

From THE DEPARTMENT OF WOMEN'S AND CHILDREN'S  
HEALTH, CHILDHOOD CANCER RESEARCH UNIT  
Karolinska Institutet, Stockholm, Sweden

**THE EFFECTS OF PARENTING A CHILD DIAGNOSED WITH  
CANCER: DISTRESS, RESILIENCE AND VITAL EXHAUSTION**

*LIVING WITH DEATH IN YOUR FACE*

Eygló Guðmundsdóttir



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THE EFFECTS OF PARENTING A CHILD DIAGNOSED WITH CANCER: DISTRESS,  
RESILIENCE AND VITAL EXHAUSTION  
LIVING WITH DEATH IN YOUR FACE

THESIS FOR DOCTORAL DEGREE (Ph.D.)

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To my three most important persons in life:

Nikulás Ingi (a.k.a. Nikki), Hrafnhildur Tekla

(a.k.a. Krumma) and Benjamín Nökkvi (a.k.a.

Benjó). YOU ROCK!!!



# ABSTRACT

## Study I

*Aim.* Studies of parental reactions to a child's cancer have traditionally been carried out within the framework of psychiatry and psychopathology. We studied the significance of individual resource factors strengthening parents' resilience to long-term cancer-related distress, a focus that has rarely been used.

*Participants and methods.* The two-nation Nordic sample included 333 parents; 159 of whom had experienced a child's cancer, and 174 reference parents. We studied the sense of coherence (SOC) using the SOC-13 questionnaire. For assessing distress reactions we used a primarily illness-specific 11-dimensional Parental Psychosocial Distress in Cancer (PPD-C) self-report questionnaire developed for use with parents of childhood cancer patients, and the General Health Questionnaire (GHQ). Resilience was defined as absence of/less severe distress.

*Results.* Low SOC was significantly associated with more severe distress in all dimensions of the PPD-C and GHQ. The influence of SOC varied with parents' gender, showing a stronger modifying influence among mothers. Mothers and fathers also differed in their utilization of professional psychosocial support when confronted with the child's cancer.

*Conclusion.* Parental resilience to cancer-related distress varies with identifiable strength factors. A strengths-oriented approach helps in understanding parental adjustment to childhood cancer. Addressing resilience helps to identify parents at risk and in need of professional support when faced with a child's cancer.

## Study II

*Aim.* Determining the incidence of disease-related distress symptoms in parents from two treatment sites: a large specialized childhood cancer (CC) center in Sweden and a smaller pediatric unit in Iceland. The two groups were compared by considering differences in center type and care organization.

*Methods.* Participants were 306 parents of 188 CC patients, in- or off-treatment. Illness-specific distress was assessed using the multi-dimensional Parental Psychosocial Distress in Cancer (PPD-C) questionnaire. General psychiatric symptoms were assessed using the General Health Questionnaire (GHQ-12). Swedish and Icelandic groups were compared and outcomes studied with regard to site characteristics. Parents in the general population served as a reference group.

*Results.* Distress outcomes in both clinical groups exceeded the levels of the reference group. Systematic differences were evident between the parent groups, Icelandic parents scoring higher on 5 of the 11 distress subscales in the PPD-C and in a majority of the illness-specific domains.

*Conclusions.* Distress outcomes exceeding those of the comparison group were indicated in both clinical groups. Significant distress differences were demonstrated between the Swedish and the Icelandic parents. Analysis of the outcomes indicates that center type and related differences in patient influx rate and local organization of care are viable explanations for these findings. Methods are proposed for enhancing family care at small centers in order to compensate for conditions associated with burden of parents of children with cancer.

### Study III

*Aim.* Assessment of levels of symptoms of Vital Exhaustion (VE) in childhood cancer (CC) parents and its relationship to Traumatic Stress Symptoms (TSS) is a necessary prerequisite for developing support programs.

*Methods.* Participants were 471 Swedish and Icelandic parents of CC patients diagnosed between the years 1986-2007. Our reference group comprised of 174 parents of children without any known chronic or lethal disease. Parental Vital Exhaustion was assessed using the Maastricht Questionnaire (MQ-21) and Traumatic stress symptoms assessed using the Impact of Events Scale-Revised (IES-R).

*Result.* Comparison of parents in the clinical and non-clinical groups (NCG) revealed a significantly higher mean level of VE score in the clinical group. There was also a significant difference in MQ mean score between males and females in the clinical group, women having a higher mean MQ total score than men, but no such difference was evident in the non-clinical group. Time from diagnosis significantly affected VE scores. Type of child cancer diagnosis also affected levels of VE scores, although non-significantly ( $p=0.55$ ), while the number of differential treatments had no significant effect on levels of VE. Analysis of MQ and IES-R total scores demonstrated a strong relationship between VE and TS. Further analysis of subscales indicated a correlation between MQ total score and symptoms of Intrusion ( $r.536 - p<0.001$ ), Avoidance ( $r.463 - p<0.001$ ) and symptoms of Hyperarousal ( $r.692 - p<0.001$ ).

*Conclusion.* Due to their elevated levels of VE, parents of children diagnosed with cancer could be at risk of developing other physical conditions (e.g. cardiovascular disease) as apparent in studies of other populations in which VE scores are elevated, in addition to other known psychological consequences. These results may therefore add to further knowledge and understanding of the complexity and diversity of childhood cancer-related parental burden over time that needs attention in care and long-term follow-up.

## LIST OF SCIENTIFIC PAPERS

- I. Gudmundsdóttir, E., Schirren, M., Boman, K. K. (2011). Psychological resilience and long-term distress in Swedish and Icelandic parents' adjustment to childhood cancer. *Acta Oncol*, 50(3), 373-380.
- II. Gudmundsdóttir, E., Hörnquist, L., & Boman K. K. (2013). Psychological outcomes in Swedish and Icelandic parents following a child's cancer—in the light of site-related differences - *Support Care Cancer*, 21:1637–1645
- III. Gudmundsdóttir, E., Harris, R. A., Gísladóttir, B., Lindahl Norberg, A. Parental Vital Exhaustion in the aftermath of a child's cancer diagnosis (manuscript)

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## LIST OF ABBREVIATIONS

ALL	Acute lymphoblastic leukaemia
AML	Acute myeloid leukaemia
ANOVA	Analysis of variance
CC	Childhood cancer
CNS	Central nervous system
FANOVA	Factorial analysis of variance
GHQ-12	General Health Questionnaire
IES-R	Impact of Event Scale-Revised
MQ	Maastricht Questionnaire
NHL	Non-Hodgkin's lymphoma
PPD-C	Parental Psychosocial Distress in Cancer
PTSD	Post Traumatic Stress Disorder
SOC	Sense of coherence
SOC-13	Sense of Coherence Scale
SPSS	Statistical Package for Social Sciences
TSS	Traumatic Stress Symptoms
VE	Vital Exhaustion

*I looked at the doctor's face and I knew she was coming with bad news. "The sentence "your son has cancer" had not even crossed my mind, I mean a 9-week-old child doesn't get a lethal disease, I mean, not for real, not in MY world, just something that happens to "other" people.*

*"According to the white-bloodcounts of 250.000 this might be Leukemia....but as I said I can't confirm nothing, you just have to wait."*

*I handed over Benjamín into my mother's arms, went out of the room to call my husband, the moment he answered I sank down to the floor. Sitting on the floor at the Children's Emergency Unit, sobbing and trying to put some words together to a sentence the soft blanket of blackout wraps itself around my brain, cotton-wrapping all feelings of that I'm on the edge of death because people can't really survive if they lose their children?!"*



# INTRODUCTION

## OVERVIEW

Although a rare disease and despite improvements in efficient treatment (Gustafsson, Heyman, & Vernby, 2007; Howlader, Noone, Krapcho, Miller, Bishop, Altekruse *et al.*, 2010), childhood cancer is still one of the most leading causes of death in children in developed countries, being the fourth most common cause of death of children under the age of 20 after accidental death, birth defects and deliberate harm (Centers for Disease Control and Prevention (CDC), 2007).

Learning that one's child has a potential lethal disease such as paediatric cancer should be understood as an extraordinarily distressing event for parents (Valdimarsdottir, Kreicbergs, Hauksdottir, Hunt, Onelov, Henter *et al.*, 2007; Wakefield, McLoone, Butow, Lenthen, & Kohn, 2011), the cancer diagnosis constituting a parental stressor that existentially threatens the conception of life as predictable and safe, and for most parents is followed by the immediate fear of losing their child. The cancer diagnosis of one's child can thus be understood as being a highly traumatic experience from a parental point of view.

Furthermore, the changes to everyday life following a child's cancer diagnosis requires coping with a suddenly altered life-situation characterised by strain, escalated situational stress and heightened parenting demands, these components adding to an already extraordinary stressful situation (Boman, Viksten, Kogner, & Samuelsson, 2004; Dixon-Woods, Findlay, Young, Cox, & Heney, 2001; Giammona, & Malek, 2002; Kazak, 1998; Santacroce, 2002; Van Dongen-Melman, Pruyn, De Groot, Koot, Hahlen, & Verhulst, 1995).

Results from earlier studies on parental reactions associated with their child's cancer diagnosis indicate that subsequent to the shock of the child's unexpected and life-threatening cancer diagnosis, many parents experience feelings of uncertainty concerning the final outcome of the child's treatment but also regarding different physical and psychological sequelae possibly followed by an invasive cancer treatment. Taken together, earlier studies have demonstrated that the diagnosis of a child's cancer evokes a period of multifaceted stressors for the parents of the sick child. For some parents these escalated symptoms of distress are still persistent several years after the child's successfully completed treatment (Boman, Lindahl, & Björk, 2003; Gudmundsdottir, Hörnqvist, & Boman, 2013; Howlader *et al.*, 2010; Kazak, Lindahl-Norberg, & Boman, 2008; Ljungman (L), Hovén, Ljungman (G), Cernvall, & von Essen, 2015; Stuber, Barakat, Meeske, Guthrie, & Meadows, 1998; Stuber,

Christakis, Houskamp, & Kazak, 1996; Vrijmoet-Wiersma, Egeler, Koopman, Norberg, & Grootenhuis, 2009; Van Dongen-Melman *et al.*, 1995).

In the field of occupational psychology the state of excessive levels of long-term psychological distress is commonly known as ‘burnout,’ referring primarily to employees experiencing a state of exhaustion after working in persistent stressful situations for extended periods of time (Freudenberger, 1974; Hobfoll, & Freedy, 1993; Lazarus, 1966; Melamed, Ugarten, Shirom, Kahana, Lerman, & Froom, 1999). Related to burnout (Freudenberger, 1974) is the condition termed ‘Vital Exhaustion’ described in the medical field by Ad Appels (e.g. 1987). This condition has been studied in medicine, primarily in the field of cardiovascular diseases, scientific findings indicating an association of chronic burnout with cardiovascular disease in workers experiencing symptoms of emotional exhaustion, physical fatigue and cognitive weariness (Appels, 2004; Melamed *et al.*, 1999). Furthermore, studies in the medical field have confirmed that traumatic experiences such as being diagnosed with cancer evokes the risks of both suicide and death from cardiovascular causes (Fang, Fall, Murray, Mittleman, Sparén, Weimin *et al.*, 2012). Other studies have demonstrated that there are certain psychosocial risk factors (e.g. experiencing a major life event in the past year) associated with increased risk of acute myocardial infarction, i.e. the presence of these psychosocial stressors in an individual’s life elevates the risk of the person experiencing a myocardial infarction (Rosengren, Hawken, Ôunpuu, Sliwa, Zubaid, Almahmeed *et al.*, 2004). In addition, studies of patients with a range of chronic physiological conditions (e.g. chronic heart failure, chronic obstructive pulmonary disease, and sleep apnea) report that levels of fatigue/exhaustion are high in this population (Falk, Granger, Swedberg, & Ekman, 2007; Hayakawa, Fujita, Ishida, Usami, Sugiura, Kayukawa *et al.*, 2002; Tselebis, Bratis, Kosmas, Harikiopoulou, Theodorakopoulou, Dumitru & Tzanakis, 2011).

In addition, newer epidemiological studies demonstrate a relationship between exhaustion, heart conditions and mortality. Results from the Copenhagen City Heart Study, including approximately 9500 men and women not having any known heart condition, indicated that vital exhaustion is a risk factor for ischemic heart disease as well as for all-cause mortality (Prescott, Holst, Grønbæk, Schnohr, Jensen, & Barefoot, 2003).

During the past 3-4 decades studies worldwide have investigated parental reactions to a child’s cancer, leading to increased knowledge concerning the psychosocial effects of the illness. The research focus of this subject has varied, but in addition to investigating many distress indicators and their severity, earlier studies have also addressed the influence on

parental distress of factors such as parental gender, ethnicity, number of children and parental education, or aspects related to illness-treatment, age of child at diagnosis, time passed since diagnosis and type of cancer (Boman, & Bodegard, 2000; Boman, & Lindahl, 2002; Steele, Dreyer, & Phipps, 2004; Vrijmoet-Wiersma, Egeler, Koopman, Norberg, & Grootenhuis, 2009; Wijnberg-Williams, Kamps, Klip, & Hoekstra-Weebers, 2006).

However, to our knowledge there are no studies addressing childhood cancer patient's parent's response to ongoing and long-term distressing conditions with symptoms of chronic stress in terms of Vital Exhaustion (Appels, Hoppener, & Mulder, 1987). Furthermore, research concerning the possible relationship between levels of parental traumatic and long-term distress symptoms may provide better and more specific understanding about adverse reactions due to a child's cancer diagnosis.

In this context, consideration of possible differences in healthcare services, such as size and type of medical centre and routines for psychosocial follow-up for families of childhood cancer patients could be of importance when it comes to highlighting components essential in supporting parents. Investigating factors associated with effectiveness of psychosocial intervention programs could facilitate the improvement of support services for parents, as current intervention programs designed for this population have not been so promising (Cernvall, Carlbring, Ljungman, & von Essen 2013; Cernvall, Carlbring, Ljungman (L), Ljungman (G), & von Essen, 2015). The aim is thus to minimize adverse acute and long-term reactions as well as preventing the possible development of psychological and physical exhaustion following the difficult life-situation associated with a child's cancer.

## **MEDICAL FEATURES AND INCIDENCE OF CHILDHOOD CANCER**

This thesis involves two national sites treating childhood malignancies where the number of children annually diagnosed with cancer differs greatly. In Sweden, with a population of ~10 million, approximately 300 children are diagnosed each year (Gustafsson *et al.*, 2007). The annual influx rate at the Icelandic site is 12-14 children from a population of ~320 thousand (NOPHO-Annual-Report, 2010). The incidence of paediatric cancer patients in the two Nordic countries is thus approximately equivalent.

Reports on incidences for 1985-2004 of eleven main diagnostic groups of childhood cancers in the Nordic countries reveal that the most frequent diagnosis is acute lymphoblastic leukaemia (ALL, ~30%), followed by central nervous system tumours (CNS, ~27%), lymphomas/histiocytosis (~12%), and bone tumours (~10%) (NOPHO-Annual-Report, 2010). Incidences of AML, ALL and CNS tumours have been stable in the Nordic countries

during the past two decades, with the incidence of childhood CNS tumours being among the highest in the world (Hjalgrim, Rostgaard, Schmiegelow, Soderhall, Komannskog, Vettenranta, 2003; Schmidt, Anderson, Bingen, Hoag, Kupst, & Warwick, 2010). Childhood malignancies vary regarding a number of factors: e.g. peak age at diagnosis and occurrence in boys and girls (NOPHO-Annual-Report, 2010). Cancer in children is most frequent at the age of 5-6 years, and boys are at greater risk of developing cancer than girls (Gustafsson, Kogner, & Heyman, 2013). The distribution of types of childhood malignancies in Nordic countries is presented in Figure 1.

