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INDIRIZZO DI PSICOLOGIA DELLO SVILUPPO E DEI PROCESSI DI SOCIALIZZAZIONE

XX CICLO

FAMILY FACTORS PREDICTING SHORT- AND LONG-TERM ADAPTATION AND QUALITY OF LIFE OF LEUKEMIC CHILDREN. A DESCRIPTIVE AND LONGITUDINAL STUDY

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ABSTRACT

The main focus of my research has been the identification of family factors predicting short and long-term child adaptation and quality of life of leukemic children. As a doctoral student I was research assistant with the tasks of data collection in the pediatric onco-hematologic clinic, data coding and analyses.

In particular, the focus was directed towards several aspects: Child's quality of life at the diagnosis, with the devise of an empirical model of psycho-social context; psycho-social state of ill children and their families throughout the several therapies' time points; the identification of possible post-diagnosis predictors of psycho-social adaptation of children after 12 months of therapies and of the possible predictors of Post-Traumatic Stress Disorder symptoms in their parents.

The rationale for this study is related to the advancement of therapies for cancer illnesses, especially leukemia (Ostroff et al., 2002), with an increasing attention on adaptation and quality of life of children with cancer and of their families (Eiser et al., 2005; Magal Vardi et al., 2004; Pickard et al., 2004). However the literature is not sufficiently completed on these psycho-social aspects during the therapies and on predictive factors identifying children and families more at risk for psycho-social problems.

A longitudinal approach was used to assess young patients and their parents at several steps of the therapy: 118 in the second week after diagnosis communication (T1), 110 in the second month (T2), 97 after 6 months (T3), 78 after 1 year (T4) and 45 after 2 years (T5). Loss of participants was due to several reasons: 11 deceased, 4 changed health

center, 5 relapsed or were in grave illness situation and only 5 families dropped out from the study (3.9%). Children's (61 girls and 66 males) mean age at the first assessment is 5.89 years (SD = 4.21). Parents mean age is 37.39 years (SD = 6.03), with a mean of 13 years of school (52.2%). These patients were recruited at the Haematology-Oncologic Clinic of the Department of Pediatrics, University of Padova.

In this study a large number of instruments for the assessment of both parents and children has been used, adopting a multi-method approach: Questionnaires, self-report, in depth interviews and psychological tests. All the instruments were derived from the international literature of this field. Among the several instruments used there are for example the Vineland Scales (VABS, Sparrow et al., 1984; Italian edition 2003) for child's assessment, the Ecocultural Family Interview (EFI-C) (Axia & Weisner, 2003; Tremolada et al., 2005) and a questionnaires battery from the Childhood Cancer Survivor Study to assess the parent's psycho-social status.

The principal results are the following:

1. At one year from the diagnosis children's development delays are evident by VABS: Socialization is the most delayed (78.2% of delays), followed respectively by Motor area in children aged 0-6 years (63.8%), by Daily Living Skills area (51.3%), and by Communication area (24.4%). The model tested (R^2 = 0.40; p = 0.0001) shows early child's coping (β = 0.69) mediated by Parenting factor (β = -0.11) as the best predictor of child's adaptive behavior post 1 year.

2. Longitudinal analyses on mental health of parents show that: DPTS symptoms don't change throughout time ($F_{(2,140)}$ = 1.09; p = 0.34); current life own perception increases during time ($F_{(2,144)}$ = 31.17; p = 0.0001); cognitive dysfunctioning doesn't modify during time ($F_{(2,140)}$ = 0.06; p = 0.93); depressive ($F_{(2,144)}$ = 3.58; p = 0.030) and arousal

($F_{(2,144)}$ = 4.26; p = 0.016) symptoms dampen. Also state anxiety at 6 months dampens significantly to 1 years post-diagnosis ($t_{(71)}$ = 2.71, p = 0.008). Parental psycho-social dimensions have the following trends: Emotional coping doesn't change along time ($F_{(2,144)}$ = 1.003; p = 0.37) and so does perceived Social support ($F_{(2,144)}$ = 0.22, p = 0.76); while Trust in medical care ($F_{(2,144)}$ = 52.52, p = 0.0001), Communication about illness ($F_{(2,144)}$ = 25.31, p = 0.0001), Routine and time reorganization ($F_{(2,144)}$ = 47.54, p = 0.0001) and couple connectedness ($F_{(2,144)}$ = 6,24, p = 0.004) increase along time.

3. An empirical model of path-analysis was estimated to evaluate child's quality of life at the second week from the diagnosis inside the psycho-social context. This model ($\chi^2(4)$ = 5.03; N = 128; p = 0.28; RMSEA = 0.045: NNFI = 0.99; CFI = 1) shows that child's quality of life is predicted by Parental trust in the medical staff, by Child Coping and Child Adaptability. These last two predictors are in turn sustained by the fixed factor Child age and by the modifiable factor Parenting.

4. An empirical model of path-analysis is estimated to identify early predictors of parental DPTS symptoms. This model ($\chi^2(9)$ = 8.83; N = 100; p = 0.45; RMSEA = 0.0001; NNFI = 1; CFI = 1) shows that emotional coping and support received are key elements impacting, the first, on parental memory abilities, and, the second, on the perceptions of their current lives. All these family factors are also related to parents' BSI-18 global score assessed at the diagnosis and indicative of short-term PTSS problems.

Specific psycho-social intervention programmes for ill children and their families can be proposed and structured basing on the empirical information collected.

RIASSUNTO

Il lavoro di ricerca di questo triennio di dottorato si è indirizzato su numerosi aspetti legati alla malattia e al trauma in età pediatrica, prestando attenzione sia ai bambini che ai loro genitori. Lo scopo principale della mia ricerca è stato l'identificazione dei fattori familiari predittivi dell'adattamento e della qualità di vita, a breve e a lungo termine, dei bambini leucemici. Come studente di dottorato ho condotto la ricerca occupandomi della raccolta dati presso la clinica di oncoematologia pediatrica ed ho successivamente analizzato e codificato i dati.

In particolare, il focus è stato rivolto su diversi aspetti: la valutazione della qualità di vita dei bambini alla diagnosi, con la creazione di un modello empirico del contesto psico-sociale; l'assessment dello stato psico-sociale del bambino malato e della sua famiglia lungo le diverse tappe del percorso terapeutico; l'identificazione dei possibili predittori post-diagnosi dell'adattamento psico-sociale nei bambini dopo 12 mesi di terapia e dei predittori dei sintomi di Disturbo Post-Traumatico da Stress (DPTS) nei loro genitori.

La ragione per cui è stato condotto uno studio di questo tipo è legata al miglioramento delle terapie per le malattie tumorali, soprattutto la leucemia (Ostroff et al., 2002), con una sempre maggiore attenzione all'adattamento e alla qualità di vita dei bambini con cancro e delle loro famiglie (Eiser et al., 2005; Magal Vardi et al., 2004; Pickard et al., 2004). Comunque la letteratura non è ancora sufficientemente completa su questi aspetti psico-sociali durante le terapie e sui fattori predittivi che possano identificare i bambini e le famiglie più a rischio di problemi psico-sociali.

Il lavoro di raccolta dati di tipo longitudinale ha previsto la valutazione dei giovani pazienti e delle loro famiglie in diversi momenti della terapia: 118 nella seconda settimana dopo la comunicazione della diagnosi (T1), 110 nel secondo mese (T2), 97 dopo 6 mesi (T3), 78 dopo 1 anno (T4) e 45 dopo 2 anni (T5). Nei diversi momenti delle valutazioni abbiamo perso alcuni partecipanti per diverse ragioni: 11 sono deceduti, 4 hanno cambiato centro di cura, 5 sono ricaduti o erano in stadio terminale e solo 5 famiglie hanno interrotto lo studio (3.9%). L'età media dei bambini (di cui 66 maschi e 61 femmine) alla prima valutazione è di 5.89 anni (DS = 4.21). L'età media dei loro genitori è di 37.39 anni (DS = 6.03), con una scolarità media di 13 anni (52.2%). Tali pazienti sono stati reclutati presso la Clinica Oncoematologica del Dipartimento di Pediatria di Padova, Università di Padova.

In questo studio è stato utilizzato un grande numero di strumenti per la valutazione dei genitori e dei bambini, adottando un approccio multi-metodo: questionari, self-report, interviste in profondità, e test psicologici. Tutti gli strumenti derivano dalla letteratura internazionale sul campo.

Tra i diversi strumenti utilizzati vi sono ad esempio le Scale Vineland (VABS, Sparrow et al., 1984; ediz. italiana 2003) per l'assessment del bambino, l'Ecocultural Family Interview (EFI-C) (Axia & Weisner, 2003; Tremolada et al., 2005) e una batteria di questionari del Childhood Cancer Survivor Study per valutare lo stato psico-sociale del genitore.

I risultati principali sono i seguenti:

1. Ad un anno dall'inizio delle terapie sono stati evidenziati nei bambini i possibili deficit di sviluppo tramite le VABS: l'area della socializzazione risulta essere la più colpita (78.2% di deficit), seguita rispettivamente da quella motoria nei bambini 0-6

anni (63.8%), dall'area delle abilità quotidiane (51.3%), e, infine, da quella della comunicazione (24.4%). Il modello tesato (R^2 = 0.40; p = 0.0001) mostra come predittore del comportamento adattivo del bambino a un anno il suo coping iniziale alla diagnosi (β = 0.69) mediato dal fattore parenting (β = -0.11).

2. Le analisi longitudinali sulla salute mentale del genitore mostrano che: la quantità di sintomi di DPTS non si modifica nel tempo ($F_{(2,140)}$ = 1.09; p = 0.34); la percezione soggettiva della propria vita migliora nel tempo ($F_{(2,144)}$ = 31.17; p = 0.0001); il malfunzionamento cognitivo non si modifica nel tempo ($F_{(2,140)}$ = 0.06; p = 0.93); i sintomi depressivi ($F_{(2,144)}$ = 3.58; p = 0.030) e di arousal diminuiscono ($F_{(2,144)}$ = 4.26; p = 0.016). Anche l'ansia di stato misurata a 6 mesi e misurata a un anno decresce in modo significativo ($t_{(71)}$ = 2.71, p = 0.008). Per quel che riguarda le dimensioni psico-sociali del genitore: il Coping Emotivo non si modifica nel tempo ($F_{(2,144)}$ = 1.003; p = 0.37) così come il grado di Supporto Sociale percepito ($F_{(2,144)}$ = 0.22, p = 0.76); mentre migliorano col tempo la Fiducia nello Staff Pediatrico ($F_{(2,144)}$ = 52.52, p = 0.0001), la quantità di comunicazione sulla malattia ($F_{(2,144)}$ = 25.31, p = 0.0001), la capacità di riorganizzazione della routine familiare ($F_{(2,144)}$ = 47.54, p = 0.0001) e la coesione di coppia ($F_{(2,144)}$ = 6,24, p = 0.004).

3. Un modello empirico di path-analysis è stato stimato per valutare la qualità di vita (QdV) del bambino nella seconda settimana dalla diagnosi all'interno del suo contesto psico-sociale. Tale modello (χ^2(4) = 5.03; N = 128; p = 0.28; RMSEA = 0.045: NNFI = 0.99; CFI = 1) mostra come la QdV del bambino sia predetta dalla fiducia che i genitori hanno nel Reparto, dalle abilità di coping del bambino stesso e dalla sua adattabilità. A loro volta i due ultimi predittori citati sono sostenuti da un fattore strutturale, l'età del bambino, e da un fattore familiare, il parenting.

4. Un modello empirico di path-analysis è stato stimato anche per identificare i predittori precoci dell'insorgenza di DPTS nel genitore. Tale modello (χ^2(9) = 8.83; N = 100; p = 0.45; RMSEA = 0.0001; NNFI = 1; CFI = 1) mostra come il coping emotivo del genitore e il supporto ricevuto al momento del post diagnosi influenzino rispettivamente le capacità di memoria e la propria percezione della vita. A loro volta tali elementi sono associati alla quantità di sintomi (depressivi, fisici e di arousal) del genitore al momento del post diagnosi, che predicono la quantità di sintomi da trauma dello stesso nel mese successivo.

Sulla base delle informazioni empiriche raccolte possono essere proposti e strutturati programmi mirati di intervento psico-sociale per i bambini malati e per le loro famiglie.

INTRODUCTION

This study is the first part of a larger longitudinal project on family factors predicting short- and long-term adaptation and quality of life of leukemic children. The original research project aims at investigating the psycho-social effects of a diagnosis of cancer on both child adaptation and parental issues. In this way we should be able to propose and increase, on empirical basis, specific intervention projects for children newly diagnosed with cancer and their families.

The research team is multi disciplinary, it was directed by prof. Vanna Axia, from the Department of Developmental and Social Psychology at the University of Padova and it is supervised methodologically by Prof. Thomas Weisner, Director of the Fieldwork and Qualitative Data Laboratory in the Mental Retardation Research Center at UCLA (USA) and by Prof. Lonnie Zeltzer, Director Pediatric Pain Program in the Mattel Children's Hospital at UCLA (USA).

This study involves a pediatric onco-hematologic clinic in Italy, the unit of the Department of Pediatrics of the University of Padova (Director, Professor Carli). Several medical doctors belonging at this Unit have taken part as investigators: Dr. M. Pillon, Dr. S. Varotto and Dr. C. Messina.

The rationale of this study is related to the growing importance of psycho-social aspects in pediatric oncology. The family factors predicting short and long-term adaptation of children with leukemia and their psychological functioning throughout therapies' timing are, nowadays, an ongoing concern. Since as a result of advances in treatments, almost 80% of children who receive a diagnosis of Acute Lymphoblastic Lukemia become a long-term survivors (Ries et al., 2005), while this percentage decrease at 50% in children with Acute Myeloid Leukemia (Woods et al., 2001). The large number of survivors has prompted studies of long-term health and psychological

consequences of treatments for childhood cancer both in childhood survivors (Patenaude & Kupst, 2005; Nathan et al., 2007; Clarke & Eiser, 2007) and in their families (Bruce et al., 2006; Manne et al., 2002) showing generally several negative psychological consequences. However, only a few studies have assessed the psychological functioning of parents of children with leukemia throughout the therapies' timing (Magal-Vardi et al., 2004; Phipps et al., 2005; Kazak et al., 2005) and there are no existing prospective studies, adopting an ecocultural point of view, that identifies possible early predictors of PTSS in parents and possible family predictors of newly diagnosed child's adaptation and quality of life. The prospective design and the multi-method approach (questionnaires, self-report measures, in-depth interviews) of this study allow filling up this gap in the literature.

The project was aimed at following children and parents from the diagnosis of leukemia for the two following years of therapies. More specifically, the focus of the whole project is on three main issues: identifying the possible family predictors of short and long term psycho-social adaptation and quality of life in children with leukemia; assessing child's and parent's psycho-social risk and their psychological functioning throughout therapies' timing; identifying early predictors of PTSD symptoms in parents of children under therapy for leukemia. The first refers to the ways in which family, child and illness factors impact upon the child's quality of life early after the diagnosis and upon child's adaptive functioning after one year of therapies. The second focuses on the identification of parents and children more at risk for psycho-social problems by a screening assessment at several time points of the two years of therapies. The third issue centers on the way in which parents' post traumatic stress symptoms behavior along the therapies' time in order to identify the possible stable and modifiable factors associated.

In the next sections, in order to justify the hypotheses of my research, I will present some relevant issues related to children with leukemia and their families and the methodological aspects involved in pediatric psycho-oncology research.

The most relevant studies and main theoretical frameworks are taken under consideration in the first two chapters in the following order:

Chapter 1 addresses the effects of pediatric leukemia and describes the context of childhood cancer in term of: Leukemia incidence and survivorship in children; effects of leukemia ongoing treatments on pediatric patient's development; long-term effects in childhood cancer survivors and their families; theoretical issues in pediatric psycho-oncology such as adaptation and adjustment, stress and coping, quality of life, locus of control.

Chapter 2 describes the following literature themes: Child's coping and adjustment to cancer throughout the therapies; child's quality of life under treatment, according to child and parents' perceptions; the concept of Caring niche; parents' coping and adjustment to child illness; parents' mental health to their child's cancer; parenting a child with cancer and, finally, family factors related to psychological adjustment of pediatric cancer patients.

Chapters 3 to 5 describe the method, results and conclusions of this research; more specifically:

Chapter 3 addresses the main aims and hypotheses of this study and method. It includes description of cancer participants, procedure, timing and instruments used both for the child and parent direct and indirect assessments.

Chapter 4 presents the results in three parts. The first part considers concurrent analyses upon child's and parent's dependent variables at the several time points related also to illness variables. The second part considers longitudinal analyses upon parent's dependent variables throughout the several time points. The last part is an investigation along the several time points of possible prediction, mediation and moderation effects in child-clinical and pediatric research respectively on child's adjustment and parent's psychological health and adaptation.

In Chapter 5 the results are discussed, limits and future directions are presented

together with some clinical suggestions and general conclusions.

THEORETICAL FRAMEWORK

CHAPTER 1

ILLNESS DURING PEDIATRIC AGE: THE CASE OF LEUKEMIA

"To say the truth, I think that also an adult does not really adapt, even though children are adaptable one hundred times more than us, she is ill at ease here. She cannot do what she wants, she is tied to a line, she does not have the mobility she enjoys at home…a number of things which are limitative, she cannot see her brother, she cannot look at the TV with the whole family, she will not meet her grandparents…a number of things that, even though she is not aware of them, they still make her say that she does not want to be here"

The diagnosis of a malignant disease is probably one of the most severe stressors that children and parents can experience (Kazak et al., 1998). This may change patients' personality and their relationship with family. Although recent advances in treatment have lead to a significant increase in survival (Ries et al., 2005), children often undergo multimodal treatment including surgeries, chemotherapy and radiation, which can cause numerous acute and long-term side effects. The experience of treatment for cancer is an exhausting, time- and energy-consuming complex process. Painful procedures, hospitalizations, and uncertain prognosis are common stressors that can pose a substantial threat to the adjustment of children and families (Sloper, 2000). Children newly diagnosed with leukemia come to the hospital in poor health and not rarely in distressed mental conditions which may prevent an accurate assessment of their current Health- Related Quality of Life (HRQL) and also of their coping resources, adaptation potentials, and resilience. This is aggravated by the fact that leukemia is more frequent in children aged from 0 to 14, peaking around 4-5 years of age (seer.cancer.gov), and

young children may have serious difficulties in communicating verbally about their inner and bodily states.

Parents become very important here as they can inform health professionals about their children's states and quality of life especially at the beginning of the treatments when doctors and nurses do not yet know them. At this purpose, socio-ecological theories suggest that a person's well-being is dependent not only on personal characteristics, but also on the social systems and resources around them (Broffenbrenner, 1979). The family system is an important and proximal factor for children with a chronic illness (Kazak, Rourke & Crump, 2003).

Specifically, in this initial chapter I will examine the following topics: First, the pediatric leukemia incidence and survival, with a brief description of the two common types of leukemia; second, the short (par 1.1.2) and the long term (par 1.1.3) main effects of leukemia treatments on pediatric patient's development and their families (par 1.1.4); third a brief explanation of the theoretical issues in pediatric psycho-oncology.

1.1 Pediatric leukemia incidence and survival

The two main different typologies of leukemias in pediatric age are: Acute Lymphoblastic Leukemia (ALL) and Acute Myeloid Leukemia (AML). The SEER Cancer Statistics Review (CSR), a report of the most recent cancer incidence, mortality, survival, prevalence, and lifetime risk statistics, is published annually by the Cancer Statistics Branch of the NCI. I took into consideration the edition including statistics from 1975 through 2004, the most recent year for which data are available (Figure 1.1 and 1.2). Leukemia is the most common type of pediatric cancer, showing the rate of 44.2% per 1.000.000 populations. Ries et al. (website, 2007) reported a significant annual percent increase for leukemia (all types combined) of 0.7% from 1975 to 2001, even if the mortality incidence became less in the last years.

Figure1.1 - Childhood Cancer SEER Incidence Rates by ICCC Group, 2001-2004 Under 20 Years of Age, Both Sexes, All Races (Source: SEER 9 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta). Rates are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130). International Classification of Childhood Cancer is based on ICD-0-3. Steliarova-Foucher E, Stiller C, Lacour B, Kaatsch P. International Classification of Childhood Cancer, Third Edition. Cancer. April 1, 2005: Vol 103, No. 7, pg 1457-1467. Rate for Group III (Brain/CNS) includes benign brain tumors and is based only on cases diagnosed in 2004).
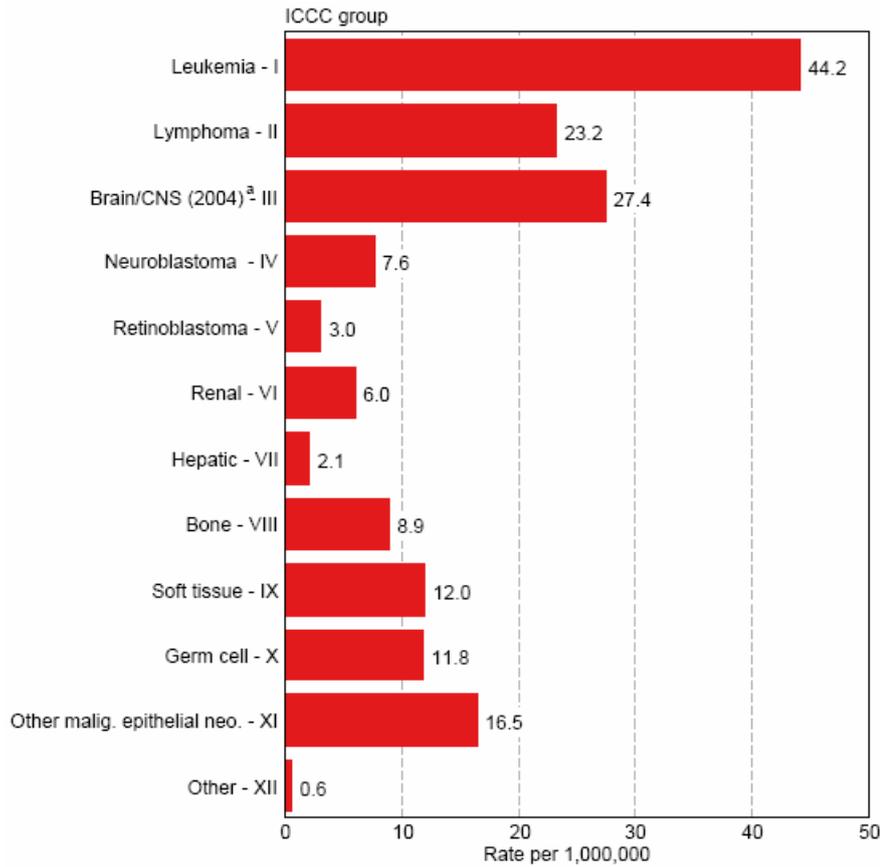
The relative contribution of leukemia to the total childhood cancer burden varies markedly with age, being 17% in the first year of life, increasing to 46% for 2 and 3 year olds, and then decreasing to only 9% for 19 year olds. To further illustrate the contribution, Figure 1.3 gives the incidence rates for both leukemia and total cancer (the sum of leukemia and non-leukemia) by single year of age.

Figure 1.2 - SEER Delay-Adjusted Incidence and US Mortality All Childhood Cancers, Under 20 Years of Age Both Sexes, All Races, 1975-2004 (Source: SEER 9 areas and NCHS public use data file for the total US. Rates are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103). Regression lines are calculated using the Joinpoint Regression Program Version 3.0, April 2005, National Cancer Institute).
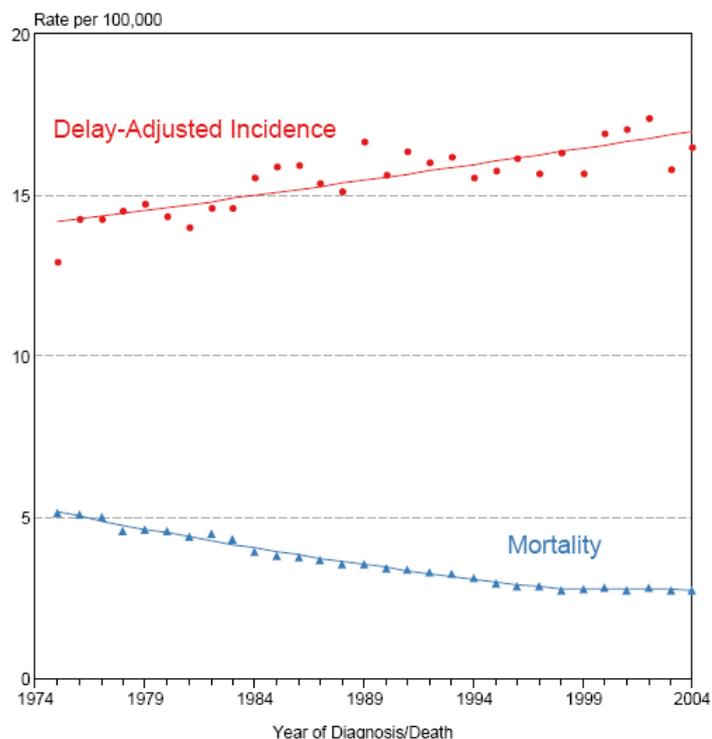
Figure 1.3 - Total childhood cancer age-specific incidence rates by leukemia versus non-leukemia, all races, both sexes, SEER, 1986-1994.
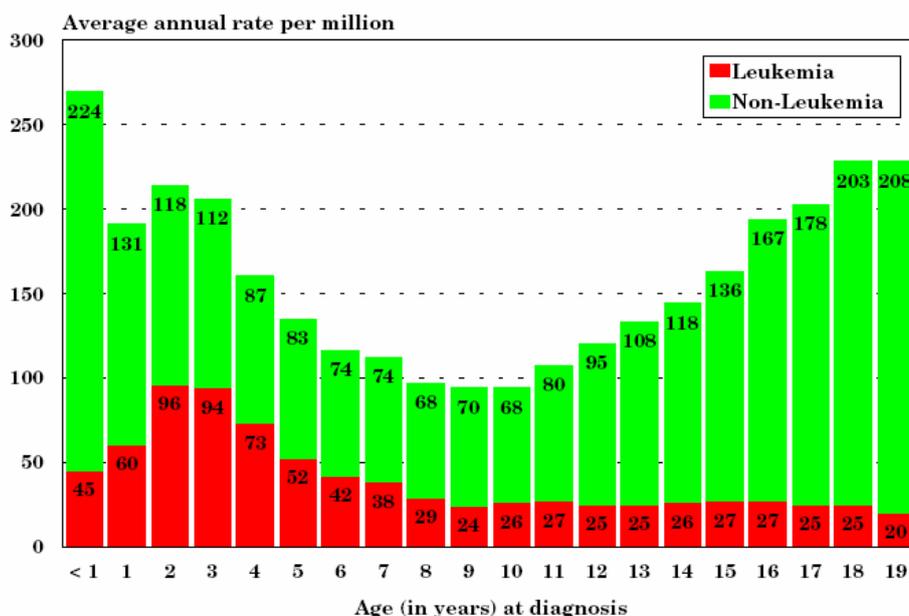
1.1.1 Acute Lymphoblastic Leukemia

Definition

Acute Lymphoblastic Leukemia (ALL) is the commonest malignancy in children, comprising about 30-35% of all childhood cancers. It affects lymphocytes, a type of white blood cells. Leukemic cells accumulate in the bone marrow, replace normal blood cells and spread to other organs including liver, spleen, lymph nodes, central nervous system, kidneys and gonads.

Incidence

In the United States, about 3,000 children each year are found to have acute lymphoblastic leukemia**.** The incidence of leukemia among children varies considerably with age. Figure 1.4 illustrates that this variation is the result of a sharp peak in ALL incidence among 2-3 year old children (incidence over 80 per million), which returns to a rate of 20 per million for 8-10 year old children. The incidence of ALL among 2-3 year old children is approximately 4-fold greater than that for infants and is nearly 10-fold greater than that for 19 year olds. In conclusion, peak incidence occurs from 3 to 5 years of age.

Figure 1.4 - ALL and AML 1986-94 age-specific incidence rates, all races, both sexes, SEER.
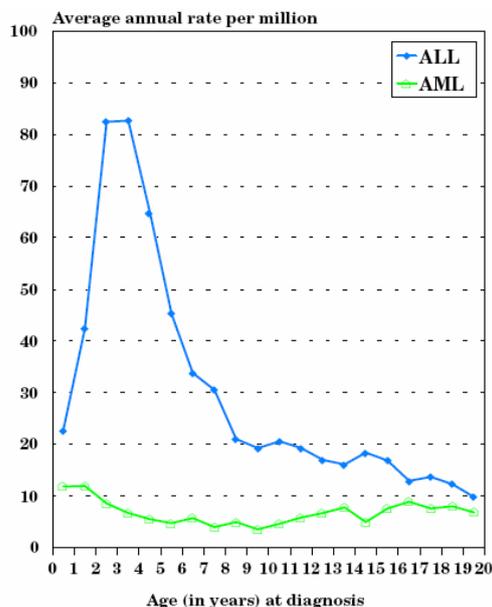
Influencing Factors

ALL affects slightly more boys than girls. It occurs more frequently among whites than blacks. Although siblings of leukemic children have a slightly higher risk of developing the disease, the incidence is relatively low (no more than one in 500).

Survival Rates

Only 30 years ago this disease was fatal within 6 months in the vast majority of children. However, today, approximately 80% of children and adolescents with ALL are cured. About 98 to 99 percent of children with newly diagnosed acute lymphoblastic leukemia attains initial complete remissions (absence of detectable leukemic cells by microscopic examination) in four to six weeks. Patients who remain leukemia-free for 10 years or more can be considered cured. Furthermore, 20-30% of children with leukemic relapse have a long lasting second remission with the chance of cure with second-line treatment. Despite this progress in treatment outcome, the absolute number of children with ALL who relapses and eventually dies of own leukemia still exceeds the absolute number of children with newly diagnosed AML (Smith & Hann, 2006).

Treatment Strategies

Chemotherapy is used to kill leukemia cells. All chemotherapy is stopped after two years of treatment. Hematopoietic stem cell transplantation is an option for very high-risk cases (e.g., Philadelphia chromosome-positive ALL or slow responders to remission induction therapy) or those who develop an early relapse in the bone marrow.

The AIEOP ALL protocol[1] consists principally of several steps of therapies, followed by a continuous bone marrow control of their effects. Figure 1.5 summaries the principle steps of the first year of ALL treatment responses given to the parents of children. The toxicity effect scales throughout all the therapies and the clinical sheet are presented in the appendix.

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[1] AIEOP: Associazione Italiana Emato-Oncologia Pediatrica, Italian Association of Pediatric Onco-haematology

Figure 1.5 - AIEOP ALL protocol: The first year.

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┌──────────────────────┐   ┌──────────────────┐
│ Peripheral blood     │   │ Bone marrow      │   ┌──────────────────────┐
│ exam: Prednisone     │   │ aspiration:      │   │ Bone marrow aspiration: │
│ good/bad responder:  │   │ count of N       │   │ count of N malignant    │
│ count of N malignant │   │ malignant cells; │   │ cells; re-attribution of│
│ cells; attribution of│   │ re-attribution of│   │ risk group: SR, MR, HR  │
│ risk group (HR o NO- │   │ risk group       │   │                         │
│ HR)                  │   │                  │   │                         │
└──────────────────────┘   └──────────────────┘   └──────────────────────┘

┌──────────────┐  ┌──────────┐  ┌──────────┐  ┌──────────┐
│ Day 0        │  │ Day +8   │  │ Day +33  │  │ Day +78  │
│ Diagnosis    │  │          │  │          │  │          │
└──────────────┘  └──────────┘  └──────────┘  └──────────┘
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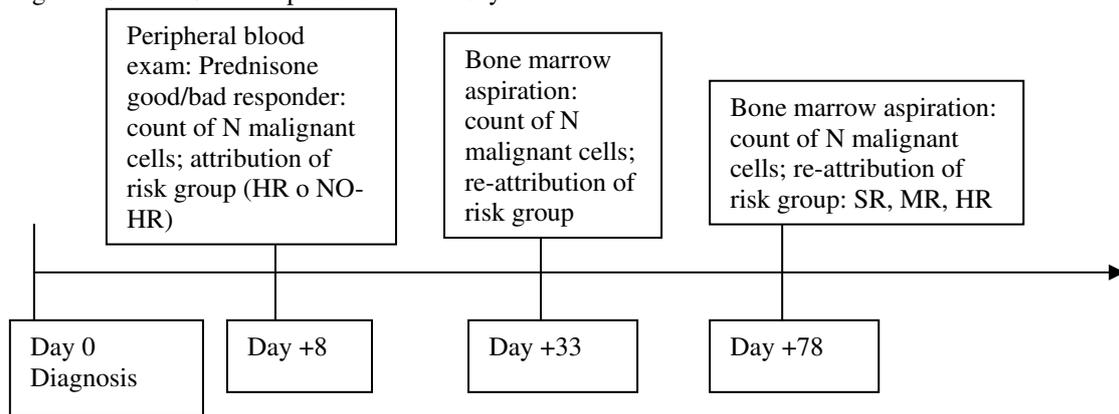
Legend: Prednisone = type of chorticolsteroid; SR = Standard Risk; MR = Medium Risk; HR = High Risk; NO-HR = Not High Risk.

1.1.2 Acute Myeloid Leukemia

Definition

Acute myeloid leukemia (AML) affects various white blood cells including granulocytes, monocytes and platelets. Leukemic cells accumulate in the bone marrow, replace normal blood cells and spread to the liver, spleen, lymph nodes, central nervous system, kidneys and gonads.

Incidence

Each year, approximately 10.000 children (ages 0-21 years) worldwide develop AML. Current epidemiologic studies predict approximately 600 new cases of AML in the USA and 100 new cases of AML in UK per year (Kean et al., 2006). AML is the major subtype of acute leukemia in adults, but only presents 15% of newly diagnosed cases of acute leukemia in children. It usually occurs in people older than 25, but sometimes is found in teen-agers, toddlers and infants. AML is the most common second malignancy (a different or second cancer found in a patient previously treated for cancer) in children treated for malignancies. The incidence of AML in children also varies with age, but with a different pattern than that for ALL. AML rates are highest in the first 2 years of life, but subsequently decrease with a nadir at approximately 9 years

of age, followed by slowly increasing rates during the adolescent years.

Influencing Factors

There is a greater incidence of leukemia among people exposed to large amounts of radiation and certain chemicals (e.g. benzene).

Survival Rates

Currently, most large studies achieve 5-year event-free-survival (absence of leukemic cells) approaching 50% (Woods et al., 2001). The complexity and challenge of AML is revealed in the fact that despite its relatively low prevalence, it nonetheless accounts for over 30% of the annual pediatric mortality attributed to leukemia (Kean et al., 2006). Between 40 to 50 percent of children with AML achieve long-term remissions with chemotherapy.

Treatment Strategies

Chemotherapy is the most common form of therapy for children with AML. Allogeneic blood stem cell (harvested from bone marrow, cord blood or peripheral blood) transplantation is preferred treatment for those patients with AML who are at a high risk of relapse or who have disease that is resistant to other treatments. Allogeneic transplants use stem cells from a donor. Autologous blood stem cell (harvested from bone marrow or peripheral blood) transplantation may be performed as part of treatment. Autologous transplants use the patient's own stem cells and should be considered an experimental form of treatment at this time.

