPEN SURGERY

258. Daniel Kondziella: GLIAL-NEURONAL INTERACTIONS IN EXPERIMENTAL BRAIN DISORDERS

259. Vegard Heimly Brun: ROUTES TO SPATIAL MEMORY IN HIPPOCAMPAL PLACE CELLS

260. Kenneth McMillan: PHYSIOLOGICAL ASSESSMENT AND TRAINING OF ENDURANCE AND STRENGTH IN PROFESSIONAL YOUTH SOCCER PLAYERS

261. Marit Sæbø Indredavik: MENTAL HEALTH AND CEREBRAL MAGNETIC RESONANCE IMAGING IN ADOLESCENTS WITH LOW BIRTH WEIGHT

262. Ole Johan Kemi: ON THE CELLULAR BASIS OF AEROBIC FITNESS, INTENSITY-DEPENDENCE AND TIME-COURSE OF CARDIOMYOCYTE AND ENDOTHELIAL ADAPTATIONS TO EXERCISE TRAINING

263. Eszter Vanky: POLYCYSTIC OVARY SYNDROME – METFORMIN TREATMENT IN PREGNANCY

264. Hild Fjærtøft: EXTENDED STROKE UNIT SERVICE AND EARLY SUPPORTED DISCHARGE. SHORT AND LONG-TERM EFFECTS

265. Grete Dyb: POSTTRAUMATIC STRESS REACTIONS IN CHILDREN AND ADOLESCENTS

266. Vidar Fykse: SOMATOSTATIN AND THE STOMACH

267. Kirsti Berg: OXIDATIVE STRESS AND THE ISCHEMIC HEART: A STUDY IN PATIENTS UNDERGOING CORONARY REVASCULARIZATION

268. Björn Inge Gustafsson: THE SEROTONIN PRODUCING ENTEROCHROMAFFIN CELL, AND EFFECTS OF HYPERSEROTONINEMIA ON HEART AND BONE

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269. Torstein Baade Rø: EFFECTS OF BONE MORPHOGENETIC PROTEINS, HEPATOCYTE GROWTH FACTOR AND INTERLEUKIN-21 IN MULTIPLE MYELOMA

270. May-Britt Tessem: METABOLIC EFFECTS OF ULTRAVIOLET RADIATION ON THE ANTERIOR PART OF THE EYE

271. Anne-Sofie Helvik: COPING AND EVERYDAY LIFE IN A POPULATION OF ADULTS WITH HEARING IMPAIRMENT

272. Therese Standal: MULTIPLE MYELOMA: THE INTERPLAY BETWEEN MALIGNANT PLASMA CELLS AND THE BONE MARROW MICROENVIRONMENT

273. Ingvild Saltvedt: TREATMENT OF ACUTELY SICK, FRAIL ELDERLY PATIENTS IN A GERIATRIC EVALUATION AND MANAGEMENT UNIT – RESULTS FROM A PROSPECTIVE RANDOMISED TRIAL

274. Birger Henning Endreseth: STRATEGIES IN RECTAL CANCER TREATMENT – FOCUS ON EARLY RECTAL CANCER AND THE INFLUENCE OF AGE ON PROGNOSIS