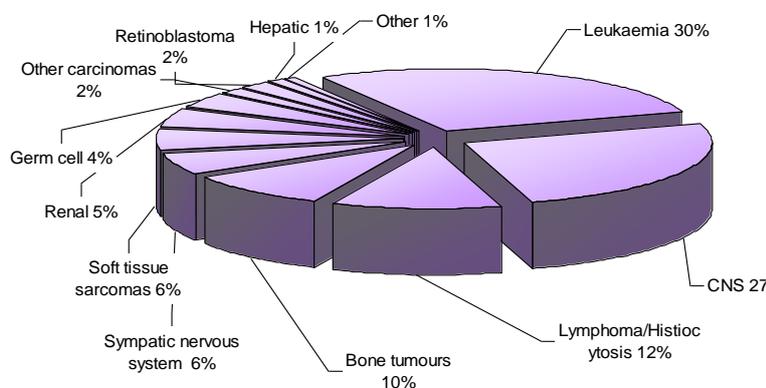


Figure 1. Distribution of different childhood malignancies in the Nordic countries

### But is cancer just cancer?

It is important to briefly explain the differences in the world(s) of oncology, both regarding differences in type of neoplasms diagnosed (benign vs malign) and treatments used for ‘cancer termination’, as there are large differences when it comes to diagnosis of cancer in childhood and adulthood, both regarding incidences of different cancer types as well as choice of treatment. Firstly, there are different types of cancer. In most cases benign tumours are just that, i.e. a lump of cells stationed in the body, usually unable to spread throughout the body. Overall this type of tumour usually responds well to treatment, in most cases the tumour is surgically removed (if possible) and prognosis for survival is quite favourable. Conversely, malignant types of tumours are formed from abnormal cells having the ability to multiply in an uncontrollable manner as well as travelling via the bloodstream, circulatory and lymphatic system, thus spreading to different parts of the body. These kinds of tumours usually require surgery followed with chemotherapy and/or radiation. The prognosis for survival is far less favourable than in cases of benign tumour (<http://neoplasm.imedpub.com>, 2017; Marino-Enriquez, & Fletcher, 2014).

Comparing incidences of different cancer diagnosis, we see a completely different picture between childhood and adulthood cancers. Leukaemia's and lymphomas account for approximately 40% of cancer types in children, the incidence of Central Nervous System tumours being ~27% (Gustavsson *et al.*, 2013), and these diagnoses are not even included in the dominating four cancer categories covering 50% of all adult cancer diagnoses. Interestingly enough, the converse is also true, the most prominent/common diagnosis of adult cancer in more developed countries are: Breast cancer (13.1%); Prostate and Lung cancer (12.5%); Colorectal cancer (12.1%). Acute Lymphoblastic Leukaemia accounting for approximately 30% of all childhood diagnoses, does not even have an own category in some reports concerning global epidemiology of adult cancer. Regarding mortality due to cancer in adulthood, Lung cancer has the highest mortality rate (19.4% of all cancer deaths), followed by breast cancer (15.4%) (Jemal, Bray, Center, Ferlay, Ward, & Forman, 2011; Ward, DeSantis, Robbins, Kohler, Jemal, 2014).

### **Surviving childhood cancer**

Advances in research into childhood cancer have led to improvements in diagnostics and more efficient treatments. The overall result has been a significant increase in survival rates during the last 50 years, from a period when paediatric cancer was considered an inevitably lethal disease to the present time where around 80% of children living in developed countries become long-term survivors (defined as having finished treatment and being disease-free for at least 5 years) (Cantrell, & Conte, 2009; Gustafsson *et al.*, 2007; Steliarova-Foucher, Stiller, Kaatsch, Berrino, Coebergh, & Lacour, 2004; Ward *et al.*, 2014).

Results from 45 population-based cancer registries in 20 countries on 24 620 European children aged from 0 to 14 years diagnosed with malignancy in the period 1990-1994, the survival variation for all cancers combined was from 45% in Estonia to 90% in Iceland. The Nordic countries (except Denmark) having the highest survival in four of seven major types of neoplasms - nephroblastoma (92%), acute lymphoid leukaemia (85%), CNS tumours (73%) and acute non-lymphocytic leukaemia (62%), whilst the eastern countries had the lowest rates of survival: 89% for Hodgkin's disease, 71% for nephroblastoma, 68% for acute lymphoid leukaemia, 61% for non-Hodgkin's lymphoma, 57% for central nervous system (CNS) tumours and 29% for acute non-lymphocytic leukaemia (Gatta, Corazziari, Magnani, Peris-Bonet, Roazzi, Stiller, & the EURO CARE Working Group, 2003).

The greatest improvements in survival rates occurred between the 1970s and 1980s, most prominently among children with ALL and Non-Hodgkin's Lymphoma (NHL) (Gustafsson *et al.*, 2013).

The peak age of ALL is between 2-8 years old, this also being the most curable type of malignant childhood cancer with above 85% of children under the age of 15 years surviving 5-years post-diagnosis. ALL is also the cancer type that has the longest continuous treatment protocol in the Nordic countries, active chemotherapy covering 30 months (Smith, Altekruse, Adamson, Reaman, & Seibel, 2014; Toft, Birgens, Abrahamsson, Griskevicius, Hallböök, Heyman *et al.*, 2017).

In contrast, if diagnosed with ALL before 1 year-old or after the age of 15 years-old the prognosis for survival is less, (approximately 78% of patients diagnosed between 15-19 years old are still alive 5-years post-diagnosis). Children diagnosed with the so-called Infantile ALL (under 12 months old) having a survival prognosis of less than 50% (Brown, 2013; Nachman, La, Hunger, Heerema, Gaynon, Hastings *et al.*, 2009; Smith *et al.*, 2014).

The survival rates for various childhood cancers in the Nordic countries over the past 55 years (1950-2005) are presented in Figure 2.

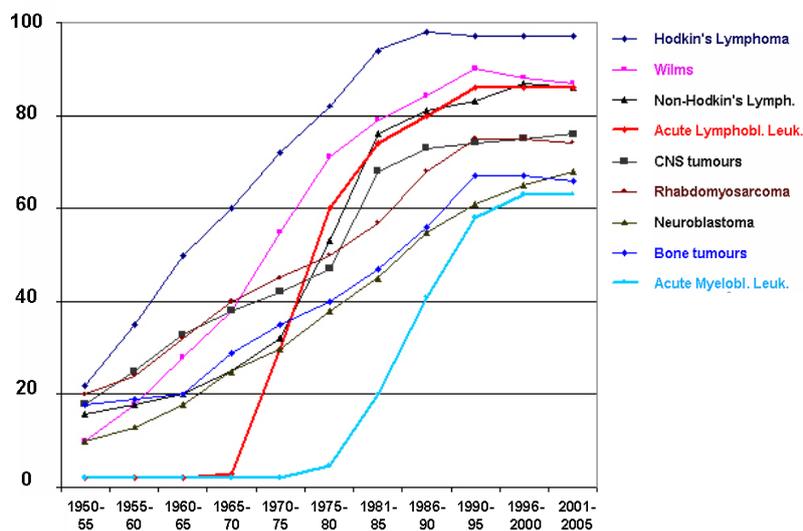


Figure 2. Survival rates for various childhood malignancies in the Nordic countries over the past 55 years (1950-2005). Source: Göran Gustafsson, Swedish Childhood Cancer Register, 2010.

## **What is the possible price of survival?**

### *Late effects and quality of life*

In industrialized countries substantial progress in paediatric oncology treatment has dramatically increased the overall survival rate during past decades (Howlader *et al.*, 2010; Gustafsson *et al.*, 2007), this resulting in a growing population of childhood cancer survivors (Stuber, Christakis, Houskamp, & Kazak, 1996). In the early days of childhood cancer every child that survived was a 'winner', a proof that being diagnosed with cancer as a child was NOT equal with a death-sentence. It seemed that children tolerated more harsh treatment than did adults, and much effort was directed at lengthening the life of the cancer-sick children, for some of whom this meant survival. From initially being a lethal disease, childhood cancer became approx. 80% curable within only half a century (Gustafsson *et al.*, 2007; Reinfjell, Lofstad, Veenstra, Vikan, & Diseth, 2007; Schmiegelow *et al.*, 2010).

Until the early beginning of the 1980's full-body irradiation was integral in leukemia treatment, and knowledge about the devastating late-effects of full-body radiation on a young child was still in its infancy. In the short-term it seemed that combining radiation and chemotherapy increased the chances of the child surviving. Unfortunately, even if the full-body irradiation was plausible in the cure of cancer, signs of the negative effects of radiation on very young children started to become increasingly apparent, sometimes being lethal or having deleterious effects on vital inner organs such as lungs and heart, inducing severe cognitive impairments in the undeveloped brain. These negative consequences led to that in the 1980's radiation was mainly/most excluded as part of the ALL treatment protocol. Today, full-body irradiation of children under the age of three is not used other than in exceptional cases (Schmiegelow *et al.*, 2010).

## **Life and death, is it so simple?**

Knowledge about late effects after treatment in childhood has fortunately increased during recent years. Despite improvements in survival rates there are potentially negative consequences of having been treated for cancer during childhood in terms of survivors' physical, psychological, and social well-being (Dieluweit, Debatin, Grabow, Kaatsch, Peter, Seitz, *et al.*, 2010; Hovén, 2010; Lof, Winiarski, Giesecke, Ljungman, & Forinder, 2009; Lund, Schmiegelow, Rechnitzer, & Johansen, 2011; Schmidt, Anderson, Bingen, Hoag, Kupst, & Warwick, 2010; Seitz, Besier, Debatin, Grabow, Dieluweit, Hinz *et al.*, 2010). Associated risks of having been treated for paediatric cancer include recurrence of primary

cancer, increased risk of developing subsequent malignant neoplasms, hormonal abnormalities, other chronic diseases, as well as different forms of functional impairments (Madanat-Harjuoja, Pitkaniemi, Rantanen, Malila, Lähtenmäki, & Vettenranta, 2017; Stuber *et al.*, 1996; Ward *et al.*, 2014). In addition to all of this, findings in a study by Olsen *et al.* suggested that patients treated with intensive, multiple-agent chemotherapy (1975-2005) had a relatively high incidence of age-specific secondary cancer (Olsen, Møller, Anderson, Langmark, Sankila, & Tryggvadottir, 2009). Survivors of childhood cancer do have a persistently high risk for subsequent cancer throughout the remainder of their lives, children diagnosed with low-risk ALL having the highest risk of secondary cancer (Nielsen, Eriksson, Rosthøj, Andersen, Forestier, & Hasle *et al.*, 2017).

In common language the late-effects after being treated for cancer in childhood can include a secondary cancer later in life; hormonal abnormalities as in physically not growing enough until the ‘skeletal-lines’ close and the possibility of growing is ‘locked’ (dwarfism), diabetes, infertility; the development of chronic lethal as well as non-lethal conditions (e.g. severe heart-damage needing heart-transplantation); chronic non-curable lung-diseases, only hope for surviving being transplant of lungs; hearing impairments, at worst total deafness; sight impairments, at worst blindness; chronic intestinal problems (e.g. not gaining weight because of ‘leaky guts’); bleedings in the intestines, the consequences of a fragile mucus resulting from chemicals so harsh that handling infants using diapers parents are instructed to wear a robe and disposable gloves; in some cases of Osteosarcoma (skeletal/bone cancer) the functional impairments can include the amputation of a limb.

Taken together the life experiences of young adult cancer survivors is obviously not normal, with restriction in their physical possibilities, ability to mature in sync with their peers, often spending more time with adults, bearing emotional scars and experiencing a perceived feeling of isolation. Children diagnosed as teenagers often develop severe anxiety problems, often in somatic forms, when they reach the ability of connecting chains of memory (e.g. treatment-associated pain, long periods in hospital away from home).

### **“Saved from Death but Sentenced to Life”**

*Referring to this statement coming from a young adult having survived cancer the question remains regarding Life, Death, and Quality of Life – how long shall we continue treatment, when is it time to stop treating and focusing of the patients Quality of Life instead of possible survival but with at a high personal cost, and who should decide?*

## DEFINITION OF CORE CONCEPTS

This research thesis is based on theoretical models and concepts from both the psychological and biological fields. To facilitate the comprehension of my study results as well as theoretical hypotheses regarding the development of an eclectic psychobiological intervention protocol, these models and concepts are defined and summarized in the following section.

### CARE AND ORGANISATION

In recent years there has been a growing understanding regarding the necessity of dealing with psychosocial needs following the diagnosis of a severe illness as pediatric cancer. Results of earlier studies have added to the understanding that it is not only the psychosocial needs of the sick child that must be considered, but the needs of the entire family have to be taken into account. This realization has resulted in the knowledge that psychosocial services are a critical component of the complete cancer treatment (Kukkola, Hovén, Cernvall, von Essen, & Grönqvist, 2017; Pai, Drotar, Zebracki, Moore, & Youngstrom, 2006).

Concerning the possible psychosocial needs of childhood cancer patient parents, mapping and analyzing contributing factors conceivably related to parents' psychological reactions due to the child's diagnosis and treatment is of great help in designing and developing functional and tailored follow-up procedures. In this context, adding possible differences in healthcare services such as size and type of medical centre, and routines for psychosocial follow-up for families of childhood cancer patients could be of importance when highlighting components essential in supporting families/parents of childhood cancer patients.

### SENCE OF COHERENCE

In my thesis this concept is based on a theoretical construct termed the 'salutogenic model', originally formulated by Aaron Antonovsky following his observations of holocaust survivors (Antonovsky, 1987). Antonovsky *et al.* defined sense of coherence (SOC) as representing salutogenic (origin-of-health) resources that enable individuals to treat life experiences as comprehensible, manageable and meaningful (Antonovsky, & Sagy, 1986). The salutogenic approach thus defines strong SOC as constituting a flexible, adaptive disposition, allowing individuals to successfully cope with adverse experiences (Surtees, Wainwright, & Khaw, 2006). This approach therefore addresses the following question: *What it is that enables some people but not others, to adapt to stress and manage crisis without being harmed in the process - or even, to be strengthened?* (Antonovsky, 1987).

## **RESILIENCE**

The capacity to resist adverse psychological reactions despite risk experiences is referred to as resilience (Rutter, 2006). This concept thus implies the relative resistance to serious negative outcomes following experience of severe adversities, resilience thus defined as an interactive concept combining adverse experiences and a relatively positive psychological outcome despite those experiences (Rutter, 2006)

In viewing resilience as an individual property, the focus is on personal differences rather than on seeing it as a general attribute (Gudmundsdottir, Schirren, & Boman, 2011; Hoge, Austin, & Pollack, 2007). As such, resilience differs from both social competence and traditional concepts of risk and self-protection in the sense that it focuses on individual variations in response to comparable experiences. Resilience includes both psychological and biological characteristics intrinsic to the individual; characteristics that might be modifiable and that confer protection against the development of psychopathology in the face of stress (Hoge, *et al.*, 2007).

In other words, resilient individuals will show a relatively good psychological outcome despite having gone through serious risk experiences including e.g. severe distress and/or adversity, generally expected to bring about serious adverse psychological consequences (Hart, Wilson, & Hittner, 2006; Rutter, 2006).