1.1.3 Effects of leukemia ongoing treatments on pediatric patient's development

With this spectacular success of 5-year survival rates in children treated for leukemia (paragraph 1.1), more attention has been paid to the quality of life of children with leukemia and to the neuropsychological impairments related to this kind of illness. However the literature reporting on developmental outcomes during leukemia treatments is still poor. These studies focus mainly on: The mood/behavior effects

related to the high doses of steroids[2], the cognitive impairments related to antitumoral drugs (methotrexate, cytarabine) and to the blood stem cell transplantation, the general psycho-social difficulties related to the illness (emotion regulation, schooling, social relationships).

A consistent field of research applied during ALL treatments has investigated the effects of corticosteroid therapy (oral prednisone, oral dexamethasone, and intrathecal hydrocortisone) on children's functioning behaviors. The glucocorticoid steroids are a standard component of therapy for acute lymphoblastic leukemia (ALL) throughout several time points along the protocol treatment (phases of Induction and Re-induction). The response of lymphoblasts to corticosteroids has emerged as a powerful prognostic tool as well as a therapeutic tool for this leukemia (Gaynon & Carrel, 1999). Despite their therapeutic utility, children may experience emotional and behavioral side effects from steroids during their treatment for leukemia, resulting in same instances in a syndrome of "steroid psychosis" (McGrath & Pitcher, 2002). Emotional lability is identified in 53-67% of children with ALL (Drigan et al., 1992) and any psychological side-effects are stressed in 75% of children with ALL (Harris et al., 1986): The pediatric patients become increasingly nervous, less able to bear physical pain and fatigue and more aggressive.

In addition to the behavioral problems, steroids have been shown to damage the hippocampus (Brown et al., 2004), and hippocampal damage has, in turn, been implicated in affective (Hochhauser et al., 2005) and memory (Alderson & Novack, 2002; Keenan et al., 1996) dysfunctions. Waber and colleagues (2000) have demonstrated how leukemic pediatric patients treated with dexamethasone were more at risk for neurocognitive late effects. Specifically, the pediatric patients performed more poorly on two of the four measures of academic achievement (i.e., reading

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[2] Corticosteroids: hormones that are produced synthetically for use of drugs in the treatment of a very large variety of diseases including many inflammatory conditions. Large doses and/or prolonged use is associated with many side effects, including increased susceptibility to infection, fluid retention and emotional changes.

comprehension and arithmetic calculation). Health related quality of life (HRQOL) implications of treatment with dexamethasone for children with ALL was also studied by Eiser et al. (2005) by standardized questionnaires assessing parent and child HRQOL at two time points (3-6 months after the diagnosis; 1 year later). Child HRQOL scores improved and behavior problems decreased significantly along time.

The experience of parents of caring for their child during treatment with steroids has also to be taken into consideration. Parents experienced the children's emotional states as very demanding, and this was exacerbated by the fact that the children were up all night eating and did not sleep. Some parents reported that this was to a worrying degree and that the child's emotional state confronted them with a sense of death and hopelessness. A set of strategies to cope with this difficulties are used: Positive personal strategies, professional help requests and normalisation activities (McGrath & Pitcher, 2002). The effects of steroids on children and their families were evident during treatment with dexamethasone, further studies are needed to address whether these deficits remain as treatment ends. The literature addressing child cognitive functioning secondary to anti-tumoral drugs treatment mainly focuses on long term effects (studies on survivors). The rationale is that deficits in neurocognitive functions may not be apparent in the immediate period following treatment, yet it is commonly thought that testing shortly after the diagnosis is not feasible because children are seriously ill and have to cope with medical procedures and intensive treatment (Jansen, Kingma, Tellegen, et al., 2005). However, a few longitudinal studies were conducted and addressed child development from the first year of therapies to the off therapy stage. One example is the study of Jansen et al. (2005) that showed no adverse effect of illness and psychological factors on IQ and neuropsychological functioning of patients recently diagnosed with ALL. Another prospective longitudinal study (Kingma et al., 2002) confirmed that also at the end of the therapies the use of chemotherapy only had not more major cognitive impairment, especially in school achievement.

The cognitive impairments in the children with leukemia can be related also to the blood stem cell transplantation (SCT)[3]. Kramer et colleagues (1997) prospectively assessed the intellectual and adaptive functioning of children receiving a SCT by IQ and Adaptive Behavior scores (Vineland Adaptive Behavior Scales) between baseline and at 1-year follow-up. IQ and adaptive behavior scores dropped significantly during the first year, but did not change between the 1 year and 3 following year evaluations.

A set of further aspects may affect child development in the short term dealing with the general psycho-social area such as emotional regulation (emotional and behavioral symptoms) and socio-emotional development (the possibility of school experience and of social relationships).

One issue concerns the impact of childhood cancer on emotional regulation. In the first weeks following the diagnosis of leukemia, children must cope with repeated painful medical procedures such as bone marrow aspirations, lumbar punctures and venepunctures (Wallander & Varni, 1998). In the last years, most of the more painful medical procedures in pediatric settings are made under sedation (Ljungman et al., 2001) in particular when done to younger children that show more distress than older ones, especially after repeated pain experiences (Jacobsen et al., 1990). However, the experience of physical pain and high levels of distress are nearly always present in the life of chronically ill children. Pain is a psychobiological phenomenon, encompassing biological mechanisms of pain transmission and inhibition but it also has psychosocial and ecological aspects (Zeltzer et al., 1997). Pain episodes occur in the context of children's everyday lives and influence the child's reactivity and temperament (Boyce et al., 1992) that may impact on the child way of coping with pain (Sanger & Copeland, 1991). Children's reactions to painful events vary widely (Schecter et al., 1991) but there is a fairly wide consensus on the fact that children with cancer may have special difficulties in dealing with the stressful medical procedures needed for the treatment of

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[3] Stem cell transplantation: to transfer part of the specialized soft tissue found in within the bone. Red bone marrow is essential for the formation of red blood cells.

their disease (Sourkes, 2000). Individual factors such as the children's temperament and intelligence contribute to their style of coping and thus may influence the short and long term effects of hospitalization (Bonn, 1994). Even the memories of such events may cause a state of anxiety (Chen et al., 2000). In particular, children diagnosed with leukemia undergo a long therapeutic process involving repeated exposure to these distressing experiences.

The experience of illness and aspects related to it – as hospitalization and the total change in daily life routines – may impact on socio-emotional development as well. This may cause unusual child and parent behavior and emotional symptoms. A significant proportion of them suffers from some degree of emotional disturbance due to own experience. Prolonged and repeated hospitalizations increase the chance of later problems. However the emotional disturbance doesn't always cause evident psychological symptoms: A recent study of Michalowski et al (2001) founds no significant difference on the scores of the CBCL[4] internalization dimension (anxiety, depression, somatic symptoms and withdrawal) between children with ALL and healthy controls.

However, no particular attention has been paid to the possible effects of prolonged hospitalizations and physical-psychological restrictions related to the illness. Children with leukemia are often hospitalized for long periods because of their immunosuppressed status and because of the therapies; this may place them at further risk for psychosocial developmental delays. Children are frequently forced to long periods in bed or in a restricted area (such as hospital room) where they are not allowed to meet friends or relatives. Long hospitalization can cause delays in school learning and development (White, 2003). Childhood cancer patients results at school, assessed by self-report and proxy (teachers, parents)-report questionnaires, differed significantly from both the siblings' and the healthy controls' results: The school marks in

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[4] CBCL: Child Behavior Checklist is a behavioral and emotional symptom checklist for children from 4 to 18 years of age that records 112 child's problems and 3 areas of competency as reported by parents.

mathematics and in foreign languages tended to be worse in cancer patients with also bullying behavior more predominant (Lähteenmäki et al., 2002). Another study (Adamoli et al., 1997) confirmed the difficulties of leukemic children in or out of the therapy in the tests of learning, socialization and emotionality as reported by teachers, with children irradiated and under 6 years of age more at risk. The literature about returning to school of child with cancer is recently reviewed (Vance & Eiser, 2002) investigating their school absence, behavior problems and social relationships. Specifically, it emerged that school absences were higher in cancer patients compared with children of other chronic conditions. While there was a mixed evidence about whether children have significant behavioral problems in school, studies involving social behavior and peer relationships generally concluded that children with cancer were more sensitive and isolated than peers, according to both peer and teacher reports.

Findings from studies conducted during cancer treatment give disaccording results and need to be more carefully investigated. As mentioned before, neurocognitive deficits may not be evident in the period immediately following treatment, but may become evident at a later time, for example with the re-entry of the child at school. Longitudinal design and multi-method approach may be useful to assess child's general quality of life throughout the therapies to identify children more at risk for developmental delays or deficits.

1.1.4 Long-term effects: Developmental outcomes in childhood cancer survivors

With modern therapies and supportive care, survival of childhood cancer has increased considerably. But what happened to the children survivors in their quality of life? The literature on this topic is really very huge. We can consider this rich field of study by the following point of view: The three big aspects of the concept of Quality of Life (par. 1.2.3) - physic area; psycho-social adaptation, psychological wellness - (Eiser et al., 2000) adapted to the model of Maslow's needs scale (1954) (Fig. 1.6).

Fig. 1.6 - Survivors' needs scale (Axia e al., 2004, pg. 122).
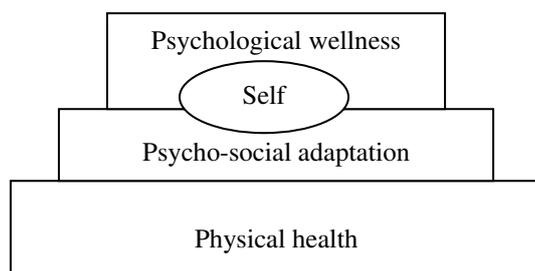
This pyramidal model can be read as follow. The physical and physiological needs are at the baseline (organ damage, decreased growth, and infertility), in the secondary level are placed the social re-adaptation needs (scholar performance, capacity of wedding, type of love relationships, type of job, educational level) and at the top level of this hypothetical pyramid is the global psychological wellness (self perceptions, body perceptions, identity of self, possible psychological symptoms). The meaning of this model is that the baseline needs (physical/medical) can influence all the other superior needs (social adaptation, psychological wellness). All these needs are related one to each other: The physical health in danger evokes the person's strategies to adjust to this event, but all this strength reactions obviously influence his/her own psychological and social wellness. The degree of this influence and the following psychological status on the survivor vary along several personal (type of reactions, personal characteristics, gender, socio-demographic status, age), environmental (family, social relationship..) and cancer factors (type of therapy, type of prognosis…).

The field of late effects has burgeoned and there is now a formidable late-effects literature (Friedman & Meadows, 2000). To make a synthetic exposition of this topic we can take into consideration principally the more recent reviews.

Patenaude & Kupst (2005) review all the studies dealing with the psychosocial functioning in pediatric cancer. They underline that long-term effects of cancer treatment dealing with the physical area vary and can include neurocognitive deficits

(Butler & Mulhern, 2005), organ damage, decreased growth, and infertility (Oberfiled & Sklar, 2002). Not surprisingly, these physical sequelae can affect social functioning and relationships (Boman & Bodegard, 2000; Byrne et al., 1989); academic success (Hays et al., 1992; Katz et al., 1988); employment (Hays et al., 1997; Mackie et al., 2000; Zeltzer et al., 1997), personal functioning (Greenberg et al., 1989; Madan-Swain et al., 2000; Mulhern et al., 1989; Smith et al., 1991), and family functioning (Kazak et al., 2001; Kupst & Shulman, 1988). From these studies, emerging over the past two decades, we have learned with increasing specificity that no child with cancer remains unchanged by the experience.

Now we can make a synthetic review of the major findings of long-term effects divided for the several areas of survivor's quality of life.

Neurocognitive sequelae

To evaluate the impact of treatment for cancer on neurocognition we have to consider the researches from the 1990s, when the therapies have evolved. The majority of the studies found significant neurodevelopmental sequelae such as difficulties with attention, memory, information processing, and other executive functions in children surviving central nervous system (CNS) cancers or CNS treatments (Peterson & Drotar, 2006). Being younger at the time of diagnosis, female, of lower socioeconomic status, with a CNS cancer and a cranial radiation therapy may negatively affect the neurocognitive status of children treated for cancer (Challinor et al., 2000). Negative outcomes are observed most frequently in survivors of acute lymphoblastic leukemia and brain tumors (Nathan et al., 2007).

Psycho-social adaptation

The neurodevelopmental sequelae in childhood cancer survivors just mentioned can have a range of effects on their psychological adjustment and quality of life as they reintegrate into school and social settings. Survivors facing such difficulties may be influenced by their family environment, and these struggles may in turn impact the

perceived burden of their parents and family system (Peterson & Drotar, 2006). Areas that have been found to be problematic for pediatric survivors include academic achievement (Haupt et al., 1992), employment difficulties (Hays et al., 1997), impaired or decreased social relationships (Mackie e al., 2000). Behavioral and social competences are important for a successful transition from cancer therapy to survivorship and for a successful adult life. Survivors were reported to be withdrawn and socially isolated and to have fewer same-age friends than their peers (Challinor et al., 2000).

Another area taken into consideration deals with the health behaviors in childhood cancer survivors. A recent review (Clarke & Eiser, 2007) illustrates an optimistic picture of low participation in substance use amongst survivors, although based mainly on smoking. However, smoking might not be the major problem for survivors and attention must also be directed to other health behaviors including exercise and healthy diet.

In conclusion, it appears that time of the evaluation (on-treatment vs off-treatment) may have an effect on the outcome of an assessment of social competence and acceptance. Therefore, it is important to determine the behavioral and social competence of the child before the diagnosis, and the pattern during treatment, before making a conclusion about the current situation of the survivor (Challinor et al., 2000).

Psychological wellness

Some problematic areas in pediatric survivors are related to psychological wellness included self-concept, self-esteem or identity (Madan-Swain et al., 2000). Most studies have found little evidence of serious maladjustment or maladaptation in pediatric cancer patients: Most survivors show good adjustment on psychological self-report measures and their scores are not significantly different from those of the norms, controls or comparison groups. Similarly, they tend to have fewer emotional and behavioral problems based on report of others (e.g. teachers, parents, peers) (Patenaude

& Kupst, 2005). Recent studies (Eiser et al., 2000; Zebrack & Zeltzer, 2003) found that survivors did not show deficits on measures of anxiety, depression or self-esteem when compared to the general population. However, these findings must be viewed with caution. Some researchers have suggested that comparing symptomatology scores in children with cancer may not be appropriate, because children with cancer may underreport their depressive/anxiety symptoms (Challinor et al., 2000). Similarly, recent review examining prevalence of posttraumatic stress symptoms (Bruce, 2006) has found that moderate to severe symptoms are present in about 5-20% of survivors, with young adult survivors experiencing more PTSD symptoms than younger survivors. Research on stressors and adverse outcomes for pediatric oncology has found that distress in one area may occur despite generally good functioning in other domains (Simms et al., 2002).

1.1.5 Long-term effects: Psycho-social outcomes in families of childhood cancer survivors

The long-term effects of children's cancer can be showed also in their families and, especially, in their parents. For them the fear of recurrence over time can remain high and the completion of the therapy often does not mean total cure. The realisation that radiotherapy and chemotherapy carry many risks for the child means that parents are frequently confronted with the news that the child may need further treatment for the large number of late effects already described. Many families can feel confused and let-down by this information: Feelings of loss and perseverations of problems prevailed (Van-Dongen-Melman et al., 1998); uncertainty and loneliness were most often reported by parents (Van-Dongen-Melman et al., 1995).

Concerning the families of childhood cancer survivors the literature is mainly focused on psychological symptomatology such as Post-traumatic stress disorder (PTSD), Post traumatic stress symptoms (PTSS), Anxiety and Depressive disorders.

Also factors related to this symptomatology such as emotional adjustment and adaptability, social support and family functioning are taken into consideration as dynamic predictors. A recent review of Bruce et al. (2006) examined the incidence of Post-traumatic stress disorder (PTSD) and Post traumatic stress symptoms (PTSS) in parents of childhood cancer survivors. Studies using the SCID-PTSD[5] reported in parents indices of current cancer-related PTSD ranging from 6.2% (Manne et al., 1998) to 25% (Hobbie et al., 2000). For the PTSS rates the studies showed a range from 9.8% (Kazak et al., 1997) to 44% (Fuemmeler et al., 2001) exhibiting clinically severe levels of PTSS indicative of PTSD caseness. The latter prevalence was found in a sample of parents of childhood brain tumor survivors. Overall, mothers appeared to demonstrate higher level of PTSS symptoms than fathers of childhood cancer survivors. Trait anxiety symptom levels in mothers of survivors were superior to those of other stressed and traumatized groups, while state anxiety symptom levels of both mothers and fathers were lower (Kazak et al., 1997). Parents (especially mothers) appear to be at grater risk, suggesting that the experience of parenting a child with cancer may be inherently more traumatic than actual cancer survivorship (Smith et al., 1999).

On this topic also dynamic predictors of PTSS or PTSD were considered: Perception of cancer and treatment factors, family functioning, social support and coping style. Individual perception and appraisal of type of cancer and treatment was repeatedly shown to predict cancer-related PTSD and PTSS (Barakat et al., 2000; Best et al., 2001; Hobbie et al., 2000; Kazak et al., 1998; Stuber et al., 1997). Family functioning was also found to significantly contribute to the variance of cancer-related PTSS reported by mothers (Brown et al., 2003; Kazak et al., 1997). Specifically, greater family (Brown et al., 2003) and social (Manne et al., 2002; Kazak et al., 1998) support were associated with fewer PTSS. Also emotion-focused coping strategies were correlated with PTSS in parents of childhood survivors (Fuemmeler et al., 2001).

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[5] SCID-PTSD: it is a semi-structured interview to identify the Post Traumatic Stress Disorder (QUOTE)

1.2 Theoretical issues in pediatric psycho-oncology

Pediatric psycho-oncology is a research and clinical field that focuses on suffering children and adolescents and their families in their adjustment to the illness. Psychosocial functioning in pediatric cancer patients and families is particularly monitored. For this reason this type of scientific field is constituted by different theoretical concepts useful to understand and to cure the psychological difficulties of the young patients and their parents. In this paragraph I will describe the theoretical key elements involved in this research and clinical field: Adaptation and adjustment, with particular attention to the caring niche of the child; coping; quality of life; Stress and the associated symptomatolgy; and locus of control.

1.2.1 Adaptation and adjustment

Adaptation, in the psychological sense, refers to processes employed to manage environmental demands (Lazarus & Folkman, 1984). Adjustment is an achievement, accomplished well or badly, or a process whereby people adjust under different circumstances. According to the AAMD (American Association on Mental Deficiency), Adaptive behavior is defined as the effectiveness or degree with which individuals meet the standards of personal independence and social responsibility expected for age and culture group (Grossman, 1983, p.1). Then, in 2002, Adaptive behavior is defined as the collection of the conceptual, social, and practical skills that have been learned in order to function in their everyday lives. Its assessment should relate to an individual's typical performance during daily routines and changing circumstances, not to maximum performance. The following common elements are founds in definitions of adaptive behavior: The developmental nature of the behaviors; common dimensions of adaptive behavior; recognition of cultural influences and situational specificity; and emphasis on performance rather than skills or ability (Harrison, 1990). Deficits in adaptive behavior

are identified as significant limitations in meeting standards of learning, maturation, personal independence, and social responsibility and are determined through clinical assessment and standardized scales (Harrison, 1990). Most adaptive behavior scales emphasize the developmental qualities of the construct by providing age-based norms and items that cover a wide range of developmental activities such as sensorimotor, communication, self-help and socialization skills. These skills are important during infancy and early childhood, while in later childhood and adolescence also other skills related to the learning process become more relevant such as: Reading and writing; applying concepts of time, number, and money; responsibility and interpersonal relationships (Grossman, 1983). Specifically, social skills and adaptive behavior represent two subdomains of the superordinate construct of social competence, with the adaptive behavior as the effectiveness and degree to which an individual meets social/cultural standards of personal independence and social responsibility (Gresham & Elliott, 1987). Thompson (1999) describes the functional and structural characteristics and Adaptive and Maladaptive behavior, identifying the following adaptive behavior factor clusters: Cognitive, Communication and Academic Skills (i.e., conceptual skills); Social Competence Skills (i.e., social skills) and Independent Living Skills (i.e., practical skills). Some limitations in these adaptive skills may include: Not knowing how to perform the skill (acquisitions deficit); not knowing when to use learned skills (performance deficit); or other motivational factors that can effect the expression of skills (performance deficit). Consistent with this view, most adaptive behavior instruments measure the "skill level a person typically displays when responding to challenges in his/her environment" (Widaman & McGrew, 1996, p.98). It is necessary to make two annotations: 1. Adaptive skill limitations often coexist with strengths in other adaptive skill areas; and 2. a person's strengths and limitations in adaptive skills should be documented within the context of community and cultural environments typical of the person's age peers and tied to the person's individualized needs for

supports. Factors influencing the Adaptive behavior can be the cultural or ethnic expectations that individual must meet and the demands of the specific situation (Harrison, 1990).

1.2.2 Coping

Although there are many definitions and theoretical approaches used to understand coping, it can be generally defined as a cognitive and/or behavioral attempt to manage (reduce or tolerate) situations that are appraised as a stressful to an individual. Moreover, no single coping strategy or dimension can be considered (mal)adaptive. The quality of the coping strategy and process should be evaluated according to its impact on the outcome of importance (Aldridge & Roesch, 2007). From the previous conceptual definition, Folkman and Lazarus (1980; 1985; Lazarus and Folkman, 1984) have distinguished two primary categories of coping: *Emotion-focused* and *problem-focused*. These coping categories describe efforts to either alter the source of stress in the environment or to alleviate the personal emotional stress induced by the stressors. The emotion-coping dimension includes strategies that involve self-preoccupation, fantasy, or other conscious activities related to affect regulation, including for example social support fro emotional reasons and positive reappraisal. The problem-focused coping dimension, on the other hand, involves strategies that attempt to solve, reconceptualize, or minimize the effects of a stressful situation, including for example instrumental social support and planful problem-solving (Lazarus and Folkman, 1984). In addition to this model problem-emotion focused, a taxonomy of coping that stressed the focus of the orientation of the coping strategy has also been emphasized. Many terms have been used to explain how cognitive and behavioral coping attempts are orientated towards a stressor (Roth & Cohen, 1986): Vigilance versus nonvigilance (Averill & Rosenn, 1972); vigilance versus avoidance (Cohen & Lazarus, 1973; Janis, 1997; Miller, 1987); attention versus inattention (Kahnemann,

1973), intrusion versus denial (Horowitz, 1976); and engagement versus disengagement (Compas et al., 2001; Connor-Smith et al., 2000). However, a common label given to coping activity directed toward a threat is termed *approach* and coping activity that is deflected from a threat is often termed *avoidance* (Holhan & Moos, 1987; Moos & Schaefer, 1993). Avoidance-oriented coping is "removal" from experiencing or thinking about a stressful situation (Billing & Moos, 1981; Carver et al., 1989), and has also been explained as withdrawal from the situation or associated emotions (Roth & Cohen, 1986). Positive reappraisal, self-control (types of emotion-focused coping), planful problem-solving and seeking information (types of emotion-focused coping) may be regarded as approach coping strategies (Roesch & Weiner, 2001; Roesch et al., 2005). In contrast, approach-oriented coping is directed towards dealing with the problem or related emotions (Roth & Cohen, 1986). Religion and distancing (types of emotion-focused coping) may be regarded as avoidance coping strategies.

Several coping models are proposed by the researchers. A specific extended model for family coping with chronic diseases will be introduced and briefly explain in the second chapter. I am now presenting a summary schema of models about child and family coping with cancer (Figure 1.7)

At the center of the figure it is presented Groothenhuis et al. model (1997): The illness is the stressful situation; the primary appraisal is the first evaluation of this event that can result as irrelevant, positive or stressful, with respectively three correspondent forms of lost, crisis and change. With the secondary appraisal several situation components and possible solutions are evaluated; this is the start of coping processing. Along minor or major adaptation after coping or possible situation changes, the individual makes a reappraisal of situation with the possibility of adoption of new coping strategies. Several factors influence this process:

- the illness parameters: Type, severity and related treatment that characterize the stressful event and its intensity (Thompson et al., 1994)

- the personal factors: Internal child characteristics, cognitive abilities related to age and development reached and his/her temperament (Hoekstra-Weebers et al., 2001; Kupst, 1993)

- the social factors: Support received or negated from the proximal environment (parents and siblings), but also from peers, friend and the large community (Kupst, 1993; Hoekstra-Weebers et al., 2001).

Recent reviews on coping structure, however, have also argued that coping is "multidimensional" (Skinner et al., 2003): The several categories cited above are not mutually exclusive, rule out several important coping categories (e.g. rumination, aggression), and lack clear cut category definition.

Coping assessment reflects the same complexity of its theoretical construct. Self-report measures (with interindividual or intraindividual approach) are principally used to assess coping reactions and responses (Parker & Endler, 1996). The researchers have to take into consideration a salient key lesson in measuring individual coping strategies: What is stressful, what is evidence of stress, and what is evidence of coping it all depends heavily on the purposes and perspectives of both the focal person experiencing stress and the researcher studying it (Beehr & McGrath, 1996).

1.2.3 Quality of life

The World Health Organization (WHO) definition described health as "A state of complete physical, mental and social well-being, not merely the absence of disease or infirmity (WHO, 1947), introducing the concept that health was more than just physical functioning. Others have addressed the issue of the subjective nature of the concept, defining the quality of life (QoL) as "The individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals expectations, standards and concerns. Quality of life is multidimensional. It includes but is not limited to the social, physical and emotional functioning of the child

and adolescent and, when indicated, his or her family" (Bradlyn et al., 1996). The term Quality of life (QoL) is difficult to define. It is fundamentally a subjective phenomenon and, when assessing quality of outcome it is important that, wherever possible, the perceptions of the survivors themselves are addressed, at least as part of the overall evaluation. When considering the assessment of QoL in children with cancer, the authors added that "Measurement of QoL must be from the perspective of the child, adolescent and family and it must be sensitive to changes that occur throughout development". The instruments typically assess physical, psychological, social and spiritual/existential domains and address concerns regarding health status and physical function, sexuality and fertility, emotional distress, future outlook, school and work performance, social and family relationships, and spirituality, as well as other key medical, demographic and psycho-social elements. There has been substantial debate about both definitions and measurement approaches in psychosocial and quality-of-life studies of childhood cancer patients and survivors (Eiser & Jenney, 1996; Parsons & Brown, 1998).

Figure 1.7 - Summary schema of models about child and family coping with cancer (Axia et al., 2004, pg 91).

Illness parameters	**Personal factors**
- type	- cognitive resources/abilities
- severity	- age/past experiences
- treatment	- gender
(Thompson et al., 1994)	- temperament
	(Hoekstra-Weebers et al., 2001; Kupst, 1993)

Cancer event

Theoretical model of Grootehhuis et al., (1996)

Reappraisal

Stressful situation

Primary appraisal
Judgement of the situation

Secondary appraisal
Problem/emotion focused coping

Adaptation outcome
Future levels of stress, timing of stress

Positive

Negative

Illness parameters
- type
- severity
- treatment
(Thompson et al., 1994)

Personal factors
- cognitive resources/abilities
- age/past experiences
- gender
- temperament
(Hoekstra-Weebers et al., 2001; Kupst, 1993)

Social factors
- protective factors and/or risks related to family
(its characteristics and type of support given)
- peers support
- environment support
(Kupst, 1993; Hoekstra-Weebers et al., 2001)

Questions regarding validity and reliability abound: Sample sizes has varied considerably. Psychometric instruments standardized on "physically normal" populations or normed instruments directly on the clinical populations have been under inquiry. Other approaches include designed questionnaires, open-ended questions and intensive personal and small group (focus group) interviews.

Another important consideration deals with quality of life at different ages. As a child matures, change is normal. It follows that the impact of any type of stress event and its short and late sequelae on the QoL of the child may also change. For many authors, maturity may bring with it an acceptance or adjustment to the situation, thus altering the impact of the late effect on the quality of life and of survival (Jenney e& Levitt., 2001).

A Quality of Life model applied to cancer survivors is that of Ferrel et al. (1991), also recently cited in Hicks et al. (2003). Figure 1.8 shows this model.

Figure 1.8 - The Quality of Life model applied to cancer survivors (Ferrel et al., 1991).
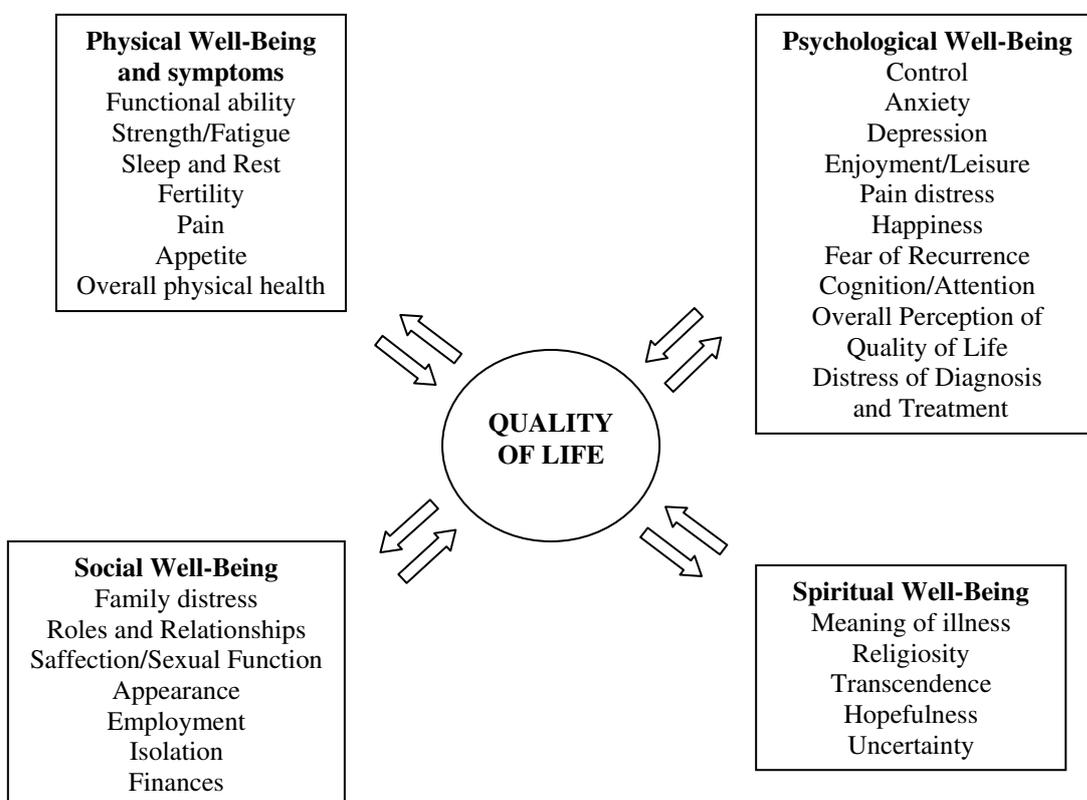
This model, consisting of four domains (physical, psychological, social, and spiritual well-being) provided the conceptual framework for this study. These domains are consistent with the predominant views of the major dimensions of QoL within the oncology literature (Aaronson, 1988; Cella and Tulsky, 1990; Haberman & Bush, 1998). This model has been tested in previous studies involving patients diagnosed with cancer and provides a way to examine the multidimensional impact of the disease and treatment from the individual's perspective (Dow, Ferrell, & Anello, 1997; Ferrell, Dow, & Grant, 1995).

1.2.4 Stress

Stress is a stimulus event of sufficient severity to produce disequilibrium in the homeostatic physiological systems (Selye, 1982). Stress has also been conceptualized variously as a non-specific response of the body to any demand that exceeds the person's ability to cope, as a person-environment relationship that threatens or taxes personal resources, and as a mental state in response to strains or daily hassles (Lazarus & Lunier, 1978; Lazarus et al., 1985; Rutter, 1983).

A variety of dissimilar situations that happen to children and their families can produce stress, including for example the experience of a physical illness or pain. Researchers have focused on several components of stress: Stressor; how a person perceives that stressor; the coping resources a person has, the support systems available internally and externally; and the person's skill in making coping or adjusting responses when stressed. A stressor is "an acute life event or a chronic environmental situation that causes disequilibrium" (Blom et al., 1986, p.9). The severity of the stress consequences depends partly on how the person understands and feels about the stressor. The stress response, seen as an "imbalance between requirements to make an adaptive response and the repertoire" of the stressed person (Zegens, 1982; p.140) shows several stages: Alarm (physiological changes); appraisal (evaluative process that

imbues a situational encounter with meaning for the person); searching for a coping strategy; and implementing coping strategies.

1.2.4.1 Symptomatology related to stress

The person who experienced stress events may develop also some psychological difficulties that can be related also to psychiatric disorders. The major of these difficult mental conditions in experiencing the traumatic event of a childhood cancer are the following: Post-Traumatic Stress Disorder (PTSD) or Post-Traumatic Stress Symptoms (PTSS) are the most common sequelae, followed by other general Anxiety disorders and Depression.

The DSM-IV (APA, 1994) defines PTSD as a serious mental condition following "an individual experiencing, witnessing, or being confronted with a traumatic event/s that involved actual death or threatened death or serious injury; or a threat to the physical integrity of himself or herself or others" (p. 427). While no discrete diagnostic taxonomy exists for children, differences in symptom manifestation are outlined within the six primary criteria for PTSD diagnosis.

The event must elicit "reactions of intense fear, helpness or horror" (p. 428) in the individual (criterion A). To meet the criteria for a diagnosis of PTSD such reactions must subsequently mobilize three specific symptom clusters. The first cluster (Criterion B) is characterized by re-experiencing symptoms of the traumatic event (i.e., intrusive memories, nightmares, a sense of reliving of the traumatic event, as well as psychological or physiological distress at reminders of the trauma). The individual must experience one (or more) of these symptoms. The second cluster (Criterion C) is characterized by persistent avoidance of stimuli associated with the trauma and numbing in general responsiveness (i.e., effortful avoidance of thoughts, feelings and reminders of the trauma, inability to recall certain aspects of the trauma, withdrawal from others and normal activities, emotional numbing, and a sense of foreshortened

future). The individual must experience three (or more) of these symptoms. The third cluster (Criterion D) is characterized by persistent arousal (i.e., insomnia, irritability, concentration difficulties, hypervigilance, as well as exaggerated startle response). The individual must experience two (or more) of these symptoms. PTSD symptoms must persist for at least one month following exposure to the traumatic event (Criterion E) and significantly impair the individual's day-to-day functioning (Criterion F).

The literature on adult cancer survivors also investigated the relationship between Post Traumatic Stress Disorder and possible deficit in memory functions. A study (Nakano et al., 2002) revealed that hippocampal volume was significantly smaller in the persons with a story of distressing cancer-related collections than in those without any such history. Also a significant visual memory delay was observed in adult breast cancer survivors. These results were confirmed also by a recent meta-analysis on this topic (Kitayama et al. 2005) suggesting also that this phenomenon was present only in adults, not in children with PTSD. Some authors have suggested that neurodevelopmental plasticity and normal development increases in the hippocampus may mask any effects of traumatic stress on children with PTSD (De Bellis et al., 2001).