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276. Mansour Akbari: HUMAN BASE EXCISION REPAIR FOR PRESERVATION OF GENOMIC STABILITY
277. Stein Sundstrøm: IMPROVING TREATMENT IN PATIENTS WITH LUNG CANCER – RESULTS FROM TWO MULTICENTRE RANDOMISED STUDIES
278. Hilde Pleym: BLEEDING AFTER CORONARY ARTERY BYPASS SURGERY - STUDIES ON HEMOSTATIC MECHANISMS, PROPHYLACTIC DRUG TREATMENT AND EFFECTS OF AUTOTRANSFUSION
279. Line Merethe Oldervoll: PHYSICAL ACTIVITY AND EXERCISE INTERVENTIONS IN CANCER PATIENTS
280. Boye Welde: THE SIGNIFICANCE OF ENDURANCE TRAINING, RESISTANCE TRAINING AND MOTIVATIONAL STYLES IN ATHLETIC PERFORMANCE AMONG ELITE JUNIOR CROSS-COUNTRY SKIERS
281. Per Olav Vandvik: IRRITABLE BOWEL SYNDROME IN NORWAY, STUDIES OF PREVALENCE, DIAGNOSIS AND CHARACTERISTICS IN GENERAL PRACTICE AND IN THE POPULATION
282. Idar Kirkeby-Garstad: CLINICAL PHYSIOLOGY OF EARLY MOBILIZATION AFTER CARDIAC SURGERY
283. Linn Getz: SUSTAINABLE AND RESPONSIBLE PREVENTIVE MEDICINE. CONCEPTUALISING ETHICAL DILEMMAS ARISING FROM CLINICAL IMPLEMENTATION OF ADVANCING MEDICAL TECHNOLOGY
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285. Kristin Gabestad Nørsett: GENE EXPRESSION STUDIES IN GASTROINTESTINAL PATHOPHYSIOLOGY AND NEOPLASIA
286. Per Magnus Haram: GENETIC VS. ACQUIRED FITNESS: METABOLIC, VASCULAR AND CARDIOMYOCYTE ADAPTATIONS
287. Agneta Johansson: GENERAL RISK FACTORS FOR GAMBLING PROBLEMS AND THE PREVALENCE OF PATHOLOGICAL GAMBLING IN NORWAY
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289. Charlotte Björk Ingul: QUANTIFICATION OF REGIONAL MYOCARDIAL FUNCTION BY STRAIN RATE AND STRAIN FOR EVALUATION OF CORONARY ARTERY DISEASE. AUTOMATED VERSUS MANUAL ANALYSIS DURING ACUTE MYOCARDIAL INFARCTION AND DOBUTAMINE STRESS ECHOCARDIOGRAPHY
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292. Ottar Bjerkeset: ANXIETY AND DEPRESSION IN THE GENERAL POPULATION: RISK FACTORS, INTERVENTION AND OUTCOME – THE NORD-TRØNDELAGE HEALTH STUDY (HUNT)
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296. Paul Jarle Mork: MUSCLE ACTIVITY IN WORK AND LEISURE AND ITS ASSOCIATION TO MUSCULOSKELETAL PAIN
297. Björn Stenström: LESSONS FROM RODENTS: I: MECHANISMS OF OBESITY SURGERY – ROLE OF STOMACH. II: CARCINOGENIC EFFECTS OF *HELICOBACTER PYLORI* AND SNUS IN THE STOMACH
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301. Arne Skjold: MAGNETIC RESONANCE KINETICS OF MANGANESE DIPYRIDOXYL DIPHOSPHATE (MnDPDP) IN HUMAN MYOCARDIUM. STUDIES IN HEALTHY VOLUNTEERS AND IN PATIENTS WITH RECENT MYOCARDIAL INFARCTION
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306. Lilian Leistad: THE ROLE OF CYTOKINES AND PHOSPHOLIPASE A₂S IN ARTICULAR CARTILAGE CHONDROCYTES IN RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS
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308. Mathias Toft: GENETIC STUDIES OF LRRK2 AND PINK1 IN PARKINSON'S DISEASE
309. Ingrid Løvold Mostad: IMPACT OF DIETARY FAT QUANTITY AND QUALITY IN TYPE 2 DIABETES WITH EMPHASIS ON MARINE N-3 FATTY ACIDS
310. Torill Eidhammer Sjøbakk: MR DETERMINED BRAIN METABOLIC PATTERN IN PATIENTS WITH BRAIN METASTASES AND ADOLESCENTS WITH LOW BIRTH WEIGHT
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313. Anne Brantberg: FETAL AND PERINATAL IMPLICATIONS OF ANOMALIES IN THE GASTROINTESTINAL TRACT AND THE ABDOMINAL WALL
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315. Elin Tollefsen: RESPIRATORY SYMPTOMS IN A COMPREHENSIVE POPULATION BASED STUDY AMONG ADOLESCENTS 13-19 YEARS. YOUNG-HUNT 1995-97 AND 2000-01; THE NORD-TRØNDELAG HEALTH STUDIES (HUNT)
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317. Heidi Knobel: FATIGUE IN CANCER TREATMENT – ASSESSMENT, COURSE AND ETIOLOGY
318. Torbjørn Dahl: CAROTID ARTERY STENOSIS. DIAGNOSTIC AND THERAPEUTIC ASPECTS
319. Inge-Andre Rasmussen jr.: FUNCTIONAL AND DIFFUSION TENSOR MAGNETIC RESONANCE IMAGING IN NEUROSURGICAL PATIENTS
320. Grete Helen Bratberg: PUBERTAL TIMING – ANTECEDENT TO RISK OR RESILIENCE ? EPIDEMIOLOGICAL STUDIES ON GROWTH, MATURATION AND HEALTH RISK BEHAVIOURS; THE YOUNG HUNT STUDY, NORD-TRØNDELAG, NORWAY
321. Sveinung Sørhaug: THE PULMONARY NEUROENDOCRINE SYSTEM. PHYSIOLOGICAL, PATHOLOGICAL AND TUMOURIGENIC ASPECTS
322. Olav Sande Eftedal: ULTRASONIC DETECTION OF DECOMPRESSION INDUCED VASCULAR MICROBUBBLES
323. Rune Bang Leistad: PAIN, AUTONOMIC ACTIVATION AND MUSCULAR ACTIVITY RELATED TO EXPERIMENTALLY-INDUCED COGNITIVE STRESS IN HEADACHE PATIENTS
324. Svein Brekke: TECHNIQUES FOR ENHANCEMENT OF TEMPORAL RESOLUTION IN THREE-DIMENSIONAL ECHOCARDIOGRAPHY
325. Kristian Bernhard Nilsen: AUTONOMIC ACTIVATION AND MUSCLE ACTIVITY IN RELATION TO MUSCULOSKELETAL PAIN
326. Anne Irene Hagen: HEREDITARY BREAST CANCER IN NORWAY. DETECTION AND PROGNOSIS OF BREAST CANCER IN FAMILIES WITH *BRCA1* GENE MUTATION

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