## **STRESS AND TRAUMA**

Hans Selye (1984) defined stress as, “*the non-specific response of the body to any demand,*” the most extreme form of stress resulting from a traumatic incidence i.e. traumatic stress (Rotschild, 2000). Symptoms of traumatic stress (TSS) refer to excessive stress symptoms associated with a traumatic event. Various studies have been conducted on the prevalence of traumatic stress symptoms in different groups of people for several decades, trying to explain how different events can increase the levels of traumatic stress symptoms. Empirical research has indicated that the occurrence of lifetime exposure to forceful situations, traumatic enough to cause symptoms of acute and/or prolonged stress reactions, is between 51-60% (Wilson, in Wilson & Keane, 2004). In other words, it is not that uncommon that individuals will be exposed to events potentially experienced as being traumatic during their lives.

## **POST-TRAUMATIC SYMPTOMS AND/OR POST TRAUMATIC STRESS DISORDER**

Post-traumatic stress symptoms are symptoms of distress related to the experienced traumatic event and are divided into three main categories: (1) Re-experiencing (e.g. intrusive recollections, traumatic nightmares, flashbacks); (2) Avoidance (e.g. avoiding trauma-related activities, places, and people,) and (3) Hyperarousal (e.g. insomnia, difficulty concentrating, hypervigilance), (Friedman, 2006).

A potential result of having experienced severe traumatic event(s) is Post-Traumatic-Stress-Disorder, the scientific definition of PTSD encompassing having been exposed to experiences defined as traumatic events such as exposure to war, threatened or actual sexual violence, terrorist attacks, torture, natural or human made disasters and severe motor vehicle accidents (APA, 2013).

The criteria required for the diagnosis of PTSD when using APA's Diagnostic Statistical Manual-V (DSM-V) are as follows:

**Criterion A (one required):** *The person was exposed to: death, threatened death, actual or threatened serious injury, or actual or threatened sexual violence, in the following way(s):*

*Direct exposure: Witnessing the trauma; Learning that a relative or close friend was exposed to a trauma*

*Indirect exposure to aversive details of the trauma, usually in the course of professional duties (e.g., first responders, medics)*

**Criterion B (one required):** *The traumatic event is persistently re-experienced, in the following way(s): Intrusive thoughts; Nightmares; Flashbacks; Emotional distress after exposure to traumatic reminders; Physical reactivity after exposure to traumatic reminders*

**Criterion C (one required):** *Avoidance of trauma-related stimuli after the trauma, in the following way(s): Trauma-related thoughts or feelings; Trauma-related reminders*

**Criterion D (two required):** *Negative thoughts or feelings that began or worsened after the trauma, in the following way(s): Inability to recall key features of the trauma; Overly negative thoughts and assumptions about oneself or the world; Exaggerated blame of self or others for causing the trauma; Negative affect; Decreased interest in activities; Feeling isolated; Difficulty experiencing positive affect*

**Criterion E (two required):** *Trauma-related arousal and reactivity that began or worsened after the trauma, in the following way(s): Irritability or aggression; Risky or destructive behavior; Hypervigilance; Heightened startle reaction; Difficulty concentrating; Difficulty sleeping*

**Criterion F (required):** *Symptoms last for more than 1 month.*

**Criterion G (required):** *Symptoms create distress or functional impairment (e.g., social, occupational).*

**Criterion H (required):** *Symptoms are not due to medication, substance use, or other illness (APA, 2013, p.271-272).*

## **PTSD AND RE-DEFINITIONS OF A TRAUMATIC EVENT**

The definition of a traumatic event has changed during the past decades. Trauma was first defined as a “*recognizable stressor that would evoke significant symptoms of distress in almost anyone*” in DSM-III (APA, 1980, p.238), being supplemented with “*the emotional response of the individual to the exposure of catastrophic stress, the event producing an intense, emotional response as fear, helplessness, or horror*” in DSM-IV-TR (2004). In DSM-V “*the individuals response*” was removed again, thus redefining a traumatic event (criteria A) as e.g. “*Exposure to, either directly or witnessing events occurring to others, actual or threatened death, serious injury, or sexual violence, as well as learning that a traumatic event(s) occurring to a close family member or close friend*”. In cases of actual or threatened death of a family member or friend, the event(s) must have been violent or accidental (APA, 2013, p.271). Medical incidents that qualify as traumatic events involve sudden, catastrophic events such as waking during surgery and anaphylactic shock. Witnessed events include observing threatened or serious injury, unnatural death, or a medical ‘catastrophe’ in one’s child (e.g. a life-threatening haemorrhage) (APA, 2013, p.274).

Theoretically, being informed about one’s child potentially fatal (cancer) illness and the possible sequelae can be defined as traumatic, possibly resulting in traumatic stress symptoms. In accordance with the definition in DSM-V, receiving the diagnosis is thus **not** defined as a traumatic event unless the diagnosis is associated with a violent or accidental situation (e.g. a bleeding haemorrhage being the reason for a child’s hospital admission followed by blood-tests revealing low platelets and abnormally high white blood counts, common in Acute Lymphoblastic Leukaemia).

## **TRAUMATIC EVENTS AND THE EFFECT ON BODILY FUNCTIONS**

For understanding the possible association between traumatic stress and heightened risks of the development of both adverse psychological and physical reactions due to a traumatic event, it may be useful to understand the elevation of Traumatic Stress Symptoms after experiencing a traumatic event as a normal response pattern to extremely stressful life events (Wilson, in Wilson & Keane, 2004).

Wilson (Wilson, in Wilson & Keane, 2004) explains the development of stress responses to traumatic event(s) as “*dynamically related psycho-biological processes including the brain, the nervous and hormonal systems, emotions, perception, and behavioral expressions of the organismic changes caused by trauma*”, the trauma affecting all dimensions of the individuals behavioral functioning as well as psychological responses. The impact of experiencing a traumatic event is thus not only emotionally overwhelming, but also triggers the release of hormones activating the readiness of the mode termed the ‘fight-or-flight’.

According to Wilson (Wilson, in Wilson & Keane, 2004) the experience of traumatic events has different effects in different individuals, the consequences of trauma being multiple changes affecting e.g. the brain, the nervous and hormonal systems, and behavioral expressions. The evocation of the stress response system activated in response to the traumatic experiences is psychobiological in nature, both the individuals psychological and biological systems responding to the stressful situation. As the brain is the central processing unit (CPU) it mobilizes the sympathetic nervous system (SNS) to do its job of ‘switching on’ the ‘fight-flight’ response when facing a perceived threat. The body, under control of the brain, responds automatically to the situation, releasing neurotransmitters to activate and energize the body’s adrenergic and noradrenergic response systems, preparing the body to confront the perceived danger (McEwen, 1998; 2000).

## **ALLOSTASIS**

Following the fight-flight reflex the body naturally seeks the homeostatic state and a return to baseline or normal functioning (Miller, in Wilson & Keane, 2004). This process explained by McEwen (2000) as the body’s natural need for restoration after reacting to an extraordinary stressful situation and often over a long time, wears the body out. The process of the body adapting to acute stress induced by a perceived traumatic experience is referred to as ‘Allostasis’. However, in certain circumstances the homeostatic condition may not be re-established, especially with traumas that are prolonged or repetitive, causing a prolonged hyperarousal state with an overproduction of stress hormones (McEwen, 1998; 2000).

## **ALLOSTATIC LOAD**

During a state of perceived danger, the excessive production and release of adrenal/stress hormones can be both protective and damaging. Cortisol and catecholamines are intended as acute-acting mediators and should not be chronically active. So, when the body fails to restore to homeostasis and remains in an adverse psychosocial or physical situations the

negative/adverse changes in the body are referred to as an ‘Allostatic load’ (McEwen, 1998; 2000).

## **LONG-TERM DISTRESS AND VITAL EXHAUSTION**

When the body fails in adapting to prolonged excessive stress there are not only adverse results in the physical system but also negative consequence at a psychological level. The physiologist Hans Selye (1977) conceptualized the failure of adapting to prolonged psychological stress as ‘exhaustion’. A term similar to Selye’s concept of exhaustion commonly used in the occupational field and describing the state of individuals’ excessive levels of long-term physical and psychological distress is the term *burnout* (Freudenberger, 1974; Hobfoll, *et al*, 1993; Lazarus, 1966; Melamed, Ugarten, Shirom, Kahana, Lerman, & Fromm, 1999). Concurrent with the definition of burnout the results of studies have indicated that parents of sick children are a group qualifying for a burnout diagnosis ((Lindström, Åman, Anderzén-Carlsson, & Lindahl Norberg, 2016; Nilsen, Skipstein, & Demerouti, 2016; Roskam, Raes, & Mikolajczak, 2017).

In the medical field yet another term similar to burnout and exhaustion exists, originally referred to by Ad Appels (1987) as Vital Exhaustion. This concept of exhaustion derived from research in the 1970’s when cardiologists were studying the relationship of a behavior pattern characterized by impatience, time pressure, ambition, and aggressiveness, termed the *A-pattern*. The results demonstrated that this pattern more than doubled the risk of myocardial infarction. Trying to replicate these study results both Ad Appels and his team from the Netherlands in 1987 as well as Hans Bosman in 1994 concluded that even if individuals characterized by type A behavior had an increased risk of coronary heart disease the American results were not replicated. Realizing that there had to be something possibly preceding a myocardial infarction, Appels and his team initiated clinical observations of patients having suffered from myocardial infarction, asking questions on how they felt months before their cardiac event. These observations revealed that two-thirds of these patients spoke about experiencing the feeling that their body was “like a battery losing its power”. Further questions to relatives and spouses of patients revealed that adding to the feelings of “losing power” another characteristic was increased irritability. From these observations, the Maastricht Questionnaire was developed for measurement of a mental precursor in the terms of Vital Exhaustion predictive of myocardial infarctions (Appels, 2004).

Vital Exhaustion (VE) as described by Ad Appels (1987) is defined as *“a state which is present when an individual only complains of unusual fatigue and decreasing energy but also by feeling dejected or defeated. Feeling exhausted when waking up is highly characteristic of the condition.”*

The relationship between exhaustion and elevated risks of cardiovascular conditions has been quite thoroughly studied in medicine – e.g. results indicating that elevated levels of exhaustion increase the risk of myocardial infarction in healthy individuals by 150%, even after controlling for age, smoking, blood pressure and cholesterol (Appels, & Mulder, 1988). Individuals having sleeping complaints in the form of problems staying asleep as well as waking up feeling very tired also have an increased risk of MI (Appels, 1990). Another study addressing whether fatigue is a possible precursor of stroke indicated that elevated levels of vital exhaustion increased the risk of first stroke by 13% per vital exhaustion point (using the Maastricht Interview Vital Exhaustion scale) (Schuitemaker, *et al.*, 2004). Studies of other populations such as patients with a range of chronic physiological conditions also report high levels of fatigue/exhaustion (Falk, *et al.*, 2007; Hayakawa, *et al.*, 2002; Tselebis, *et al.*, 2011).



## **WHAT ARE THE POSSIBLE EFFECTS ON PARENTS FOLLOWING THEIR CHILD'S CANCER DIAGNOSIS?**

*What about parents fighting for their child's life, what are the effects on them? Could they be suffering from traumatic symptoms, acute- as well as long-term distress and (vital) exhaustion, possibly heightening their risk of developing severe physical and/or psychological conditions, during or even after the battle?*



## PREVIOUS RESEARCH OF PARENTAL DISTRESS

The way parents respond psychologically to their child's cancer has been investigated in a growing number of studies, beginning about 3 decades ago and expanding substantially thereafter (Best, *et al.*, 2001; Gudmundsdottir *et al.*, 2013; Hovén *et al.*, 2008; Kazak, & Meadows, 1989; Koocher, 1986; Lindahl-Norberg *et al.*, 2008; Peck, 1979; Vrijmoet-Wiersma *et al.*, 2009, Ljungman *et al.*, 2015).

Collectively, these have shown that the psychosocial situation of parents is strongly affected both during treatment and follow-up, and even decades after the treatment is completed (Barakat *et al.*, 1997; Boman *et al.*, 2004; Dixon-Woods *et al.*, 2001; Giammona *et al.*, 2002; Kazak, 1998; Lindahl-Norberg *et al.*, 2008; Santacroce, 2002; Van Dongen Melman *et al.*, 1995). The trauma associated with a child being diagnosed with a potentially lethal disease affects the whole family, parents in particular, regardless of the individual's psychological resources. Nevertheless, as there appear to be more and less adaptive ways of coping (Forinder, 2004; Lindahl Norberg *et al.*, 2005), individual strengths and resources may influence the individual vulnerability for psychological distress (Kazak *et al.*, 2003).

High levels of distress have been associated with the uncertainty about final treatment success, adding to the initial traumatic experience of being told that the child has cancer. This strained life situation, characterized by on-going disease and treatment-related distress, makes parents vulnerable to acute and lasting psychological adverse consequences. For some, the strain can become so overwhelming that it may threaten their ability to function as parents, both for the sick child and for other family members (Dixon-Woods *et al.*, 2001; Giammona, & Malek, 2002; Mu *et al.*, 2002; Gudmundsdottir *et al.*, 2013; Hovén *et al.*, 2015; Ljungman *et al.*, 2015; Van Dongen Melman *et al.*, 1995).

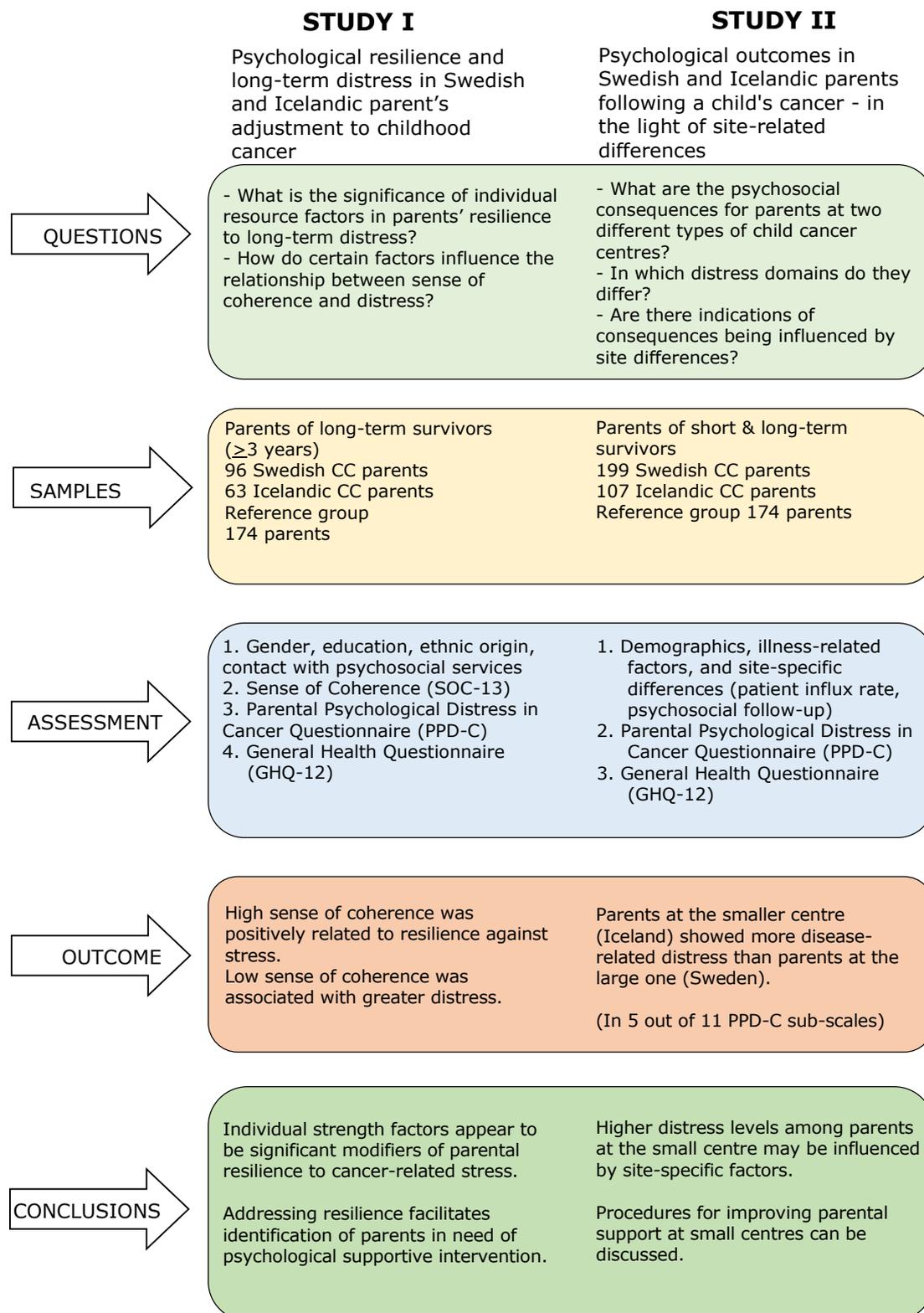
However, earlier studies have been inconsistent in their findings, possibly due to different study designs. Study groups might have been small, thus making it difficult to draw definitive conclusions based on the trends observed (Best *et al.*, 2001; Kazak *et al.*, 1989; Lahteenmaki, Salmi, & Salo, 1996).