Intrusive recollection in adult cancer survivors may be also associated with a smaller volume of the amygdala, one of the regions in the limbic system of the brain, critical for enhancement of explicit memory associated with emotional arousal (Matsuoka et al., 2003). Also the orbitofrontal cortex, which is thought to be involved in the extinction of fear conditioning and the retrieval of emotional memory, might play an important role in the pathophysiology of adult cancer-related PTSD (Hakamata et al., 2007). No studies investigated this phenomenon in parents of children with cancer affected by PTSD.

Recognition and utilization of the concepts of PTSD and PTSS in childhood cancer survivors and their parents clearly bestows a number of advantages: The reactions are easily recognizable and treatable; rapid and succinct communication of

potentially very complex problems can be provided; psychotherapeutic and specific interventions can be implemented. Nevertheless, conceptualization of cancer within the PTSD nosological framework is not without its difficulties and remains under continuous debate (Kangas et al., 2002). For this reason, a model of pediatric medical traumatic stress (PMTS) has been developed providing a useful heuristic for understanding the short and long-term psychological consequences of cancer on the child and their family as well as a guide for psychological interventions (Kazak et al., 2006; Pai & Kazak, 2006). Figure 1.10 illustrates the PMTS model.

Figure 1.9 - Model of medical traumatic stress (PMTS) for pediatric patients and their families.
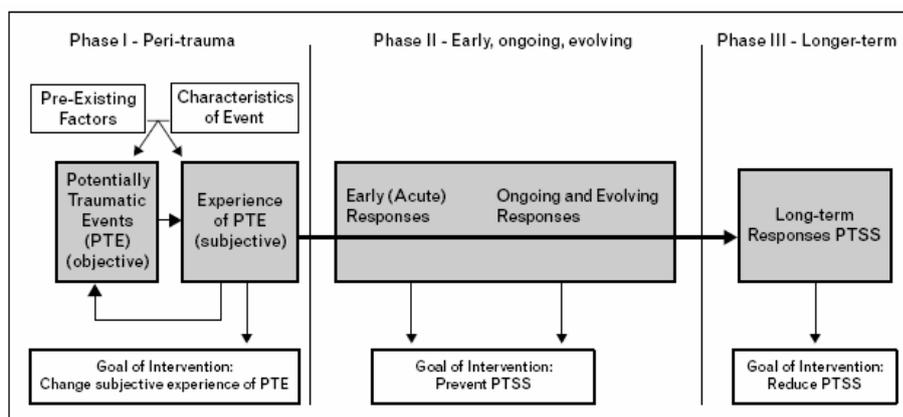
Source: Kazak AE, Kassam-Adams N, Schneider S, Zelikovsky N, Alderfer M, Rourke M. An integrative model of pediatric medical traumatic stress. J Pediatr Psychol 2006; 31: 343–355.

The family is central to the PMTS model. The child is seen within the context of the family who must negotiate multiple potentially traumatic events. For example, parents are usually told the diagnosis of life-threatening conditions before pediatric patients and parents make numerous and difficult treatment decisions. Although multiple family members experience the same events, the reaction of individual family members to these events may be variable (Kazak et al., 2003). Indeed, illness events are called potentially traumatic events (PTE) because the same objective event may not be equally traumatic to all individuals. Rather, it is the interaction between the objective nature of the event and the subjective interpretation of an event that determines whether

a particular event is perceived as traumatic (Stuber et al., 1997). There are three phases in the PMTS model, each characterized by the time elapsed since a particular PTE.

Phase I involves the occurrence of the PTE and its immediate aftermath. For children with cancer and their parents Phase I includes the diagnosis of cancer or subsequent PTEs (i.e. admission to the intensive care unit, sudden and serious complications). Two factors are posited to contribute to an event being perceived as traumatic: Pre-existing factors and characteristics of the event. For instance, pre-existing factors such as pre-morbid psychological difficulties (Kazak et al., 1998; Manne et al., 2004) and perceived levels of social support (Stuber et al., 1997; Kazak et al., 1998) have been associated with subsequent posttraumatic stress symptoms (PTSS) in parents of cancer survivors. Characteristics of the event also contribute to the perception of an event being traumatic. Consistent with the traditional traumatic stress framework, the event must entail life threat, and/or evoke fear, horror, and helplessness (APA, 2000).

Phase II encompasses the early (acute), ongoing, and evolving traumatic stress responses that unfold with the physical sequelae of cancer and cancer treatment. For instance, children with cancer and their families may be required to negotiate multiple procedures and adverse side effects.

Finally, Phase III refers to longer-term traumatic responses when the immediate physical sequelae, acute threat, and medical treatment have resolved or ended. The timing and duration of these phases vary depending on the nature and the course of cancer treatment. Potentially traumatic events may be recurrent or cyclical with the possibility of subsequent episodes of trauma.

The PMTS model is supported by a substantive literature on childhood cancer survivors and their families, highlighting the relevance of the PMTS model in pediatric cancer and the importance of a family systems approach to psychological care.

The instruments and procedures used throughout studies to measure PTSD and PTSS in children with cancer and in their parents varied considerably. Specifically,

while some used diagnostic interviews others implemented single and multiple informant self-report questionnaires. Consequently, it is important to distinguish between rates of PTSD diagnosis (measures by a clinician using the SCID-PTSD) and rates of PTSS (reported by participants using self-report questionnaire/s) indicative of PTSD caseness (Bruce, 2006).

1.2.5 Locus of control

Locus of control refers to an individual's generalized expectations concerning where control over subsequent events resides. In other words, who or what is responsible for what happens. It is analogous to, but distinct from, attributions. According to Weiner (1974, 1980) the "attribution theory assumes that people try to determine why people do what they do, i.e., attribute causes to behavior." There is a three stage process which underlies an attribution. Step one: The person must perceive or possibly observe the behavior. Step two is to try and figure out if the behavior was intentional, and step three is to determine if the person was forced to perform that behavior. The latter occur after the fact, that is, they are explanations for events that have already happened. Expectancy, which concerns future events, is a critical aspect of locus of control.

Locus of control is grounded in expectancy-value theory, which describes human behavior as determined by the perceived likelihood of an event or outcome occurring contingent upon the behavior in question, and the value placed on that event or outcome. More specifically, expectancy-value theory states that if (a) someone values a particular outcome and (b) that person believes that taking a particular action will produce that outcome, then (c) they are more likely to take that particular action.

Julian Rotter's original (1966) locus of control formulation classified generalized beliefs concerning who or what influences things along a bipolar dimension from internal to external control: "Internal control" is the term used to describe the belief that

control of future outcomes resides primarily in oneself while "external control" refers to the expectancy that control is outside of oneself, either in the hands of powerful other people or due to fate/chance. Hannah Levenson (1973) offered an alternative model. Whereas Rotter's conceptualization viewed locus of control as unidimensional (internal to external), Levenson's model asserts that there are three independent dimensions: Internality, Chance, and Powerful Others. According to Levenson's model, one can endorse each of these dimensions of locus of control independently and at the same time. For example, a person might simultaneously believe that both oneself and powerful others influence outcomes, but that chance does not. Generally, the development of locus of control stems from family, culture, and past experiences leading to rewards. Most internals have been shown to come from families that focused on effort, education, and responsibility. On the other hand, most externals come from families of a low socioeconomic status where there is a lack of life control.

Since its introduction, the locus of control construct has undergone considerable elaboration and several context-specific instruments have been developed. Locus of control's most famous application has probably been in the area of health psychology, largely thanks to the work of Kenneth Wallston. Scales to measure locus of control in the health domain are reviewed by Furnham and Steele (1993). The most famous of these would be the Health Locus of Control Scale and the Multidimensional Health Locus of Control Scale, or MHLC (Wallston, Wallston, & DeVellis, 1978; Wallston, Wallston, Kaplan & Maides, 1976). Furnham and Steele (1993) argue that health locus of control is better at predicting health-related behavior if studied in conjunction with health value, *i.e.* the value people attach to their health, suggesting that health value is an important moderator variable in the health-locus of control relationship.

Health locus of control is defined as the set of beliefs a person has about his or her personal influence on health. This set of beliefs includes: Internal locus of control (if the individual believes that personal actions or thoughts can affect their outcomes) and

external locus of control (if the outcome is believed to be determined by powerful others such as God, health professionals, or if chance is believed to control the outcome) (Wallston, 1991; De Vellis, De Vellis, Blanchard, Klotz, Luchok, & Voyce, 1993). Empirical research suggests that health locus of control may play a significant role in determining people's health-related behaviors (Odgen, 1996). Parents have an important role in the promotion of their children's health especially when their children are very young. It is therefore of interest to assess parental locus of control relative to children's health (Bornstein & Cote, 2004).

In this starting chapter, I focused on the key elements necessary to enter the pediatric psycho-oncology field. In the next chapter, I'm going to examine the literature about the global psycho-social aspects of children with cancer and their families, focusing alternatively to children and to parents.

CHAPTER 2

PSYCHO-SOCIAL ASPECTS OF CHILDREN WITH CANCER AND THEIR FAMILIES

"Think positive, I mean, if we started thinking negative…I wouldn't be here, I'd be crying in another room"

"We can talk freely with the doctors, with great ease…thousands of questions and still they are always available, really…yes, this is a good thing because…for something which hits you so out of the blue, all together, this helps, yes, this helps greatly…even a simple word which may be banal, for us is a big help, yes, a big help".,
"They seem all very nice to me, very…human, very…I feel as if we were in a large family here"

The life of a child who has been recently diagnosed with cancer is completely altered and accompanied by a flood of emotions. These changes range from numerous invasive medical procedures to the disruption of normal activities (e.g, going to school). The stressors related to cancer and the therapies used to treat this disease are numerous. Most children suffering from cancer report pain, weakness, nausea, vomiting, and toxing reactions (Woodgate & McClement, 1998). The major stressors for both children and parents in a recent study (McCaffrey, 2006) can be identified principally as: Medical procedures (needles, lumbar punctures, bone marrow tests), chemotherapy problems, loss of control, hospital environment, relapses, fear of dying, check-up worries, hair loss, infections, isolation from friends. Other specific parents' stressors are the following: Lack of family structure, neglect of siblings, lack of communication with partner, siblings farmed out, adult friends drift away. The management of stressors

(such as frequent hospitalization, repeated intrusive procedures, extensive chemotherapy, dependence, immobility, vulnerability, apprehension, anger and anxiety) can be often be inappropriate, with children perceiving these stressors more frequently and intense with a related high level of anxiety and lower self-esteem (Hockenberry-Eaton et al., 1995). General psycho-social adjustment, such as attitude towards the illness, body image, self-esteem and self-worth, affects an individual's ability to cope.

We have just seen above the psychological adjustment of pediatric cancer survivors (par. 1.1.3) and the effects of cortisone and chemotherapy on psychological health of children under therapy (par 1.1.2). In this chapter we will report the following literature themes: Child's coping and adjustment to cancer throughout the therapies; child's quality of life under treatment, according to child and parents' perceptions; the concept of Caring niche; parents' coping and adjustment to child illness; parents' mental health to their child's cancer; parenting a child with cancer and, finally, family factors related to psychological adjustment of pediatric cancer patients.

2.1 Children with cancer: Adjustment, coping and quality of life throughout the therapies

2.1.1 Child's coping and adjustment to cancer throughout the therapies

The disease poses huge problems for the child, because treatments are lengthy, complex and demanding. Normal life and routine of the children are disrupted by frequent hospital visits, medication and invasive procedures. There are risks of neutropenia (when a child's immunity is significantly impaired by the chemotherapy) which can necessitate hospitalization, and school attendance is interrupted, especially as children have lowered immunity and are susceptible to childhood viruses. School absence can lead to rejection from friends, and aggravate "feeling different". Children

also have to cope with changes to body appearance and deal with fears about the future. Anger, distress and withdrawal have been reported (Sawyer et al., 1997). Behavior problems may be further exacerbated by specific aspects of treatment protocols (Woodgate & Degner, 2004). For example we have just seen that corticosteroids have been linked to clingy and irritable behavior (Drigan et al., 1992). The precise way in which child response likely depends on many factors, including also chronological age and gender. Age is likely to reflect knowledge and understanding of the illness and may impact on coping and adjustment. Equally, the issues of concern for males, such as whether or not they can play their best sport, may differ from girls who may be more concerned about hair loss.

Within the literature conflicting findings concerning children's adjustment to cancer have frequently surfaced. Possible explanations for this incongruence may result from research that indicates overall adaptive functioning may still occur even in the presence of situational distress, including positively perceived changes in focus, a reordering of life priorities, an increased resilience, and a greater appreciation of life and relationships (Patenaude & Kupst, 2005).

But which are the coping strategies most efficacious for stress reduction and better adjustment? On the whole, the literature suggests that for acute stressors avoidant coping may be more beneficial, whereas approach coping in response to more chronic stressors has been associated with better adjustment outcomes (Compas et al., 1992). Related to perceived control, findings suggest that for more controllable stressors approach strategies such as attentional or problem-focused coping are related to improve adjustment, but not for uncontrollable stressors (such as invasive medical procedures) where are better avoidant or emotion-focused coping strategies (Weisz et al., 1994), even if the majority of the studies suggests that children who use more approach or problem-focused coping are better adjusted than children using avoidant strategies (Kliewer, 1997). More detailed dissemination about child coping styles with

pain can be found in the par. 1.1.2 of the first chapter.

The findings of a recent meta-analysis of these studies (Aldridge & Roesch, 2006) do not confirm this statement, finding that children who used problem-focused coping experienced worse overall adjustment. A number of explanations are plausible for these findings. First, children that take an active, problem-focused role accompanying uncontrollable stressors may be overwhelmed by the sheer amount of information and decision-making that accompanies the illness. Second, the illness itself may be perceived as uncontrollable. Third, it is important to take into consideration possible moderators and mediators such as: Time since diagnosis, type of leukemia, and type of stressor (illness-related factors); child age and gender (child-related factors) and family styles, functioning and type of coping (ecological factors). It is possible that time from diagnosis is an important factor that influence the types of coping strategies adopted by the child. The benefit of emotion-focused coping, such as social support and threat minimization, in close proximity to a cancer diagnosis is particularly adaptive in diminishing the negative emotions surrounding this time, allowing the child to recoup or regain strength. The secondary control constructs (comparable to emotion-focused coping strategies) seem to divert or minimize harm that comes from the loss of control (Heckhausen & Schulz, 1995). But prolonged use of this emotion-focused coping is not useful for a good psychological adaptation: An implementation of problem-focused coping during the following and latter stages of treatment can become more adaptive. So we can conclude that emotion-focused strategies may be more adaptive predecessors to the effective implementation of problem-focused ones during the several steps of treatment (Aldridge & Roesch, 2006).

Another factor to take into consideration is the age of the child: Developmental differences can be found in several studies. Particularly, older children use more cognitively oriented coping methods, such as emotion-focused coping (Compas et al., 1988), information-seeking (Peterson & Toler, 1986), problem solving (Tyc et al.,

1995) and secondary coping that requires more abstract thinking (Band & Weisz, 1988). Younger children, instead, use more active coping to change the environment (approach, problem focused) rather than cognitive abstraction to manage stressors (Band & Weisz, 1988).

Especially for the younger children, it is necessary to take into consideration parents' description of their behaviors to understand their possible psychological reactions to the illness and to its treatments. A recent study of Earle & Eiser (2007) extracted from 32 interviews with mothers of children with ALL themes related to their adjustment and behavior in relation to school, friendship, appearance and understanding the illness. Mothers described children aged 0-4 years as adjusting well because of their limited understanding and ability to integrate treatments into normal life. Children in the 5-9 year group were adjusting less well, experiencing social problems and worries about appearance. Older children (10-14 years) adjusted least well, with socially difficulties and look and feel normal concerns.

The paragraph 2.4 will show also the family factors related to child's coping and adjustment, an important issue for these research hypotheses. A good use of coping styles and strategies can allows the child to maintain as possible a dignified quality of life both during the hospitalizations and their own daily life.

2.1.2 Child's quality of life throughout the therapies and parents' health perceptions

Quality of life assessment is a complex challenge for pediatric researchers and clinicians. Several instruments have been used to assess survivors of childhood cancer, but their application in studies of children receiving active therapy for cancer has been limited. Most prospective pediatric clinical trials include scales for the measurement of specific therapy-related toxicities (such as pain or diarrhea), but these are not the only

measures or Health Related Quality of Life (HRQL). It is important to note that the evidence on HRQL in children with cancer is mostly based on preformatted, rigid measures such as questionnaires. Some recent reviews on the health-related quality of life in pediatric lymphoblastic leukemia identified the HRQL measures most used (Pickard et al., 2004). The questionnaires are devised by clinicians and researchers and are based upon research on adults with cancer, developmental theories and clinical impressions. Wallander and colleagues (2001) have identified four developmental factors that should be considered when designing a pediatric HRQL instrument: a) developmental differences in HRQL markers; b) child relevance; c) comprehension and d) time frame. In order to be sensitive to developmental differences in HRQL markers, instruments must evaluate HRQL domains and markers that are appropriate for the age and developmental stage under study (Nathan et al., 2004). In order to be child relevant, a HRQL instrument should assess specific domains and marker that are important to children themselves. The questionnaires not always map the whole range of the pediatric patients' experience about their HRQL as they view it (Hinds et al., 2004). Sometimes, questionnaire-based information may not facilitate the communication between doctor and patient, especially when the patient is a young child and the communication must pass through the parents. Thus, the existing questionnaire-based evidence on the quality of life of children with cancer should be complemented by evidence drawn from open-ended verbal reports by the parents and also by the patients, when they are mature enough to report their HRQL by complex verbal means.

Some studies are now developing on this new trend, taking into account children's own perceptions. McGrath et al. (2004) shows children and parents' experiences of the diagnosis of AML and the early hospitalization experience by analysing the narratives during interviews respectively of children and parents. Woodgate (2005) describes the core narrative of "life is never the same" lived by the children and their families and Hicks et al. (2003) explore quality of life in children with leukemia aged 5-9 years old

in the period of post 6 months from diagnosis or in the off-therapy time.

Also parents are very important for child's health throughout the therapies as they can inform health professionals about their children's states and quality of life, especially at the beginning of the treatments when doctors and nurses do not yet know them. One would expect most parents to be reliable informants, but the evidence shows that parents and pediatricians may differently perceive the quality of life of chronically ill children (Janse et al., 2005) and that parent-child agreement (Chang & Yeh, 2005) is influenced by elicitation method (Sung et al., 2004). For example questionnaire given to children and to their parents (proxy) can measure a concept of quality of life different from the same concept using in depth interviews. Another possibility for these disagreements may rest in the fact that doctors and parents may attribute importance to different aspects of children's HRQL and hence communication about these issues may be difficult. However maternal perceptions of their children's quality of life may be reliable enough (Tremolada et al., 2005). In this study, during the interviews, mothers were never asked for judgments or evaluations about their children's skills or quality of life, simply narrating everyday facts and events in a holistic manner. They were hardly biased by the well-known subjective effects that may occasionally skew the data from questionnaires which ask parents to rate their children. The reported episodes were scored only afterwards by independent judges. Moreover, it is worth noting that the variable Quality of Life drawn from parental narratives is associated with objective variables (i.e., CVC[6] implantation and Age of the child) in the expected directions, thus giving support to the validity of the parental interview data.

Qualitative methods are vital when developing an understanding of the meaning of quality of life (QOL) for the patient. The themes regarding the effects of leukemia and treatment on Quality of Life stressed by the literature are: Tiredness, activities affections, medication and treatment effects, relation changes, hair loss. The factor that

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[6] CVC: Central Venous Catheter is placed during the first week of hospitalization to administer the several therapies directly to the heart of the patient. It allows children to stop the painful venipunctures.

most affected QoL by Hicks and colleagues (2003) was fatigue (related to: Procedures, sedation, venous access device, staff interactions, symptoms due to its causing limitations on activity). According also to Davies et al. (2002), fatigue is exacerbated by the emotional and mental energy needed to cope with facing the unknown and the unfamiliar routine of coming to the clinic or hospital. Also psychosocial issues such as hopefulness, family/peer isolation impact on the short and long term adaptation of the children and of their families. Focusing on possible predictors of HRQOL, Yeh (2002) identified Communication with others as the best factor predicting HRQOL. The importance of how to tell patients they have cancer, especially children, is showed in several studies (Clarke et al., 2005; Cline et al., 2006), stressing also the bad effects of a mutual pretense and a conspiracy of silence between parents and children. A parent has also to consider the cognitive capacity of children at different developmental stages when communicating children with cancer. Parents' role becomes a key element so that we now are going to analyse it and also the possible effects of the child illness on their own psychological health.

2.2 Adjustment to cancer: The Caring niche

In most pediatric tumors, different phases can be identified. First there is the acute phase, characterized by the diagnosis and the first, intensive treatments in the hospital. The second is the chronic phase, characterized by check-ups and treatments which can be carried out during (often brief) intermittent hospitalizations or in day-hospital. For example, for leukemia this phase may last up to two years. Then, there is the remission or off-therapy phase, during which the children are followed-up but they do not receive treatment; this phase lasts for 5 years. If there is no recurrence of the disease, after 5 years the child is considered healthy again. Each phase requires its own adaptations, yet the first, acute phase is the one which requires the complete modification, often the

upturning, of the previous family life and routines.

Adopting an ecocultural point of view, this phase can be defined as the one in which the previous developmental niche of the child (Super and Harkness, 1986; Weisner, 1984, 1998, 2001, 2002) is revised and a modified one takes place. Axia (2004) defined the new niche of the child with cancer as the "caring niche" which is activated in Western societies when the existing niche appears to be unable to make the child survive. The new niche takes care of children's survival by specialized means which are out of the reach of the parents and extended family. As represented in Figure 1.2.1, the caring niche is immersed in its own specific ecocultural context which is made of the overall economy and resources, the health policies and resources allocation (Weisner, 1984), including in this case resources for cancer research. Further parts of the broader context relevant for the caring niche of the children with cancer are the local presence and training of volunteers in the pediatric onco-ematology hospital, the place social services for the families and the flexibility of the school system. For example, in some pediatric hospitals there are specialized teachers from local schools who take care of the academic work of the hospitalized children; the local social services may sometimes provide low cost or no cost rooms or apartments for parents in the surroundings of the children's hospital, etc.. The caring niche is sustained and influenced by all these ecocultural aspects of the local context.

Differently from the developmental niche which is basically one system, the caring niche is made up of two different but highly interconnected systems. On one side, there is the child's "natural system" provided by his or her family and ecoculture, including the daily routines and their settings. On the other side, there is the "expert system" which is activated to preserve the child's survival when the natural system cannot guarantee it any longer. The expert system has specific settings (e.g., the hospital), specific daily routines and activities, and is made by people who are specialized in treating physical and mental health, in preserving physical and mental life

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(i.e., oncologists, pediatricians, nurses, psychologists, psychiatrists). The balance and the relationships between the two subsystems of the caring niche change over time. A great deal of activity and of communication between the two subsystems is needed to preserve good functioning all along the various phases of pediatric cancer diseases. However, the most interesting and telling phase is the first one, when children and families require huge adaptations. During the acute phase, the previous well established niche is completely upturned, and a new one must be created. Some parts of the new caring niche are already there in the ecocultural context, but other parts are the outcome of an intense, sometimes desperate, adaptation process which involves equally the children with cancer and their family. From the family perspective, there is the question of making sense of the new niche and of its potentials. The major task is to create actively new ways to live ordinary, meaningful lives in a different, more complex ecocultural niche.

Figure 2.1 - The caring niche (Axia et al., 2004, pg. 31).
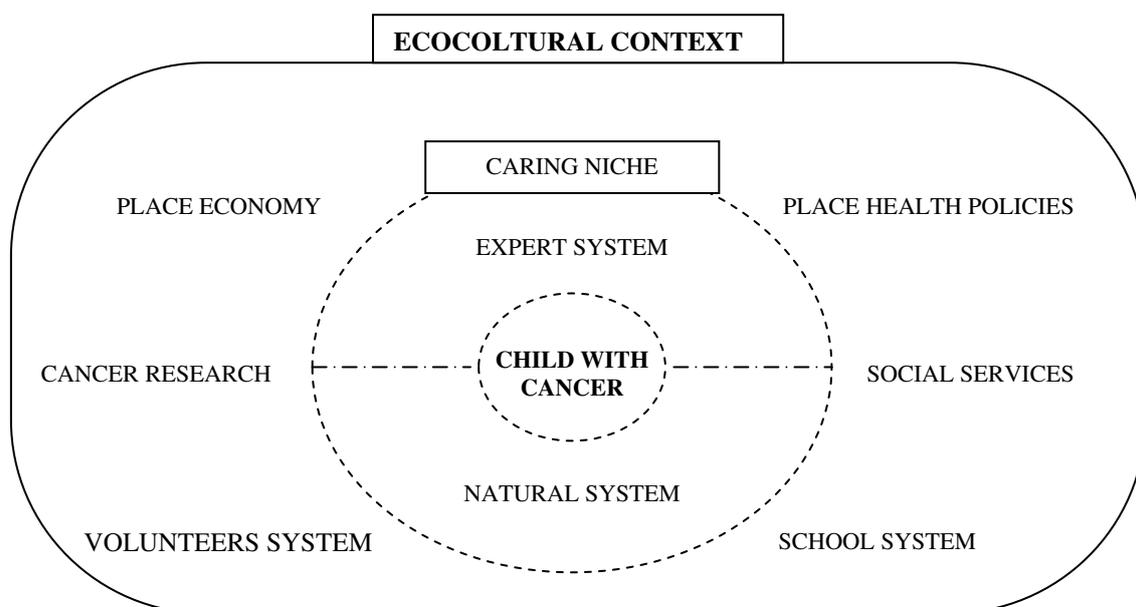
2.3 Parents of children with cancer: An ecocultural approach

The ecocultural approach considers human development and human experiences as inextricably related to the context in which they occur. When a child is diagnosed with cancer, the whole family system, and often the broader social context, is affected and the previous accommodations and homeostasis are broken. This effect is so strong that pediatric cancer was often defined as a "family disease" (Chesler, 1993). As the father of a 3-year old girl with a brain tumor told us: *"Frances* (fictitious name) *is ill but we also are ill. The patient is not only one here, the three of us…we are also ill, her mom and her dad. When she cries, it is my heart that cries. When she is in pain, I feel my bones aching..and..when she is in despair, I am in despair too"*.

In most pediatric tumors, different phases can be identified. First there is the pre-diagnostic phase where uncertainty and threats involved can provoke high levels of parents' anxiety and isolation from others.

The second is the acute phase, characterized by the diagnosis and the first, intensive treatments in the hospital. Parents may experience decision making difficulties and immediate treatment threats. In this phase coping resources may differ depending on adequate communication between pediatric staff and family members.

The third is the chronic phase, characterized by check-ups and treatments which can be carried out during (often brief) intermittent hospitalizations or in day-hospital. For example, for leukemia this phase may last up to two years. The attempt to define and return to normalcy may arouse the most family discord.

Then, there is the remission or off-therapy phase, during which the children are followed-up but they do not receive treatment; this phase lasts for 5 years. If there is no recurrence of the disease, after 5 years the child is considered healthy again.

Each phase requires its own adaptations, yet the first, acute phase is the one which requires the complete modification, often the upturning, of the previous family life and routines.

Consideration of parent/caregiver variables is critical when conducting research with children facing life-threatening illness, given the impact of parent functioning on child functioning. Moreover, because parents are often used as proxies to assess the quality of life and functioning of the child, their perceptions, functioning and adjustment need to be considered.

Historically, findings from the caregiver literature on parents' adjustment to a child's cancer diagnosis are equivocal, with same studies revealing generally good parent adjustment (Frank et al., 2001; Kazak & Meadows, 1989) and others indicating high rates of significant disease (Sloper, 2000; van Dongen-Melman et al., 1995; Vannatta & Gerhardt, 2003). These discrepant findings may reflect the method by which adjustment is assessed and a reliance on tolls less sensitive to the experience of parenting a child with a life-threatening illness (Eiser, 1998; Streisand et al., 2001). Measures has focused on important domains such as impact on family (Stein & Reissman, 1980), aspects of illness-related functioning (Streisand et al., 2001), post-traumatic stress (Bruce, 2006), maternal worry (DeVet & Ireys, 1998) and parental beliefs (Kazak, McClure et al., 2004). Also the subjective parent distress is an important factor in child outcomes: Perceived uncertainty (Woodgate & Degner, 2002), continual loss experiences and emotional self-efficacy are important factors in this sense (Bonner et al., 2006). Parents' distress can lead to inefficiency in keeping equilibrium in family functioning in a variety of ways: They may not understand what the illness involves; they may experience overwhelming guilt; they may experience financial strain; they may feel inadequate for meeting support needs to each other; they may feel unable to give their other children reassurance and support; it may later their own vocational responsibilities; it may interfere with normal recreational and churchgoing activities, thus depriving them of social support networks that are necessary at these times (Melamed, 2002).

2.3.1 Parents' coping and adjustment to their child's cancer

The concept of family resilience is defined as the coping and adaptational process of the family unit as a whole. Basing on in-depth interviews, McCubbin et al. (2002) identified resiliency factors that helped the family recover: Internal family strengths; rapid mobilization and reorganization; social support from the health care team, extended family, the community, and the workplace; and changes in appraisal to make the situation more comprehensible, manageable, and meaningful. Specifying the family and the illness characteristics and defining the phase of diagnosis or treatment is critical when examining resilience and coping strategies involved. Each phase of the disease confronts parents with different problems and thus requires the learning of new coping skills and patterns (Eiser, 1993; Swallow & Jacoby, 2001; Yeh et al., 2000).

Although it has been noted that coping is not a linear process but a series of "ups" and "downs" which are often exacerbated by unpredictable events, two major approaches had been suggested to explain family coping with a child's cancer.

The first approach, called the "stages" framework, has a developmental perspective and depicts four phases that parents go through as they adapt: Disbelief, anger, demystification, and conditional acceptance (Austin, 1990). Other authors (Fortier & Wanlass, 1984) describe five stages in this order: Impact, denial, grief, focusing attention, and closure. In this view, the diagnosis causes feelings of shock, anxiety and depression whereas parental adaptation occurs over a period of time through the use of active behaviors that were employed, especially, during the last two stages. Also Yeh et al. (2000) enumerates five components of the coping process in childhood cancer: Confronting treatment, maintaining family integrity, establishing support, maintaining emotional well-being, and searching for spiritual meaning. In Yeh's study the identified components of parental coping included the following: Confrontation of reality, management of treatment issues, cognitive and affective shifting, recognition of the situation, and adjusting properly.

The second approach includes models (McCubbin & Patterson, 1982; Lazarus & Folkman, 1984) that directed attention to parents' perceptions of the situation, providing a comprehensive framework for psychosocial research and a useful tool for assessment and intervention in the clinical setting. Examining variation in coping behavior can be a mean to explain some of the variability that appears in individual response and adjustment to illness-related stress among persons (Miller, 2000).

Incorporating aspects of both "the stages" and the "coping-adaptation" approaches is useful in practice and research.

Hoekstra-Weebers et al. (2000) summarized about 20 years of findings and showed an interesting model (Figure 2.2) as a framework to explain the variability in parental psychological functioning by identifying concurrent and prospective predictors of maladjustment.

Childhood cancer is viewed as an ongoing stressor to which each parent has to adapt. The diagnostic phase is considered as an acute traumatic stressor of life. Three basic components and their interactions influence parents' adaptation outcomes. The first is the type of child leukemia, the duration and outcomes of the therapy (see also, Stuber et al., 1996) – all considered as <u>main stressors</u>. The second component is made by the stable variables which can influence parental adjustment outcomes: SES (Hoekstra-Webers et al., 1998b; Kazak et al., 2003), life events (Breslau et al. 1985) and parents' personality traits, such as anxiety (Dalquist et al. 1996; Frank et al., 2001). They are called <u>stable moderators</u>.

Figure 2.2 - Model for parental psychological functioning (Hoekstra-Weebers et al., 2000, pg. 259, adapted).
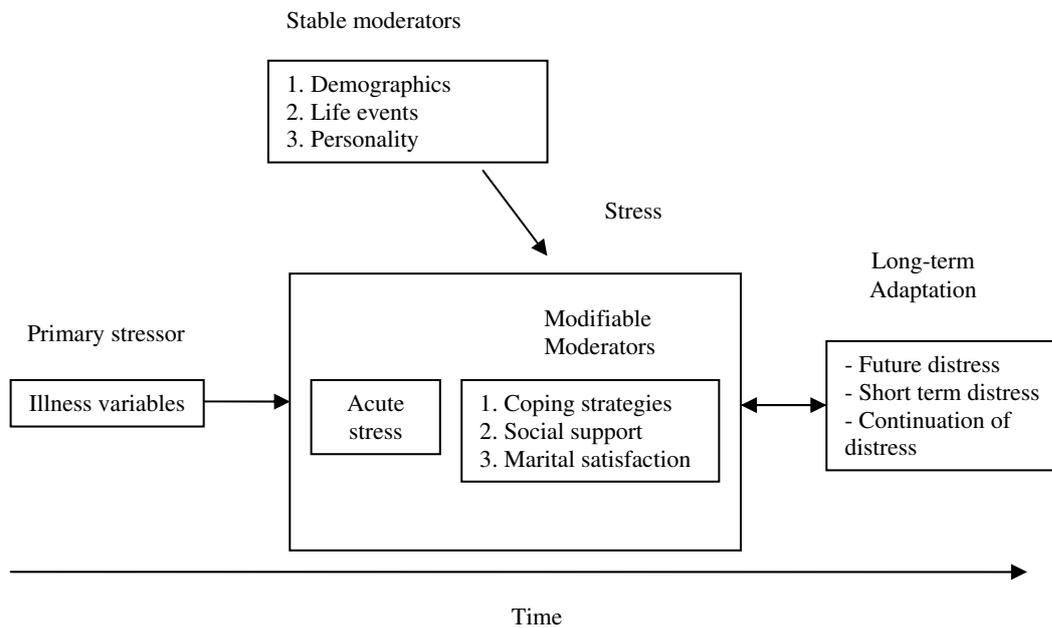
The third component is made of more flexible variables such as parental coping strategies (Goldbeck, 2001; Grootenhuis et al., 1996; Grootenhuis and Last, 1997), available social support (Manne et al., 2000; Dockerty et al., 2000; Kazak et al., 1997; 1998), and marital satisfaction (Ruccione et al., 1991; Brown et al., 1993). These are called <u>modifiable moderators</u>. Stable moderators influence modifiable moderators which in turn impact upon stress and adjustment outcomes.

In childhood cancer, studies have found that parents employ both emotion- and problem-focused coping behaviors to deal with the stressors associated with their child's illness. Nevertheless, the same parents primarily rely on emotion-focused strategies when they are faced with the other uncertainties of the illness such as those related to their parenting role and the final outcome of the child's disease (LaMontagne et al., 1999; Sterken, 1996). Parental coping strategies include maintaining family stability and cohesion, open communication, role flexibility, shared values and beliefs, search for information about the child's illness and its treatment, living one-day-at-a-time, acceptance, a consistent philosophy of life, optimism and hope (Chesler and

Barbarin, 1987; Eiser, 1994; Eiser et al., 1995; Spinetta et al., 1988; Grootenhuis and Last, 1997; Patistea, 2005). Maintaining balance in family life and strengthening family bonds, especially have been reported as a continuous source of stress and anxiety for parents (Atkin and Ahmad, 2000; Rocha-Garcia et al., 2003). Religion, prayer and faith in God also seem to play a crucial role in both parents' coping efforts (Goldbeck, 2001; Patistea et al., 2000).