Several studies have restricted their focus to only one or two dimensions of psychological reactions, and assessment instruments have often failed to cover illness-specific reactions associated with the unique problems relevant for this population. Additionally, many studies have only addressed mothers (Greenberg, Kazak, & Meadows, 1989; Steele *et al.*, 2004). While mothers and fathers might have different experiences Gudmundsdottir *et al.*, 2011;

Yeh, 2002), it is important to acknowledge that a complete evaluation of parental reactions to a child's illness is warranted.

Studies of parental reactions due to their child's cancer diagnoses have rarely adopted a resources-oriented perspective, in terms of sense of coherence and resilience, exploring the possibility that individual resistance factors might have a distress-buffering effect. Outcomes of studies investigating parental reactions to other paediatric illnesses or medical conditions have indicated the potential of SOC in boosting resilience against distress (Margalit *et al.*, 1992; Hedov *et al.*, 2002; Hintermair, 2004; Svavarsdottir *et al.*, 2005). Nevertheless, prior studies have, as far as I know, not addressed the **relationship** between SOC and a variety of symptoms of disease-related distress among parents of children with life-threatening cancer. Furthermore, previous studies of parents have typically involved samples from single countries. As far as I know, research on site-specific determinants and differences in organisational care, possibly influencing the outcome of parental stress due to a child's cancer, has not been carried out in a comparative approach between countries.

While parents of sick children may warrant a burnout diagnosis (Lindström *et al.*, 2016; Nilsen *et al.*, 2016; Roskam *et al.*, 2017) there are no studies addressing parent's response to ongoing and long-term distressing conditions with symptoms of chronic stress in terms of Vital Exhaustion (Appels *et al.*, 1987). Focusing on possible determinants of parental short- and long-term distress may provide better and more specific understanding about adverse reactions due to a child's cancer diagnosis. This will be of great help in designing and developing functional and tailored follow-up procedures in terms of psychosocial support interventions. In this context, examination of possible differences in healthcare services, such as size and type of medical centre, and routines for psychosocial follow-up for families of childhood cancer patients, could be of importance. The effectiveness of reducing parental distress following their child's cancer diagnosis, in earlier intervention programs designed for this population has been poor (Cernvall *et al.*, 2013; Cernvall *et al.*, 2015), and thus this represents a currently unmet medical need.



### STUDY III

#### Parental Vital Exhaustion in the aftermath of a child's cancer diagnosis

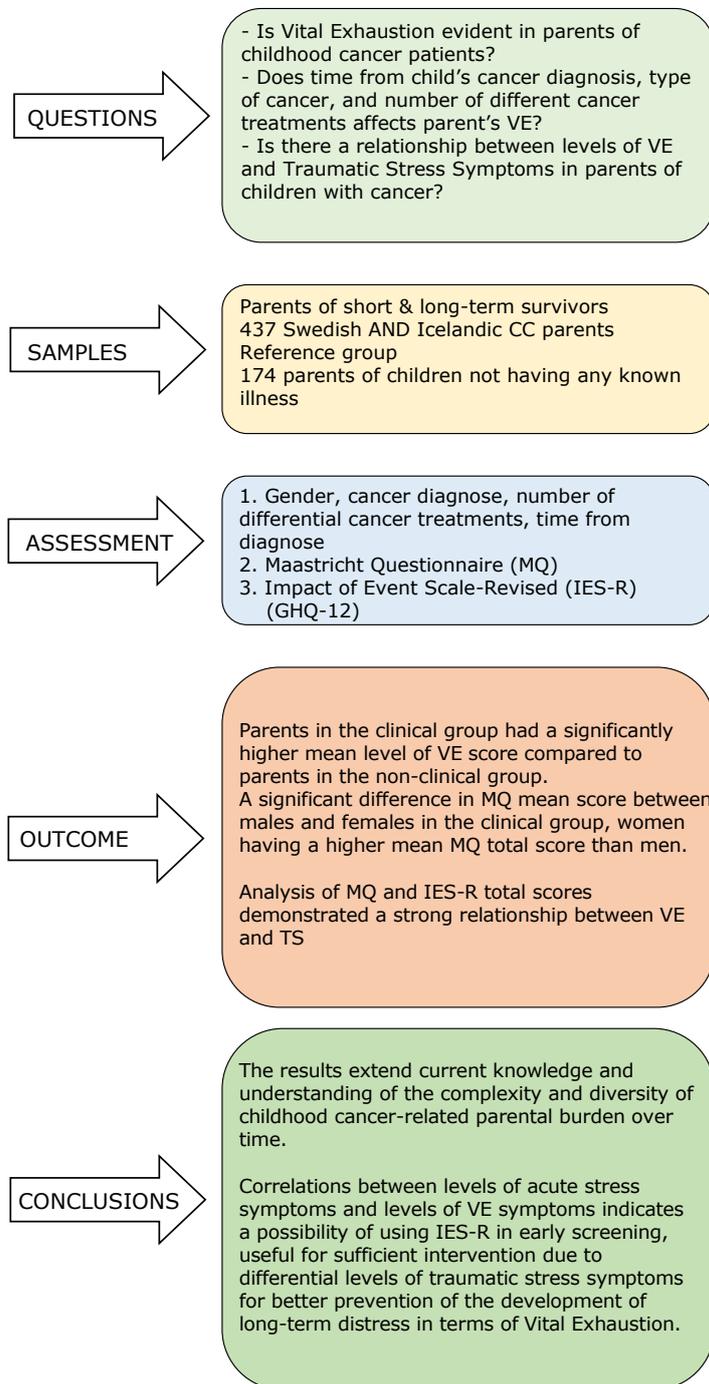


Figure 3. Overview of thesis studies

## **HYPOTHESIS**

The hypothesis addressed was that current healthcare practices for parents of cancer-diagnosed children are inadequate and that increased understanding of the factors contributing to parental stress would facilitate development of improved practices.

## **GENERAL AIM**

The general aim of this thesis was to present further and more detailed evidence about the psychological reactions of parents of children diagnosed with cancer. It is an extension of the study of risk and resilience factors that influence parent reactions. The Nordic sample of parents from two different types of treatment centre allowed for exploration of influence of centre characteristics on parental outcomes. The continued project adheres to recommendations received from the board of examination following my licentiate examination.

An ultimate goal was to gain sufficient knowledge to develop individualized care and clinical follow-up protocol for families of children with cancer.

## **SPECIFIC AIMS OF STUDIES I-III**

### **Study I**

The aim of the first study was to examine the significance of individual strength factors (as defined by sense of coherence (SOC)) on parental distress related to childhood cancer. The specific focus was on the relationships between parental SOC and illness-specific and generic distress symptoms. We also wanted to study whether parental (a) *gender*, (b) *level of education*, and (c) *use of professional psychological support* influenced the relationship between sense of coherence and distress.

### **Study II**

The aim of the second study was to determine the incidence of disease-related distress symptoms in parents treated at two quite different types of site in two Nordic countries. We wanted to compare the two groups regarding distress outcomes to assess whether findings could be understood in the light of national, site-specific, and/or organisational determinants; i.e. whether parental reactions in parenting a child diagnosed with cancer might be influenced

by such determinants. The study thus addressed the question of how differences in type and size of centre, and/or national and local solutions regarding care may predict parents' distress outcomes.

### **Study III**

The aim of the third study was to present further and more detailed evidence about the psychological reactions of parents of children diagnosed with cancer, focusing on mapping and analyzing levels of long-term distress in terms of Vital Exhaustion. As theoretically there could be a relationship between levels of Traumatic Stress (TS) and levels of Vital Exhaustion, this study examined the possible association of levels of acute stress symptoms and levels of vital exhaustion symptoms with the purpose of possible early screening, sufficient intervention and prevention.

# METHODS

## PARTICIPANTS AND PROCEDURES

### Procedures studies I-III

#### *Clinical groups*

The three studies comprised a total of 471 parents of children diagnosed with cancer between the years 1986-2007 treated at three different sites: a specialized CC treatment centre at Astrid Lindgren Children's Hospital in Stockholm (ALCH), Sweden, Linköping University Hospital, Linköping (LUH), Sweden, and at the Children's Hospital in Reykjavik (CHR), Iceland. Exclusion criteria were children diagnosed over 18 years of age, known fatal diagnosis at time of study, palliative treatment phase, or insufficient knowledge of Swedish or Icelandic in order to complete the questionnaires. In Iceland the procedure was a little different than in Sweden as those cc-patients that were 18-years old at the time of the study also had to give informed consent of their parents' participating in the study. The total response rate of clinical groups was ~69% (ALCH ~73%; LUH ~78%; CHR ~56%).

Data collection for the studies were done in two phases as the data collected for the studies included in this thesis are a part of a larger study, based at Karolinska Institutet in Sweden, investigating the psychosocial situation of parents of children with cancer. The data collection of this larger study had begun in 1999 and collection of data in Sweden finished in 2002. The investigator (Eygló Guðmundsdóttir) presenting the three studies included in this thesis was included in the larger project in 2006 and was therefore not a part of the first phase of data collection, i.e. the Swedish sample. Phase two of the data collection, i.e. the Icelandic sample, was conducted between 2007-2008, all responsibilities and procedures being carried out by me. As mentioned above the total number of parents in the clinical group comprised of 471\* parents, the number of parents of CC patients in the various studies being: n=159 (study I); n=306 (study II); n=471 (study III). The explanation of why the number of parents in the three studies varies is that in study I we excluded all parents having children diagnosed prior to 36 months; in study II we included all parents of children diagnosed between 1986-2007 (maximum 21 years post-diagnosis); regarding study III data collected from Linköping University Hospital were included in that study as well as that we excluded parents of children diagnosed post 15 years.

Table 1. Characteristics of the clinical groups

Sub-study groups\*

		Study 1 % (n)	Study 2 % (n)	Study 3 % (n)
Mothers		59.1 (94)	59.8 (183)	58.1 (254)
Fathers		40.2 (65)	40.2 (123)	41.9 (183)
Child's Cancer diagnosis	Leukemia/Lymphoma	61 (58.7)	98 (52.1)	141 (55.3)
	CNS-tumour	12 (11.5)	24 (12.8)	30 (11.8)
	Sympatic nerve system	3 (2.9)	13 (6.9)	15 (5.9)
	Renal tumour	4 (3.8)	8 (4.3)	21 (8.2)
	Skeletal tumour	8 (7.7)	12 (6.4)	13 (5.1)
	Soft tissue sarcoma	8 (7.7)	13 (6.9)	20 (7.8)
	Other/unspecified	8 (7.7)	20 (10.6)	15 (5.9)
	<b>Total/mean</b>	<b>104 (100)</b>	<b>188 (100.0)</b>	<b>255 (100.0)</b>
Age of child at diagnosis	Leukemia/Lymphoma	6.4 (SD 4.8)	6.7 (SD 4.6)	6.8 (5.0)
	CNS-tumour	5.7 (SD 5.2)	7.4 (4.7)	7.1 (5.2)
	Sympatic nerve system	0.6 (SD 0.8)	2.3 (2.5)	2.5 (2.9)
	Renal tumour	4.4 (SD 3.6)	5.8 (4.9)	5.2 (4.3)
	Skeletal tumour	14.0 (SD 4.3)	14.4 (3.8)	13.6 (3.8)
	Soft tissue sarcoma	10.3 (SD 7.8)	9.0 (7.6)	9.2 (6.3)
	Other/unspecified	3.4 (SD 4.1)	6.2 (6.8)	4.6 (5.5)
	<b>Total/mean</b>	<b>6.7 (SD 5.4)</b>	<b>7.1 (5.4)</b>	<b>6.8 (5.3)</b>
Time elapsed since diagnosis (years)	Leukemia/Lymphoma	8.7 (SD 4.8)	5.2 (5.0)	3.9 (3.2)
	CNS-tumour	6.5 (SD 2.5)	4.5 (3.4)	5.2 (3.4)
	Sympatic nerve system	9.5 (SD 5.3)	3.3 (4.2)	5.4 (3.6)
	Renal tumour	6.9 (SD 4.4)	4.1 (4.3)	4.4 (3.5)
	Skeletal tumour	7.4 (SD 4.9)	4.3 (3.3)	3.9 (3.3)
	Soft tissue sarcoma	6.8 (SD 3.4)	4.5 (4.7)	5.1 (4.6)
	Other/unspecified	3.4 (SD 4.1)	4.2 (4.3)	4.1 (3.3)
	<b>Total/mean</b>	<b>6.7 (SD 5.4)</b>	<b>7.1 (5.4)</b>	<b>4.3 (3.4)</b>

\*Several parents were involved in more than one sub-study

### Reference group

The reference group were parents of children not having any known lethal disease. Two-hundred mothers of children living in the catchment area of Astrid Lindgren Children's Hospital in Stockholm and having at least one child corresponding in age to that of the children in the Swedish clinical group, were randomly selected. In a letter of invitation both parents were asked to participate. The response rate in the non-clinical group was ~50%.

Parents in both the clinical and non-clinical groups received a letter of invitation or phone/email contact together with information about the project, informed consent being obtained from all participants prior to inclusion. Mothers and fathers were instructed to complete their questionnaires independently. After completion parents returned questionnaires by mail using pre-paid envelopes. The study was approved by the Swedish Regional Ethics Board and the Icelandic National Bioethical Committee, respectively.

## **ASSESSMENT**

### **The General Health Questionnaire 12 (GHQ-12)**

#### *Studies I & II*

The General Health Questionnaire 12-item version (GHQ-12) is a reliable and sensitive tool for screening of non-pathological psychiatric symptoms (Van Dongen Melman *et al.*, 1995). Items relate to the mastering of daily problems, self-esteem, stress, depression and anxiety. Cronbach's alpha for GHQ in the clinical groups, in studies I and II, was 0.86.