Another significant resource for both mothers and fathers of children with cancer is support from spouses, relatives, friends and other parents having children with the same health problem (Eapen and Revesz, 2003; James et al., 2002). Low social support has been associated with poor emotional health of parents and inadequate psychosocial adjustment (Dockerty et al., 2000; Han, 2003). According to fieldwork studies (Gibson, 1995; Last and Grootenhuis, 1998), nurses and doctors also need to support parents of chronically ill children and help them develop the necessary knowledge, competence and confidence (a process called "empowerment") that would enable them to adapt to their situation and increase their sense of control over their lives. There are research accounts indicating that health care professionals are indeed a significant source of support for parents in coping with their child's lifethreatening illness (Hodgkinson and Lester, 2002; Wittrock et al., 2000). Other study findings, however, have revealed that health practitioners may act as constraints to parental efforts to deal with childhood chronic illness (Swallow and Jacoby, 2001b; Thorne and Robinson, 1988). Parents have commented that sometimes, health care professionals do not respect their time and do not acknowledge the expertise they develop in caring for the sick child (Ray and Ritchie, 1993). Positive relationships between parents of children with cancer and the members of the health care team have been associated with improved spousal relationships and more effective overall coping with the caregiver role (Shapiro et al., 1998).

Previous research has failed to report statistically significant correlations between

parental coping and the sociodemographic and illness-related variables it examined. For example, Eapen and Revesz (2003) have shown that parents' coping was not associated with their education, occupation or socio-economic status. Similarly, based on their findings, Eiser et al. (1995) have concluded that mothers do not differ from fathers in their ratings of the helpfulness of different coping strategies. Other investigators (Eiser and Havermans, 1992; Han, 2003; Sterken, 1996), however, have supported the view that there is a direct relationship between parental coping and some of the sociodemographic factors such as the age of the father, the age and the gender of the child, and the length of time since diagnosis.

Research concentrating on gender differences and preferences in coping with childhood malignancy has provided contradictory results. For instance, McGrath (2001) has found no correlation between gender and coping with childhood leukemia. Similarly, based on their findings, Eiser et al. (1995) have concluded that mothers do not differ from fathers in their ratings of the helpfulness of different coping strategies. Nevertheless, other researchers have indicated that fathers are more likely to use active problem-focused coping as compared to mothers who tend to cope through palliative reaction patterns (Hoekstra-Weebers et al., 1998).

In addition, fathers seem to use more denial, avoidance and emotional withdrawal than do mothers (Chesler and Barbarin, 1987; Chesler and Parry, 2001). Using drugs, alcohol and food, driving alone and putting increased energy into work are among the avoidance coping styles most commonly reported by fathers (Sterken, 1996). Gender differences have also been observed in social-support seeking (Hoekstra-Weebers et al., 1998; Jones and Neil-Urban, 2003). Fathers have been found to receive less social support as compared to mothers and thus they have a higher risk of psychological distress (Katz, 2002; Speechley and Noh, 1992). Sterken (1996) has characterised paternal coping styles as evasive, optimistic, and emotive. Crying and praying have been the most frequent emotive coping strategies used by fathers (Cayse, 1994; Sterken,

1996). In the study conducted by Eiser and Havermans (1992), mothers gave higher ratings in all four coping subscales examined (autonomy, medical care, social support, family support). Overall, mothers tend to report more frequent and more effective coping as compared to their male partners (Goldbeck, 2001; Koch et al., 1996).

The type of coping style adopted by parents can be strongly related also to their mental health. For example in the study of Norberg et al. (2005) a more frequent use of active problem-focusing, and a less frequent use of avoidance behavior and passive reaction pattern was related to lower levels of anxiety and depression in parents of children with cancer. The contextual demands in each time points after the diagnosis influence the relation between coping and anxiety/depression.

2.3.2 Parents' mental health related to their child cancer

Being confronted with the diagnosis of childhood cancer in the family causes various emotional reactions. The word "cancer" is associated with death, and for most people cancer cannot be associated with children. There is a vast literature on the psycho-social consequences of child cancer on parental well-being and quality of life.

In general, the literature converges upon two major facts. The first is that the most difficult period for parents and families happens just after the diagnosis (Sheeran et al., 1997) and along the first year following it, when child undergoes several invasive medical procedures (e.g., bone marrow aspirates, lumbar punctures) and treatments (e.g., chemotherapy, bone marrow transplantation). Several studies showed that the acute phase is the most stressful period for parents (LaMontagne et al., 1999; Sawyer et al., 1986; 1997; 2000; Sloper, 1996) in which a new family "reality" must be built up (Clarke-Steffen, 1993). Parental distress related to these painful pediatric procedures is highly stressed (Boyer & Barakat, 1996), especially related to bone marrow transplantation (Streisand et al., 2000). Thereafter, stress tends to decrease (Bracken, 1990), but it does not go back to normal values (Hoekstra-Webers et al., 1996). For

example, marital dissatisfaction in parents of children with cancer may be present in about one parent of every four (25% of mothers, 28% of fathers, according to Dahlquist et al., 1993), even if neither mothers nor fathers' mean of marital adjustment scores changed over time (Dahlquist et al., 1996). Also self-perceived social support decreased with time, becoming a risk factor only for fathers (Hoekstra-Weebers, 2001), while the parents' psychological distress decreased significantly from the time of the diagnosis to 5 years later (Wijnberg-Williams et al., 2006).

The second point highlighted by the literature is that there are different pathways for adjustment and quality of life open to the families of children with cancer. Unfortunately, a notable percentage of parents is not able to make it and remains indelibly scorched by the experience.

Common emotional difficulties among parents of children with cancer are sleep disturbances, hypervigilance, difficulty concentrating, guilt, anger, uncertainty, loneliness, problems with parenting the sick child and siblings, an inability to meet each other's emotional needs and financial strain (von Essen et al., 2004). Researchers who have focused on parents of newly diagnosed children with cancer, or children who are in treatment, report increased emotional distress, such as anxiety or depression, in these parents against normative data (Dahlquist et al., 1993; Manne et al., 1995). In longitudinal studies also increased negative emotions such as anxiety, depression, insomnia or somatic and social dysfunctioning shortly after diagnosis are found (Sawyer et al., 2000; Pelcovitz, 1996; Van-Dongen Melman et al., 1995). In some cases this psychological distress was also greater than in healthy controls (Sawyer et al., 1993). A number of other studies report that parents are experiencing emotional problems 1 year after diagnosis; for example, a high percentage of mothers are diagnosed as overanxious and fathers are diagnosed with major depression or increased feelings of depression (Brown et al., 1992).

Other studies, which included children with cancer both in and off treatment, also found increased psychological stress in the parents with children in active treatment (Hughes & Lieberman, 1990; Larson et al., 1994; Hoekstra-Weebers, 1998). Brown et al. (1993) found that 34% of the mothers of children with cancer in various phases of their child's disease were diagnosed with a psychiatric disorder. Women diagnosed with a psychiatric disorder had higher depression scores on the Beck Depression Inventory (BDI) than mothers who were not diagnosed with a psychiatric disorder. The scores of mothers both with and without a psychiatric disorder were in the normal range, however. On the other hand, no differences were found between parents of children with cancer against normative data about their general mental health in the study of Dockerty et al. (2000).

A few investigators analysed within-group differences based on the treatment phase of the child. Brown et al. (1992) found that mothers of children who were off treatment had significantly lower depression scores than mothers of newly diagnosed children, and mothers of children 1 year after diagnosis. Van Dongen-Melman et al. (1995) reported that late psychological consequences did not differ for parents with children off treatment less than 2 years ago, between 2 and 5 years ago, and for parents of children off treatment more than 5 years ago. Lack of prediction of time since diagnosis has also been found by Grootenhuis and Last (1997; Sloper et al., 2000). When treatment is terminated many parents experience ambivalence. On the one hand, they may experience relief that the treatment is completed, but on the other, their fear about the child's future life may increase. These results correspond well with findings demonstrating that some parents show symptoms of Post-traumatic Stress Disorder (PTSD) still years after the termination of treatment (Pelcovitz et al., 1996; Kazak et al., 1997). Parenting stress, parent report of child quality of life during treatment for childhood leukemia and later PTSS and state anxiety were found strongly associated (Kazak & Barakat, 1997). Adaptive styles may be correlated to PTSS in parents of

children with cancer (Phipps et al., 2006): Parents identified as "low anxious" or "repressors" (high defensiveness) self-reported lower levels of PTSS than did high anxious.

Numerous studies have reported on the increased incidence of PTSD and PTSS compared to parents of healthy children, especially in mothers (see paragraph 1.1.4). Fewer studies have reported the PTSS incidence in parents of children in active treatment and also comparing it with that of parents of long-term survivors.

A recent study of Phipps and colleagues (2005) underlined that parents of recently diagnosed children appeared to show elevations on self-reported PTSS, and that these incidences were still present approximately 2 years following diagnosis. Symptom levels in parents of children who were long-term survivors were significantly lower and comparable to normative values. Parents of children on treatment face numerous ongoing stressors that can lead to symptoms of distress that are common to many psychiatric conditions, and are not unique of PTSD. For example, in their work with parents of children undergoing BMT, Manne et al. (2001; 2004) found diagnosable cases of Major Depressive Disorder, Panic Disorder, and Generalized Anxiety Disorder, in addition to PTSD in this population. It may be appropriate to view this as an indication of overlapping symptom patterns, especially occurring as a contingent response to concurrent stressors throughout child treatment. In the study of Phipps et al. (2005) parental PTSS and child self-reported PTSS were also significantly correlated, suggesting a clustering of symptoms within families. It is easier to find this kind of association by utilising the full distribution of PTSS as a continuous variable, than by using PTSD as a dichotomous variable. Focusing on the full continuum of PTSS may be more informative.

Another longitudinal study (first 6 months) about psychiatric morbidity in parents of children with malignancies (Magal-Vardi et al., 2004) after the diagnosis found that approximately 20% of the parents had scores of PTSS above the cutoff point in the first

evaluation within 2 weeks post diagnosis. PTSS scores for mothers and fathers were similar on admission, and no significant interaction was found between their symptoms and children's risk level. Only the fathers' symptoms decreased over time, and they were positively associated with the children's symptoms at the 1-month and 6-month follow-ups. Landolt et al., (2003) gave a different light to the functional status of children, showing as important predictor to more PTSS in children and parents. The authors didn't find associations between child's PTSS and parents' PTSS.

The study of Kazak et al. (2005) investigated the presence of PTSS in parents of children currently in treatment and their association with treatment intensity and length of time diagnosis: All but one parent endorsed PTSS, with two thirds of mothers and one half of fathers reporting PTSS in the moderate-to-severe range. A recent preliminary italian study of Axia et al. (2006) gave more comfortable results with only 34.5% of 58 mothers having a full PTSD. Mothers of children with ALL fared better than mothers of children with AML. Preliminary analyses showed that child age and sex, parental education and employment, and family SES did not affect mothers' PTSD symptoms. Predictors for later PTSD symptoms were found since the second week after the diagnosis, i.e. mothers' evaluations of their current lives and their cognitive functioning.

Whereas previous literature on parent adjustment to having an ill child has looked primarily at anxiety and/or depression, the findings related to these outcomes have been variable and of somewhat utility. That is, anxiety is elevated at diagnosis but declines for most parents as treatment is initiated and the family accommodates to the new "routines" in their lives (Steele et al., 2004). Depression, although seemingly understandable, has not been reported as a consistent or clinically significant outcome for parents (Steele et al., 2004). Alternatively, PTSS such as intrusive thoughts about the child's diagnosis or other particularly salient moments during the child's treatment (e.g., admission to the intensive care unit, trips to the emergency room, death of a

roommate), physiological arousal at reminders of cancer and thoughts about avoiding cancer and its treatment are closely linked to clinical care and continue to be common among parents for many years after treatment (Kazak et al., 2004). It would be inappropriate to assume that PTSS indicate psychiatric impairment. They are, for many, part of the process of responding and reacting to one's circumstances and may be adaptive in certain ways. This is an important clinical information and it becomes important to identify the parents more at risk of elevated PTSS just in the fist hospitalization of the child.

In this sense, it is of paramount importance to identify predictors and mediators of psychological adjustment in parents of children with cancer under treatment, especially related with possible psychiatric disorders. Kazak et al (1998) developed an interesting exploratory model to examine correlates of post-traumatic stress in mothers and fathers of childhood cancer survivors, looking at the relative contributions of several factors: Personality (trait anxiety), current individual and family systems variables (parental appraisal of life threat and treatment intensity, life events, social support, and family functioning), post-treatment variables (length of time since treatment ended, child's current anxiety, medical sequelae of treatment), and treatment-related events (child's age at diagnosis, type and intensity of treatment). In this model, anxiety was the strongest predictor of post-traumatic stress symptoms. The current family and individual variables also contributed significantly, particularly with respect to the individual contributions of perceived life threat, perceived treatment intensity, and social support. Objective medical data did not contribute to post-traumatic stress symptoms.

The literature on predictors and mediators of psychological adjustment in parents of children with cancer under treatment and not survivors deals with some longitudinal studies. It has been repeatedly shown that social support seems to be a key factor in dealing with experience of pediatric cancer diagnosis and treatment (Brown et al., 2003; Dockerty et al., 2000; Sloper, 2000). Studies have showed that lack of perceived social

support is associated with increased risk for development of post-traumatic stress symptoms (Best et al., 2001; Kazak et al., 1997; Kazak et al., 1998; Manne et al., 2000). In addition, studies have shown that parents who have been able to adjust well to their child's cancer have received better family and overall support (Hoekstra-Weebers et al., 2001; Kupst & Shulmann, 1988; Kupst et al., 1995; Smith et al., 1999). In contrast, at least one study has shown no effects for social support on PTSD symptoms (Pelcovitz et al., 1996). The few studies that have included data for fathers have shown differences between mothers and fathers. Some authors have hypothesized that fathers may enjoy a greater deal of social support during the child illness than mothers who usually are the main caretakers and spend most of their time with the ill child. For example, fathers may have greater support in their work ambience (Weiss, 1990) and they experience more ample and varied roles during the child disease than mothers (Frank et al. 2001; Holmebeck et al., 1997).

Another possible predictor of parental psychological adjustment is the family cohesion. Sloper et al. (2000) showed how family cohesion was predictive of low level of distress at 6 months after the diagnosis. Family cohesiveness also had a contributory role in the maintenance of parent depressive symptoms (Manne et al., 1995). Family cohesion suggests families with strong relationships that become closer as a result of the illness, in contrast to those who felt that the illness had caused problems in relationships. Dolgin and Phipps (1996) suggest that the construct of family cohesion is related to the idea of centripetal and centrifugal forces, which operate around events in the normal life cycle to draw families together or put them apart.

Other possible good prognostic elements at 6 and 18 months post-diagnosis were, for mothers, their appraisal of the strain of the illness-related demands and their own ability to deal with it, so related to their coping styles. For fathers, risk factors of employment problems and the number of hospitalization were significant, along with appraisal and family cohesion (Sloper et al., 2000).

Also anxiety during treatment can be a significant predictor of PTSS for mothers, but not for fathers. Self-efficacy, post-traumatic growth and length of time since treatment ended were associated with parental avoidance (Best et al., 2001).

Child behavior problems are also a strong predictor of parent psychological adaptation, in particular for parent depressive symptomatology (Manne et al., 1995).

In conclusion, positive correlates of parental psychological adjustment to pediatric cancer identified in the literature include: Effective coping strategies (Kupst and Shulman, 1988; Kupst et al., 1984); the child's physical well-being (Van Dongen-Melman et al., 1995); lack of other concurrent stress and strains (Van Dongen-Melman et al., 1995); and good family support (e.g. Speechly & Noh, 1992). The child's functional impairment and behavior problems were found to be the strongest predictors of parental depression at 3 months post-diagnosis (Manne et al., 1995). Studies assessing the relationship between parental coping strategies and psychological adjustment to pediatric cancer report inconclusive, but significant, findings (Noll et al., 1995). At this purpose, Barrera et al. (2004) found that in mothers of children newly diagnosed with cancer emotion-focused coping and child behavior both predicted depression, anxiety and global mental health, while concurrent stress and strain mediated the relationship between child behavior and depression and between emotion-focus coping and each measure of adjustment.

How the clinicians can identify the family more at risk for psychological difficulties facing with the child's cancer?

Kazak et al. (2003) devised a quick measure to assess most of the factors indicated by the literature above. The Psycho-social Assessment Tool is a 20 item questionnaire which can be filled out by the caregivers and give information on 10 domains: Family structure, family resources, social support, child knowledge of cancer school attendance, child cognitive, emotional and behavioral concerns, child maturity, marital or family problems, family beliefs and other stressors. A 14 items version can be

filled out by doctor and nurses. The authors found that the most common risk factors were financial difficulties, having more than three children living in the home, a history of emotional problems in the families and single parenthood. However, only 7.2% to 5.6% (depending on the respondent) of families were targeted for psychosocial risk, with a further proportion of 36.3% to 14.4% of families potentially selected for psychosocial risk. Most families were not at risk. Not surprisingly, there is long term stability for families' psychosocial risks (as measured here) in the time range from 3 to 6 months after the diagnosis.

Questionnaires given to parents can measure their mental health status, resources (SES) or psychosocial risk level (Kazak 2003). The main characteristic of such questionnaires is that they score people along scales in which there are fixed cut-off points for psychological risk, including mental health (anxiety, post-traumatic stress, etc.). They certainly inform us about the mental functioning of parents of children with cancer and they also inform us about their chances for positive adaptation. However, they tell us little on how parents of children with cancer strive to extract a meaning from their ongoing experience and how they use it to create a routine which can be meaningful to them. These arguments may be investigated by in-depth interviews and in the next paragraph we are going to describe the role of parents throughout the therapies of children with cancer.

2.4 Parenting a child with cancer

The main task of parenting is to give care. Caring for children involves responsibility for their well-being, and knowledge about their needs and how to accommodate them. Most importantly, there is an emotional bond between parents and their children that is essential to children's development and happiness (Ainsworth, 1969). The central task for parents is not simply to keep the child alive, or provide

appropriate discipline, but "create the conditions in which children can develop their fullest capacity both inside and outside the family" (Cowan et al., 1997). The responsibilities and challenges involved in childcare are numerous, but because there is caring and concern, parents usually finds ways to manage, even in extreme conditions such when a child has cancer. Knowing how to parent an ill child is difficult and challenging. Parents of children diagnosed with cancer must negotiate a myriad of potentially stressful situations daily: Talking with the child about the illness, learning how to correctly perform a home care regimen, managing the parent's own emotions about the child's disease and survival, advocating on the child's behalf within a complex health care system, providing care for unaffected siblings, and fulfilling extra-familiar obligations (employment, financial, or otherwise) during periods of child sickness or hospitalization (Enskar et al., 1997a). This pediatric parenting stress can also be associated with poorer family functioning (Streisand et al., 2003). Family functioning consists of examining mutual and reciprocal influences between members. Parents who report experiencing more frequent pediatric stressors, particularly those pertaining to emotional issues, are more likely to simultaneously report having difficulty with the level of behavioral control exhibited among their family members. Specifically, parents who experience heightened communication difficulties around the illness reported less emotional expression within their families.

The major themes that emerged from the parents' stories (isolation versus support; uncertainty versus certainty, control versus loss of control, honesty versus secrecy, survival versus capitulation) capture the essence of the crisis a parent is plunged into once his or her child is diagnosed with cancer (Papaikonomou & Nieuwoudt, 2004). Biographical disruption begins for parents when they first notice something wrong with their child, and intensifies with diagnosis, altering their sense of self and their social identity. Especially for mothers, caring evokes an intense emotional interdependence with their sick child, and involves a range of technical tasks and emotional work,

including acting as "brokers" of information for their child and managing the cooperation with treatment (Young et al., 2002).

When a child has cancer, parents enter a world where the terrain is unfamiliar and their basic childrearing tasks are challenged. Problems such as overprotectiveness, difficulty with consistent discipline and expression of appropriate anger towards the child and concerns about "spoiling" the child can occur in parenting tasks (Davies et al., 1991).

Adherence to pediatric cancer treatment can be difficult for families, especially when the child is a young child and the required tasks include medical procedures (mouth care, conducting physical exams). More important, certain of these difficulties are related to the parent's child-rearing attitudes and practices, with the supportive parenting style as the best one, encouraging children to express their needs and also attend more to the child' physical and emotional reactions to the treatment (Manne et al., 1993).

Important aspects of care and assistance mentioned by parents of children are several: Accessible care (possibility to contact the ward), clinical competence of the medical pediatric staff (knowing what to do), continuity (to meet the same doctor and nurse), emotional support (staff availability to talk with parents), information (about the child conditions), participation in care and in decision making, physical ambience of the hospital, social competence of the staff (polite, nice, helpful), the own child is well cared for by the staff and time spent by staff with parents (von Essen et al., 2001).

"Building a new normality" is a statement that summarize mothers' experiences of caring for a child with acute lymphoblastic leukemia: They felt as important for children's day-to-day lives to continue as normal as possible in order to facilitate adjustment to the illness and reintegration with friends both during and at the end of treatment (Earle et al., 2006). Leading a normal life is very important for mothers, but not easily achieved. Normalization of routine in the face of illness is an important sign

of resilience in families. Thus, the resilient family is both a system that has adapted to the chronic stress associated with a child's illness needs, as well as a mediator or cause of the child's psychosocial development or resilience (Patterson, 1991). Specifically, we are now showing the family factors that are associated to psychological adjustment of pediatric cancer patients.

2.5 Family factors related to psychological adjustment of pediatric cancer patients

Parents' behavior may affect the child's reactions to treatment and general adjustment in several ways. First, parent-child relationships during medical procedures are examined: Certain parent behaviors such as use of distraction, parental coaching, and positive reinforcement have been associated with decreased child distress and anxiety prior to and during medical procedures (Vance & Eiser, 2004).

A second field of literature deals with the relationship between parent behaviors and compliance with treatment: Permissive parents are more likely to experience problems gaining the child's collaboration and establishing adherence to home-based care and treatment.

A third way to study child-parent bounds is related to parents' use of discipline: Parents of ill children may feel that it is inappropriate to discipline a sick child, or lack the energy to deal with the situation so that children exhibit particularly difficult behavior. The literature on this topic is less focused in everyday situations that are common to all families.

Drotar (1997) reviewed the studies concerning the relationship between parent and family functioning with psychological adjustment of children with chronic health conditions: More adaptive and cohesive family relationships and parental psychological adjustment were associated with positive psychological adjustment while less adaptive family relationships (e.g., greater conflict and maternal psychological distress)

consistently predicted problematic adjustment.

A related priority is to develop and test explicit models of how family processes influence the psychological development of children with chronic health conditions. For example, Kliewer et al. (1994) identified three alternative pathways by which families influence children' adaptation to stressful events: (a) coaching or direct instructions, including reinforcement of appraisals and coping patterns that suggest specific courses of action in responding to stress; b) modelling of coping styles and strategies of illness management; c) general contextual influences that shape family environments in which stable patterns of coping are learned (e.g., quality of family routines, communication, and/or relationships).

Studies about the last mentioned trajectory have emphasized the importance of family communication and support (Kupst et al., 1984; Rodrigue et al., 1994) and of general family factors in exacerbating or attenuating the impact of the disease on the child (Ostroff et al., 2000; Stuber et al., 1996). Results of a study on childhood survivors and their families (Fuemmeler et al., 2003) showed that the variable of perceived family relationships characterized by support moderated the association between repressive adaptation and adjustment for caregivers but not for children. Perhaps peer relationships or parent distress and/or parenting practices may represent more salient factors in children's adjustment and adaptation.

Socio-ecological theories suggest that a person's well-being is dependent not only on personal characteristics, but also on the social systems and resources around them (Broffenbrenner, 1979). The family system is an important and proximal factor for children with a chronic illness (Kazak, Rourke & Crump, 2003). According to these theories, the adjustment of children to a stressor may be influenced by the adjustment of those around them and the family's available resources. Parent distress has been found to be positively related to distress in children. For example children of depressed mothers display a variety of internalizing and externalizing symptoms, above and

beyond those displayed by children of nondepressed mothers (Brennan et al., 2002; Langrock et al., 2002) or they showed more depressive symptoms (Mulhern et al., 1992). Similarly, anxiety in parents has been linked to anxiety in children (Langrock et al., 2002; Whaley et al., 1999) due to their less use of modelling and reassurance of their children's fears (Dolgin et al., 1990). The diagnosis and treatment of cancer may disrupt the family environment (McGrath, 2001), possibly leaving children vulnerable to internalizing problems. Parents, particularly mothers, of children with cancer may display more internalizing difficulties than parents of healthy children (Dahlquist et al., 1996; Dockerty et al., 2000; Hoekstra-Weebers et al., 1999), which in turn may leave children with cancer more vulnerable to internalizing difficulties.

Parental social support may buffer the association between parent and child distress (Cohen & Wills, 1985) even if the quality and the timing of support are not clearly established.

Another factor linked to distress in children is the quality of their family environment. Children raised in environments high in conflict may be more prone to adjustment problems (Hammen et al., 2004; Varni et al., 1996). However children in a positive family environment (e.g., high expressiveness and cohesion, and low conflict) are more likely to adjust well (Drotar et al., 1997; Varni et al., 1996). For a child with cancer, cohesive and expressive families may be more capable of ensuring the adjustment of each family member, and thereby buffer parent and child distress (Hammen et al., 2004). Varni and colleagues (1996) tested family functioning as a predictor of child psychological and social adaptation to a new diagnosis of cancer. Specifically, the relationship dimensions of family cohesion and expressiveness were the most consistently predictive of child adaptation across both concurrent and prospective (6 and 9 months post-diagnosis), with fewer internalizing problems.

Despite increased attention to the psychological effects of chronic illness, theoretical and methodological limitations in the literature make it difficult to draw firm

conclusions. Existing research has focused on either medical or psychosocial variables as predictors of functioning in children. The possibility that these factors may have an additive or mediational effect on functioning is less frequently considered. A recent study of Robinson and colleagues (2007) aimed at identifying some factors (e.g., family environment, parental social support, child age and gender, cancer diagnosis, and treatment severity) that influence the association between parent and child distress among children with cancer and comparison peers. Significant association was found between parent and child distress. The identified models showed the following significant mediators of the specific association between father and child distress: The family environment; child gender (boys more vulnerable to distress than girls) and child age (younger children more vulnerable). The specific association between mother and child distress is nor mediated or moderated by other factors, because it was a significant main effect, pervasive (e.g., Brennan et al., 2002; Langrock et al., 2002; Whaley et al., 1999).

In conclusion, children whose parents were distressed were more likely to be distressed themselves and it is necessary to identify mechanism of risk and resilience of children and their families, developing specific family-based interventions.

THE STUDY

CHAPTER 3

METHOD

"One is not able to plan any kind of future development. The friction with the external world (outside the hospital) is generated by this incapacity, let's call it so, to be able to plan a future, to be able to plan future necessities…and this influences anything else."

3.1 Research design

This study is the first part of a larger longitudinal project on family factors predicting short- and long-term adaptation and quality of life of leukemic children. The original research project aims at investigating the psycho-social effects of a diagnosis of cancer on both child adaptation and parental issues. The project was aimed at following children and parents from the diagnosis of leukemia for the two following years of therapies. More specifically, the focus of the whole project is on several topics: Post-diagnosis predictors of psycho-social adaptation in children with leukemia post 12 months of therapies; quality of life in children under treatment for leukemia in their psycho-social context; predictors of PTSD symptoms in parents of children under therapy for leukemia; psycho-social risk in parents of children with leukemia; the psychological health and the re-adaptation of the children with leukemia and their parents to their daily lives at the stop-therapy time.

Data were collected adopting a multi-method approach: Parents were interviewed (direct measure) and filled in several self-reports questionnaires (indirect measure) about 10 days after the diagnosis (T1) and longitudinally at 1 month later (T2), 6

months later (T3), 12 months later (T4) and 24 months later (T5). Information about the child at T1 were collected through parent's interview, at T2 through self-report and parent-report of his/her coping with pain, at T3 through parent's reports on his/her reactions to cortisone, at T4 through parent's interview and reports, at T5 directly through an interview (only for school-age-children) and indirectly by parent's interview. Therefore, this multi-method study included direct and indirect measures of child adaptation and quality of life (e.g., adaptive behaviors, coping with pain, quality of life during hospitalization, mood reactions to cortisone), direct and indirect measures of parental psychological health state (e.g., anxiety levels, PTSD symptoms, cognitive functioning, life self-perceptions), of their psycho-social context factors (e.g., social support, communication about the illness, emotional coping, trust in the medical care, sibling involvement, routine and time reorganization…) and measures of parenting behaviors (e.g., parent believes on development, parent health locus of control).

The present work presents findings exclusively derived from child and parent's measures presented in the Table 3.3, although the entire project is much more complex. This selection is due to timing and methodological issues so we will focus here on the data at the first 4 time-points, during the first year of therapy. Data from the last assessment are not included in this study, because data collection is still in progress. Figure 3.3 describes the main constructs, measures and data sources used at each time-point.

The principal goal of the project is to identify the relative impact of two types of factors on the psychological development of children under treatment of leukemia and when the therapies end so that specific psychosocial, supportive programs may be implemented on empirically based information. The independent variables are of two kinds:

1. Medical variables: Type of leukemia, age at the diagnosis, time from the diagnosis, type of therapies;

2. Child and family variables: Child age, child gender, child temperament, family SES.

Dependent Variables are:

1. Child variables: Child adaptation to illness, child coping with medical procedures and with hospitalization, child Quality of Life.

2. Family variables: Parental mental health, Quality of Life, adaptation and emotional coping.

3.2 Research questions and hypotheses

3.2.1 PART A: Concurrent hypotheses upon Child's QoL and Adaptation at the several time points

3.2.1.1 Which family and child factors are responsible for quality of life of leukemic children in the second week after the communication of the diagnosis?

The present study aims at verifying a hypothetical model of the family factors responsible for short- quality of life of leukemic child. The basic model is reported in Figure 3.1 and derives from published studies (Frare et al., 2002; Napoli et al., 2002) on families of children with headache which adopted our interview technique (EFI). In these studies unidirectional model fitting analyses (LISREL) showed that family factors are causal independent variables which impact upon children's coping abilities and on children's QoL.

In the present study the examined variables referred to Child (Age and Gender; Coping styles; Adaptation to Illness), to Family (Parental Emotional Coping; Level of communication on the child illness, Trust in the medical care and in the hospital community, Routine and time reorganization, Social support; Connectedness of the

parental couple; Sibling involvement, SES and Subsistence Level; Previous Family Traumas) and to Leukemia (type, % of survival probability, reaction to the first cortisone therapy). LISREL model-fitting analyses will assess the relationships among our variables.

Figure 3.1 – Hypothesis.
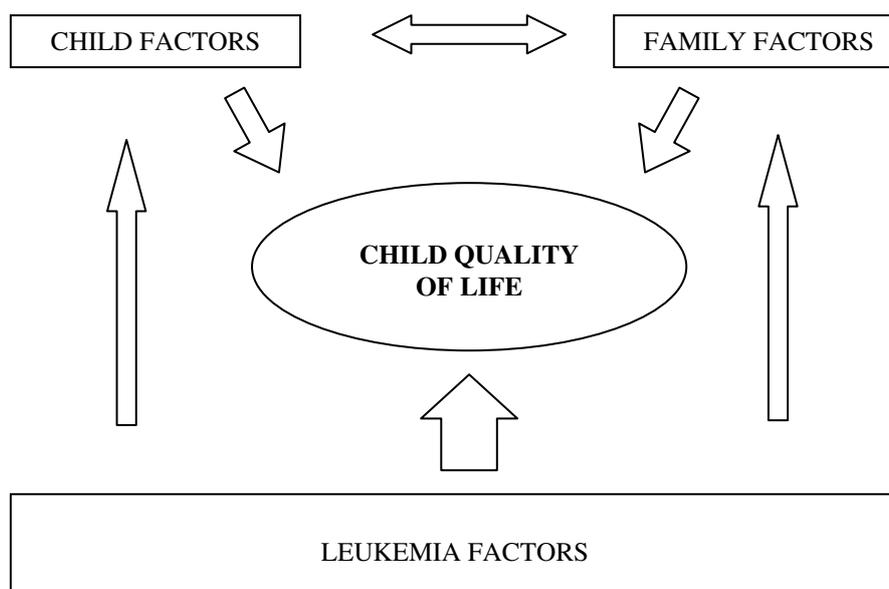
In particular, we want to focus on Health Related Quality of Life (HRQOL) of children with leukemia assessed by parents' perceptions. We have seen in paragraph 2.1.2 that mothers can be reliable enough in these perceptions and we have noted that in-depth interviews can give more information of the meaning of Quality of Life for the children with leukemia during their first hospitalization. Yeh et al (2002) have identified Communication with others as the best predictor of HRQOL and the literature stressed also the role of Parental communication with the child in the early period after the diagnosis. We have also underlined the important role of the Caring Niche of the child with cancer (see paragraph 2.2). In this sense there is no study that verifies an empirical model that linked the several context psycho-social variables useful to maintain a

positive quality of life in children with cancer in their first hospitalization. In this sense, the aim is to identify the weight of fixed factors and modifiable moderators of child and his/her family on child's quality of life, following the definition of Hoekstra-Weebers et al. (2000) illustrated above in Figure 2.2. We expect that a fixed factor as Child Age have an impact on Child's Quality of Life and also the modifiable factor Child's Coping as the literature have stressed (Aldrige & Roesch, 2006; Earle & Eiser, 2007). Reading the model of Caring Niche cited above and the literature of parenting (see paragraph 2.4), we can hypothesize that Parenting dimension can be an important modifiable family factor that can impact on Child's Quality of Life. Finally, we think that illness factors at the beginning of therapies don't have an impact on Child's Quality of Life.

3.2.1.2 Which child's styles of coping with pain are adopted and which are their associations with disease and family factors in the second month after the diagnosis communication?

We have seen in paragraph 1.1.3 that pain episodes occur in the context of children's everyday lives during hospitalization so that children's coping with painful procedures is necessary, especially in the first month. We have stressed also that in problem/emotion focused coping three factors categories must be examined: Illness parameters (type, severity, treatment), personal factors (cognitive resources, age and past experiences, gender, temperament) and social factors (protective or risk factors related to family, peers support, environment support) (Axia et al., 2000; Figure 1.7). In an Italian study on coping with pain in healthy school-aged children (Bonichini & Axia, 2000) Seek for social support is identified as the best strategy used by Italian children, while American children preferred the Cognitive strategies. The Italian children used more cognitive strategies such as Problem Solving and Cognitive Self-Instruction with increasing age. In this sense we expect to confirm some of these results: The Cognitive strategies just mentioned increase with child's age; seek for social support is the most

used strategy; there are no gender differences adopting the several coping strategies. For the child's Catastrophizing behavior we expect a direct influence of parent's Symptomatology and an indirect relation with child's Coping and Adaptability factors assessed at the diagnosis-time. We don't expect a diagnosis effect on children's coping with pain, because we think that these aspects assessed at the first month of hospitalization for treatments are similar in both types of leukemias.