### **The Parental Psychosocial Distress in Cancer (PPD-C)**

#### *Studies I & II*

The Parental Psychosocial Distress in Cancer (PPD-C) is a standardized self-report distress measure originally developed by van Dongen-Melman *et al.* to study illness-specific distress symptoms characteristic for parents of children who survived cancer (Van Dongen Melman *et al.*, 1995). The conceptual framework for the assessment model is based on theory, literature, and in-depth interviews with parents of childhood cancer patients.

The PPD-C consists of 11 subscales: *uncertainty, loss of control* (regarding personal functioning, parenting the patient, the sibling(s)), *self-esteem, anxiety, disease-related fear, loneliness, sleep disturbances, depression, and psychological and physical distress*. The response format of the 125 items asks parents to respond according to 2-, 3- or 4-point Likert scales. The in-depth interviews with parents, which were part of the construction of the original questionnaire, ensure construct validity of assessment (Van Dongen Melman *et al.*, 1995).

Cronbach's alpha for the sub-scales of PPD-C ranged from 0.70-0.95 in Study I and 0.68-0.95 in Study II.

### **The Sense of Coherence-Scale (SOC-13)**

#### *Study I*

For assessing comprehensibility, manageability and meaningfulness in the clinical study group, Swedish and Icelandic versions of the 13 item Sense of Coherence-Scale (SOC-13 scale) (Antonovsky, 1993) were used. SOC has been recognised as a resource related to resilience indicating a positive subjective state of health (Eriksson, & Lindstrom, 2006; Hart

*et al.*, 2006; Surtees *et al.*, 2006). The SOC-13 is a standardized scale that has been found to be cross-culturally applicable and versions have been developed for use in both Sweden and Iceland (Eriksson & Lindstrom, 2005). Summary scores were calculated for parents individually. In prior studies using SOC-13 the internal reliability has ranged from 0.74-0.91, and the instrument has demonstrated high content, face and constructs validity as well as temporal stability (Antonovsky, 1993; Feldt, Lintula, Suominen, Koskenvuo, Vahtera, & Kivimaki, 2007). In our study the estimation of the reliability of the SOC questionnaires by Cronbach's alpha resulted in 0.88 for the clinical groups and 0.86 for non-clinical groups.

## **The Impact of Event Scale-Revised (IES-R)**

### *Study III*

Levels of TSS were assessed using the 22-item instrument Impact of Event Scale-Revised (IES-R) (Weiss, in Wilson & Keane, 2004), a revised version of the original 15-item version designed by Horowitz (1979) which is widely used in research assessing self-reported psychological stress following psychological trauma. The IES-R covers three aspects of stress reactions: intrusion (8 items); avoidance (8 items); and hyperarousal (6 items). In our study Cronbach's alpha coefficients for the three subscales ranged from 0.82-0.89 (Intrusion 0.89, Avoidance 0.82, Hyperarousal 0.84). Cronbach's alpha for IES-R total score was 0.93.

As suggested from its developers we adapted the instrument, referring the supposed trauma to a single event using the statement "*Related to your child's disease*" before each item/statement. For this reason the comparison of levels of TSS between the clinical cancer and reference groups was only possible in an explorative manner as the statement "*Related to the most traumatic event that you have been through*" before each statement would be considered to be far too subjective.

## **The Maastricht Questionnaire (MQ-21)**

### *Study III*

For assessing levels of VE we used The Maastricht Questionnaire (MQ-21) consisting of 21 items that encompass self-reported excessive fatigue, loss of vigour, increased irritability and feelings of demoralization (Appels *et al.*, 1987). The instrument was developed as a research tool assessing premonitory symptoms of myocardial infarction (MI), i.e. if levels of experienced feelings of VE predict the onset of MI. The reliability of the instrument is good (Meesters, & Appels, 1996), with high internal consistency of items (Cronbach's alpha 0.89),

suggesting the instrument is a valid tool for assessing mental precursors of myocardial infarction (MI) (Appels *et al.*, 1987). Cronbach's alpha in the present study for the combined cohort group was 0.88 (0.86 in the non-clinical group and 0.90 in the clinical group). The response format of each of the MQ's 21 statements had the answer alternatives Yes (scored 2), No (scored 0), and Don't know (scored 1) except for items 9 and 14 for which the scoring was reversed. The maximum score was 42; a suggested clinical cut-off point is 14.0, a further high-limit clinical cut-off score is 20 (e.g. Appels, 1990).

### **Background variables**

In all studies, for the purpose of being possible confounders affecting primary focus outcomes in some way, data regarding children's age at diagnosis, illness and treatment-related background were collected. Information regarding parents' utilisation of professional psychological support, the family structure, educational level, ethnic background, and home language were also collected in studies I-II.

	Variables	Study I	Study II	Study III
Disease-related stress (PPD-C)	- Uncertainty	X	X	
	- Control (personal functioning)	X	X	
	- Control (parenting the patient)	X	X	
	- Control (parenting the sibling(s))	X	X	
	- Self-esteem	X	X	
	- Anxiety	X	X	
	- Disease-related fear	X	X	
	- Loneliness	X	X	
	- Sleep disturbances	X	X	
	- Depression	X	X	
- Psychological and physical distress	X	X		
Resilience (SOC)	- Comprehensibility	X		
	- Manageability	X		
	- Meaningfulness	X		
General mental health (GHQ)	- Self-esteem	X	X	
	- Stress	X	X	
	- Depression Anxiety	X	X	
Traumatic stress (IES-R)	- Intrusion			X
	- Avoidance			X
	- Arousal			X
Long-term distress – Vital Exhaustion (MQ)	- Fatigue			X
	- Irritability			X
	- Demoralization			X

*Table 2. – Variables analyzed in the three studies*

## **STATISTICAL ANALYSES**

### **Study I**

Analysis related to the primary focus on the relationship between SOC and distress was carried out by conducting linear regression analyses adjusted for time passed since diagnoses. In these analyses distress symptom outcomes were inserted as the dependent variable in separate analyses, with the individual SOC-sum score inserted as the independent predictor variable.

With two-way ANOVA in a combined main and interaction effects model, we also examined whether the relationship between parental SOC and distress was influenced by potentially modifying factors (parent gender, level of education, and utilization of professional support).

## **Study II**

In this study the main outcomes were compared between parents at the Swedish and Icelandic study sites, and descriptive statistics for groups were presented regarding different background variables (e.g. education, utilized professional psychological support, ethnicity, and number of children in the family) and illness-related factors (diagnosis, child's age at diagnosis, time since diagnosis). Comparisons between the two clinical site groups (Sweden/Iceland) regarding these variables were performed using the Chi-Square test ( $\chi^2$ ), variables being either categorical or ordinal.

Study sites were compared concerning distress outcomes of the PPD-C and GHQ-12, using t-test for independent groups. Distress outcomes were compared with normative reference data using an independent t-test.

## SUMMARY OF RESULTS

The main finding for studies I-III are presented separately

### STUDY I

#### Basic outcomes

Comparison of background factors in the clinical study group showed that parents' educational levels\* were similar. Conversely, the proportion of parents with an immigrant background\*\* was lower in the Icelandic group and their mean number of children per family\*\*\* was higher. The utilisation of professional psychological support when confronted with the child's cancer differed between mothers and fathers in both groups, with mothers using such support more frequently.

#### Sense of coherence and distress

Outcomes indicated that levels of SOC had a modifying effect on generic distress symptoms, physical and psychological stress symptoms, anxiety and depression. The relationship between SOC and distress was inverse, with low SOC scores being associated with more severe distress in all dimensions of the PPD-C and GHQ. The influence of SOC varied with parents' gender, showing a stronger modifying influence among mothers.

Associations were evident for all the dependent distress variables, showing a negative correlation coefficient (Pearson's  $r$ ) from moderate ( $r$  -0.23) for the subscale (uncertainty - PPD-C) to strong ( $r$  -0.73) for GHQ. Outcomes showed a significant interaction effect between gender (independent background variable), SOC, and disease-related fear ( $p=0.008$ ).

Outcomes indicated a stronger negative relationship between SOC and the distress variables were stronger for mothers than fathers. This tendency, although less strong, for this interaction effect between gender and SOC was seen regarding other distress variables as well.

Concerning the interaction effect between other background variables, SOC, and distress, a significant effect of education and SOC ( $p=0.013$ ) on the *psychological and physiological distress* variable (subscale of PPD-C) was apparent, this being indicative of a greater protective effect of SOC in parents with a lower level of education. Initial comparison of SOC outcomes between the clinical and non-clinical groups were similar although higher

SOC was significantly evident for parents in the non-clinical group demonstrated a ( $t = -2.181$ ,  $df = 297.992$ ,  $p < 0.05$ ).

## STUDY II

### Basic outcomes

When comparing the clinical sites regarding different background factors (\*; \*\*; \*\*\*) the same results as in study I were evident. Conversely, the two sites differed in “utilised professional psychological support”: 54.1% of Icelandic parents having used some kind of such support, compared to 34.8% of Swedish parents ( $t = -2.50$ ,  $df = 205$ ,  $p < 0.05$ ).

Regarding illness-related factors, there were significant differences between the national sites concerning the child’s age when diagnosed ( $t = -2.22$ ,  $df = 108.532$ ,  $p < 0.05$ ), and time from diagnosis to assessment ( $t = -4.89$ ,  $df = 83.755$ ,  $p < 0.001$ ).

### Main distress outcomes

Comparing the two national sites there were significant differences concerning illness-specific distress, Icelandic parents (at the smaller site) scoring higher. The majority of the subscales where the Icelandic study group scored higher concerned disease-related symptoms. In the entire clinical group of Swedish and Icelandic parents, distress among parents generally exceeded the level of our reference group data collected from the non-clinical group.

Results from t-tests regarding all studied dimensions of distress (PPD-C) showed that Icelandic parents scored significantly higher on 5 of the 11 subscales (*uncertainty* ( $p < 0.001$ ); *loss of control regarding parenting the sick child* ( $p < 0.01$ ); *disease-related fear* ( $p < 0.001$ ); *sleep disturbances* ( $p \leq 0.00$ ); and *K: psychological and physical distress* ( $p = 0.001$ )).

For the remaining 6 subscales the outcomes were similar when comparing the two sites, showing no significant difference between the clinical study groups. Outcomes of the GHQ-12 concerning non-pathological psychiatric symptoms were similar for the two national groups.

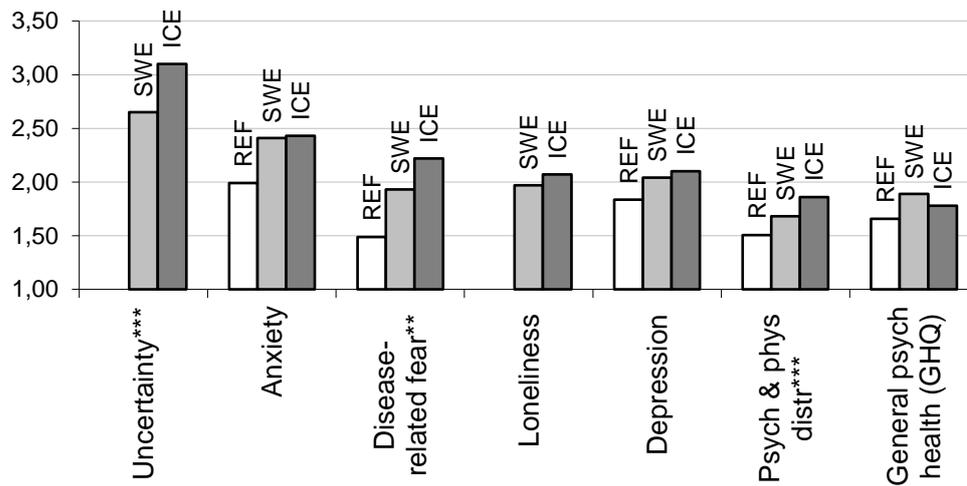


Figure 4. Group-wise outcomes for 4-point distress symptom scales (scale range=1-4). REF=reference parents, non-clinical; SWE & ICE= Swedish and Icelandic childhood cancer parents, respectively. \*\*\*= $p < 0.0001$ , \*\*= $p < 0.001$ , \*= $p < 0.01$  in Sweden - Iceland clinical groups comparisons. Note 1: Uncertainty and Loneliness scales are illness-specific, and not applicable for the non-clinical reference group.

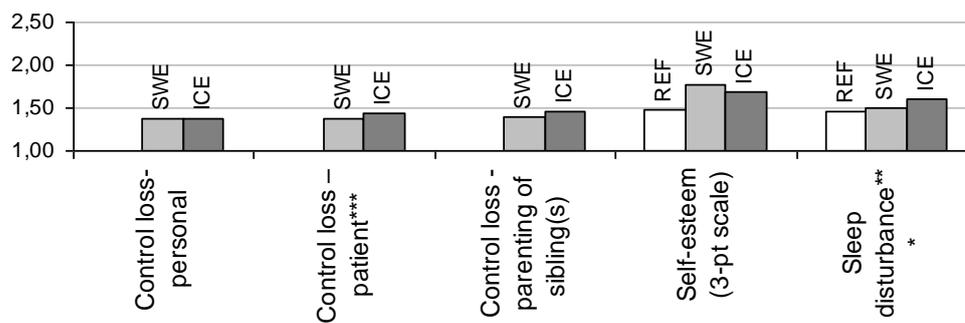


Figure 5. Group-wise outcomes for 3 & 2-point distress symptom scales. REF=reference parents, non-clinical; SWE & ICE= Swedish and Icelandic childhood cancer parents, respectively. \*\*\*= $p < 0.0001$ , \*\*= $p < 0.001$ , \*= $p < 0.01$  in Sweden - Iceland clinical groups comparisons. Note 1: Control loss sub-scales are illness-specific, and not applicable for the non-clinical reference group.

## Reflections on learning – Studies I & II



*The study that resulted in these published papers provided me with a number of learning experiences. As a new PhD student I gained knowledge about cancer as a spectrum of diseases, including both the clinical physical reality as well as the treatment regimes for patients. I learned the structure and purpose of the various questionnaires as well as the process of convincing parents to take part in the study. Recruitment of these individuals during such a stressful time is not something to be taken lightly. Other practical experiences that were new to me included construction of the database and statistical analyses, as well as scientific writing. The comparative approach of the two study populations also open my eyes to the structure and functioning of healthcare providers, as well as the importance of the presiding cultures within these organizations.*

*During the process of thesis evaluation, it became apparent that there has been a lack of scientific precision in these first two published papers. The data included were inaccurate and the statistical analyses inappropriate. Quite late in my training I was thus forced to learn new lessons in critical thinking and data quality control. I embarked on an intensive re-learning of statistics with an expert in the field. With the experience of hindsight and somewhat improved scientific maturity, I welcomed the chance to re-assess these data and to critically re-analyse the scientific interpretations.*

*An over-arching reflection of these two different learning phases is how useful a critical re-appraisal of one's own scientific data is, and should possibly represent a practice that every researcher could adopt, even when the original data are sound, in order to promote scientific reflection.*



## **STUDY III**

### **Main distress outcomes**

Comparison of parents in the clinical and non-clinical groups (NCG) revealed a significantly ( $p<0.001$ ) higher mean level of VE score in the clinical group. Comparing groups regarding the suggested VE clinical cut-off score ( $\geq 14$ ), the results revealed that the number of parents in the clinical group above the cut-off score were significantly higher than in the non-clinical group (CG=59.8%; NCG=40.1%,  $p<0.001$ ). Furthermore, comparison of the two groups regarding the higher cut-off threshold score demonstrated a highly significant difference with almost half of the cancer parents having a cut-off score of  $\geq 20$  (CG=45.4%; NCG=17.4%,  $p<0.001$ ).

Time from diagnosis significantly affected VE scores. Type of child cancer diagnosis also affected levels of VE scores, although non-significantly ( $p=0.55$ ), while the number of differential treatments had no significant effect on levels of VE.

### **Vital Exhaustion and gender**

Comparisons between the groups regarding gender revealed that there was a significant difference in MQ mean score between males and females in the clinical group with women having a significantly higher mean MQ than men ( $p<0.001$ ). Regarding the suggested VE clinical cut-off score ( $\geq 14$ ), the results further demonstrated that the proportions of mothers above the cut-off score were significantly higher than were fathers (mothers=58.9%; fathers=45.2%,  $p=0.003$ ). The same was evident regarding the  $\geq 20$  clinical cut-off score, with 42.8% of mothers compared with 26.4% of fathers,  $p<0.001$ . There was no significant difference between genders in the non-clinical group.

### **Vital Exhaustion and Traumatic Stress Symptoms**

Analysis of MQ and IES-R total scores in the clinical group demonstrated a strong relationship between VE and TS ( $r.641 - p<0.001$ ). Further analysis of subscales indicated a correlation between MQ total score and symptoms of Intrusion ( $r.536 - p<0.001$ ), Avoidance ( $r.463 - p<0.001$ ) and symptoms of Hyperarousal ( $r.692 - p<0.001$ ).

### **Comparison of Traumatic Stress Symptoms**

The comparison of levels of TSS between the Clinical and Non-Clinical group were investigated for explorative purposes only, the definition of the traumatic event not being

identical between the two groups. Results of the t-test between independent groups demonstrated that levels were significantly higher in the clinical group in all categories of the IES-R except for the sub-category Avoidance (IES-R Total mean  $p=0.003$ ; Intrusion  $p=0.006$ ; Hyperarousal  $p<0.001$ ).

### **Comparison of Traumatic Stress Symptoms and gender in clinical group**

This trend was the same when comparing parental gender in the clinical group, i.e. statistical significance in all dimensions of TSS except for the category Avoidance, mothers having a significantly higher score than fathers in three categories of four (IES-R Total,  $p=0.001$ ; Intrusion,  $p=0.002$ ; Hyperarousal,  $p=0.001$ ).



### **Reflections on learning – Study III**

*This study provided me with increased subject-specific knowledge of the field, and a realization of the many different aspects that could be studied. There was thus the chance to critically compare and contrast the use of different grading tools, as well as the relative importance of the variables in focus. The study also provided me with the opportunity to deepen my knowledge of statistics through use of new analysis methods.*

*It became clear to me through the writing phase of this study that there was a lack of systematic review of the specific research field, and I thus took the initiative to conduct an extensive review of the literature. This gave me the opportunity to increase my skills in literature searches, critical appraisal of other's work, and to gain a tremendous overview of the subject area knowledge. By learning how to apply critical criteria the results of these protracted endeavours resulted in a selection of only 7 relevant studies from a total of over 500 reviewed published papers. While this sample size precluded writing of a publishable review article, it still represents significant personal learning experiences.*



## GENERAL DISCUSSION

The general aim of the studies in this thesis was to increase knowledge concerning short- and long-term consequences of having a child with cancer, and possible factors associated with those consequences. This includes the investigation of parental distress in general, as well as specific risks and strength factors, including variations in organisation of care due to treatment centre type. The aim was to increase our understanding of the determinants of parental reactions and needs. This facilitates the development of the care and follow-up routines for families, paying attention to both individual risk and resilience factors, and to ways in which limitations related to treatment centre and organisational characteristics could be compensated for.

Findings of earlier studies indicate that parents of children with cancer experience extraordinary strain which, in turn, can increase their vulnerability for developing various serious psychological symptoms (e.g. depression, anxiety, sleep-disturbances and symptoms of post-traumatic stress) (Boman *et al.*, 2004; Cernvall *et al.*, 2013; Cernvall *et al.*, 2015; Gudmundsdottir *et al.*, 2013; Kazak *et al.*, 2004; Lindahl-Norberg *et al.*, 2008; Ljungman *et al.*, 2015; Van Dongen Melman *et al.*, 1995). Thus, as earlier studies have shown (Boman *et al.*, 2004; Hovén *et al.*, 2008), and the outcomes of study II and III appear to confirm, the negative psychological symptoms have been found to persist years after diagnosis and successful treatment.

### GENERAL DISCUSSION – SUMMARY

Results from numerous studies worldwide have shown that the unexpected and life-threatening cancer diagnosis, often followed by invasive medical treatment, evokes a period of multifaceted stressors for the parents of the sick child. These, now well documented facts, confirm that psychosocial services are a critical component in complete paediatric cancer care (Pai *et al.*, 2006; Cernvall *et al.*, 2013; Cernvall *et al.*, 2015; Kukkola *et al.*, 2017).

The findings in this thesis indicate that parental resilience to cancer-related distress varies with identifiable strength factors. Addressing resilience simultaneously as screening for possible adverse symptoms associated with a child's cancer helps identifying parents at risk and in need of intensified psychosocial support. That is, prior intervention studies have not screened for distress to triage participants to appropriate intensity of intervention. Instead, all participants have been allocated to the same intervention irrespective of reported distress level or perceived need.

Distress and needs for illness-related information was more prominent among parents at the smaller Icelandic site. This finding indicates a need for routines to meet parental uncertainty, adapted to conditions prevailing at a low-influx centre with limited resources for specialized psychosocial follow-up.

Differences between study groups indicate that compensatory measures in local/national and/or site-related arrangements for care, surveillance and information are possible means by which parental psychosocial services can be improved. Differences in this study in parental outcomes may partly be due to the larger centre having more favourable preconditions for providing a multifaceted caring context, including parental fellowship where informal mutual support and shared information contribute to resilience against illness-related distress.

The results of study III extend current knowledge and understanding of the complexity and diversity of childhood cancer-related parental burden over time that needs attention in care and long-term follow-up. The correlations between levels of acute stress symptoms and levels of vital exhaustion symptoms indicates a possibility of using IES-R in early screening, useful for sufficient intervention due to differential levels of traumatic stress symptoms for better prevention of the development of long-term distress in terms of Vital Exhaustion.

Furthermore, early screening might also be beneficial for the purpose parents of children diagnosed with cancer possibly being at risk of developing physical conditions (e.g. cardiovascular disease) as apparent in studies of other populations in which VE scores are elevated (Appels, 2004).

## **Study I**

As far as is known, few studies have investigated the effect of resilience-related individual characteristics among parents of children with cancer, although studies concerning children suffering from other medical conditions (Hedov *et al.*, 2002; Olsson, & Hwang, 2002; Svavarsdottir *et al.*, 2005) have shown that SOC is a positive and helpful factor for parents in these stress-related circumstances.

Following Antonovsky's theory on sense of coherence (Antonovsky, 1987; Antonovsky & Sagy, 1986), and inspired by earlier studies investigating the effect of sense of coherence (SOC) on parents experiencing long-term distress due to illness-related situations (Hedov *et al.*, 2002; McCubbin, Balling, Possin, Friedrich, & Bryne, 2002; Olsson *et al.*, 2002; Sivberg, 2002; Svavarsdottir, McCubbin, & Kane, 2000), our hypothesis was that high SOC would be related to parents' being more resilient against distress when faced with their child's cancer.

Overall, the outcomes of Study I showed that levels of sense of coherence were associated with higher resilience, here operationalised as lower levels of reported distress symptoms. Conversely, lower levels of SOC were significantly associated with parents' showing more severe distress in all dimensions of the Parental Psychosocial Distress in Cancer (PPD-C) questionnaire and the General Health Questionnaire (GHQ). These results supported the primary study question whether individual resistance factors, operationalised as sense of coherence, being of significance for parents' experienced levels of distress.

The impact of SOC varied with parental gender, where levels of SOC had a stronger modifying effect among mothers than fathers. Also, regarding parents' level of education, the protective effect of SOC had a stronger influence on distress in parents with a lower level of education compared to those with a higher level.

When designing the study we were aware that studying parents shortly after the child's cancer diagnosis might influence the levels of parental SOC. Antonovsky, the founder of the theory of sense of coherence, points out that situations involving intense stress may influence parental coping and be associated with a decrease in SOC (Antonovsky, 1987). To reduce the possible bias of such a potential decrease of SOC due to intense stress, in Study I we stipulated 36 months as the minimum time from child's diagnosis to assessment for parental inclusion. The period directly after diagnosis and the initial treatment period were not covered, since this is a period known to be characterised by the most intense stress (Boman *et al.*, 2003; Levi *et al.*, 2000; Poder *et al.*, 2007; Vrijmoet-Wiersma *et al.*, 2009).

The focus on medium-to-long-term parental distress instead of acute stress following diagnosis meant that the study group was composed of parents whose children had already completed 2–2.5 years of cancer treatment. Among these parents, SOC was at a level similar to those in the non-clinical reference-group, indicating relative stability of SOC across situational circumstances, at least when these are not characterised by acute and intense stress.

The clinical implications of the outcomes are that using the SOC scale, in order to counteract psychological vulnerability, screening for strengths can facilitate the detection of parents at risk, predicting the severity of stressful reactions, which in turn can improve the identification of parents in need of intensified professional psychological support and psychosocial follow-up, when facing childhood cancer.

## Study II

The aim of Study II was to improve the understanding of possible determinants influencing parental psychological reactions to childhood cancer. It therefore focused not only on the occurrence of distress, or the influence of demographical or cancer-related factors, but particularly on differences in healthcare services, such as size and type of medical centre, and routines for psychosocial follow up for families of childhood cancer patients.

Earlier studies addressing parental reactions following childhood cancer have rarely, in a comparative approach, included samples from more than single nation samples. In our study we collected data from two national sites, one in Sweden and one in Iceland, quite different in size and frame of organisation. This enabled us to compare and study parental distress outcomes, and to investigate both national and site-specific potential determinants of parental psychological distress accompanying childhood cancer.

Regarding a focal question of the study, systematic differences in psychosocial outcomes were evident between the parents at the two studied sites, with Icelandic parents presenting stronger disease-related distress symptoms than Swedish parents.

This finding was to some extent unexpected, especially since a longer period of time had passed since diagnosis for the parents at the Icelandic site - although the two samples were within the same range of elapsed time from diagnosis to follow-up. These results were noteworthy, since earlier studies have usually shown disease-related distress to generally decrease with time. In contrast to our findings, other studies have sometimes indicated that parents of children with cancer report levels of distress symptoms similar to parents of healthy children (Jurbergs *et al*, 2007).

Another unexpected finding was that Icelandic parents had utilised more professional psychological support services than had Swedish parents, while at the same time exhibiting stronger, not less, distress symptoms. Explaining this outcome is difficult. One explanation may be that the Icelandic group experienced more disease-related distress, and consequently sought more professional help. Conversely, the outcome could be explained by the fact that the difference in the mean number of contacts is very small from a clinical perspective (Icelandic parents had on average received professional help 2.7 times, and Swedish parents 1.6 times). This may not be of clinical significance when it comes to reducing the severe distress symptoms evident in the childhood cancer parent population.

Another aim was to investigate whether and how parental psychological outcomes might be influenced by certain modifying factors, including parental gender, ethnicity, number of children in the family, and parental education, as well as factors related to the child's illness, such as age at diagnosis, type of cancer and time passed since diagnosis. In studying two treatment sites that exhibited considerable differences (e.g. regarding size, patient influx rate, psychosocial services), we also were especially interested in whether differences in distress in study groups might be attributable to differences in type of medical centre, and centre-specific routines for psychosocial services and follow-ups.

The significant differences in parental distress between the two sites remained strong even when adjusted for modifying factors (parental factors, patient factors, education, and utilisation of professional psychological support). Icelandic parents scored significantly higher on 5 of PPD-C's 11 subscales, indicating that there may be site-specific factors influencing distress outcomes.

One of these could be the population difference in the two nations, affecting the influx rate of childhood cancer patients at each site. Sweden has ~9.4 million inhabitants, large enough to allow for a number of specialised childhood cancer centres treating ~300 newly diagnosed patients annually, while Iceland with a population of ~320 thousand has only one small treatment centre (with no specialized ward when it comes to in-patient treatment) responsible for treating 12-14 newly diagnosed paediatric cancer patients annually.

The limited influx of CC patients is likely to result in less peer support for parents and families during the child's treatment and thereafter. The parental fellowship with mutual support and sharing of experiences naturally occurring at a large centre probably functions as a modifier of parental uncertainty, providing a variety of informal illness and treatment-related information. However, the lack of such inter-parental support at a small low-influx centre could be compensated for, by for example establishing regular meetings in an intensified and structured co-operation between the hospital and the local parental organisations. The establishment of volunteer-based groups, including parents with longer time elapsed since diagnosis and treatment could be a part of such routines, implemented in collaboration between the parent organisation(s) at the smaller treatment site as part of a structured follow-up.

### **Study III**

Prolonged and recurrent distress – often experienced by parents – can result in cumulative stress and fatigue symptoms developing into Vital Exhaustion, bringing with it risks of

different physical conditions. Our results confirmed that this is a risk for parents of children with cancer. Mapping and analysing general, traumatic, and long-term parental distress from novel angles, and with novel assessments addressing neglected potential symptoms, is important in developing specialized screening tools for detecting 'signs of warning' of severe distress at an earlier stage. Such screening can be used to identify support needs and prevent the development of persistent psychological and possible physiological burden of parents.

Studies have reported that symptoms of fatigue are common in the general population, confirming earlier observations that they convey a substantially increased risk of IHD and some mortality risk (Prescott *et al.*, 2003). Although the biological mechanisms relating fatigue symptomatology to IHD are not yet fully understood, we feel that symptoms of exhaustion should begin to become part of risk assessment in clinical practice.

Hypothetical explanations that fatigue/exhaustion might be a marker of chronic stress and an affected HPA-axis could definitely explain why parents of children with cancer have so high level scores of Vital Exhaustion symptoms. Knowing that earlier studies have demonstrated that your child's cancer diagnosis is experienced as a traumatic event, levels of traumatic stress symptoms in study III indicate that parents of children with cancer score significantly higher than do parents of children with no known illness. Results of the same study revealing that levels of Vital Exhaustion are also significantly higher than in the normal population (GP's) support that having a child with cancer evokes high levels of both acute and chronic stress symptoms.

## **REPRESENTATIVITY AND GENERALISIBILITY**

The relatively low response rate in the studied clinical groups (total response rate for all 3 studies ~64%) must be acknowledged when considering the generalisation of the findings for the whole population of parents of children with cancer. In particular, the lower response rate at the Icelandic site (~56%) raises the question of whether the study sample is representative of the Icelandic study population, affecting in turn generalisation of the Icelandic outcomes. Conversely, the Icelandic group represented an entire national cohort, which to some extent may compensate for the negative effect of the lower participation rate in the Icelandic group.

There are a variety of possible explanations for the lower response rate in the Icelandic group. The Icelandic nation is small, with only ~320 000 inhabitants. This can result in concerns about anonymity (fear of being identified/recognized) when participating in studies like this for which sensitive data is collected about illness and individual

psychological reactions. The situation is thus quite different from that in Sweden, where data collection involved a large city population, the risk of similar identification hardly constituting a problem at all. The relatively small group of all families of children diagnosed with cancer also constitutes the only 'national target group' for similar investigations in Iceland, a fact that may result in the group becoming the subject of a variety of similar and simultaneously on-going research studies. If so, being frequently contacted for research study purposes could make parents more reluctant to participate. Although attrition always constitutes an unwanted weakness complicating the interpretation of results, the two types of hypothetical explanations for the attrition referred to above, although they are likely to be influential, need not seriously threaten the reliability and generalisability of the findings.