3.2.1.3 Which are the types of developmental deficits in adaptive behaviors in children with leukemia and what kind of association with children temperament and with family factors there are one year after the diagnosis communication?

We have seen that children with leukemia are often hospitalized for long periods because of their immunosuppressed status and because of the therapies; this may place them at further risk for psychosocial developmental delays. Children are frequently forced to have long periods in bed or in a restricted area (such as hospital room) where they are not allowed to meet friends or relatives. Long hospitalization can cause delays in school learning and development (White, 2003), for instance the school marks in mathematics and in foreign languages tend to be worse (Lähteenmäki et al., 2002) and these children have difficulties in socialization and in emotionality, especially those under 6 years of age (Adamoli et al., 1997). The literature about returning to school by child with cancer was recently reviewed (Vance & Eiser, 2002) showing that while there was a mixed evidence about whether children have significant behavioral problems in school, studies involving social behavior and peer relationships generally concluded that children with cancer were more sensitive and isolated than peers, according to both peer and teacher reports.

So we expect that children with leukemia under treatment have socialization problems related both to interpersonal relationships and to the respect of social and community rules, particularly due to their isolation experience. We also think that

children under 6 years of age can have difficulties in their motor abilities proportionally to their days of hospitalization. The only study assessing adaptive functioning in children with cancer adopting the Vineland Scales showed a significant decrease in adaptive scores during the first year after the blood stem cell transplantation (Kramer et al., 1997). In this context of cancer no study has analysed the possible association between children's temperament factors and their behavioral adaptation. We expect to find a negative association between some child's developmental scales (Communication, Daily Living Skills, Socialization) with Negative Emotionality and a positive relation between Social Orientation and Attention (from QUIT).

3.2.2 PART A: Concurrent hypotheses upon Parent's Psychological Health and Adaptation at the several time points

3.2.2.1 What happens to the parent's psychological health and adaptation in relation to child's disease factors in the second week after the diagnosis communication?

In general, the literature converges upon two major facts. The first is that the most difficult period for parents and families happens just after the diagnosis (Sheeran et al., 1997) when child undergo several invasive medical procedures (e.g., bone marrow aspirates, lumbar punctures) and treatments (e.g., chemotherapy). Several studies showed that the acute phase is the most stressful period for parents (LaMontagne et al., 1999; Sawyer et al., 1986; 1997; 2000; Sloper, 1996) in which a new family "reality" must be built up (Clarke-Steffen, 1993). Also some family resources are posed at risk. For example, marital dissatisfaction in parents of children with cancer may be present in about one parent of every four (25% of mothers, 28% of fathers, according to Dahlquist et al., 1993).

The second point highlighted by the literature is that unfortunately, a notable percentage of parents are not able to make a pathway for good adjustment and quality of

life and remain indelibly scorched by the experience (von Essen et al., 2004). Researchers report increased emotional distress, such as anxiety or depression, in these parents against normative data (Dahlquist et al., 1993; Manne et al., 1995). In longitudinal studies there also is evidence of increased negative emotions such as anxiety, depression, insomnia or somatic and social dysfunctioning shortly after diagnosis are found (Sawyer et al., 2000; Pelcovitz, 1996; Van-Dongen Melman et al., 1995).

So in this acute first phase we expect to find lower scores in parents' Current Life Perceptions, and higher scores in their Symptomatology manifestations. We also make the hypothesis that the Diagnosis Type impacts on their Psychological State and that parents of children with AML are more in difficulty than those of children with ALL. Another factor that can be related to their mental health can be Child's Age and Parents' Age with a best situation with increasing age. At this purpose we think that older parents can have more experience to care for children and that they can be more "expert" in their parenting role in this difficult time. Taking into consideration also the social context we imagine that Social Support and Couple Connectedness perceived by parents can represent valid resources to dampen their Psychological Symptoms and to get better their Cognitive Functioning.

Particularly, for parents of children with ALL we also suppose that the Number of Blastos communicated to parents at the day +8 can increase the difficulties in their Cognitive and Psychological Functioning.

3.2.2.2 What happens to parenting behavior along the several child's ages?

Adherence to pediatric cancer treatment can be difficult for families, especially when the child is a young child and the required tasks include medical procedures (mouth care, conducting physical exams, venepunctures, bone marrow aspirations, etc.) (Manne et al., 1993). Parent's child-rearing attitudes and practices, with the supportive

parenting style as the best one, are really a key element in the child's life during the illness. So we expect that parenting behaviors will be different in relation to child's age, with a more necessary and intensive care for infants and toddlers in respect the older children. We also think that child coping strategies and child adaptability are also related to the parenting styles.

3.2.2.3 What happens to the parents' locus of control and to their psychological health in relation to child's disease factors in the second month after the diagnosis communication?

There are no specific studies on Parental Health Locus of Control in a context of children with cancer. Basing on the literature on Health Locus of Control, we expect that parents invest a lot on their Internal Locus of Control (self-perceived efficiency in their parenting role and in their psychological resources), but also in the External Locus of Control (such as the same child, health professionals or God). Particularly, we make the hypothesis that parents' Internal Locus of Control is related to a positive Perception of their Life and a lower Psychological Symptomatology and that Children's Influence on their illness is perceived more by parents with children's increasing age.

For parents' psychological health we imagine that PTSS will be high in this early phase, especially Intrusion symptoms, and related also to child type of leukemia, with a major presence of Post-Traumatic symptoms in parents (especially arousal symptoms) of children with AML.

3.2.2.4 What happens to the parent's psychological health and adaptation in relation to child's disease factors after 6 months post diagnosis communication?

We evaluate in this time-point the amount of PTSS and possible child, illness and family factors associated with it.

An interesting study on mothers and fathers of childhood cancer survivors (Kazak

et al., 1998) has developed a model of possible factors associated with PTSS. In this model, anxiety was the strongest predictor of posttraumatic stress symptoms. The current family and individual variables also contributed significantly, particularly with respect to the individual contributions of perceived life threat, perceived treatment intensity, and social support. Objective medical data did not contribute to posttraumatic stress symptoms. We expect a similar finding in our sample of parents of children under treatment. We think that anxiety assessed at the same time is strongly associated with PTSS and we also imagine that parent's emotional coping influences this type of symptomatology. At this purpose, Barrera et al. (2004) found that in mothers of children newly diagnosed with cancer emotion-focused coping and child behavior both predicted depression, anxiety and global mental health. We don't presume that Social Support can be an important factor, because the literature shows varied results on this point, converge about this idea (Pelcovitz et al., 1996) and because we think support remains quite stable during the different time points and so is probably not going to predict variations (though it certainly is important for all families).

The literature identifies family cohesion as a possible factor associated with parental low level distress at 6 months after the diagnosis (Sloper et al., 2000). So we also expect that Family Routine and Time Reorganization, that deal with family cohesion, are associated with a lower Post-Traumatic Symptomatology in parents of children with leukemia at 6 months after the diagnosis.

Another parental factor that we think related to parents' PTSS is their level of cognitive functioning, including, for example memory, concentration, distraction, impulsivity, labile mood. The literature on adult cancer survivors found a relation between PTSD and cognitive functions, especially memory (Nakano et al., 2002; Kitayama et al., 2005).

Parents' experience of caring for their child during treatment with steroids has been also taken into consideration in the literature. Parents experienced the children's

emotional states as very demanding, and this was exacerbated by the fact that the children were up all night eating and did not sleep. Some parents reported that this was to a worrying degree and that the child's emotional state moved them to a sense of death and hopelessness. A set of coping strategies to confront these difficulties are used: Positive personal strategies, professional help requests and normalisation activities (McGrath & Pitcher, 2002). We expect that ALL children's bad behaviors and mood reactions to cortisone impact negatively on parental mental health, especially on their cognitive and psychological functioning.

3.2.2.5 What happens to the parent's psychological health and adaptation in relation to child's disease factors after 1 year post diagnosis communication?

We think that parents' post-traumatic stress symptoms are a bit lower at this time point, but still present. We hypothesize to confirm that the best factor associated with PTSS can be the level of State Anxiety according to the literature just mentioned above. We think also that PTSS is correlated with the other Depressive and Arousal Symptoms and with Cognitive Dysfunction. We presume that Family Routine and Time Reorganization is an important prognostic factor negatively associated with PTSS as mentioned for the precedent period of post-6 months. We think also here that Days of Hospitalization are not influential in parents' Psychological Health State.

3.2.3 PART B: Longitudinal hypotheses about Parent's Psychological Health and Adaptation throughout the several time points

3.2.3.1 What type of time trend is related to the parent's psychological health and adaptation along the several time points?

We have seen that in most pediatric tumors, different phases can be identified:

The pre-diagnostic, the acute, the chronic, the remission or off-therapy phase. Each phase requires its own adaptations, yet the first, acute phase is the one which requires the complete modification, often the upturning, of the previous family life and routines.

The literature about the longitudinal incidences of parental psychological symptoms throughout all the child's treatment mainly identified the acute phase as the most stressful period for parents (LaMontagne et al., 1999; Sawyer et al., 1986; 1997; 2000; Sloper, 1996) with the presence of negative emotions such as anxiety, depression, insomnia or somatic and social dysfunctioning (Sawyer et al., 2000; Pelcovitz, 1996; Van-Dongen Melman et al., 1995). Thereafter, psychological stress tends to decrease (Bracken, 1990; Wijnberg-Williams et al., 2006), but it does not go back to normal values (Hoekstra-Webers et al., 1996). For example, neither mothers nor fathers' mean of marital adjustment scores changed over time (Dahlquist et al., 1996) and self-perceived social support decreased with time (Hoekstra-Weebers, 2001).

Parental self-reported PTSS incidences are high at the beginning of the child's treatment and are still present approximately 2 years following diagnosis (Phipps et al., 2005). Anxiety is elevated at diagnosis but declines for most parents as treatment is initiated and the family accommodates to the new "routines" in their lives (Steele et al., 2004). There is long term stability for families' psychosocial risks (as measured here) in the time range from 3 to 6 months after the diagnosis (Kazak et al., 2003).

Based on this literature review we expect to find a significant decrease along the first year of child's therapies of the Parental General Symptomatology such as Anxiety, Arousal, Depression with a general better Perception of their lives. Instead we think that parental PTSS would remain stable and continuous during time as the literature suggest. Dealing with parental psycho-social factors we expect that: Couple Connectedness, Family Routine and Time Reorganization and trust in the Medical Care increase from the diagnosis while Social Support has a significant decrease. For other factors such as Parental Communication around the Child's Illness, their Emotional Coping and their

Cognitive Functioning we presume that they remain stable during the time, without significant changes.

3.2.4 PART C: Predictive hypotheses upon Child's Adaptation along the several time points

Numerous recent studies identified mediated and moderated effects in child-clinical and pediatric research on child adjustment. According to Baron & Kenny (1986), a moderator variable is "a qualitative (e.g., sex, race, class) or quantitative variable that affects the direction and/or strength of a relation between an independent or predictor variable and a dependent or criterion variable.." (Baron & Kenny, 1986; pp. 1174, 1178). A mediator variable is, on the other hand, "the generative mechanism through which the focal independent variable is able to influence the dependent variable of interest…" (pp. 1173, 1178) (Figure 3.2)

Figure 3.2 - Models of mediated and moderated effects. In the left model, B mediates the relationship between A and C. In the right model, B moderates the relationship between A and C.

3.2.4.1 Which family, child and disease factors just after the diagnosis communication are responsible for long-term adaptation of children with leukemia after 1 year of treatments?

In the literature (Vance & Eiser, 2004) we have seen that parents' behavior may affect the child's reactions to treatment and general adjustment in several ways: Helping

children during medical procedures (Jacobsen et al., 1990; Dahlquist et al., 2001), increasing their general compliance with treatment (Manne et al., 1993; LaMontagne et al., 1999) and, finally, using appropriately discipline (Dahlquist et al., 1994). Also more adaptive and cohesive family relationships and parental psychological adjustment were associated with positive psychological adjustment (Drotar, 1997). A related priority is to develop and test explicit models of how family processes influence the psychological development of children with chronic health conditions. Studies have emphasized on the importance of family communication and support (Kupst et al., 1984; Rodrigue et al., 1994) and of general family factors in exacerbating or attenuating the impact of the disease on the child (Ostroff et al., 2000; Stuber et al., 1996). Parental social support may buffer the association between parent and child distress (Cohen & Wills, 1985) even if the quality and the timing of support are not clearly established. Another factor linked to distress in children is the quality of their family environment (Hammen et al., 2004; Varni et al., 1996; Drotar et al., 1997) with cohesive and expressive families more capable of ensuring the adjustment of each family member, and thereby buffering parent and child distress (Hammen et al., 2004).

So we expect that family factors and disease characteristics would be causal independent variables which impact upon children's adaptive behaviors post one year of child's therapies.

In particular, we think that a general dimension such as Parenting (comprehensive of all the parental strategies to help children to cope with the illness) assessed at the beginning of the child's hospitalizations and treatments can be an important mediator that impact upon child's early coping to medical procedures and upon child's behavioral adaptation one year post diagnosis. We suppose that other family factors associated with Child's Adaptive Functioning are Routine and Time Reorganization at the diagnosis and their Family Cohesion.

3.2.4.2 Which family, child and disease factors after 1 month from the diagnosis communication are responsible for long-term adaptation of children with leukemia after 1 year of treatments?

We expect that children's use of Coping Strategies to front medical procedures and hospitalization in the first month impact on their Adaptive Functioning one year later. In particular we think that Cognitive Strategies impact positively on their use of Adaptive Behavior while the Emotional Strategies are related negatively as the literature on Child's Coping and Adaptation has suggested (Aldrige & Roesch, 2006). We also suppose that the Parental Perceptions about children's control on their health can positively impact on their Adaptive Functioning, due to the believe that they have the power and the possibility to work on the situation to cope in the best way.

3.2.4.3 Which family and disease factors after 6 months from the diagnosis communication are responsible for long-term adaptation of children with leukemia after 1 year of treatments?

We expect that family capacity to communicate with their children and with the other persons about the child's illness can be a positive reinforcement for the child so that his/her adaptive functioning can be continuously active and can develop a good adaptation until the first year of treatment (Kupst et al., 1984; Rodrigue et al., 1994), when then the child will re-start school and some social activities.

3.2.5 PART C: Predictive hypotheses upon Parent's Psychological Health and Adaptation along the several time points

The model presented in chapter 2 (Figure 2.2) is used as a framework in our study to explain the variability in parental psychological functioning by identifying concurrent and prospective predictors of maladjustment (Hoekstra-Weebers et al., 2000).

Childhood cancer is viewed as an ongoing stressor to which each parent has to adapt. Three basic components and their interactions influence parents' adaptation outcomes. The first is the type of child leukemia, the duration and outcomes of the therapy (see also, Stuber et al., 1996) – all considered as <u>main stressors</u>. The second component is made by the stable variables which can influence parental adjustment outcomes: SES (Hoekstra-Webers et al., 1998b; Kazak et al., 2003), life events (Breslau et al. 1985) and parents' personality traits, such anxiety (Dalquist et al. 1996; Frank et al., 2001). They are called <u>stable moderators</u>. The third component is made of more flexible variables such as parental coping strategies (Goldbeck, 2001; Grootenhuis et al., 1996; Grootenhuis and Last, 1997), available social support (Manne et. Al, 2000; Dockerty et al., 2000; Kazak et al., 1997; 1998), and marital satisfaction (Ruccione et al., 1991; Brown et al., 1993). These are called <u>modifiable moderators</u>. Stable moderators influence modifiable moderators which in turn impact upon stress and adjustment outcomes.

We will run hierarchical regressions to show which family factors (stable or modifiable) and child's disease characteristics (stable factors) are causal independent variables which impact upon parent's global psychological health.

3.2.5.1 Which family and child factors are responsible for short-term PTSS of parents of children with leukemia one month after the diagnosis?

We have seen above the possible factors associated with parental PTSS at concurrent time. Here the question is if there are just some family and child factors at the post diagnosis (T1) predictive of PTSS one month after (T2).

Considering the several parental psycho-social factors we presume that Emotional Coping and Support received can be key elements impacting upon parents' symptomatology assessed at the diagnosis and indicative of future PTSS problems.

In only ALL children we also suppose that another illness element, such as the

Communication of Blastos at day +8, can be an important moderator of the increase of Parental Psychological Symptoms that can predict the PTSS incidence on month post diagnosis. No study in the literature has examined the possible consequences of this specific communication by medical staff on parent's mental health.

3.2.5.2 Which family and child factors are responsible for psychological functioning of parents of children with leukemia 6 month post-diagnosis?

We suppose that family factors such as Routine and Time Reorganization and Social Support received at the time of the diagnosis (T1) can be related to the Parental Perception of their current lives post 6 months of therapies (T3). For the demographic factors we think that older age of parents and of children can be an important factor for a better Parental Psychological Functioning. In fact, older parents can have more caring instruments and parenting experiences that help them to cope better with the illness difficult situation. We also presume that PTSS symptoms assessed at one month (T2) can be strongly associated also to the other symptomatology (such as Depression, Arousal, Cognitive Dysfunctioning) measured at 6 month post diagnosis (T3).

3.3 Participants

Patients at time point one were 128 leukemic children and their families recruited at the Haematology-Oncologic Clinic of the Department of Pediatrics, University of Padova (Director, Professor Carli). All parents were Caucasian with a mean age of 37.39 years (SD = 6.03). Most parents had 13 years of school (52.2%); 33.6% had 8 years; 6.2% had college education; 6.2% had degree or diploma and 1.8% had 5 years of school. Parents' incomes were average (52.7%), high (24.1%) and low (23.2%) for Italian norms, but above poverty. The average of job hours/weekly were mostly around 35 (28.4%) and 45 (22%), even if the major part of parents was temporarily relieved of

their work or they were housewives (43.4%). The parents who participated were mostly mothers (N = 111) and only a few were fathers (N = 17) because the mothers were more proximal to the child during hospitalization while fathers stayed with other siblings or continued to work to maintain the family. In the preliminary analysis we have controlled the possible differences between fathers and mothers. There were no significant differences in our variables so we decided to consider them all together.

Children's mean age was 5.89 years (SD = 4.21, range = 10 months-17 years). Mostly children had Acute Lymphoblastic Leukemia (ALL) (N = 104), while 24 had Acute Myeloid Leukemia (AML). Children were enough equally distributed by gender with 61 girls and 66 males.

These children and their parents participated at the first assessment. All eligible families agreed to participate to the study except two families that declared that they didn't feel well to speak about their feelings to anyone. From this initial group of 128 families of children with leukemia, 118 filled in questionnaires battery above the in-depth interview, while the remained 10 had only the in-depth interviews assessment because they participated to an early exploratory phase of the study. At the following time-points we had a loss of participants due to several reasons: 11 deceased, 4 changed health center, 5 relapsed or were in grave illness situation at the assessment moment and only 5 families dropped out from the study (3.9%).

Table 3.1 shows the patients and families assessed from June 2003 to November 2007.

Table 3.1 - Patients and families assessed at the different time-points.

	2° week	2° month	Post 6 months	Post 12 months	Post 24 months
ALL	98	90	84	68	41
AML	20	20	13	10	4
TOTAL	118	110	97	78	45

Table 3.2 shows the child's characteristics at the diagnosis and at the different

time points.

For children with AML, seen the low number in our sample, we took into consideration only the days of hospitalization and not other variables such as therapies' toxicity.

Table 3.2 - Child's illness status at the different time points (T1, T2, T3 and T4).

Characteristics	First assessment N = 118	Second assessment N = 110	Third assessment N = 97	Fourth assessment N = 78
Illness status in ALL children				
Level of risk: SR, MR, HR (%)	-	-	SR: 16.7% MR: 60.2% HR: 23.1%	SR: 18.3% MR: 65.6% HR: 16.1%
N blastos day +8 Mean (SD)	2312.93 (18240.79)	-	-	-
N blastos day +33 Mean (SD)	-	1.25 (6.86)	-	-
N blastos day +78 Mean (SD)	-	-	0.74 (1.76)	0.74 (1.76)
Toxicity status Mean (SD)	-	0.53 (0.97)	1.61 (1.62)	1.61 (1.62)
Cortisone effects Mean (SD)	-	-	6.88 (1.93)	6.88 (1.93)
Illness status in children with all leukemias				
Days of hospitalization Mean (SD)	-	-	60.66 (38.25)	63.09 (53.40)

Legend: SR: Standard Risk; MR = Medium Risk; HR: High Risk; blastos = malignant cells.

3.4 Procedure

The families were contacted by a clinical psychologist during the first hospitalization of their children, about one week after the diagnosis. Project aims were

explained and informed consent was asked for. Informal contacts with the participants were kept up on a daily basis, to provide support and motivation for the project. The parents were interviewed in a separate room of the Clinic. The questionnaires were compiled in the child's room, with the clinical psychologist's assistance, during a quiet period of the day. The participants were informed that they were free to drop out at any moment of the study. Each family was contacted again at the several established time points: 1 month later, 6 months later, 12 months later and 24 months later. The assessments were carried out at the Day Hospital or in the library of the Clinic. The psychologist remained (and is still now) constantly in touch with the child and the family for the duration of the study with frequent telephone contacts and direct contacts during the DH check-ups. Before the assessments, the psychologist contacted by telephone the parent to agree about the meetings.

3.5 Timing

The data collection phase of the study required several steps. The timing followed four main events: A first contact with the family and five sessions for the child's assessment respectively in the second week after the communication of the diagnosis (T1), 1 month later (T2), 6 months later (T3), 12 months later (T4) and 24 months later (T5). The first contact took place while the child was under the initial therapy in the Clinic and the next assessment was done when the child and the family were in day hospital visits.

Timing is illustrated in figure 3.3 above

Figure 3.3 – Timing.

	T0	**T1**	**T2**	**T3**	**T4** **T5**
	Communication of diagnosis	+8-12 days from T0	+ 1 month from T1	+ 6 months from T1	+ 12 months from T1 / + 24 months from T1

CHILD	**EFI-C** parent on child (0-18 ys old)	**PPCI** - parent on child (4-16 ys old)	**Cortisone psycho-social effects questionnaire** parent on child (0-18 ys old)	**Vineland Scales** parent on child (0-18 ys old) **QUIT** parent on child (0-11 ys old)	**EFI-C** - Child (≥6 ys old) - parent on child (0-18 ys old) **Vineland Scales** parent on child (0-18 ys old)
PARENT	**EFI-C** Parent **BSI-18** Parent **Ladder of life** Parent **Problem scale** Parent **SES** questionnaire	**PHLOC** parent **PTSD symptom inventory** parent	**EFI-C** questionnaire parent **BSI-18** parent **Ladder of life** parent **Problem scale** parent **STAI** parent **PTSD symptom inventory** parent	**EFI-C** questionnaire Parent **BSI-18** Parent **Ladder of life** parent **Problem scale** parent **STAI** parent **PTSD symptom inventory** parent	**EFI-C** parent **BSI-18** parent **Ladder of life** parent **Problem scale** parent **STAI** parent **PTSD symptom inventory** parent

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3.6 Instruments

In this study a large number of instruments for the assessment of both the parents and the children were used. All the instruments were derived from the previous literature; some were new for the Italian culture. Mostly of the international instruments were taken from the Childhood Cancer Survivor Study (CCSS). CCSS was established in 1993 through funding from the National Cancer Institute and exists as a large research program for studies of childhood cancer survivors. Coordinated through the Department of Pediatrics at the University of Minnesota, the CCSS represents the largest and most comprehensively characterized epidemiological research cohort of childhood cancer survivors ever assembled in North America. The population derived from a group of 20.267 individuals treated for cancer (several diagnoses) during childhood and adolescence at 25 centers across the United States and Canada. The CCSS protocols and questionnaires were approved by the Institutional Review Boards of all collaborating Institutions. A 24-page baseline questionnaire provided information about demographics, personal and family medical history, medical late effects, functional limitations, psychological outcomes, work history and living circumstances Study questionnaires can be viewed at www.cancer.umn.edu/ccss.

The table below summarizes the instruments used by both the child and his/her family and briefly describes the kind of assessment, the instrument measures and to whom it is designated. All instruments will be later described in detail.

Table 3.3 - Instruments used for the assessment of children and families.

Instruments	Kind of assessment
CHILD ASSESSMENT	
1. Adaptation, Coping and Quality of Life	
▪ Ecocultural Family Interview-Cancer (Weisner et al., 2003; Tremolada et al., 2005)	Interview with the parent about child's coping, quality of life in the hospital and adaptability (proxy)
▪ PPCI (Varni, 1994; italian version by Bonichini & Axia, 1996)	Questionnaires about the child coping with pain, parent version (of children aged 4-12; proxy)
▪ Vineland Scales (Sparrow et al., 1984; italian edition 2003)	Interview for parents about their child's growth and adaptation (proxy)
▪ QUIT (Axia, 2002)	Questionnaires about the child temperament to be filled in by parents (proxy)
2. Medical information	
▪ Cortisone psycho-social effects questionnaire	Questionnaire about the child behavior related to cortisone assumption to be filled in by parents (proxy)
▪ Medical charts	Type of leukemia, days of hospitalization, number of malignant cells at several protocol steps, therapy's grade of organ toxicity
PARENT AND FAMILY ASSESSMENT	
1. Demographics: ▪ *SES questionnaire*	Questionnaire to be filled in by parents
2. Psychological Symptoms	
▪ PTSD symptom inventory (CSSS)	Questionnaire to be filled in by parents on their own symptoms of PTSD
▪ LADDER OF LIFE (CCSS)	Questionnaire to be filled in by parents on their own life perceptions
▪ BSI-18 (Derogatis, 1982)	Questionnaires to be filled in by parents on their own psychological symptoms
▪ PROBLEM SCALE (CCSS)	Questionnaire to be filled in by parents on their own cognitive difficulties
▪ STAI (Spielberger, 1983)	Questionnaire to be filled in by parents on their level of anxiety, both trait and state
3. Adaptation and Locus of control	
▪ Ecocultural Family Interview-Cancer (Weisner et al., 2003; Tremolada et al., 2005)	Interview with the parent about daily routines of family life
▪ PHLOC (DeVellis et al., 1993)	Questionnaires to be filled in by parents on their types of locus of control

PART A: Instruments used for child's assessment

A set of questionnaires filled in either by the child himself or by the mother evaluated the child's psychological symptoms, child adaptation to illness, QoL and

temperament.

3.6.1 Adaptation and Quality of Life

3.6.1.1 EFI-Cancer, parent version

The EFI-C is a parent interview which explores the daily routines of family life and the salient concerns regarding how that routine is organized. The EFI is not a question-answer formal interview, but it has more the sociolinguistic form of an everyday conversation about daily life. The interview is a mix of conversation, probing questions by the interviewer and preplanned questions. Participants use their words and emphases. The interviews start with a question such as: "Would you guide me through your daily life? What is your and your child's routine?" The EFI interview form flows from our theoretical and epistemological approach, which starts with the observation that the family daily routines and actions are aimed at adaptation tasks, in which various people participate. Such tasks are carried out in practice according to the family resources and through specific scripts or sets of actions, which are meaningfully linked to the beliefs and values of the broader ecology and culture and which show the emotions and motivations held in them. When people talk about their everyday life and routines, they spontaneously talk about all these things as this is how the topic is stored in memory. When the adaptation tasks are overloaded by negative emotion, as often in our case, the participants sometimes can find relief during the interview process (Scrimin et al., 2005). The EFI can also be experienced as a kind of life review – a chance to step back from the ongoing flow of events and reflect on them – which is itself of potential value. After being introduced to the study method, the parents might have taken the chance to narrate their lives and concerns to psychologists even in their role as researchers. The EFI is also based on the theory that using the parents' own categories and stories, with the themes and topics embedded in them, the researcher gets

closer to the parents' points of view and experiences (Kazak, 1997; Smith, 1995). Despite the naturalistic flow and ease of the talk, the interviewer gently but firmly guides the narratives upon events, facts, and actions (e.g., "What happened during the doctor's last visit?", "How did your child react?", "What did you do?").

The EFI was originally devised to study the adaptation process in families of disabled children by T.S.Weisner and his associates, at the Neuropsychiatric Institute, UCLA, USA (Nihira et al., 1994). Different versions of this interview have been developed for the study of various issues in pediatric psychology, with Italian families, such as reactivity to pain (Axia & Weisner, 2002), or children with headache (Frare, Axia, Battistella, 2002) and, finally, children with cancer (Tremolada et al., 2005). For the reliability of the EFI-C in this special population, it has been administered by now to 128 parents of children with cancer receiving treatment at the Onco-hematologic clinic of Padova. A total of 98 items were extracted from the parental narratives with several research group discussions and an explorative factor analysis was run to identify the global dimensions containing these items. Appendix 1 shows a synthesis of this codebook containing the total 98 items grouped into the 11 major dimensions. One-fourth of the total 128 interviews (N = 32) was coded with a score ranged 0 (low presence of variable) to 8 (high presence of variable) by two-independent judges, showing a good Spearman inter-rater reliability (rho = .833; p = 0.001).

A good internal consistency in the several dimensions also was demonstrated (Table 3.4).

Three dimensions deal with child: Coping, Quality of life and Adaptability. See also paragraph 2.1 where these constructs are explained in detail.

Table 3.4 - EFI-C dimensions 128 interviews.

Dimension	Alpha	N of items
Parental emotional coping	.75	13
Levels of communication on the child illness	.57	8
Parenting the child in the hospital	.81	9
Trust in the medical care and in the hospital community	.79	6
Routine and time reorganization	.79	16
Social support	.71	5
Connectedness of the parental couple	.93	9
Sibling involvement	.68	5
Child coping with procedures and hospitalization	.89	12
Child quality of life in the hospital	.72	7
Child adaptability/temperament	.91	8
Total	.94	98

3.6.1.2 Waldron/Varni Pediatric Pain Coping Inventory (PPCI) (Varni et al., 1996; Italian version by Bonichini & Axia, 1996)

PPCI is a patient-report and parent-report instrument with a total of 41 items designed to provide a standardized assessment of the child's and parent's perception of the strategies that the child utilizes to cope with physical pain. A three-point Likert-type is developed for clarity and ease of administration and is scored as 0 = never, not at all, 1 = sometimes", or 2 = often, a lot.

According to the authors, children in pain can adopt 5 different coping strategies which represent 5 subscales of the questionnaire. These scales are:

1. Cognitive Self-Instruction (Alpha = 0.74): This scale includes internal self-statements that deal with the child's pain at cognitive level (number of items = 7).

2. Problem-Solving (Alpha = 0.67): This scale includes overt acts that are intended to manage pain (number of items = 10).

3. Distraction (Alpha = 0.66): This scale includes items that shift the child's attention to things other than pain (number of items = 9).

4. Seek for Social Support (Alpha = 0.66): This scale includes items in which the child seeks aid, comfort, or understanding from parents, peers, and others (number of items = 9).

5. Catastrophizing/Helplessness (Alpha = 0.57): This scale includes items that assess feelings of victimization and powerless over the pain (number of items = 6).

The relationship between PPCI scales and demographic variables shows that age is significantly correlated with Factor Seek for Social Support (r = -0.41, p<0.001) and Factor Distraction (r = -0.27, p<0.001). The intercorrelations between the PPCI scales and parent-rated patient pain intensity and adjustment are good.

The questionnaire PPCI has been adapted and validated for the Italian population. In the Italian study (Bonichini & Axia, 2000) the Cronbach alpha in the several subscales of the parent version of PPCI is not very high, but acceptable: Distraction (alpha = .81), Seek for Social Support (alpha = .61) are the most good; while Problem Solving (alpha = .60) and Cognitive Self-Instruction (alpha = .48) are less good. The Scale of Catastrophizing is not been included in the Italian version because the alpha score is too low (alpha = .37). For the standardization 122 PPCI questionnaires are compiled by mothers of children aged 7-11 years old and 100 are compiled by mothers of ill children of the same age hospitalized.

In the Italian sample: There is a most use of Seek for Support strategy than the

others ($F_{(3,288)}$ = 13.40; p<0.001); Distraction is most used for children hospitalized for surgery than the others ($F_{(1,98)}$ = 2.90; p<0.01); Cognitive Self-Instruction is preferred by increasing of hospitalization days ($F_{(1,98)}$ = 4.86; p<0.01); Seeks Support is more used by hospitalized children than the healthy ones ($t_{(284)}$ = 4.77; p = 0.001).

3.6.1.3 VINELAND ADAPTIVE BEHAVIOR SCALES (VABS) (Sparrow et al., 1984; italian edition by Balboni & Pedrabissi, 2003)

The VABS are useful in assessing an individual's daily functioning throughout several domains of adaptive functioning (personal and social). They can be used as an evaluation and diagnostic tool for individuals who are mentally retarded or individuals with other handicaps. They can also be used to develop individual educational, rehabilitative, and treatment programs and can monitor progress during such a program. Finally, the VABS can be used in research in which the development and functioning of handicapped and non-handicapped individuals are investigated. The Italian version was been validated by Balboni & Pedrabissi (2003).

There are two versions of the revised Vineland that can be used with infants and toddlers. Each version differs in the number of items and materials and the method of administration. The Interview Edition, Survey Form, which is more similar in content to the original VABS, is administered to a parent or caregiver in a semi-structured interview format. The Interview Edition, Expanded Form, Italian version, has 540 items, including 261 from the Survey Form. This form yields a more comprehensive assessment of adaptive behavior and gives a systematic basis for preparing individual educational, rehabilitative, or treatment programs. The Expanded Form can be used by itself or as a follow-up to obtain more information about deficits suggested by the Survey Form. Both versions are organized around four Behavior Domains: Communication, Daily Living Skills, Socialization, and Motor Skills. For the Survey Form, items are organized in domains in developmental order. For the Expanded Form,

items are in clusters, which are organized in developmental order under sub-domains that make up the domains. Administration time for the Survey Form is from 20 to 60 minutes, for the Expanded Form from 60 to 90 minutes. Professionals administering the VABS should be a social worker, psychologist, or equivalent. In this study we used the Expanded form and we checked the age equivalents for each domain and sub-domain in the normal standardization scales.

Adaptive behaviors investigated are: Communication, Daily Living Skills, Socialization and Motor abilities. The Communication domain is comprised of three sub-domains: Receptive, Expressive, and Written Language. The Daily Living Skills scale includes the Personal, Domestic, and Community sub-domains. The Socialization scale is comprised of the Interpersonal, Play and Leisure, and Coping Skills sub-domains. The Motor scale includes Gross and Fine motor abilities.

Factor analyses studies concerning adaptive behavior have overwhelmingly found there are only four distinct factors, as in the Vineland domains. The four domains of *Vineland Adaptive Behavior Scales* include information on all areas defined by AAMR[7]. For example, the assessments of the AAMR areas of "home living," "self-care," "community use," "health and safety," and "work" are all included in the *Vineland* Daily Living Skills domain.

Studies confirming the reliability and validity of the VABS have solidified this measure as one of the most widely used assessments of adaptive behavior (Sparrow & Cicchetti, 1985). Using a checklist to assess adaptive behavior may limit the information an interviewer gathers about the various activities involved in an individual's behavior. A checklist also may allow the respondent to bias the outcome of the assessment because he or she might not fully understand the intent of certain items or might not know the criteria for scoring. Consciously or unconsciously, the respondent might choose scores that do not reflect the individual's true behaviors.