## POINTS OF PERSPECTIVE

### THE EXPERIENCE OF CHILDHOOD CANCER DIAGNOSIS – A TRAUMATIC EVENT?

Various studies have been conducted on the prevalence of traumatic stress symptoms in different groups of people for several decades, trying to explain how different events can increase the levels of traumatic stress symptoms. Empirical research has indicated that the occurrence of lifetime exposure to forceful situations, traumatic enough to cause symptoms of acute and/or prolonged stress reactions, is between 51-60% (Wilson, in Wilson, & Keane, 2004). In other words, it is not that uncommon that individuals will be exposed to events potentially experienced as being traumatic during their lives.

Despite many parents experiencing their child's cancer journey as very traumatic a life-threatening illness or debilitating medical condition is **not** necessarily considered a traumatic event according to scientific definition. The scientific definition of a traumatic event having changed over the past decades, according to DSM-V a traumatic event "*must have been violent or accidental*" (APA, 2013, p.271). For most parents the diagnosis of a lethal disease as childhood cancer will neither be violent or accidental, the event not fulfilling criteria "A" in definition of traumatic events in the DSM-V, thus not qualifying this situation as fitting into the category of "POST-TRAUMATIC STRESS DISORDERS" even though all other criteria's might be fulfilled.

Thus, according to the new diagnostic manual, DSM-V, the definition of an existential event does not fit the earlier studies now directing the event of having your child diagnosed with cancer in the category of "Adjustment Disorders" (APA, 2013, p.286). This change must be seen as a setback for all researchers specializing in trauma studies, groups studied earlier fitting into the category of 'post-traumatic stress' now defined in terms of 'Adjustment disorder', a term quite different and less "emotionally charged" than the term traumatic stress.

Furthermore, this change might also change the view of societies, in many senses, as well as parents themselves not being recognized as having gone through the traumatic experience/journey of their child suffering from a lethal disease, but having problems adjusting to the fact that their child's lives are threatened. Not only can this become a problem regarding social security in the sense of recognizing the right of sick-leave due to your child's illness, but also regarding the recognition from family, friends, and society as a whole that the parents have gone through a severe traumatic event followed by long-term excessive stress. Thus this changes of terms could affect the parents own experiences,

following their child's cancer diagnosis feeling "shameful" perceiving themselves as "weak" for not "adjusting" better to their child's illness.

### **WHAT SHOULD WE MAKE OF ASSOCIATIONS BETWEEN LEVELS OF VITAL EXHAUSTION AND PARENTING A CHILD WITH CANCER?**

When a child is diagnosed with cancer the information not only results in parental feelings of traumatic distress but also brings with it a great deal of uncertainty (Mishel, 1981). Fatigue and stress also limit the parents' ability to understand. In a high-anxiety situation, parents often block after being informed of threatening conditions and do not hear the remainder of the conversation. Anxiety, denial, and anger can all cause the parents to distort information (Miles, 1979).

Although advances in medical knowledge alter survival rates in children diagnosed with cancer, the cure of cancer can bring with it certain costs in the form of different late effects, i.e. the child is living and cured from cancer but might be left with other chronic conditions which might bring with it the need for special support for the rest of his/her life and some of them will never be able to live a normal life.

### **TRAUMA, VITAL EXHAUSTION AND PSYCHOBIOLOGY**

The well-known biological result when faced with traumatic situations is 'fight-or-flight'. Concurrent with theories of an affected HPA-axis due to traumatic stress, the production of cortisol is elevated so the person can survive the traumatic situation, normally followed by the body seeking back to the state of homeostasis as soon as the experienced dangerous situation is not experienced as "risky" anymore (Rotschild, 2001; Wilson, in Wilson, & Keane, 2004). In a "normal" fight-flight situation the production of cytokines will be impeded as the body needs to over-produce cortisol for surviving the experienced dangerous situation/trauma. A study on victims of rape demonstrated that levels of cortisol increased when victims were reminded of the traumatic situation (Gola, Engler, Schauer, Adenauer, Riether, Kolassa *et al.*, 2012). Contrary to the normal biological reaction to traumatic situations, there are studies demonstrating an abnormal production of pro-inflammatory cytokines (McEwen, 2000) indicating that levels of different pro-inflammatory cytokines are elevated when individuals are undergoing long-term excessive stress (Tian, Hou, Li, & Yuan, 2014).

Referring to studies on heart patients the results of several studies demonstrate that patients experiencing severe heart conditions (e.g. cardiac arrest) have high scores on symptoms of Vital Exhaustion, supporting the speculation regarding a connection between Allostatic Load

with an overproduction of pro-inflammatory cytokines over prolonged time. There are studies demonstrating interactions between levels of heightened levels of inflammatory markers (cytokines) and different conditions, (e.g. interleukin 1; IL-6; IL-1 $\beta$ ; IFN $\gamma$ ; and TNF $\alpha$ , these cytokines showing increased levels in PTSD, Anxiety, Major Depression, and Eating Disorders) (Bremner, Vythilingam, Vermetten, Adil, Khan, Nazeer *et al.*, 2003; Moonga, Lekander, von Blixen, Rönnelid, Holmgren, & af Klintenberg, 2011; Passos, Vasconcelos-Moreno, Costa, Kunz, Brietzke, Quevedo *et al.*, 2015; Zunszain, Anacker, Cattaneo, Carvalho, & Pariante, 2011).

Hypothetically, over-production of pro-inflammatory cytokines might even associate with different kinds of psychological and physical conditions defined as autoimmune diseases (e.g. Alopecia Areata; Fibromyalgia; Chronic Fatigue) (Ong, Benson, Zautra, & Ram, 2017).

### **Trauma, vital exhaustion, and psychobiology in the context of parents of childhood cancer patients**

Going through the journey of your child's cancer there can be different situations triggering excessively stressful cognitive and/or bodily memories of the "originally" traumatic event (your child's cancer diagnose – "My child has cancer and can actually die!"). Thus, although the traumatic situation in itself is over, the experience of trauma is still evident. The body is thus not able to turn back to a state of homeostasis and in these situations the body "settles" into a mode of Allostatic Load as it is forced to "gear down" from fight-or-flight, otherwise the body will physically collapse with a risk of death. Furthermore, the child's cancer diagnosis is often followed by different factors adding to the already excessively stressful situations. These include lack of sleep, insufficient food intake, information overload (e.g. sub-diagnosis, intervention methods, medicaments, the vocabulary of cancer, technicality in terms of "monitors"; "syringes"; "saturation"; "intravenous lines"; etc.), as well as *taking care of the whole family and possible siblings*.

It would be rational to expect that the body continues to have excessive levels of Cortisol under continuous extraordinary strain, stressing the body to stay in an alert position, thus making it very difficult for the body to revert to the homeostatic state. But, as mentioned above, there are studies on other populations demonstrating that individuals kept in excessively strained situations for a long time unexpectedly do NOT have excessive levels of cortisol. Furthermore, other studies have shown that contrary to what should be expected, levels of cortisol have even been at the lowest levels when fatigue/exhaustion is expected to be the greatest (Nicolson *et al.*, 2000; Glover *et al.*, 2002).

Thus the ongoing excessive stress levels that direct the body to ‘settle’ for levelling down from the fight and flight mode to the state of Allostatic Load. Needing to stay in that state for a long period of time will lower the production of cortisol, but levels of different pro-inflammatory cytokines will be heightened, evoking inflammation in the body (e.g. in the arteries), this leading to a heightened risk of serious psychological and/or physiological conditions in parents of children with cancer.

### MODEL OF “VICIOUS CYCLE”

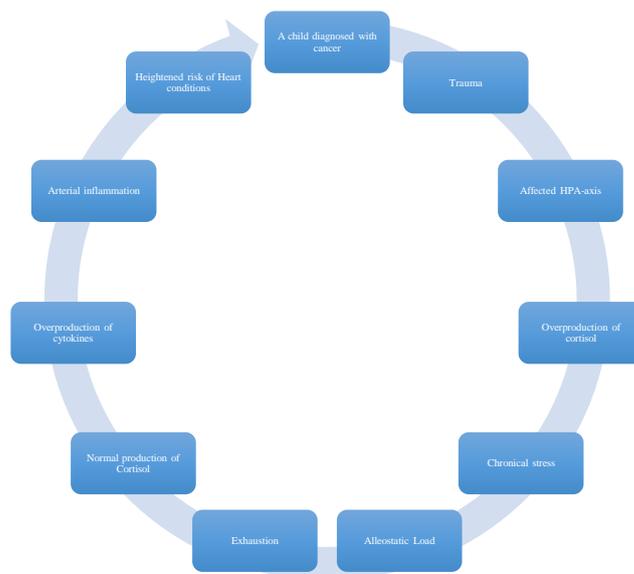


Figure 6. Vicious cycle

*Might parents get worn out not only fighting their child's cancer but also for the family's Quality of Life?*



*A sibling to a cancer child patiently waiting that someone will take her out of the hospital and into the warm summer – longing for running, jumping, and climbing trees.....*

## CONCLUSIONS

The results from my studies provide expanded knowledge of the risk and resilience factors affecting parental distress in parenting a child diagnosed with cancer. In this project we, among others, studied long-term distress in the terms of Vital Exhaustion, an outcome related to burnout, which has not been addressed before in this population and rarely in international studies regarding parental distress.

Findings of the studies from this PhD project revealed, not surprisingly, that parenting a child diagnosed with cancer entails levels of both general and long-term distress sub-ordinate to levels evident in parents of children with no known lethal illness. Results demonstrated that the proportions of parents having levels of long-term distress in the terms of Vital Exhaustion were large (59.8%) and 40.1% of parents had levels exceeding the suggested clinical cut-off ( $\geq 14$ ), levels not beginning to decline until 2.5 years after child's cancer diagnosis.

Proportions of parents scoring at the "high clinical cut-off" ( $\geq 20$ ), thus being at excessive risk of developing severe cardiologic problems, were even more worrying 45.4% of the clinical group having this score compared to 17.4% of parents not having a child diagnosed with cancer. Further, when it comes to symptoms of long-term distress, in terms of Vital Exhaustion, results indicate that not until approximately 10 years from diagnosis before parents scores are in line with the general population. The findings thus confirmed the need for a long-term intervention program following parents over a much longer time than those intervention models evaluated in this thesis.

## FUTURE PERSPECTIVES

### HUMANISTIC/EXISTENTIAL PSYCHOLOGY: A MISSING LINK IN THE DEVELOPMENT OF PSYCHOLOGICAL INTERVENTION PROGRAMS FOR PARENTS OF CHILDREN WITH CANCER?

*“The fear of death plays a major role in our internal experience; it haunts as does nothing else; it rumbles continuously under the surface; it is a dark, unsettling presence at the rim of consciousness.” (Yalom, 1980).*

In existential theories one of four main concerns in life is death (Yalom, 1980).

Despite that a child dying before its parent must always have been experienced as an unnatural cycle of life, the death of children has in Western societies become very rare compared to the raising of children 100 years ago. This fact has brought us to the reality that losing a child has become an even more un-natural part of life. Concurring with Yalom the death of your offspring could thus most certainly be understood as the fifth and even greatest “life-worry” a parent can imagine. Even so horrifying that parents will not even bring it up to consciousness as being a part of reality.

Results of numerous studies investigating the effect of having a child diagnosed with cancer clearly document various and extensive adverse outcomes for parents’ well-being.

Experiencing one of your greatest fears brings with it the importance of acknowledging this as a situation in which severe symptoms of distress in parents is normal. Feelings of despair and anguish in these situations are not the result of dysfunctional thought patterns and they are not ‘curable’ through reframing cognitions. Experiencing emotions of despair, hopelessness and fear are normal reactions to an unfamiliar situation for which one is hopelessly unprepared. This is a perfectly normal human response.

Existential psychotherapy is supportive suiting in a situation with “real” life-crisis. Normalizing the fear/anxiety/anguish as well as other feelings “followed” being a parent on his/hers child’s cancer journey, and supporting the parents in these feelings in what way fitting the individual situation as no family is identical to the next.

Summarizing this thesis there is an evident need for more effective intervention programs to reduce different variations of distress in parents of childhood cancer patients, preventing the possible consequences of excessive levels of long-term strain, in terms of Vital Exhaustion.

Through combining already attained evidential knowledge, using varied psychotherapy techniques, acknowledging the essential fact that parental distress is normal and not an object of psychopathology, should all be important aspects in developing an effective eclectic intervention program in this setting.

Do we believe that a family's cancer journey can result in severe long-term distress in terms of vital exhaustion, putting parents at elevated risks for adverse psychological and physiological conditions?

The study results of all three studies show that levels of general distress and vital exhaustion are significantly higher in parents of children with cancer than in parents of children with no known severe or chronic diseases. Levels of stress symptoms due to a traumatic event (in this thesis, a child's cancer diagnosis), were not comparable with our reference group as the directions of the assessment tool used (IES-R) suggests that if no defined traumatic event the evaluation of what is experienced as a traumatic event becomes too subjective, lowering the power of the instrument, thus risking the validity of the scores attained.

Conversely the results demonstrate that so-called stable personality characteristics or elements of the individuals personality developed through the life-span, such as SOC and General Mental Health, did not differ between the clinical and reference groups. Comparing the groups in different demographical areas did not show differences explaining the much higher levels of different distress symptoms in the groups of childhood cancer parents – the only clear differences between these 2 groups were that one of them had experienced having their child diagnosed with cancer and the other had not. No matter how much we would like to analyse the results in different more complicated ways, these are the facts from the results of these three studies, and they are so significant that I can't see how we shall look past them and not believe in them?

Is it because it is an ugly truth? That parents even up to ten years after their child was diagnosed with cancer have levels of symptoms of vital exhaustion so high that they might be at risk for severe biological consequences? Or is it because we can't imagine that if the child survived the cancer there should only be happiness, resilience, learned Mindfulness in the sense that you've seen death in the eyes, through your offspring, and thus you now know what is really important in life, this giving you automatically a better Quality of Life?

It might be all of this, but the importance here is that having your child diagnosed with cancer is a journey, and for many families a very, very long journey, including experiencing things you as a parent never imagined you would be able to go through without losing your mind, or even still standing on your feet. But the battle takes its toll, and as explained in this thesis parents experience the diagnosis as a highly traumatic event, watching your child suffer should obviously be recognised as traumatic experience.

When it comes to your child's cancer the cancer is out of your control, it can hurt your offspring in so many different ways, both physically and psychologically, and you can't fix it, you need to rely completely on someone else (doctors/nurses) or something else (operation, radiation, chemotherapy). Your life as you knew it is beyond your control, your child's survival is beyond your control, and you don't have the power to do anything except wait, trust, hope, and try your best.....to fix it.

*When you try your best, but you don't succeed*

*When you get what you want, but not what you need*

*When you feel so tired, but you can't sleep*

*Stuck in reverse*

*And the tears come streaming down your face*

*When you lose something, you can't replace*

*When you love someone, but it goes to waste*

*Could it be worse?*

*Lights will guide you home*

*And ignite your bones*

*And I will try to fix you*

Using the findings of the studies from this project is useful and gives ideas to parameters important developing effective intervention programs. I have developed the following protocol that could be implemented in this context – Welcome to the EGG-protocol!

## THE EGG-PROTOCOL

This is how a protocol could look like taking the results of the three studies into account:

- 1) Screening for traumatic stress symptoms using IES-R as well as establishing the baseline level of long-term distress symptoms using the Maastricht Questionnaire – this should be done approximately 1-2 weeks after the child’s diagnosis.
- 2) Theoretically parents can be in a state of *Allostatic load* the first weeks after their child’s diagnosis focusing on fighting for their child’s survival, this could cause difficulties for them being in “realistic” contact with their own psychological well-being which could cause the first results to be “false positive”. For this reason, measuring parent’s levels of cortisol levels could give a more “true” and “stable” insight into parent’s stress levels during the first weeks after their child’s cancer diagnosis.

As early as the child’s diagnosis, there should be an *active* psychological contact in that sense that a psychologist has introduced himself to the family. This should be by the hospitals initiative, and the parents should be informed that a psychologist is available when needed. It is of great importance that the contact with the psychologist continues to be active and structured in that way that this person will check-up on the family/parents at least once a week while they are staying at the hospital. If the family is not staying at the hospital the contact should be continued via telephone or through other possible and appropriate ways. Considering studies showing that the families financial situation will be affected in one way or the other (e.g. Hovén *et al.*, 2013), a social worker should relate to the family taking care of everything that has to do with keeping the families economy as intact as possible.

- 3) Two-to-four weeks after the child’s diagnosis, parent’s resilience should be evaluated using the self-report instrument measuring Sense of Coherence, results from Study 1 showing the high scores on this scale can give an insight into parent’s resilience this being a protective factor regarding the development of severe distress.

Adding together levels of traumatic stress symptoms, baseline levels of long-term distress, measurement of cortisol levels, and the scores of SOC assuming parent’s resilience, parents should be divided into one of three arms of intervention, the one best suitable for their group.\*

4) Three months after the child's diagnosis traumatic stress symptoms should be measured for the second time, using the IES-R, as well as levels long-term distress for the purpose of following a possible level of the condition in terms of Vital Exhaustion. Subsequent to this is measurement of cortisol levels followed by a baseline measurement of concentrations of pro-inflammatory cytokines e.g. interleukin 1; IL-6; IL-1 $\beta$ ; IFN $\gamma$ ; and TNF $\alpha$ , these cytokines showing increased levels in PTSD, Anxiety, Major Depression, and Eating Disorders e.g. Bremner *et al.*, 2003; Moonga *et al.*, 2011; Passos *et al.*, 2015; Zunszain *et al.*, 2011) – this considering chronic low-grade inflammation as a potential target or biomarker (Passos *et al.*, 2015).

5) Six months after child's diagnosis measures should be the same as in 3, though adding measurement of oestrogen and testosterone in context with gender and age. The rationale for this is based on studies indicating that the risk of women developing a serious heart condition increases after the age of 50, possibly due to lowering levels of oestrogen which serve to buffer against these effects. Similar but juxtaposed indications have been implicated in studies of men, i.e. men getting testosterone replacement therapy are at elevated risk for severe/serious heart conditions.

6) One year after child's diagnosis the same measures should be conducted as in #3 and #4 with the only change of focusing on items measuring sleep and sleep quality using both IES-R and VE for this purpose. Physiological measurement should stay the same.

7) Two-and-a-half year after child's diagnosis, concurring with medical protocols on Acute Lymphoblastic Leukaemia used in Europe/Northern countries this being the longest continuous treatment protocol (30 months), exactly the same procedures as in #5 should be followed.

8) Five years after child's diagnosis, in line with the "Magical Five" some children being both 5 years after diagnosis as well as five years after treatment termination (those children with operable cancers NOT followed by radiation and/or cytostatic), procedures regarding measurements should follow #6 with the change of not measuring traumatic stress symptoms using IES-R. The reason for this is that according to Study 3 scores have diminished down to levels of the norm-population 5 years after a child's diagnosis.

9) The last organized follow-up for measuring parents psychological well-being using both psychological and physiological techniques should be performed 7.5 years after child's diagnosis following the procedures of #7. The results of Study 3 revealed that parents VE-scores do not align with the "norm" until 7.5 years after child's diagnose.

\*The intervention groups should be divided into:

***1 = high levels of traumatic stress symptoms, mean levels of long-term distress, high Cortisol levels, high resilience ->***

This group should receive the Standard intervention program, this including: meeting with a psychologist at least once a week for 3 months; psychoeducation using theories of cognitive behavioural therapy, teaching relaxation techniques, as well as focusing on helping parents getting sufficient quality of sleep this being one of the crucial things trying to prevent the development of Vital Exhaustion.

***2 = high levels of traumatic stress symptoms, high levels of long-term distress, high Cortisol levels, high resilience ->***

This group should receive the Standard intervention program with addition of physical examinations ensuring and preventing the development of different physical conditions and medication if needed, if levels of hyperarousal and sleep deficiency are higher than in 75% of the cancer parent group.

***3 = high levels of traumatic stress symptoms, high levels of long-term distress, high Cortisol levels, low resilience ->***

This group should receive both the Standard intervention program as well as the intervention used in group 2 with addition of support focusing on strengthening parent's resilience, e.g. teaching them different coping techniques useful for developing better ways in how they can handle this extremely stressful and straining situation, as well as working with possible difficult life-experiences having occurred earlier in life and/or ongoing difficult life situations NOT "connected" with the child's illness (e.g. earlier psychological problems; having experienced violence and/or other form of abuse; traumatic life-events; drug use; bad economic situation; unemployment).

## EPILOGUE

What makes people choose a field of interest to study in a scientific way?

Pure coincidence, as in it was the field advertising for PhD students for a project at a fancy university, personal fascination in the subject since early on, personal experiences, etc.?

And stick with it, maybe still with passion, maybe not.

Being a clinical psychologist I hardly knew the world of cancer, neither scientifically nor personally, until life introduced me to this world, in a very personal manner. The year was 2003.

*Here I had decided that I would “twist” the truth a little having been warned (both “kindly” and “less kindly” from the academic world that my studies would not be taken “seriously” if I told the truth. That my results would risk that they would be perceived as “subjectively filtered” from just “another mom” not being able to change between the different “hats” of being a clinical psychologist, a mother of a child diagnosed with cancer, and latest a “true” scientist.*

*For years I never presented myself as a “cancer mom” in situations where I was supposed to present my “scientific” results, neither at forums (e.g. parents of childhood cancer patients) where it was more beneficial not being judged as a “dry, scientific person, that did not know anything about having a child with cancer....”**yet another scientist coming with all these p-values, making us feel stupid not connecting our reality to those 12-minute presentation in which words such as “sequale” are used instead of late-effects”** - and the experience from the parents were often experienced as yet another “time-waste” from my battle of my child’s survival, trying to understand everything I needed to know regarding childhood cancer so I would have better chances that my child would “make it”.*

*I decided that it was a disgrace to my own intelligence and abilities of changing “hats”, so after thorough consideration I hereby choose to not “hide” anymore, especially not in the scientific world as in that world there are so much more prejudices, for some kind of reason, in the sense that it is “experienced” as shameful and non-scientific doing research for personal reasons, for a group dear to your own heart. Instead you can sit at a conference, having deep personal connection to the topic, experiencing that scientists have lost themselves in micro-details, re-polishing a screening instrument for 5 years but when they get the question of what they do if individuals are 1 score below the “cut-off point” you get the*

*devastating answer, replied in embarrassment, that “we only personally contact those reaching the cut-off point.” You realize that to some extent research is done for the “researchers” themselves, the reality of what they are studying not really being theirs, as long as they get paid and other scientists praise them for the results that the “sensitivity” of the psychological screening instrument got better. After spending 3 years of getting that result, they believe that they are doing a good deed, and they are, maybe just not so practical especially as theories and populations have changed a lot during those 10 years they’ve spent on sensitizing an instrument to people they have never met!*

*Sorry, lost track there, tend to do that at times, as you have already discovered if you kept on reading through this thesis.*

I still remember my confusion sitting at a meeting at the Children’s Hospital in Iceland, the year was 2003, and my youngest of three children, only 9 weeks-old, was diagnosed with a very, very bad prognostic type of cancer (*Infant ALL*). Present were a priest, three paediatric oncologists, an oncology nurse and a social worker. As I later, and of course subjectively, looked at my own face in the mirror, I saw a face as if made of stone, with eyes that understood what was going on but at the same time they had this empty, glazy look, that I had seen before when I had, due to my profession, met individuals in a severe traumatic state, and I remember thinking “*where is the psychologist that is part of this “a-child-newly-diagnosed-with-cancer-team”?*”

I got the answer at the end of the meeting - there wasn’t any. In professional misery, I tried to reason to myself the explanation I got when asking about psychological support: – ***If a parent/family member felt they needed a psychologist they should call the Children’s Hospitals Psychiatric Ward, situated 5 km away, and explain their situation and that they were not feeling well and needed a psychologist!!***

Nobody could explain to me how long it could take from making the appointment until you could expect to meet up with the psychologist, dependent on the load of the ward where the psychologist was stationed. These psychologists’ specialty was the field of psychiatric conditions of children, quite far from handling parents whose child just got diagnosed with cancer!

Watching the absurdity in this situation and as the time went by, my son being admitted in the hospital for several weeks, he was 9 weeks old, and me living there with him, apart from my 5 year-old as well as my 2 year-old children, I learned to know about paediatric cancer, as well as both the children and their parents involved in this horrible disease.

I watched kids (including my own) losing their hair, parents holding brave faces but turning their heads away with sorrow in their eyes when yet another pile of hair was stuck in the hairbrush instead of on the child's head. I heard sobbing when walking through the corridor, a 14 year-old boy knowing there was nothing left to do and death was waiting for him – in love for his parents, seeing their exhaustion even though they fiercely tried to hide it from him, keeping up a positive spirit, he had sent them home saying he could manage. I asked if I could hold him, and in my arms he cried out the anguish no 14 year-old should have, bearing the knowledge that your life is over.

He died three days later.

I watched the same families coming and going, at times there were happy faces, things going well. Treatment finish lines. A few times I watched the backs of parents, walking like their legs were made of Jello, to the end of the hospital corridor with personal belongings in plastic bags, leaving their dead child behind.

I decided to contact the Children's Cancer Organization and offered my work to them, the least I could do for all these brave families and being a psychologist.

Through the years I have met all kinds of people, the one and only thing all of them having in common being that their child had been diagnosed with cancer, and the experience of living on the edge of what is possible for a human being. Too many have I met that fought for their child's survival for years, sleepless, beyond anxious, having to live with the uncertainty of the possible relapse of the disease, staying in the ***“waiting-room of Hell”*** for the Holy five years post-diagnosis, falling down in pieces both mentally and physically years after a ***Happy Ending Story***, explaining their perception of self like ***“an empty shell”***; ***“beyond extra batteries”***; ***“ashamed”***, as in *“I mean everything went well, my kid is alive, nobody understands that 10 years after my daughters diagnosis I haven't recovered, and I am too ashamed to tell them that I'm even worse 'cause I haven't had any time recovering. Life, you know, taking care of mortgages, day-care, our kid almost blind and deaf as consequences of the harsh treatment, the middle child having developed some kind of illness- phobia thinking he is having all kinds of diseases, probably a consequence of having seen his sibling so sick. I haven't slept without sedatives for years, no energy to do anything for myself and the marriage is down the drain.....”*

Since the year 2003 I had wondered what needed to be done to better help these families, living the 'Cancer Journey'. Having had several meetings with all kinds of professionals working at the Children's Hospital I ended up realizing that the most prominent reason for a

structured or non-structured psychosocial support for parents of children with cancer - (this was also the case regarding all chronic diseases in children, but as this thesis is about childhood cancer I will focus on that) – was lack of scientific knowledge regarding the effect of having a child with cancer, without scientific proof there is difficult to get money to build organized support into a system already economically disadvantaged.

In the year 2005 I learned about a project at Karolinska Institutet focusing on the effects of parents having a child diagnosed with cancer, I contacted the project manager at KI and through our co-operation this bi-national project was born.

And this thesis represents the results from a long, quite bumpy ride – and **YES**, my youngest died, surviving cancer twice, the late-effects (Bronchiolitis Obliterans) of the experimental (but fortunate!) double bone-marrow transplantation led to his death, 10 years after beating his cancer prognosis (Infantile ALL), and he died as he lived “*Live your Life Living as long as you are Alive*”.

*In the memory of my beloved AngelBoy, Benjamín Nökkvi, who fought and loved life for almost all the 12 years of his almost 12-year-old life.*





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**Krister K. Boman.** Thank you for believing in me and accepting the challenge to go into this project knowing my life circumstances. Being understanding over the years but still showing me the respect of not “pampering” me and knowing that even though things have been difficult at times, the quality of my work should be at the same level as that of others. Thank you for that. Last but not least I want to thank you for all the great conversations we have had over the years, keeping the passion alive for my “call in life”.

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**Desirée Gavhed!** How can I not love you?! Over all the years, you have always been there explaining all administrative things confusing to me. From becoming a colleague in the beginning, I see you today as a wonderful person and friend with a warm hearth and a great spirit one cannot walk by without falling a bit in love.

Kära kära **Astrid Häggblad** – din underbara, fantastiska människa! Älskar dig på ett sätt som en tokig isländska kan älska sin förälder även om du inte är det. Alla våra snack genom åren, chokladen jag (inte!) försökt muta dig med, dina raka ”rör” och hur reglerna ”ÄR” på KI tillsammans med din uthållighet med alla mina frågor, förseningar, missförstånd (jag har alltså ADHD!), och inte minst ditt vackra bemötande med mig, alltid, men inte minst när min Benjamín gick bort. Du är verkligen den jag vill dricka Champagne med och ha en ordentlig ”bitch-snack” om livet med. Jag älskar dig!

**Anna Sandberg** – Huff, hur du har hjälpt mig! Du tog över Astrids position med bravör. Believe me, I will not try to” bribe” you with Icelandic chocolate. You are definitely one of the big reasons I kept on with it. On the other hand, do you like Icelandic liquorice.....?..... supposed to be great.

And “Hey there”, **Robert A. Harris** – my main supervisor! The way you fought for me, kept my passion alive, denied me “giving up”, believed in me as a person as well as “student” – how shall I say this..... you got me here ‘cause somewhere you believed that it is a good thing people thinking “outside the box”, that it is not a “scary” thing for senior researchers or others but a way of letting research go forward. Maybe the hypotheses will fail or prove as being non-valuable or non-useable – but let’s try it and check it out! That is the way a great supervisor should dare to think and this you did. Fucking THANK YOU for that!!!

My love, **Gustav Anders Wollmén**, you know me, you stood by me, you believed in me..... yeah, and you still stood by me! All the years with a “distant-minded” woman, hardly (at times) knowing your name (or even my own!), you were there, believing I was doing something good for parents of children diagnosed with cancer (and we both know that Journey). THANK YOU for sticking with me and still believing!

Last but definitely not least I want to thank my big wonderful Icelandic family, without grandparents, aunts, cousins, siblings, etc., this would never have worked out. You were always there for me when I needed help and stood up every time needed.

A humble TRIBUTE goes to my children who have been extremely patient over the years, especially at “dead-line” times, when I have “disappeared” into my little “closet” for days and days, coming out grumpy and not so patient. My children not understanding why I am so passionate about this research but showing it respect and accepting having a mother like this!

**Nikulás Ingi, Hrafnhildur Tekla, and Benjamin Nökkvi** – you are my heroes and greatest role-models in life. THANK YOU for being so great and wonderful and my love for you is not measurable but endless.

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