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[7] AAMR: American Association on Mental Retardation.

Reliability studies indicate that the professionally conducted and scored interviews have higher reliability and validity than checklists.

Each item is rated "2" (behavior is usually or habitually performed), "1" (sometimes or partly performed), or "0" (never performed). In addition, there is a code ("N") for cases when the child has never had the opportunity to perform the activity and a code ("DK") to use when the caregiver does not know if the child performed the activity.

The manuals provide users with instructions for scoring caregiver responses. Domain and, in the Expanded Form, sub-domain raw scores are obtained by summing the numerical values of the responses. Using tables in the manuals, the raw scores can be converted into standard scores (with a mean of 100 and standard deviation of 15), percentile ranks, stanines, and age equivalents. The sum of the domain standard scores is used to obtain the composite standard score. A table is then used to obtain the stanines and percentile rankings for the composite from the standard scores. The age equivalents for the composite score can be either the mean or median of the domain age equivalents. The manuals provide instructions for calculating the mean and median age equivalents. The domain standard scores are reported by age increments of 1 month up to first 2 years of age and 2-month increments between 2nd and 3rd years. Children under 6 years old share the same standard composite scores (Balboni & Pedrabissi, VABS manual, pg. 250-266).

Psychometric properties for normal population and for Expanded Form in the Italian standardization version are the following, dealing with reliability (Balboni & Pedrabissi, VABS manual):

(1) Split half-reliability: Internal reliability tests of the Expanded Form were performed on caregivers of children under age 19. The Expanded Form split half coefficients for the several age groups are quite good: It ranged from .61

to .96 for the single Domains and from .61 to .98 for the Adaptive Behavior Composite.

(2) Internal coherence: The Expanded Form Cronbach alpha coefficients for the several age groups are quite good ranging from .52 to .93 for the single Domains and from .59 to .97 for the Adaptive Behavior Composite.

(3) Test-retest reliability (2-4 weeks between tests): The Survey Form reliability coefficients for caregivers of children between the several age groups ranged from .77 to .94 for the Domains. There were no test-retest reliability tests for the Expanded Form.

For the Validity:

(1) Content validity included a literature review and field tests with caregivers (Balboni & Pedrabissi, VABS manual, pg. 77).

(2) Criterion-related validity: The correlations between the Adaptive Behavior Scales and other intelligence tests (i.e., PMA – Primary Mental Ability -, WIPPSI, PM38) among caregivers of children between 5 months and 12 years of age increased with the major age. The differential magnitudes of these correlations is said to support the assumption that adaptive behavior scales, intelligence and achievement scales measure different areas of functioning.

3.6.1.4 QUIT- *Questionari Italiani del Temperamento (used with parents on children aged from 1 month to 11 years)*

The Questionari Italiani del Temperamento are a group of questionnaires that measure temperament in children aged from 1 month to 11 years. The QUIT are constructed of different sub-scales that measure: Attention, motor activity, social interaction, and positive and negative emotions. There are 4 versions of this questionnaire, according to different age ranges: 1-12 months; 13-26 months; 3-6 years;

7-11 years. Each questionnaire is composed of 60 items to be filled in by the parent. Completion time requires approximately 15 minutes. The QUIT, which was administered to parents of 775 children distributed over two age groups (1-12 months and 13-36 months), demonstrates good internal consistency (Cronbach alphas ranged from .59-.83).

3.6.2 Medical information

3.6.2.1 Child's Medical chart

A medical sheet was filled for each child with leukemia (Appendix 2). In this sheet various information were collected in collaboration with the medical doctors such as: The type of leukemia; the therapies and their effects at the several assessment time points; the number of days of hospitalization; the number of blastos at crucial time points for ALL protocol (day +8, +33, +78), the level of risk for ALL protocol (SR, MR, HR).

3.6.2.2 Cortisone psycho-social effects questionnaire

A specific parental report questionnaire was devised to measure the possible mood effects of corticosteroids therapy during the phase of Re-Induction in ALL protocol, about 6 months after the diagnosis communication. This 15-items check-list describes several possible positive (i.e., the child is able to draw or to make homework; the child makes calm plays, etc.) or negative behaviors (i.e., sudden cry, motor hyperactivity, etc.) of children under treatment with cortisone (see Appendix 3).

PART B: Instruments used for Parent and Family assessment

A set of questionnaires were used to assess the parent psychological status (e.g.: Presence of PTSD or depressive symptoms, cognitive functioning), the family SES and the parent adaptation to the child's illness.

3.6.3 Demographics

3.6.3.1 SES Questionnaire

Parental education and occupational status were measured. In particular, the following variables were considered: Number of years of school achievement, type and average hours of job, economical status, number of familiars and sons in the family.

3.6.4 Psychological Symptoms

3.6.4.1 The PTSD symptom inventory (CCSS)

It is a 17-item-check-list assessing the presence of symptoms of Post Traumatic Stress Disorder (PTSD) that may arise after a very stressful situation (adapted from, Derogatis, 2000). It is an adapted version of the LFTU Study version (part k) used in the CCSS Childhood cancer survivor study. There is a list of possible problems related to the communication of the diagnosis of cancer of their children. Parents fill in the questionnaire about the presence/absence of these experiences in their lives in the last month after the communication of the diagnosis. These 17 items are divided into intrusion, avoidance and arousal symptoms (DSM IV). For the reliability of the PTSD symptom inventory in this special population, it has been administered by now to 118 parents of children with cancer receiving treatment at the Onco-hematologic clinic of

Padova demonstrating a good internal consistency (Cronbach alpha = .72).

3.6.4.2 LADDER OF LIFE (CCSS)

The parent had to evaluate, using a 1 to 10 points scale, the quality of her/his present life, the quality of her/his life 5 years before the child's disease and how satisfying her/his life will be in the future (5 years later from the son's/daughter's diagnosis). With this instrument we can have information about individual perception of the past, the present and the future. This scale was recently published in Axia et al. (2006).

3.6.4.3 BRIEF SYMPTOM INVENTORY BSI-18 (Derogatis & Spencer, original copyright 1982)

The BSI-18 includes 18 items divided into three dimensions (somatization, depression and anxiety). These items serve as a screen for depression, somatization, and anxiety in medical and community populations. Respondents are asked to refer about how they felt the last 7 days and each item is rated on a 5-point Likert scale from 0 (not at all) to 4 (extremely). Each dimension includes six items and it takes approximately 4 minutes to complete it. Scores are calculated by adding up the values for the six items in each dimension (range 0–24). In addition, it provides a global or total score, the Global Severity Index (GSI), which summarizes the respondent's overall emotional adjustment or psychological distress by adding up the values for the three dimensions (range 0–72). Interpretation of the scores on each sub-scale and the GSI scores are based on gender-keyed norms published from a sample of oncology patients in the USA (N = 1.543) (Zabora et al., 2001b). In this same study reliability and validity were determined and Cronbach alpha was 0.89, the majority of participants were men (52%) and mean age was 55. According to the guidelines in the BSI 18 manual (Derogatis, 2000), raw scores

are converted to standardized T scores which are characterized by a distribution with a mean of 50 and a standard deviation (SD) of 10.

The BSI 18 is a shortened version of the BSI, which is a 53-item self-report symptom inventory used in a distress screening programme managed by James Zabora and research colleagues at the John Hopkins Oncology Center in Baltimore USA (Zabora et al., 2001b). Coefficients of internal consistency of the BSI have been reported to range from 0.71 to 0.85 and test-retest reliability to be 0.68–0.91 (Derogatis & Melisaratos, 1983). The BSI was developed from its parent instrument the SCL-90-R. Test-retest and internal consistency reliabilities are shown to be very good for the primary symptom dimensions of the BSI and the correlation with comparable dimensions of the SCL- 90-R are high ranging from 0.92 to 0.99 (Derogatis & Melisaratos, 1983). Although the BSI 18 test is relatively new, and reliability and validity studies on the instrument are few, BSI 18 has been shown to be reasonably comparative to the longer instrument BSI with internal consistency ranging from 0.74 to 0.90 (Derogatis, 2000). Additionally, in a study (Zabora et al., 1990) attempting to predict future psychological distress in newly diagnosed cancer patients, it was found that the BSI measurement identified a future distress of 16 of 19 patients.

The BSI is acknowledged as one of the most widely used self-report scales for identifying psychological distress (Derogatis & Melisaratos, 1983; Boulet & Boss 1991) for psychiatric patients; (Stefanek et al., 1987; Zabora et al., 1990, 1997, 2001b; Gilbar et al., 2001; Baider et al., 2003); for identifying psychological symptoms status of medical patients; (Ruipérez et al., 2001; Gilbar & Ben-Zur, 2002).

Recently BSI-18 was used to assess psychological outcomes in long-term survivors of childhood cancer (Zebrack et al., 2004; Recklitis et al., 2006) and in mothers of children under treatment for leukemia (Axia et al., 2006).

For the reliability of the BSI-18 in this special population, it has been administered by now to 118 parents of children with cancer receiving treatment at the

Onco-hematologic clinic of Padova, demonstrating a global good internal consistency (Cronbach alpha = .92). Also the specific domains show a good internal consistency: Depression, Cronbach alpha = .84, Physical, Cronbach alpha = .83; Arousal, Cronbach alpha = .83.

3.6.4.4 PROBLEM SCALE (CCSS)

It is a 25-item questionnaire, recently published in Axia et al. (2006), that investigates the presence and intensity (range from 1 = "never a problem" to 3 = "often a problem") of cognitive problems dealing with childhood cancer experience in the last 2 weeks. The questionnaire is filled in by parents. A Varimax rotated confirmatory factor analysis was run to identify the factors that more specify the kind of these cognitive problems. The results on 118 parents of children with cancer showed that five factors can be extracted according to Kaiser's rule, explaining totally a good proportion of the total variance (56,63%). The factors are (Appendix 4): Memory (N = 5 items; alpha = 0.78; 14.02 of variance); Mental Disorganization (N = 8 items; alpha = 0.82; 13.89 of variance); Labile mood (N = 3 items; alpha = 0.75; 10.46 of variance); Impulsivity (N = 4 items, alpha = 0.73; 10.35 of variance); Concentration (N = 5 items; alpha = 0.67; 7.90 of variance). Internal consistency of the sub-scales is good. Correlations among the several factors showed that the scales are moderately independent from each other.

3.6.4.5 Anxiety test (STAI) (Spielberger, 1983)

The State-Trait Anxiety Inventory (STAI) measures anxiety in adults. The STAI differentiates between the temporary condition of "state anxiety" and the more general and long-standing quality of "trait anxiety". The essential qualities evaluated by the STAI-Anxiety Scale are feelings of apprehension, tension, nervousness, and worry.

Scores on the STAI-S Anxiety scale increase in response to physical danger and psychological distress, and decrease as a result of relaxation training. On the STAI-T-Anxiety scale, consistent with the trait anxiety construct, psychoneurotic and depressed patients generally have high scores (Spielberger, 1983). The reliability of the scale is really high: Cronbach's alpha = .93 for the STAI-S (N = 20 item) and .90 for the STAI-T (N = 20 item).

3.6.5 Adaptation and Locus of control

3.6.5.1 EFI-Cancer, parent version

It is a parent interview which explores the daily routines of family life in which the child with cancer and parent participate, and the salient concerns regarding how that routine is organized. We have just presented it above. Particularly, the family dimensions are the following: Parental emotional coping; Levels of communication on the child illness; Parenting the child in the hospital; Trust in the medical care and in the hospital community; Routine and time reorganization; Social support; Connectedness of the parental couple and Sibling involvement.

A questionnaire based only on these family dimensions was set up for this study with the same range 0-8.

3.6.5.2 PHLOC (DeVellis et al., 1993)

It is a 30-items questionnaires assessing parent's type of internal or external locus of control about child's health. The PHLOC was used to assess mothers' beliefs about the health of her child. Child's well-being can depend on destiny (absolutely not controllable), on external information sources (pediatric staff) or on parent (fully controllable). The questionnaire assesses beliefs of Child, Divine, Fate, Media, Parental,

and Professional influences over child health. For example, the Fate subscale provides an index of the extent to which parents believe that the health status of their child is predominantly a matter of luck (e.g., *Whether my child avoids injury is mostly a matter of luck*). The American standardization (De Vellis et al., 1993) showed internal consistency reliability coefficients above .70 for all scales and test-retest (*r*) correlations all above .60.

CHAPTER 4

RESULTS

"When he has pain, he whimpers "hurt, hurt", and then they give him something to help him until he quiets down.
Then, he is the type that as soon as he feels better, he practically resurrects…and then bikes away!"
(Toddlers are allowed to use their small 3-wheels bikes along the corridors of the hospital)

Results are divided into three main parts following the hypotheses and research questions.

The first part considers concurrent analyses upon child's and parent's dependent variables at the several time points related also to illness variables (Part A: Concurrent analyses). The aim of this first part is to evaluate: Quality of life and adaptation of child at the several time points of the therapies (see paragraphs from 3.2.1.1 to 3.2.1.3), on one side, and parent's psychological health and adaptation at the same time points, on the other side (see paragraphs 3.2.2.1-3.2.2.5).

The second part (Part B: Longitudinal analyses) considers longitudinal analyses upon parent's dependent variables throughout the several time points (see paragraph 3.2.3.1). This second part aimed at investigating the longitudinal psychological health and adaptation of parents of children with leukemia along the first year of therapies.

The third part (Part C: Predictive analyses) focuses on the possible prediction, mediation and moderation effects, respectively on child's adjustment (see paragraphs from 3.2.4.1 to 3.2.4.3) and parent's psychological health and adaptation (see paragraphs 3.2.5.1 and 3.2.5.2) considering the different time points of the research

project.

4.1 Analyses plan

4.1.1 Part A (concurrent analyses)

Data were first examined for skewness, kurtosis, outliers and normalcy (Kolmogorov-Smirnov test): No transformations were necessary as the distribution was normal for all dependent variables.

Child

(T1) After preliminary descriptive analyses and Pearson's bivariate correlations to examine the associations between our variables, a LISREL path model was performed to assess whether the family (Parental Trust on the Medical Care, Parenting) and child factors (Child's Age, Coping and Adaptability) impacted concurrently on Child's Quality of Life during the first hospitalization.

(T2) Descriptive statistics were run to evaluate the Child's Pain Coping styles (1. Cognitive Self-Instruction; 2. Problem-Solving; 3. Distraction; 4. Seek for Social Support; 5. Catastrophizing) and Pearson's bivariate correlations measured their possible relations to illness parameters (type, treatment), to personal child factors (age, gender, global coping and adaptability at the diagnosis) and to family factors (parent's symptomatology).

(T4) Descriptive statistics showed the Child's Adaptive Behavior Scores, specifically the global adaptive behavior score and the scores related to each subscale (Communication, Daily Living Skills, Socialization, Motor Abilities) post 1 year of treatment. We calculated the descriptive statistics of developmental delays in these adaptive behaviors using the norms of the Vineland test. Then, Pearson's bivariate

correlations were used to assess the kind of association of these Adaptive Behaviors with Children Temperament (Negative Emotionality, Social Orientation and Attention), with family factors (parents' symptomatology) and with Illness Parameters (Type of leukemia, Days of hospitalization).

Parent

(T1) After preliminary descriptive analyses, at T1 5 hierarchical linear regressions models were performed, two referring respectively to parents of all the children with leukemia and the other three referring to parents of only children with ALL. In the first sample the first hierarchical regression had as dependent variable Parental Current Life Perception and as independent variables: Demographic and Illness factors, entered in the first step; Family Stress Events and Psycho-Social Factors, entered in the second step. The second regression had the same independent variables and as dependent variable the Parental Cognitive Problems.

In the other sample of parents of children with ALL the same two linear regression analyses were run with entry-addition Number of Blastos communicated at day +8 at the first step. Another linear regression analysis had the same independent variables and as dependent variable the Sum of Parental Symptomatology (BSI-18 global score).

An ANCOVA was performed to assess the Parenting Behavior (dependent variable) throughout the several Age Groups (fixed factor) by also the effects of Parents' Demographic Factors, Parents' Stress Events and Child's Coping, Adaptability and Quality of Life (covariates).

(T2) Descriptive statistics showed PTSD Symptomatology and its distribution among parents one month after the diagnosis and Pearson's bivariate correlations evaluated its possible associations with child's Type of Leukemia. Other descriptive statistics showed the major parents' types of Locus of Control and Pearson's bivariate correlations evaluated their possible associations with Parents' Psychological Health

(perception of their current life, psychological symptoms) and with Children's Factors (e.g., age).

(T3) Descriptive statistics showed the parental psychological health condition post 6 months of child therapies. A LISREL path model was performed to assess whether parental psycho-social factors and parents' symptoms impacted concurrently on parental PTSS. Particularly, only for parents of children with ALL, three hierarchical regression models evaluated the impact of family demographic factors, family stress events and illness parameters (days of hospitalization, number of blastos at day +78, mood cortisone effects) (first entry-step), psychological problems, symptoms and anxiety (trait and state) (second entry-step) and family psychosocial factors (third entry-step) respectively and separately upon the following dependent variables: Parental current life perceptions, parental cognitive functioning and parents' psychological symptomatology.

(T4) Descriptive analyses showed the frequency of parents' post-traumatic stress symptoms one year after the diagnosis communication. Pearson's bivariate correlations assessed the associations of parents' PTSS with the other family (demographics, stress events, symptoms, psycho-social factors, trait anxiety), child (age, gender, temperament) and illness (days of hospitalization) factors.

4.1.2 Part B (*Longitudinal analyses*)

A series of repeated measures ANOVAs were performed to see what type of time trend (Independent variable) was related to the parent's psychological health and adaptation (Dependent variables) along the several time points. For each ANOVA we controlled the Mauchly sphericity test and, if not respected, we used the Greenhouse-Geisser correction.

4.1.3 Part C (Predictive analyses)

For both moderation and mediation effects, two types of statistical strategies were applied: Multiple regression (Baron & Kenny, 1986) and structural equation modelling (SEM).

We used here the regression approach for testing the potential mediation effects. Baron & Kenny (1986) illustrated the three multiple regression analyses testing mediation effects: The significance of the path "predictor A on the mediator B" was examined in the first regression; the significance of the path "predictor A on the dependent variable C" was examined in the second regression; finally, predictor and mediator used simultaneously as predictors of dependent variable in the last equation.

Regression approach was also used here for testing moderation effects. The predictor and moderator main effects were entered simultaneously into the regression equation first, followed by the interaction of the predictor and moderator respectively centered.

Child

(T1-T4) After preliminary analyses of Pearson's bivariate correlations between the several variables tested, a model of mediation effects following the Baron and Kenny's rule (Three linear regressions) was performed to evaluate the family factors and disease characteristics at T1 which impacted upon children's adaptive behaviors (global scale of VABS) one year post child's therapies. Post hoc Sobel test was used to control the signification of mediation effects.

(T2-T4) Hierarchical regression analysis was run to assess whether family, child and disease factors after 1 month from the diagnosis communication were predictive of long-term adaptation of children with leukemia (global scale of VABS) after 1 year of treatments. In the first step of regression we entered demographic variables and illness parameters (diagnosis, days of hospitalization); in the second step we entered parental

PTSS at one month and the five parental strategies of locus of control on child illness; in the third step child's strategies of coping with pain assessed post one month of treatments were entered.

(T3-T4) Another hierarchical regression analysis was run to show whether family and disease factors after 6 months from the diagnosis communication were responsible for long-term adaptation of children with leukemia (global scale of VABS) after 1 year of treatments. In the first step of regression we entered demographic variables and illness parameters (diagnosis, days of hospitalization); in the second step we entered the several types of parental symptoms; in the third step psycho-social factors of EFI-C at T3 were entered.

Parent

(T1-T2) We performed a LISREL path model to see whether parental and family factors were responsible for short-term PTSS of parents of children with leukemia one month after the diagnosis. We entered as Y-variables: Parental PTSS at T2, memory problems at T1, mean of parents' different psychological symptoms at T1 and perception of their current life at T1. As X-variables we entered the family factors emotional coping and support derived from EFI-C assessed at T1.

Only on children with ALL we assessed the possible moderation effect of number of blastos communicated at day +8 with physical symptoms as predictor and parents' PTSS symptoms at T2 as dependent variable. The analysis used to see this effect was the regression model: The predictor and moderator main effects were entered simultaneously into the regression equation first, followed by the interaction of the predictor and moderator respectively centered.

(T1-T3) Then we run three hierarchical analyses to find whether family and child factors were responsible for psychological functioning of parents of children with leukemia 6 months post-diagnosis. In the first regression analysis we entered parents' current life perception at T3 as dependent variable and demographic and illness factors

(step 1), family psycho-social factors at T1 (step 2) and parental symptoms at T1 and T2 (step 3) as independent variables. The second regression had as dependent variable the total symptoms assessed by BSI-18 at T3 and the same independent variables. The third regression showed as dependent variable the cognitive problems at T3 and the same independent variables.

Another three hierarchical analyses tested the same research question only on children with ALL. The proceeding was similar as above, adding the independent variables of number of blastos communicated at day +78 and cortisone mood effects score.

4.2 Part A: Concurrent analyses

4.2.1 Child's QoL and Adaptation at the several time points

4.2.1.1 Child's Quality of Life at T1

Which family and child factors are responsible for quality of life of leukemic child in the second week after the diagnosis communication?

To answer this question we ran preliminary descriptive statistics. Table 4.1 presents the means and standard deviations for the scores derived from the EFI-C of child's and parental dimensions.

Table 4.1 - Descriptive statistics for the child and the parent dimensions from the interviews.

Dimension (Range 0-8)	N	Mean	SD
Parental emotional coping	128	4.89	0.83
Levels of communication on the child illness	128	4.62	0.91
Parenting the child in the hospital	128	5.16	0.95
Trust in the medical care and in the hospital community	128	4.95	1.07
Routine and time reorganization	128	4.28	0.72
Social support	128	4.46	1.33
Connectedness of the parental couple	128	5.13	1.34
Sibling involvement	96	5.61	9.72
Child coping with procedures and hospitalization	128	3.94	1.36
Child quality of life in the hospital	128	3.93	1.22
Child adaptability/temperament	128	5.39	1.22

Then, the LISREL path model was performed to test this first question and figure 4.1 showed the results.

This model showed that Child's Quality of Life was predicted by Parental Trust in the Medical Staff, by Child Coping and Child Adaptability. These last predictors were in turn sustained by the fixed factor Child's Age and by the modifiable factor Parenting. Parenting was also directly predictive of Child's QoL, but less than by Child's Coping mediation effect. Child's Age influenced both Coping and Adaptability, which in turn was sustained also by Parental Trust in Medical Staff.

Figure 4.1: Structural standardized coefficients of hypothetical model of path-analysis. All the coefficients were significative for p<.005. The model presented good fit indices ($\chi^2(4) = 5.03$; N = 128; p = 0.28; RMSEA = 0.045: NNFI = 0.99; CFI = 1) (Engel et al., 2003)
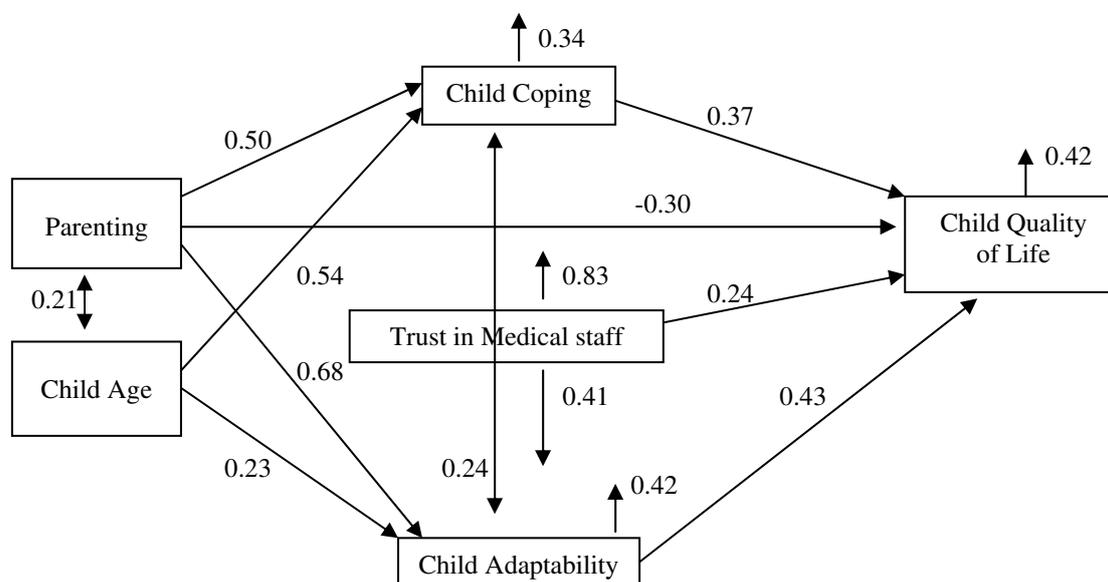
4.2.1.2 Child's Coping with Pain at T2

Which child's styles of coping with pain are adopted and which are the associations with disease and family factors in the second month after the diagnosis communication?

To answer this question we preliminary run descriptive statistics. Table 4.2 showed that style of coping with pain mostly used by children with leukemia was Seek for social support in the first month of hospitalization.

Table 4.2 - Descriptive statistics for the child's coping strategies

Coping strategies (range 0-2)	N	Mean	SD
Seek for social support	81	1.25	0.34
Problem Solving	81	0.89	0.36
Catastrophizing	81	0.86	0.32
Cognitive self-instruction	81	0.74	0.40
Distraction	81	0.58	0.37

Then, Pearson's bivariate correlations were computed between illness parameters, demographic variables, child's and family dimensions assessed at T1 and also between

parents' symptoms at T1 and child's coping strategies at T2. Specifically, all child's coping strategies were correlated one to each other except for Catastrophizing: Distraction strategies were significantly correlated with Cognitive self-instructions (r = .49; p<0.001), with Social Support strategies (r = .27; p<0.05), with Problem Solving strategies (r = .27; p<0.05); Problem solving strategies were significantly correlated with Social Support ones (r = .26; p<0.05); Social Support strategies were significantly correlated with Cognitive self-instructions (r = .30; p<0.01).

Both Problem Solving (r = .32, p<0.01) and Cognitive Self-Instructions (r = .30; p<0.01) were significantly correlated with Child's Age. Catastrophizing was significantly associated with Parental Cognitive Problems at T1 (r = .30; p<0.01).

4.2.1.3 Child's Adaptive Behaviors at T4

Which are the types of developmental deficits in adaptive behaviors in children with leukemia and what kind of association with children temperament and with family factors one year after the diagnosis communication there are?

To answer this question we preliminary calculated the age equivalents of each scale of child's adaptive behaviors. Figure 4.2 shows the situation of child's developmental delays of almost three months at T4 in the four domains of Vineland Scales.

Then, Pearson's bivariate correlations were computed between the Child's Adaptive Behaviors scores (converted in equivalent ages) and: Child's Temperament and Family Factors. The several domains were strongly correlated each other showing how child adaptive behavior was a unique construct. Communication scale was significantly correlated with Daily Living Skills scale (r = .92; p<.001), with Socialization scale (r = .86; p<.001) and with Motor abilities scale (r = .80; p<.001). Daily Living Skills scale was significantly correlated with Socialization scale (r = .94; p<.001) and with Motor abilities scale (r = .71; p<.001). Finally, Socialization scale was

significantly correlated with Motor abilities scale (r = .76; p<.001).

The Motor Development score was strongly negatively correlated with Child's Type of Leukemia (r = -0.510; p<0.001), with Days of Hospitalization (r = -0.579; p<0.001) and positively correlated with Motor Activities in Child's Temperament score (r = 0.437; p<0.01) in 46 children under 6 years of age at T4.

Figure 4.2 - Child's developmental delays of almost three months in each of the domains of Vineland Scales.
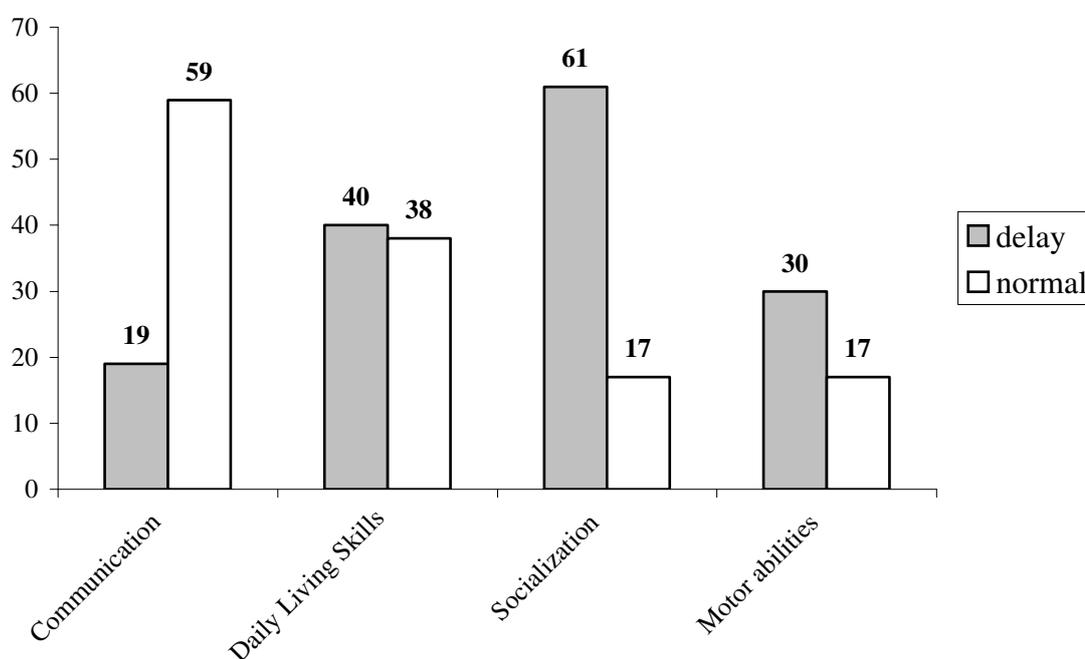
The Communication Development Score was significantly associated with the following family factors: Parent's report of Child's Mood Problems (r = -0.322; p<0.01); parent's Concentration Problems (r = -0.310; p<0.01); Parental Communication about the child illness (r = 0.392; p<0.01).

Communication score was associated with Child's Temperament, specifically in the domains of Social Orientation (r = 0.313; p = 0.013) and Negative Emotionality (r = -0.316; p = 0.012).

The Daily Living Skills development score was significantly associated with the following family factors: Parent's Report of Child's Mood Problems (r = -0.353; p<0.01); parent's Concentration Problems (r = -0.343; p<0.01); parental Communication about the child illness (r = 0.402; p<0.001). Child's Temperament was not significantly related to VABS Communication score.

The Socialization development score was significantly associated with the following family factors: Parental global Cognitive Problems (r = -0.343; p<0.01); parental Communication about the child illness (r = 0.361; p<0.01); Social Support (r = 0.344; p<0.01). Socialization score was also related to Child's Temperament, specifically in the domain of Negative Emotionality (r = -0.329; p = 0.09).

4.2.2 Parent's Psychological Health and Adaptation at the several time points

4.2.2.1 Parent's Psychological Health and Adaptation at T1

What happens to the parent's psychological health and adaptation in relation to child's disease factors in the second week after the diagnosis communication?

To answer this question we preliminary run descriptive statistics. Table 4.3 presents the means and standard deviations for the scores derived from the questionnaires of parents about their psychological symptoms.

Life perception was really low at T1, even if there was a big standard deviation that underlined the variability of parent's emotive state. Depression symptoms were the most frequent in the BSI-18 total score, followed respectively by Arousal and Physical ones. Cognitive problems score was not so high at T1, less than BSI-18 total score. Mood problems score and Impulsivity score were the most frequent sub-scales of the total Cognitive Problems score. It seemed that Emotive Problems were more intensive than Cognitive ones at T1.

Table 4.3 - Descriptive statistics for parental psychological symptoms at T1.

Symptoms scores	Range	Mean	SD
Life perceptions	0-10	4.43	2.21
Depression score	1-5	2.29	0.99
Arousal score	1-5	2.16	0.90
Physical score	1-5	1.66	0.76
Global BSI score	1-5	2.03	0.77
Mood problems score	1-3	1.72	0.56
Impulsivity score	1-3	1.65	0.47
Disorganization score	1-3	1.59	1.42
Memory score	1-3	1.56	0.47
Concentration problems score	1-3	1.52	0.41
Cognitive problems score	1-3	1.60	0.34

Hierarchical regression models were run to identify the family and disease factors associated with parental psychological symptom scores. In the first regression model we entered the following independent variables: At the first step, demographic and illness factors; at the second one, the 8 family Psycho-Social Factors derived from the interviews and the Life Stress Events and, at the last step, the 3 Child's Factors derived from the interviews. The dependent variable in this first regression was Parents' Current Life own perception. In this regression the second model was the best one ($R^2 = 0.38$; F = 3.54; p = 0.001) with Child's Diagnosis ($\beta = -0.24$; p = 0.004), Child's Age ($\beta = 0.26$; p = 0.016), Parent's Age ($\beta = 0.24$; p = 0.017) and Social Support ($\beta = 0.51$; p = 0.0001) that impacted upon parents' Current Life Perception (Table 4.4).

Table 4.4 - Hierarchical regression predicting Parents' Current Life Perception at Time 1.

Step	Variables	R^2	ΔR^2	F	P	β	p
1	**Demographic and illness factors**	0.20	0.20	0.18	4.31		
2	**Family psycho-social factors**	0.38	3.54	0.001	0.001		
	Child diagnosis					-0.24	0.004
	Child age					0.24	0.016
	Parent age						0.017
	Parent school years						ns
	Parent mean hours/weekly						ns
	Number of siblings						ns
	Emotional Coping						ns
	Trust in the medical care						ns
	Communication about the illness						ns
	Routine and time reorganization						ns
	Parenting						ns
	Support						0.0001
	Couple connectedness						ns
3	**Parental life stress events**	0.42	0.03	1.98	Ns		

The second regression model had the same independent variables and only the dependent variable changed (in this case Parents' Cognitive Problems score). In this second regression the second model was the best one (R^2 = 0.27; F = 2.13; p = 0.04) with Child's Diagnosis (β = 0.19; p = 0.034), Child's Age (β = -0.25; p = 0.035), Parent's Mean hours job/a week (β = 0.25; p = 0.010) and Couple Connectedness (β = -0.27; p = 0.021) that impacted upon Cognitive Problems score (Table 4.5).

In the third regression with global BSI score with dependent variable no significant model was found.

Table 4.5 - Hierarchical regression predicting parents' Cognitive Problems score at Time 1.

Step	Variables	R^2	ΔR^2	F	p	β	p
1	***Demographic and illness factors***	0.14	0.14	2.91	0.011		
2	***Family psycho-social factors***	0.27	0.13	2.13	0.040		
	Child diagnosis					0.20	0.034
	Child age					-0.25	0.035
	Parent age						ns
	Parent school years						ns
	Parent mean hours/weekly					0.25	0.010
	Number of siblings						ns
	Emotional Coping						ns
	Trust in the medical care						ns
	Communication about the illness						ns
	Routine and time reorganization						ns
	Parenting						ns
	Support						ns
	Couple connectedness					-0.27	0.021
	Parental life stress events						ns
3	***Child EFI-C factors***	0.28	0.01	0.38	ns		

Then we run the same three hierarchical regression models exclusively on the sample of parents of children with ALL, including also as independent variables the number of blastos at day +8 dealing with ALL protocol in the first step. The first model (R^2 = 0.56; F = 3.43; p = 0.03) showed that Cognitive Problems score was significantly predicted by: Parent's Mean hours job/a week (β = 0.29; p = 0.005); by Family's Routine and Time Reorganization (β = 0.33; p = 0.03); by Couple Connectedness (β = -0.34; p = 0.012) and by Number of Blastos at day +8 (β = 0.20; p = 0.05) (Table 4.6).

The second model (R^2 = 0.20; F = 3.58; p = 0.03) indicated Social Support (β = -.29; p = 0.006) and Number of Blastos at day +8 (β = 0.24; p = 0.02) as the best predictors of Global BSI-18 score. The last model (R^2 = 0.36; F = 3.68; p = 0.03) showed that Parental Current Life Perception was predicted by Parent's Age (β = 0.25; p = 0.02), by Social Support (β = 0.39; p = 0.009) and by Child's Age (β = 0.28; p = 0.02) (Table 4.7).

Table 4.6 - Hierarchical regression predicting Cognitive Problems score in parents of children with ALL at Time 1.

Step	Variables	R^2	ΔR^2	F	p	β	p
1	**Parents demographic factors**	0.09	0.09	3.05	0.033		
2	**Family psycho-social factors**	0.25	0.15	1.93	ns		
3	**Child illness and demographic factors**	0.31	0.06	3.43	0.038		
	Parent age						ns
	Parent school years						ns
	Parent mean hours/weekly					0.29	0.005
	Emotional Coping						ns
	Trust in the medical care						ns
	Communication about the illness						ns
	Routine and time reorganization					0.33	0.033
	Parenting						ns
	Support						ns
	Couple connectedness					-0.34	0.012
	Parental life stress events						ns
	Child age						ns
	N blastos day +8					0.20	0.058

Table 4.7 - Hierarchical regression predicting BSI-18 Global score in parents of children with ALL at Time 1.

Step	Variables	R^2	ΔR^2	F	p	β	p
1	*Parents demographic factors*	0.05	0.05	1.48	ns		
2 (stepwise)	*Family psycho-social factors*	0.13	0.08	8.15	0.005		
		0.20	0.07	3.58	0.032		
3	*Child illness and demographic factors*						ns
	Parent age						ns
	Parent school years						ns
	Parent mean hours/weekly					-0.29	0.006
	Support						Ns
	Child age					0.24	0.019
	N blastos day +8						

4.2.2.2 Parenting behavior

How child's ages affects parenting behavior at T1?

To answer this question an ANCOVA was performed with: Child's dimensions of EFI-C (Coping, Quality of Life and Adaptability) and demographic factors (parent's school years, parent's mean of job days/a week, parent's Life Stress Events) as

covariates; Age of the Child divided into three categories (0-3 ys; 4-6 ys; upper to 7 ys) as fixed factor; Parenting as dependent variable.

As expected, the analysis revealed the presence of a significant group difference on Parenting by Child's Age. When controlling for these independent variables estimated marginal means for the three groups of child's age were 5.56 for children aged 0-3, 5 for children aged 4-6 and 5.08 for the older children. Results are presented in Table 4.8.

Table 4.8 - ANCOVA comparing parenting between the three categories of child's age controlling for demographic factors and child's dimensions.

Source	*df*	*F*	$\eta^2 p$	*p*	*B*	*t*	*Sig.*
Group (child's age):	2	4.81	0.085	0.010	0.479	2.153	0.034
in order 0-3; 4-6; 7≥					-0.076	-0.492	ns
Parent school years	1	0.62	0.006	ns			
Parent mean of job days/a week	1	0.07	0.001	ns			
Parent life stress events	1	0.09	0.001	ns			
Child's coping	1	5.08	0.047	0.026			
Child's quality of life	1	0.92	0.009	ns			
Child's adaptability	1	20.11	0.163	0.0001			

4.2.2.3 Parent's Health Locus of Control

What happens to the parents' locus of control, to their psychological health in relation to child's disease factors in the second month after the diagnosis communication?

To answer this question descriptive statistics were shown on the several styles of parental locus of control on child's illness in Table 4.9. We could note that Parental Influence was the most used.

Table 4.9 - Descriptive statistics of parental locus of control styles on child's illness

Locus of control styles	Range	Mean	SD
Parental influence	1-6	4.35	0.79
Medical staff influence	1-6	4.30	0.83
Divine influence	1-6	4.03	1.64
Child influence	1-6	3.13	0.97
Fate influence	1-6	2.97	1.21
Media influence	1-6	2.56	1.27

Then we run hierarchical regression analyses to see if Parental Influence was related to a positive perception of their life and a lower psychological symptomatology. We entered: The Demographic Variables, the Illness parameters and Life Stress Events in the first step; Parent's Symptomatology scores in the second step and 11 Psycho-Social factors derived from the EFI-C in the third step. The second model resulted significative ($R^2 = 0.20$; F = 4.19; p = 0.08) with Parent's Current Life Perception tested at T1 as the best predictor of Parental Influence at T2 ($\beta = 0.37$; p = 0.003) (Table 4.10).

Table 4.10 - Hierarchical regression predicting parental internal locus of control at T2.

Step	Variables	R^2	ΔR^2	F	p	β	p
1	*Demographic and illness factors*	0.08	0.08	1.18	ns		
2	*Family psychological symptoms at T1*	0.13	0.08	8.15	0.008		
	Child diagnosis						ns
	Child age						ns
	Parent age						ns
	Parent school years						ns
	Parent mean hours/weekly						ns
	Number of siblings						ns
	Life stress events						ns
	Parent current life perception					0.37	0.003
	Cognitive problems score						ns
	BSI-18 global score						ns
3	*Family and child psycho-social factors*	0.20	0.07	3.58	ns		

Another regression analysis measured the possible factors associated with parental perceptions of their children's grade of influence on the illness. The second model ($R^2 = 0.24$; F = 3.14; p = 0.03) showed that Child's Age ($\beta = 0.36$; p = 0.002) and Parental Current Life Perception ($\beta = 0.32$; p = 0.006) impacted upon parental perceptions of their children's influence on the illness (Table 4.11).

At one month post diagnosis descriptive analyses were performed to see the distribution of parental PTSS in each subscale. Mean of total PTSS of parents was 6.13 (SD = 3.34) divided into 2.29 (SD = 1.37) of intrusion, 1.95 (SD = 1.59) of avoidance and 1.87 (SD = 1.35) of arousal. The more frequent total number of post-traumatic symptoms was concentrated between 4 to 9 (65.5%).

Table 4.11 - Hierarchical regression predicting parental perception of child locus of control at T2.

Step	Variables	R^2	ΔR^2	F	p	B	p
1	**Demographic and illness factors**	0.16	0.16	2.51	0.021		
2	**Family psychological symptoms at T1**	0.24	0.08	3.14	0.029		
	Child diagnosis						ns
	Child age					0.36	0.002
	Parent age						ns
	Parent school years						ns
	Parent mean hours/weekly						ns
	Number of siblings						ns
	Life stress events						ns
	Parent current life perception					0.32	0.006
	Cognitive problems score						ns
	BSI-18 global score						ns
3	**Family and child psycho-social factors**	0.32	0.07	0.87	ns		

4.2.2.4 Parent's Psychological Health and Adaptation at T3

What happens to the parent's psychological health and adaptation in relation to child's disease factors after 6 months post diagnosis communication?

To answer this question descriptive statistics we run preliminary correlations to see the associations between our variables. Then, a LISREL path model was performed to test whether family and illness factors were related to PTSS at 6 months post diagnosis. Figure 4.3 shows the results.

This model showed that parental PTSS at T3 was significantly sustained directly by Family Routine and Time Reorganization. A more strongly association was found by mediation effect of Parental Cognitive and Anxiety Problems at the same time point.

We run hierarchical regression analysis to assess the possible association between parental current life perceptions with illness and the following independent variables: Demographic Factors (step one), Parent's Symptoms (step two) and Psycho-Social Factors (step three). The second model was the best one (R^2 = 0.53; F = 16.42; p = 0.0001) with Child's Age (β = 0.36; p = 0.0001), BSI-18 Global score (β = -0.28; p = 0.031) and State anxiety (β = -0.55; p = 0.0001) that impacted significantly upon Parental Current Life Perception (Table 4.12).

Figure 4.3 - Structural standardized coefficients of hypothetical model of path-analysis. All the coefficients were significative for p<.005. The model presented was saturated, so that the fit was perfect ($\chi^2(0) = 0$; N = 94; p = 1; RMSEA = 0.0001) (Engel et al., 2003).
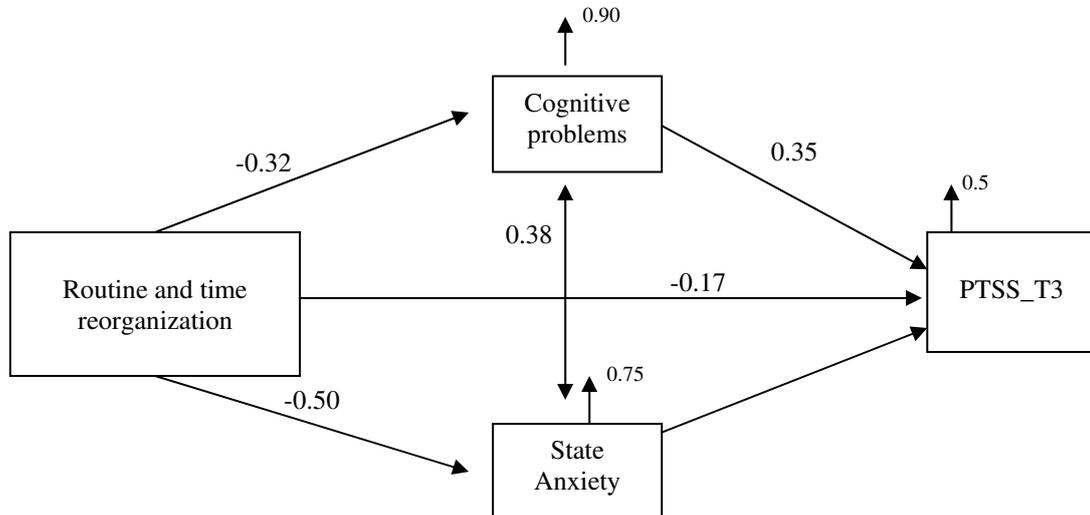
Another hierarchical regression model ($R^2 = 0.50$; F = 15.33; p = 0.0001) showed that Parental Cognitive problems score was associated significantly to Days of hospitalization ($\beta = 0.31$; p = 0.033) and to BSI-18 Global score ($\beta = 0.50$; p = 0.0001) (Table 4.13).

BSI-18 Global score was significantly related to Parental Current Life Perception ($\beta = -0.20$; p = 0.031) and Cognitive Problems score ($\beta = 0.34$; p = 0.0001) in the last regression model tested ($R^2 = 0.66$; F = 33.10; p = 0.0001) (Table 4.14).

Table 4.12 - Hierarchical regression predicting parents' current life perception at Time 3.

Step	*Variables*	*R²*	*ΔR²*	*F*	*p*	*β*	*p*
1	*Demographic and illness factors*	0.14	0.14	1.67	ns		
2	*Parent's symptoms*	0.53	0.39	16.42	0.0001		
	Child age					0.36	0.0001
	Child diagnosis						ns
	Days of hospitalization at T3						ns
	Parent age						ns
	Parent school years						ns
	Parent mean hours/weekly						ns
	Number of siblings						ns
	Parental life stress events						ns
	Cognitive problems score						ns
	BSI-18 global score					-0.28	0.031
	State anxiety					-0.55	0.0001
	Trait anxiety						ns
3	*Family psycho-social factors*	0.55	0.02	0.50	ns		

Table 4.13 - Hierarchical regression predicting parents' cognitive problems score at Time 3.

Step	*Variables*	*R²*	*ΔR²*	*F*	*p*	*β*	*p*
1	*Demographic and illness factors*	0.11	0.11	1.28	ns		
2	*Parent's symptoms*	0.50	0.39	15.33	0.0001		
	Child age						ns
	Child diagnosis						ns
	Days of hospitalization at T3					0.31	0.033
	Parent age						ns
	Parent school years						ns
	Parent mean hours/weekly						ns
	Number of siblings						ns
	Parental life stress events						ns
	BSI-18 global score					0.50	0.0001
	Parental current life perception						ns
	State anxiety						ns
	Trait anxiety						ns
3	*Family psycho-social factors*	0.55	0.02	0.50	ns		

Table 4.14 - Hierarchical regression predicting parents' BSI-18 global score at Time 3.

Step	Variables	R^2	ΔR^2	F	p	β	p
1	*Demographic and illness factors*	0.09	0.09	1.11	ns		
2	*Parent's symptoms*	0.66	0.57	33.10	0.0001		
	Child age						ns
	Child diagnosis						ns
	Days of hospitalization at T3						ns
	Parent age						ns
	Parent school years						ns
	Parent mean hours/weekly						ns
	Number of siblings						ns
	Parental life stress events						ns
	State anxiety						ns
	Trait anxiety						ns
	Cognitive problems score					0.34	0.0001
	Parental current life perception					-0.20	0.031
3	*Family psycho-social factors*	0.68	0.02	0.85	ns		

Then we run other three similar hierarchical regression models only on parents of children with ALL to see if children's bad behaviors and mood reactions to cortisone impact negatively on parental mental health, especially in their cognitive and psychological functioning.

In the first regression model (R^2 = 0.55; F = 12.84; p = 0.0001) Children's Age (β = 0.37; p = 0.001) and State Anxiety (β = -0.54; p = 0.002) impacted on Parental Current Life perceptions (Table 4.15).

In the second regression model (R^2 = 0.64; F = 19.13; p = 0.0001) Child's Mood Cortisone effect (β = 0.18; p = 0.046) and Parent's Cognitive Problems score (β = 0.37; p = 0.0001) impacted on parental BSI-18 Global score (Table 4.16).

Table 4.15 - Hierarchical regression predicting Current life perception in parents of children with ALL at Time 3.

Step	Variables	R^2	ΔR^2	F	p	β	p
1	*Demographic and illness factors*	0.16	0.16	1.36	ns		
2	*Parent's symptoms*	0.55	0.39	12.84	0.0001		
	Child age					0.37	0.001
	Days of hospitalization at T3						ns
	Parent age						ns
	Parent school years						ns
	Parent mean hours/weekly						ns
	Number of siblings						ns
	Parental life stress events						ns
	N blastos at day +78						ns
	Child's mood cortisone effects						ns
	BSI-18 global score						ns
	Cognitive problems score						ns
	State anxiety					-0.54	0.002
	Trait anxiety						ns
3	*Family psycho-social factors*	0.57	0.016	0.32	ns		

Table 4.16 - Hierarchical regression predicting BSI-18 global score in parents of children with ALL at Time 3.

Step	Variables	R^2	ΔR^2	F	p	β	p
1	*Demographic and illness factors*	0.18	0.18	1.54	ns		
2	*Parent's symptoms*	0.64	0.46	19.13	0.0001		
	Child age						ns
	Days of hospitalization at T3						ns
	Parent age						ns
	Parent school years						ns
	Parent mean hours/weekly						ns
	Number of siblings						ns
	Parental life stress events						ns
	N blastos at day +78						ns
	Child's mood cortisone effects					0.18	0.046
	Cognitive problems score					0.37	0.0001
	State anxiety						ns
	Trait anxiety						ns
	Current life perception						ns
3	*Family psycho-social factors*	0.68	0.044	1.24	0.32		

In the last regression model ($R^2 = 0.52$; F = 9.01; p = 0.0001) Child's Mood Cortisone effect (β = -0.21; p = 0.040), Parent's Mean Job hours/a week (β = 0.27; p = 0.015) and BSI-18 Global score (β = 0.50; p = 0.0001) impacted on Parental Cognitive Problems score (Table 4.17).

Table 4.17 - Hierarchical regression predicting Cognitive problems score in parents of children with ALL at Time 3.

Step	Variables	R^2	ΔR^2	F	p	β	p
1	***Demographic and illness factors***	0.23	0.23	2.078	0.045		
2	***Parent's symptoms***	0.52	0.29	9.014	0.0001		
	Child age						ns
	Days of hospitalization at T3						ns
	Parent age						ns
	Parent school years						ns
	Parent mean hours/weekly					0.27	0.015
	Number of siblings						ns
	Parental life stress events						ns
	N blastos at day +78						ns
	Child's mood cortisone effects					-0.21	0.040
	BSI-18 global score					0.50	0.0001
	State anxiety						ns
	Trait anxiety						ns
	Current life perception						ns
3	***Family psycho-social factors***	0.57	0.057	1.19	ns		

4.2.2.5 Parent's Psychological Health and Adaptation at T4

What happens to the parent's psychological health and adaptation in relation to child's disease factors after 1 year post diagnosis communication?

To answer this question we run descriptive statistics on parent's psychological symptoms and life perceptions (Table 4.18).

Table 4.18 - Descriptive statistics of the several measures of parental psychological symptoms and psycho-social factors.

Symptoms' score	Range	Mean	SD
PTSS	0-1	5.21	3,43
Current life perceptions	0-10	6.55	1.73
BSI-18 total score	1-5	1.97	0.90
Cognitive problems total score	1-3	1.58	0.35
		Sum	
State anxiety	1-4	45.09	12.52
EFI-C factors	**Range**	**Mean**	**SD**
Emotional coping	0-8	4.85	0.85
Trust in the medical care	0-8	6.23	1.08
Communication on illness	0-8	5.45	1.37
Routine and time reorganization	0-8	5.07	0.84
Support	0-8	4.47	1.82
Couple connectedness	0-8	5.58	1.60

We could see how parent's current life perceptions at T4 were enough high, showing a good life functioning in parents. Examining the other parental symptoms, we noted that PTSS were the most present, but with a big standard deviation that underlined huge variability between the parents.

A comment had to be paid also to the parental psycho-social factors: Trust in the medical care was really high, followed by Couple Connectedness and Communication on illness, even if they showed a great variability (big standard deviation); while Support and Emotional Coping were less high, in average, showing a sort of "pause" in using parental emotional and social support resources at this time point.

Then, we run a hierarchical regression analysis to assess the possible association between parental PTSS and the following independent variables at T4: Demographic factors (step one), Parent's symptoms (step two) and Psycho-Social Factors (step three). The best model was the second one ($R^2 = 0.38$; F = .23; p = 0.0001) showing Cognitive problems score ($\beta = 0.36$; p = 0.016) as the best factor associated with PTSS at one year post diagnosis (Table 4.19).

Table 4.19 - Hierarchical regression predicting parents' PTSS at T4.

Step	Variables	R^2	ΔR^2	F	p	β	p
1	*Demographic factors*	0.01	0.01	0.23	ns		
2	*Parent's symptoms*	0.38	0.37	6.23	0.0001		
	Child age						ns
	Parent age						ns
	Parent school years						ns
	Parent mean hours/weekly						ns
	Current life perception						ns
	Cognitive problems score					0.33	0.016
	BSI-18 global score						ns
	State anxiety						ns
	Trait anxiety						ns
3	*Family psycho-social factors*	0.49	0.11	1.67	ns		

4.3 PART B: Longitudinal analyses

4.3.1 Parent's Psychological Health and Adaptation throughout the several time points

4.3.1.1 Development and stability of Parent's Psychological Health

What sort of development and stability have parent's psychological health and adaptation along the several time points?

To answer this question we preliminary run descriptive statistics (Table 4.20). Then we run several series of repeated measures ANOVAs were performed to test the longitudinal behavior of parents' symptoms score and of their psycho-social factors. For each analysis we controlled the Mauchly sphericity test and, if not respected, we used the Greenhouse-Geisser correction.

Table 4.20: Descriptive statistics of parent's symptoms and psycho-social factors measured at the several time points

Parent's symptoms and Parent's psycho-social factors	Mean (SD) at T1	Mean (SD) at T2	Mean (SD) at T3	Mean (SD) at T4
Current life perceptions	4.48 (2.20)	-	5.43 (2.27)	6.55 (2.73)
Depressive symptoms	2.25 (0.95)	-	2.20 (0.95)	1.97 (0.90)
Arousal symptoms	2.15 (0.92)	-	2 (0.91)	1.84 (0.80)
Physical symptoms	1.66 (0.78)	-	1.63 (0.73)	1.55 (0.70)
Cognitive problems score	1.58 (0.33)	-	1.62 (0.38)	1.59 (0.35)
State anxiety	-	-	48.52 (13.53)	45.09 (12.52)
PTSS	-	5.76 (3.21)	5.48 (3.17)	5.21 (3.43)
Couple connectedness	5.06 (1.41)	-	5.67 (1.61)	5.58 (1.60)
Family routine reorganization	4.06 (0.84)	-	4.94 (1.04)	5.07 (0.84)
Parental communication around the child's illness	4.65 (0.94)	-	5.55 (1.35)	5.45 (1.37)
Trust in the medical care	5.13 (0.95)	-	6.14 (1.08)	6.23 (1.08)
Social support	4.55 (1.37)	-	4.44 (1.56)	4.47 (1.82)
Emotional coping	5.15 (0.75)	-	4.97 (0.90)	4.85 (0.85)

The first repeated measures ANOVA tested the possible time changes of parent's current life perception. Assuming the sphericity, results showed that there was a significance increase of Parent's Current Life Perception ($F_{(2,144)} = 31.17$; $p = 0.0001$). A second repeated measures ANOVA showed that, assuming the sphericity, Depressive Symptoms decreased significantly from the second week of hospitalization to post-one year ($F_{(2,144)} = 3.58$; $p = 0.030$). The same trend was found in the third ANOVA with Arousal Symptoms as dependent variable ($F_{(2,144)} = 4.26$; $p = 0.016$). The time behavior of State Anxiety was assessed by paired-samples t-test at time point T3 (post 6 months) and T4 (post 1 year). The results showed that State Anxiety dampened by time increasing ($t_{(71)} = 2.71$; $p = 0.008$). Figure 4.4 illustrated these significative results on parental symptoms in a synthetic way.

Instead nor Physical Symptoms ($F_{(2,144)} = 0.18$; $p = 0.83$) nor Cognitive Problems score ($F_{(2,144)} = 0.06$; $p = 0.93$) resulted significantly different in the three time points. Neither PTSS had a significant change during time ($F_{(2,140)} = 1.09$; $p = 0.34$).

We controlled also parents' PTSS stability throughout the several time-points. So we run Pearson's correlations between: PTSS at T2 and PTSS at T3 ($r = 0.60$; $p =$

0.0001); PTSS at T2 and PTSS at T4 (r = 0.69; p = 0.0001); PTSS at T3 and PTSS at T4 (r = 0.64; p = 0.0001).

Figure 4.4 - Results on parental symptoms that significantly different at the different time points.
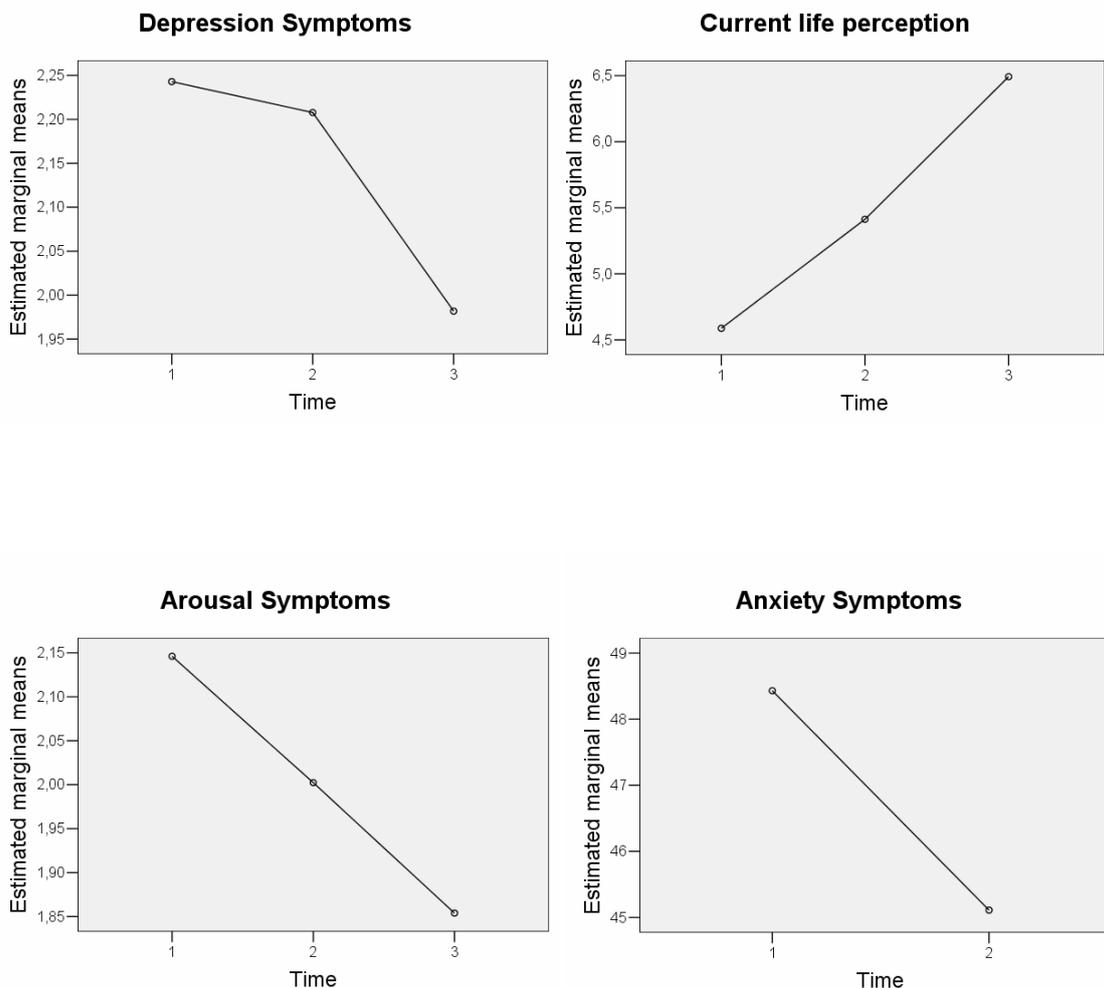
Other repeated measures analyses on parental psycho-social factors showed that Couple Connectedness ($F_{(1.74,144)}$ = 6.24; p = 0.0001), Family Routine Reorganization ($F_{(1.64,144)}$ = 47.54; p = 0.0001); Parental Communication around the child's illness ($F_{(1.72,144)}$ = 25.31; p = 0.0001) and Trust in the Medical Care ($F_{(1.74,144)}$ = 52.52; p = 0.0001) increased significantly from the diagnosis to 1 year post diagnosis. For these last analyses we used the Greenhouse-Geisser correction because the sphericity was not respected. Figure 4.5 showed these significative results on family psycho-social factors

in a synthetic way.

Figure 4.5 - Results on family psycho-social factors that significantly different at the three time points.
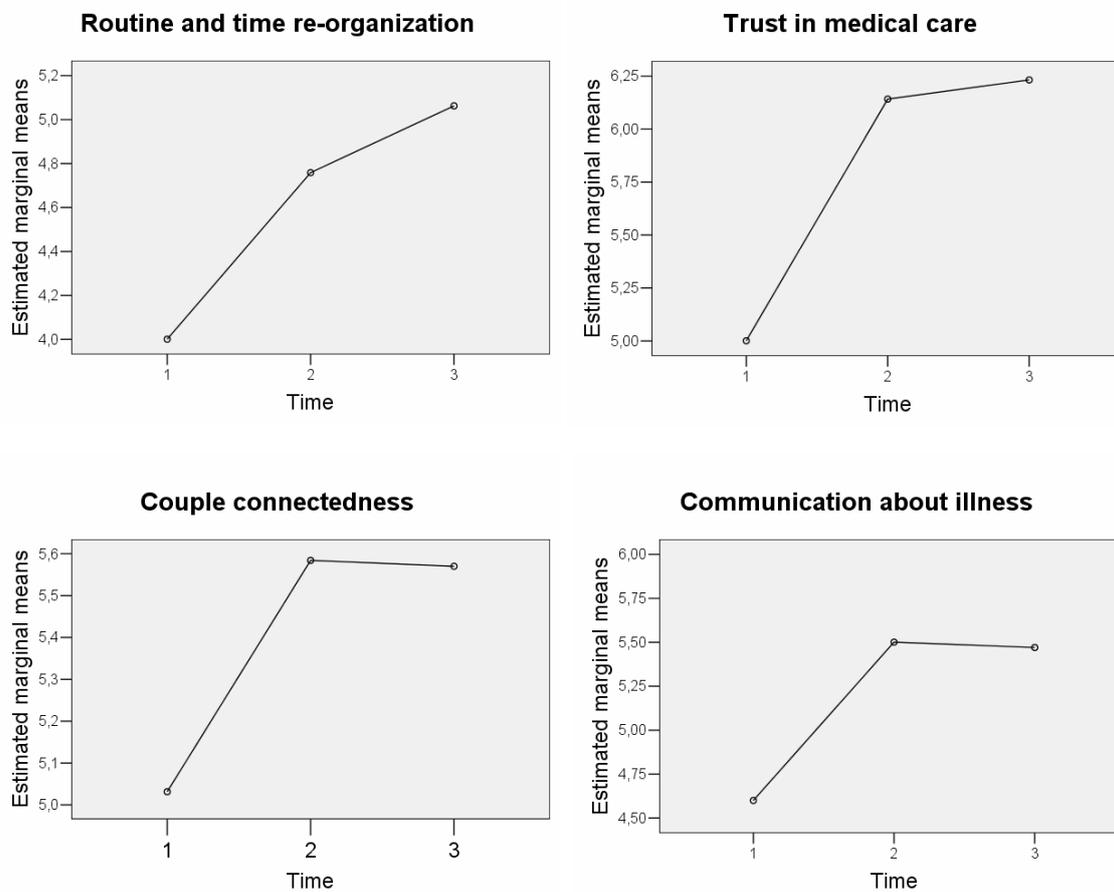
For other factors such as Social Support ($F_{(2,144)} = 0.22$; $p = 0.76$), their Emotional Coping ($F_{(2,144)} = 1.003$; $p = 0.37$) the analyses showed that they remained stable during the time, without significant changes.

4.4 PART C: Predictive analyses

4.4.1 Factors associated with child's behavioral adaptation along the several time points

4.4.1.1 Factors measured at T1 associated with Child's Behavioral Adaptation at T4

Which family, child and disease factors just after the diagnosis communication are responsible for long-term adaptation of children with leukemia after 1 year of treatments?

To answer this question three regression analyses, following Baron & Kenny (1986) rules, were used.

The significance of the path "predictor Child Coping on the mediator Parenting" was examined in the first regression ($R^2 = 0.39$; $\beta = 0.63$; $p = 0.0001$). The significance of the path "predictor Child Coping on the dependent variable VABS global scale" was examined in the second regression ($R^2 = 0.39$; $\beta = 0.62$; $p = 0.0001$); Finally, Child Coping ($\beta = 0.69$) and Parenting ($\beta = -0.11$) were used simultaneously as predictors of VABS Global Scale in the last equation ($R^2 = 0.40$; $p = 0.0001$). Mediation effect was measured by Sobel test ($Z = 4.17$; $p = 0.00003$) (Figure 4.6)

Figure 4.6: Predictor and mediator factors tested at T1 of VABS global scale tested at T4.
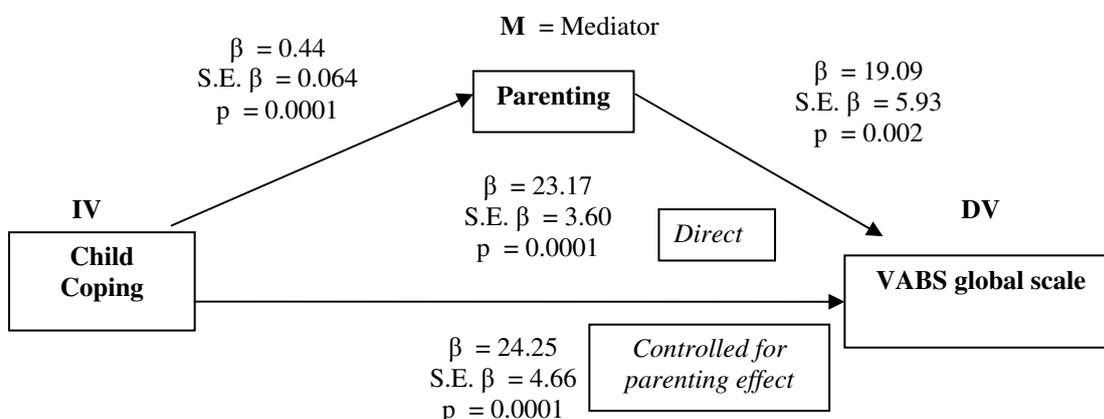
4.4.1.2 Factors measured at T2 associated with Child's Behavioral Adaptation at T4

Which family, child and disease factors after 1 month from the diagnosis communication are responsible for long-term adaptation of children with leukemia after 1 year of treatments?

To answer this question we run a hierarchical regression analysis to assess the possible predictors at T2 of VABS global scale at T4. Independent variables were entered into three steps: Demographic factors (parent's age, parent's school education, Parent's Mean Job hours/a week) and Illness factors (type of leukemia and days of hospitalization), in the first step; different parental styles of Locus of Control on child's illness cited above, in the second step and different categories of Child's Coping with pain reported by parents, in the last one. The third model resulted of signification (R^2 = 0.66; F = 5.41; p = 0.001) with Fate influence (β = -0.25; p = 0.021), Divine influence (β = 0.25; p = 0.034), Child influence (β = 0.30; p = 0.019), Child's problem solving (β = 0.27; p = 0.025) and Child's Social Support Strategies (β = -0.38; p = 0.001) that impacted upon the child's VABS Global Scale (Table 4.21).

Table 4.21 - Hierarchical regression predicting child's VABS Global Scale at T4 with independent variables assessed at T2.

| Step	Variables	R^2	ΔR^2	F	p	β	p
1	***Demographic and illness factors***	0.19	0.19	2.33	ns		
2	***Parent's PTSS and PHLOC styles***	0.41	0.22	2.35	0.040		
3	***Child coping with pain styles***	0.66	0.24	5.41	0.001		
	Child diagnosis						ns
	Parent age						ns
	Parent school years						ns
	Parent mean hours/weekly						ns
	Days of hospitalization						ns
	Parents' PTSS symptoms at T2						ns
	Parent health influence						ns
	Medical staff health influence						ns
	Divine health influence					0.25	0.034
	Child health influence					0.30	0.019
	Fate health influence					-0.25	0.025
	Media health influence						ns
	Child Seek for social support					-0.38	0.001
	Child Problem Solving					0.27	0.025
	Child Catastrophizing						ns
	Child Cognitive self-instruction						ns
	Child Distraction						ns

4.4.1.3 Factors measured at T3 associated with child's behavioral adaptation at T4

Which family and disease factors after 6 months from the diagnosis communication are responsible for long-term adaptation of children with leukemia after 1 year of treatments?

To answer this question we run a hierarchical regression analysis to assess the possible predictors at T3 of VABS global scale at T4. Independent variables were entered into three steps: Demographic factors (parent's age, parent's school education, Parent's Mean Job hours/a week) and Illness factors (type of leukemia and days of hospitalization), in the first step; several Parental Symptom scores (Current Life perceptions, Cognitive problems score; BSI-18 Global score, State and Trait Anxiety scores), in the second one, and 6 family Psycho-Social Factors, in the last one. The third model resulted of signification ($R^2 = 0.42$; F = 2.82; p = 0.018) with Current Life perceptions at T3 (β = 0.34; p = 0.019) and Communication about the child's illness at

T3 (β = 0.50; p = 0.0001) that impacted upon the child's VABS global scale at T4 (Table 4.22).

Table 4.22 - Hierarchical regression predicting child's VABS Global Scale at T4 with independent variables assessed at T3.

Step	Variables	R^2	ΔR^2	F	p	β	p
1	*Demographic and illness factors*	0.08	0.08	1.29	ns		
2	*Parent's symptoms at T3*	0.24	0.15	1.75	0.039		
3	*Family psycho-social factors at T3*	0.42	0.17	2.82	0.018		
	Child diagnosis						ns
	Parent age						ns
	Parent school years						ns
	Parent mean hours/weekly						ns
	Days of hospitalization at T4						ns
	Parent's current life perception					0.34	0.019
	Cognitive problems score						ns
	BSI-18 global score						ns
	State anxiety						ns
	Trait anxiety						ns
	Emotional Coping						ns
	Trust in the medical care						ns
	Communication about the illness					0.50	0.0001
	Routine and time reorganization						ns
	Parenting						ns
	Support						ns
	Couple connectedness						ns

4.4.2 Factors associated with Parent's Psychological Health and Adaptation along the several time points

4.4.2.1 Factors measured at T1 associated with Parent's Psychological Health and Adaptation at T2

Which family and child factors are responsible for short-term PTSS of parents of children with leukemia one month after the diagnosis?

To answer this question we preliminary run correlation between our variables. Then a LISREL path model was performed to test whether family and illness factors

were related to PTSS at 6 months post diagnosis. Figure 4.7 shows the results.

From the several parental psycho-social factors we saw that Emotional Coping and Support received were key elements impacting, the first, on their Memory abilities, and, the second, on their Perceptions of their Current Lives. All these family factors were also related also to parents' BSI-18 Global score assessed at the diagnosis and indicative of short-term PTSS problems.

Figure 4.7 - Structural standardized coefficients of hypothetical model of path-analysis. All the coefficients were significative for p<.005. The model presented good fit indices (χ^2(9) = 8.83; N = 100; p = 0.45; RMSEA = 0.0001; NNFI = 1; CFI = 1) (Engel et al., 2003).
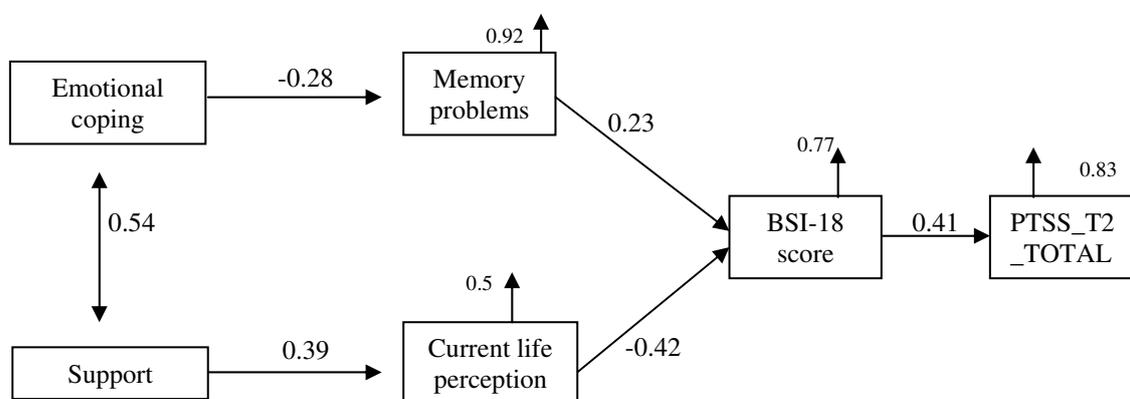
A linear regression model controlled for moderation effect was used only on children with ALL sample to identify the family and illness factors that significantly impacted upon parents' PTSS at T2. After preliminary correlations, we tested as predictor the Physical Symptoms and as moderator the Number of Blastos communicated at day +8. Figure 4.8 illustrates the results. Regression approach was used here for testing moderated effects. The predictor and moderator main effects were entered simultaneously into the regression equation first, followed by the interaction of the predictor and moderator respectively centered.

Figure 4.8: Moderation effect and predictive factor of parent's PTSS at T1 in only ALL sample.
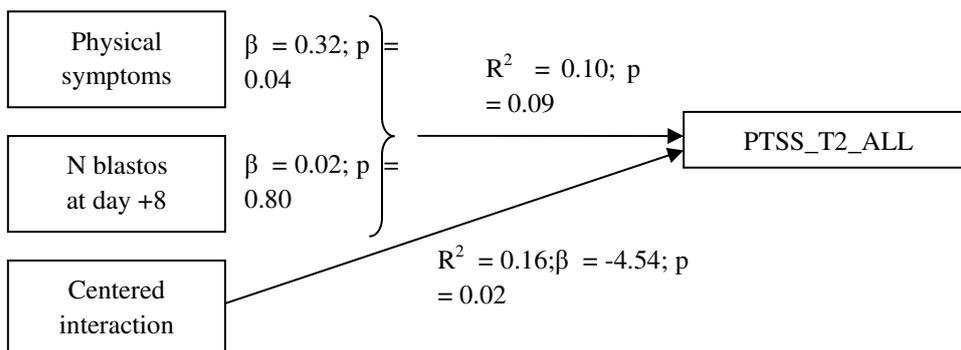
4.4.2.2 Factors measured at T1 and T2 associated with Parent's Psychological Health and Adaptation at T3

Which family and child factors assessed at T1 and T2 are responsible for psychological functioning of parents of children with leukemia 6 month post-diagnosis?

To answer this question we run a hierarchical regression analysis to assess the possible predictors at T1 and T2 of parents' psychological symptomatology at T3. The first model had as dependent variable the Parental Current Life perceptions at T3. Independent variables were entered into three steps: Demographic factors (parent's age, parent's school education, Parent's Mean Job hours/a week; parents' life stress events; child's age) and Illness factors (type of leukemia and days of hospitalization), in the first one; 6 family Psycho-Social factors assessed at T1, in the second one, and Parents' Symptoms and Cognitive functioning assessed at T1 and T2 (BSI-18 Global score; cognitive dysfunctioning score; PTSS), in the last one. The second model resulted of signification ($R^2 = 0.31$; F = 2.73; p = 0.014) with Child's Age ($\beta = 0.26$; p = 0.042), Parent's Mean Job hours/a week ($\beta = -0.22$; p = 0.048), Family Routine and Time Reorganization ($\beta = 0.31$; p = 0.049) and Support ($\beta = 0.32$; p = 0.043) that impacted upon the Parental Current Life Perception at T3 (Table 4.23).

Table 4.23 - Hierarchical regression predicting Parents' current life perception at Time 3.

Step	Variables	R^2	ΔR^2	F	p	β	p
1	*Demographic and illness factors*	0.13	0.13	1.53	ns		
2	*Family psycho-social factors*	0.27	0.13	2.13	0,014		
	Child age					0.26	0.042
	Days of hospitalization T3						ns
	Parent age						ns
	Parent school years						ns
	Parent mean hours/weekly					-0.22	0.048
	Number of siblings						ns
	Parental life stress events						ns
	Child diagnosis						ns
	Emotional Coping						ns
	Trust in the medical care						ns
	Communication about the illness						ns
	Routine and time reorganization					0.31	0.049
	Parenting						ns
	Support					0.32	0.043
	Couple connectedness						ns
3	*Parent symptoms*	0.38	0.07	2.63	ns		

The same independent variables except for a change in the third step of BSI-18 global score with Parental current life perception and a new dependent variable, BSI-18 global score at T3 were entered for the second hierarchical regression model. The third model resulted of signification ($R^2 = 0.42$; F = 7.04; p = 0.0001) with Parent's Age (β = -0.29; p = 0.012), Family Routine and Time Reorganization (β = -0.32; p = 0.035) and PTSS (β = 0.32; p = 0.004) that impacted upon the BSI-18 Global score at T3 (Table 4.24).

Table 4.24 - Hierarchical regression predicting Parents' BSI-18 global score at Time 3.

Step	Variables	R^2	ΔR^2	F	p	β	p
1	*Demographic and illness factors*	0.14	0.14	1.64	ns		
2	*Family psycho-social factors*	0.24	0.10	1.47	ns		
3	*Parent symptoms*	0.42	0.17	7.03	0.0001		
	Child age						ns
	Days of hospitalization T3						ns
	Parent age					-0.29	0.012
	Parent school years						ns
	Parent mean hours/weekly						ns
	Number of siblings						ns
	Parental life stress events						ns
	Child diagnosis						ns
	Emotional Coping						ns
	Trust in the medical care						ns
	Communication about the illness						ns
	Routine and time reorganization					-0.32	0.035
	Parenting						ns
	Support						ns
	Couple connectedness						ns
	Cognitive problem score at T1						ns
	Parent's PTSS at T2					0.32	0.004
	Parent's current life perception						ns

In the last regression analysis we entered the same independent variables of the second analysis except for a change in the third step of Cognitive Problems score with BSI-18 global score and a new dependent variable, Cognitive Problems score at T3. The third model resulted of signification ($R^2 = 0.41$; F = 7.17; p = 0.0001) with PTSS (β = 0.38; p = 0.001) that impacted upon the Cognitive Problems score at T3 (Table 4.25).

Table 4.25 - Hierarchical regression predicting Parents' cognitive problems score at Time 3.

Step	Variables	R^2	ΔR^2	F	p	β	p
1	*Demographic and illness factors*	0.12	0.12	1.37	ns		
2	*Family psycho-social factors*	0.23	0.11	1.62	ns		
3	*Parent symptoms*	0.41	0.17	7.17	0.0001		
	Child age						ns
	Days of hospitalization T3						ns
	Parent age						ns
	Parent school years						ns
	Parent mean hours/weekly						ns
	Number of siblings						ns
	Parental life stress events						ns
	Child diagnosis						ns
	Emotional Coping						ns
	Trust in the medical care						ns
	Communication about the illness						ns
	Routine and time reorganization						ns
	Parenting						ns
	Support						ns
	Couple connectedness						ns
	BSI-18 global score at T1						ns
	Parent's PTSS at T2						0.38	0.001
	Parent's current life perception						ns

We run other three hierarchical regression models only on parents of children with ALL, entering in the first step specific illness variables related to ALL protocol such as Psycho-Social Cortisone Effects and Number of Blastos communicated at day +78. The three regression models were similar to the models run for parents of children with all types of leukemia. No illness variables specific for children with ALL resulted predictor of parents' symptomatology.

CHAPTER 5

DISCUSSION

>*"These things happen, yes…one tries not to think about them…it is a hard test, a hard test for a person's balance this one…keep in mind that at the beginning one works as a person who is travelling between two parallel worlds which do not touch each other.*
>*The world of the ill and of the illness is like another world facing the normal, external world and you are in between these two worlds.*
>*If you do not have a strong shoulder to which you can lean to sustain the two worlds…it is easy to get lost."*

In the last decades there has been a growing importance of psycho-social aspects in pediatric oncology. Pediatric psycho-oncology has become an important research and clinical field that has focused on suffering children and adolescents and their families and on their adjustment to the illness. Psychosocial functioning in pediatric cancer patients and families has been particularly monitored.

The medical advance in the treatments for cancer and the increase probability of survivorship that derived from it (Ries et al., 2005) have prompted studies of long-term health and psychological consequences of treatments for childhood cancer both in childhood survivors (Patenaude & Kupst, 2005; Nathan et al., 2007; Clarke & Eiser, 2007) and in their families (Bruce et al., 2006; Manne et al., 2002) showing generally several negative psychological consequences.

However, only a few studies have assessed the psychological functioning of parents of children with leukemia throughout the therapies' timing (Magal-Vardi et al., 2004; Phipps et al., 2005; Kazak et al., 2005) and there are no existing prospective

studies, adopting an ecocultural point of view, that identifies possible early predictors of PTSS in parents and possible family predictors of newly diagnosed child's adaptation and quality of life.

The family factors predicting short and long-term adaptation of children with leukemia and their psychological functioning throughout therapies' timing are, nowadays, an ongoing concern. This study is the first part of a larger longitudinal project on family factors predicting short- and long-term adaptation and quality of life of leukemic children. The original research project aims at investigating the psycho-social effects of a diagnosis of cancer on both child adaptation and parental issues. The prospective design and the multi-method approach (questionnaires, self-report measures, in-depth interviews) of this study has allowed to fill up this gap in the literature, giving a contribution to the scant prospective literature on the psychological adaptation of children diagnosed with leukemia and their families.

The project was aimed at following children and parents from the diagnosis of leukemia for the two following years of therapies. More specifically, the focus of the whole project is been on three main issues: Identifying the possible family predictors of short and long term psycho-social adaptation and quality of life in children with leukemia; assessing child's and parent's psycho-social risk and their psychological functioning throughout therapies' timing; identifying early predictors of PTSD symptoms in parents of children under therapy for leukemia. The first has referred to the ways in which family, child and illness factors impact upon the child's quality of life early after the diagnosis and upon child's adaptive functioning after one year of therapies. The second has focused on the identification of parents and children more at risk for psycho-social problems by a screening assessment at the several time points of the two years of therapies. The third issue has centered on the way in which parents' post traumatic stress symptoms behavior along the therapies' time and the possible stable and modifiable factors associated.

The discussion of our findings upon these three main research issues will be presented following the major questions of our research both related to child and her/his parents. The several time points from the diagnosis will be used as organizer parameter, firstly presenting the concurrent hypotheses on child's and parent's adaptation and psychological health at the several assessment-steps (Part A), secondly the longitudinal hypotheses on parent's adaptation and psychological health throughout the therapies (Part B) and thirdly the predictive hypotheses about the factors that impact upon parent's adaptation and psychological health between the several time points (Part C).

5.1 Concurrent analyses upon Child's coping, adaptation and quality of life in the first year of therapies

5.1.1 Child's Quality of Life at T1

First of all, we considered which family and child factors are responsible for quality of life of leukemic child. In particular, we focused on Health Related Quality of Life (HRQOL) of children with leukemia assessed by parents' perceptions. We have seen in paragraph 2.1.2 that mothers can be reliable enough in these perceptions and we have noted that in-depth interviews could give more information of the meaning of Quality of Life for the children with leukemia during their first hospitalization.

On this topic the literature give us only some poor contributions, identifying only communication with others (Yeh et al., 2002) and child's fatigue (related to: Procedures, sedation, venous access device, staff interactions, symptoms due to its causing limitations on activity) (Hicks et al., 2003) as possible predictors of child's HRQOL. This child's fatigue might be exacerbated by the emotional and mental energy needed to cope with facing the unknown and the unfamiliar routine of coming to the clinic or hospital (Davies et al., 2002). Also psychosocial issues such as hopefulness,

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family/peer isolation might impact on the short and long term adaptation of the children and of their families. Together with the child's age and her/his capacity of coping, when she/he are diagnosed with cancer, the entire environment in which she/he is changes, transforming from a regular developmental niche (Super & Harkness, 1986) to a caring niche (Axia et al., 2004). This sudden and traumatic change requires an adaptation of the child, the parent and the interaction of the two, and puts child's development in a status of risk. Taking into account this new perspective, what are the possible early family predictors of newly diagnosed child's quality of life?

In this sense there is no study that verifies an empirical model that linked the several context psycho-social variables useful to maintain a positive quality of life in children with cancer in their first hospitalization. Specifically, the aim is to identify the weight of fixed factors and modifiable moderators of child and his/her family on child's quality of life, following the definition of Hoekstra-Weebers et al. (2000).

The path-model that we have found significative shows that Child's Quality of Life is predicted by Parental trust in the medical staff, by Child's Coping and by Child's Adaptability. These last predictors are in turn sustained by the fixed factor child age and by the modifiable factor Parenting. Parenting is also directly predictive of child's QoL, but less than by child's coping mediation effect. Child's Age influences both coping and adaptability, which is sustained also by parental trust in medical staff. Illness factors at the beginning of therapies don't have an impact on Child's Quality of Life.

To sustain these results we can consider that developmental differences have been found in several other studies: Particularly, older children use more cognitively oriented coping methods (emotion-focused coping, information-seeking, problem solving, abstract thinking), while younger children use more active coping to change the environment (approach, problem focused) (Aldrige & Roesch, 2006). Especially for the younger children, it is necessary to take into consideration parents' description of their behaviors to understand their possible psychological reactions to the illness and to its

treatments (Earle & Eiser, 2007). Also parents are very important for child's health throughout the therapies as they can inform health professionals about their children's states and quality of life, especially at the beginning of the treatments when doctors and nurses do not yet know them. Their capacity of parenting is of paramount importance because it helps the child to cope better with the illness during the hospitalization sustaining the idea of the caring niche explained above. Also parental trust in the medical care is a key element that sustains child's quality of life during the first hospitalization: Parents' capacity of acceptance of this new live environment (constituted by medical staff, volunteers, psychologists, nurses and all the comfortable allocations) allows child to adapt better to the hospitalization with an increase of her/his quality of life.

5.1.2. Child's Coping with Pain at T2

Previous studies have shown that in the first weeks following the diagnosis of leukemia child's adaptation and quality of life might be impaired by the general psycho-social difficulties in emotion regulation to cope with painful medical procedures (Wallander & Varni, 1998), in particular in younger children that show more distress than older ones (Jacobsen et al., 1990). However the emotional disturbance doesn't always cause evident psychological symptoms (Michalowski et al., 2001). The precise way in which child responses likely depends on many factors, including also chronological age and gender. Age is likely to reflect knowledge and understanding of the illness and may impact as we have seen also above on coping and adjustment (Aldrige & Roesch, 2006). Equally, the issues of concern for males, such as whether or not they can play their best sport, may differ from girls who may be more concerned about hair loss.

Children's reactions to painful events vary widely (Schecter et al., 1991) but there is a fairly wide consensus on the fact that children with cancer may have special

difficulties in dealing with the stressful medical procedures needed for the treatment of their disease (Sourkes, 2000). We have stressed also that in problem/emotion focused coping three factors categories must be examined: Illness parameters (type, severity, treatment), personal factors (cognitive resources, age and past experiences, gender, temperament) and social factors (protective or risk factors related to family, peers support, environment support) (Axia et al., 2004; Figure 1.7). Particularly, in an Italian study on coping with pain in healthy school-aged children (Bonichini & Axia, 2000) that used the same instrument adopted in our research, Seek for social support is identified as the best strategy and the use of the cognitive strategies such as Problem Solving and Cognitive Self-Instruction increase with age.

How children's age impact on their coping with the illness? Which is the best strategy adopted by leukemic children? Could family symptoms influence child's coping with pain?

Regarding these questions we expected that: The cognitive strategies increased with child's age; seek for social support was the most used strategy; child's catastrophizing behavior was directly influenced by parent's symptomatology and indirectly by child's coping and adaptability assessed at the diagnosis-time. We did not expect diagnosis effect on children's coping with pain, because we had thought that these aspects assessed at the first month of hospitalization for treatments were similar in both types of leukemias.

Our results definitely confirm this set of hypotheses showing that: Problem solving and cognitive self-instructions are more used by child's age increasing; seek for social support is the preferred strategy of our sample; catastrophizing is significantly associated with parental cognitive problems at T1 and negatively correlated with child's coping and adaptability measured at the second week from the diagnosis.

These data give relevant information on coping with pain used by children with leukemia at their first hospitalization. Specific interventions can be applied to children

taking into consideration their age and their preferred coping strategy. Other supportive interventions can be studied for parents at more risk for cognitive problems at the diagnosis so to dampen the catastrophizing using of their children, not successful for a good adaptation. Preliminary child coping and adaptability can be early predictors of their capacity to use several strategies to front pain also after one month of hospitalization.

5.1.3 Child's Adaptive Behaviors at T4

We had seen that children with leukemia are often hospitalized for long periods because of their immunosuppressed status and because of the therapies; this might place them at further risk for psychosocial developmental delays. The cognitive impairments related to antitumoral drugs and to the blood stem cell transplantation (Waber et al., 2000; Jansen et al., 2005), the general psycho-social difficulties in schooling tasks (White, 2003; Lähteenmäki et al., 2002) and in social relationships (Vance & Eiser, 2002; Adamoli et al., 1997) impact upon their development status.

Which are the types of developmental deficits in adaptive behaviors in children with leukemia and what kind of association with children temperament and with family factors one year after the diagnosis communication there are?

In regard to this question we expected that children with leukemia under treatment have particularly socialization problems related both to interpersonal relationships and to the respect of social and community rules, particularly due to their isolation experience. We also had thought that children under 6 years of age could have difficulties in their motor abilities proportionally to their days of hospitalization. The only study assessing adaptive functioning in children with cancer adopting the Vineland Scales showed a significative decrease in adaptive scores during the first year after the blood stem cell transplantation (Kramer et al., 1997). In this context of cancer no study has analysed the possible association between children's temperament factors and their

behavioral adaptation. We had expected to find a negative association between some child's developmental scales (Communication, Daily Living Skills, Socialization) with Negative Emotionality and a positive relation with Social Orientation and Attention (from QUIT).

Our findings confirm partially these hypotheses: The situation of child's developmental delays of almost three months at T4 in the four domains of Vineland Scales is particularly important for child's Socialization development, followed respectively by Motor scale and by Daily Living Skills. So also motor abilities are in significative delay and this is positively associated with child's type of leukemia and with days of hospitalization. Children with AML and with more days of hospitalization are more at risk for developmental delays in their motor abilities one year post treatment for leukemia. Motor activities score related to child's temperament is also positively related with VABS motor developmental score, showing that also child's temperament is a key element in measuring child's development. Children with a low temperamental score in Motor activities are more at risk to have a negative impact on their motor development.

All the domains of child's development assessed by Vineland scales are strongly associated one to each other showing how child adaptive behavior is a unique construct formed by several sub-domains.

5.2 Concurrent analyses on Parent's Psychological Health and Adaptation in the first year of therapies

The literature on families of children with cancer has underlined that, when a child was diagnosed with cancer, the whole family system, and often the broader social context, is affected and the previous accommodations and homeostasis are broken. Consideration of parent/caregiver variables is considered critical when conducting

research with children facing life-threatening illness, given the impact of parent functioning on child functioning. Moreover, because parents are been often used as proxies to assess the quality of life and functioning of the child, their perceptions, functioning and adjustment have need to be considered.

5.2.2 Parent's Psychological Health and Adaptation at T1

Each phase of the disease confronts parents with different problems and thus requires the learning of new coping skills and patterns (Eiser, 1993; Swallow & Jacoby, 2001; Yeh et al., 2000).

The most difficult period for parents and families happens just after the diagnosis (Sheeran et al., 1997; LaMontagne et al., 1999; Sawyer et al., 1986; 1997; 2000; Sloper, 1996) when child undergoes several invasive medical procedures (e.g., bone marrow aspirates, lumbar punctures) and treatments (e.g., chemotherapy), and when a new family "reality" must be built up (Clarke-Steffen, 1993). Also some family resources are posed at risk. For example, marital dissatisfaction in parents of children with cancer may be present in about one parent of every four (25% of mothers, 28% of fathers, according to Dahlquist et al., 1993).

Unfortunately, a notable percentage of parents are not able to make a pathway for good adjustment and quality of life and remain indelibly scorched by the experience (von Essen et al., 2004). Researchers report increased emotional distress, such as anxiety or depression, in these parents against normative data (Dahlquist et al., 1993; Manne et al., 1995). In longitudinal studies also increased negative emotions such as anxiety, depression, insomnia or somatic and social dysfunctioning shortly after diagnosis are found (Sawyer et al., 2000; Pelcovitz, 1996; Van-Dongen Melman et al., 1995).

So our question was: What happens to the parent's psychological health and adaptation in relation to child's disease factors in the second week after the diagnosis

communication?

In this acute first phase we had expected to find lower scores in parents' current life perceptions, and higher scores in their symptomatology manifestations as the literature suggested us. We also had made the hypothesis about which factors could impact on parents' psychological state: Diagnosis type, with parents of children with AML more in difficulty than those of children with ALL; child's age and parents' age, with a best situation with increasing age; social support and couple connectedness perceived as valid resources to dampen their psychological symptoms and to get better their cognitive functioning.

Our findings confirm partially these hypotheses: Child's diagnosis, child's age, parent's age and social support impact upon parents' current life perceptions. In detail, parents of children with AML perceive a worse life than parents of children with ALL. This finding is also sustained by the literature (McGrath et al., 2001). For child's age we can make the consideration that the increasing age of the child is positively associated with her/his evolutionary coping strategies so to help parents in their caregiver role, dampening the possible psychological outcomes. At this purpose we also think that older parents can have more experience to care for children and that they can be more "expert" in their parenting role in this difficult time. Social support is recognized by the literature as a valid resource to help parents coping with the child's illness, especially in this acute time (Hoekstra-Weebers et al., 2001; Sloper, 2000).

Beside the factors just mentioned, also parent's mean hours job/a week and couple connectedness impact upon specific parents' cognitive problems. Job duties at this time seem to request to parents too many resources so they react with cognitive problems such as disorganization, memory and concentration malfunctions. Couple connectedness seems to help parents in their capacity of reasoning in this difficult situation, showing how partner can be a valid resource.

We also wanted to see exclusively the psychological health of parents of children

with ALL, for whom we supposed that the number of blastos communicated to parents at the day + 8 could increase the difficulties in their cognitive and psychological functioning. This our supposition didn't derive from the literature because no study has investigated the psychological effects of this particular communication to the parents of children affected by ALL. We thought that this type of communication at this time could be crucial for parents because it just gave them a preliminary response of first therapies on child's illness status.

In this case cognitive problems are significantly predicted by: Parent's mean hours job/a week; by family's routine and time reorganization; by couple connectedness and by number of blastos at day +8. Parents' cognitive problems get worse by number of blastos at day +8 increasing and also by their strains to reorganize family's times and routines after the diagnosis communication. More social support received at this acute phase and less number of blastos at day +8 dampen parents' psychological symptomatology (BSI-18 total score). No study before has investigated the relations of this important communication to parents about their child's response to the illness and their psychological functioning.

5.2.3 Parenting Behavior at T1

Adherence to pediatric cancer treatment can be difficult for families, especially when the child is a young child and the required tasks include medical procedures (mouth care, conducting physical exams, venepunctures, bone marrow aspirations, etc.) (Manne et al., 1993). Parent's child-rearing attitudes and practices, with the supportive parenting style as the best one, are really a key element in the child's life during the illness. So we wanted to respond to this question: How child's ages affects parenting behavior at T1? We expected that parenting behaviors were different in relation to child's age, with a more necessary and intensive care for infants and toddlers in respect to the older children.

As expected, the analysis reveals the presence of a significant group difference on parenting by child's age: Infants require a higher and more intensive parenting behavior, followed respectively by scholar-age children and by pre-scholar age children. We think that these findings confirm the difficult role of parents in caring their children when they are younger: Infants routines change so much due to hospitalization in an important developmental time that need more energy directed to them. But also the scholar age can be critical in another sense, because the children have more comprehension of the situation, a capacity that sometimes is useful, but that requires intensive parents' communication and support. Parents of school-aged children have to manage their parenting functions for helping them to tolerate the school and the peer relationship absences. Probably pre-scholar aged children have fewer needs in the sense of linking with the previous routines (school, sports, social activities) and they require only the physical presence of the parent into the hospital daily activities, but not more.

5.2.4 Parent's Health Locus of Control and PTSS at T2

There are no specific studies on parental health locus of control in a context of children with cancer. Basing on the literature on health locus of control, we expected that parents invested a lot on their internal locus of control (self-perceived efficiency in their parenting role and in their psychological resources), but also in the external locus of control (such as the same child, health professionals or God). So we investigated what happened to the parents' locus of control and to their psychological health in relation to child's disease factors in the second month after the diagnosis communication.

Particularly, we made the hypothesis that parents' internal locus of control was related to a positive perception of their life and a lower psychological symptomatology and that children's influence on their illness was perceived higher by parents with children's increasing age.

Our findings show that parental influence (a type of internal locus of control strategy) is the most used, followed by the following external health control strategies: Medical staff influence; divine influence and child influence. Then we find that parent's current life perception tested in the second week after the diagnosis communication is the best predictor of parental influence post one month. This instrument of current life perception just at the beginning of child's treatment gives us a measure to identify parents more in difficulty in their parental role and self-estimation to care the child during the illness.

Other findings are that the parental perceptions of their children's influence on the illness are positively associated with child's increasing age and with better parental current life perceptions at the diagnosis time. It seems that parents of older children take more into consideration their capacity to manage the illness and that parents' current life perception is also a hope estimation that help them to believe also in their child's own resources.

There was no study that has investigated parents' psychological health at this specific time point. The literature that reviewed parental PTSS during child's treatment is really poor (Phipps et al., 2005; Kazak et al., 2005). Basing on these few studies we imagined that PTSS would be high in this early phase, especially intrusion symptoms, and related to child type of leukemia, with a major presence of post-traumatic symptoms in parents (especially arousal symptoms) of children with AML. Our findings show that parental PTSS was relatively high, with the more frequent total number of these symptoms concentrated between 4 to 9 (65.5%). Intrusion symptoms, followed by avoidance and arousal ones, are the more frequent at this time point. No difference by diagnosis type in this early phase is discovered.

5.2.5 Parent's Psychological Health and Adaptation at T3

We started our reflections from this probing question: What happens to the

parent's psychological health and adaptation in relation to child's disease factors after 6 months post diagnosis communication?

We evaluated at this time-point the amount of PTSS and possible child, illness and family factors associated with it. No study in the literature is specific at this time point, but we had taken ideas from other retrospective or longitudinal studies about PTSS in parents of children with cancer.

Particularly, we have taken into consideration an interesting study on mothers and fathers of childhood cancer survivors (Kazak et al., 1998) that developed a model of possible factors associated with PTSS: Anxiety was the strongest predictor followed by some current family and individual variables (individual contributions of perceived life threat, perceived treatment intensity, and social support). Objective medical data did not contribute to posttraumatic stress symptoms.

So we expected a similar finding in our sample of parents of children under treatment.

We thought that anxiety assessed at the same time was strongly associated with PTSS and we also imagined that parent's emotional coping (related to individual contributions also of perceived life threat and of perceived treatment intensity) influenced this type of symptomatology. At this purpose, Barrera et al. (2004) found that in mothers of children newly diagnosed with cancer emotion-focused coping and child behavior both predicted depression, anxiety and global mental health.

We did not presume that social support could be an important factor, because the literature didn't converge about this idea (Pelcovitz et al., 1996) and because we had thought that it could be quite stable during the different time points and so probably not influent.

The literature identified also the family cohesion as a possible factor associated with parental low level distress at 6 months after the diagnosis (Sloper et al., 2000). So we also expected that family routine and time reorganization, that dealt with family

cohesion, were associated with a lower post-traumatic symptomatology in parents of children with leukemia at 6 months after the diagnosis.

Another parental factor that we thought related to parents' PTSS was their level of cognitive dysfunctioning (related to memory, concentration, distraction, impulsivity, labile mood) because the literature on adult cancer survivors found a relation between PTSD and cognitive functions, especially the memory (Nakano et al., 2002; Kitayama et al., 2005).

Our findings show a model that pictures parental PTSS post 6 months of therapies as significantly sustained directly by family routine and time reorganization. A more strongly association is found by mediation effect of parental cognitive and anxiety problems at the same time point.

We can note how a new important factor as family routine and time reorganization that entries as predictor of PTSS at this time point. At this moment the ill child is under a strong therapy of chemioterapics and steroids and all the family system is involved in a consuming activity of routine and time reorganization to maintain its caring homeostasis. State anxiety problems put parents to cope worse in this family reorganization and increase their post-traumatic symptoms. Also cognitive problems tend to obstacle a good practical and psychological functioning in parents.

Taking into consideration this difficult time-therapy, we decided to analyse exclusively the behaviors of parents of children with ALL. The literature showed that parents' experience of caring for their child during treatment with steroids was emotionally very difficult, experiencing the children's emotional states as very demanding, with children up all night eating and not sleeping (McGrath & Pitcher, 2002). So we expected that ALL children's bad behaviors and mood reactions to cortisone could impact negatively on parental mental health, especially on their cognitive and psychological functioning. These expectations are unfortunately partially confirmed by our findings. Child's mood cortisone effects and parent's cognitive

problems score impact on parental total symptoms (BSI-18 global score), showing that caring children under cortisone effects added to parental cognitive disorientation represent really a consuming activity for parents. Child's mood cortisone effects, Parent's Mean Job hours/a week and BSI-18 global score also impact on parental cognitive problems score. So cortisone effects on child's mood put in crisis both cognitive functioning and psychological symptoms in parents.

5.2.6 Parent's Psychological Health and Adaptation at T4

What happens to the parent's psychological health and adaptation in relation to child's disease factors after 1 year post diagnosis communication?

No study specific at this time point is present in the literature, so we took into consideration the literature on PTSS in survivors just mentioned above. To answer this question we thought that parents' post-traumatic stress and other psychological (depressive, physical, arousal) symptoms were a bit lower at this time point, but still present (Phipps et al., 2005; Magal-Vardi et al., 2004).

Our findings confirm this hypothesis: Parent's current life perceptions are enough high, showing a good life functioning in parents. Examining the other parental symptoms, we can note that PTSS are the most present, but with a big standard deviation that underlined huge variability between the parents. A comment has to be paid also to the parental psycho-social factors: Trust in the medical care is really high, followed by couple connectedness and communication on illness, even if they show a great variability (big standard deviation); while support and emotional coping are less high, in average, showing a sort of "pause" in using parental emotional and social support resources at this time point.

We also hypothesized that the best factor associated with PTSS could be the level of state anxiety according to the literature just mentioned above. We thought also that PTSS was correlated with the other depressive and arousal symptoms and with

cognitive dysfunctioning. We presumed that family routine and time reorganization was an important prognostic factor negatively associated with PTSS as mentioned for the precedent period of post-6 months. We thought also here that days of hospitalization were not influent to parents' psychological health state.

Our findings don't confirm totally these hypotheses: Cognitive problems score is the unique factor associated with PTSS at one year post diagnosis. Other our hypothetical factors such state anxiety, depressive and arousal symptoms and family routine and time reorganization don't impact upon parental PTSS at this time point. Probably, state anxiety, depressive and arousal symptoms are lower at this time point because less stable during time respect the PTSS. Family routine and time reorganization is not influent because at this time point the child is under a less strong therapy, only oral and with less hospitalizations and day-hospital check-ups. Cognitive problems instead have a characteristic more permanent during time (Nakano et al., 2002; Kitayama et al., 2005) and for this reason they can be an important factor that impact on parental PTSS at long term. Cognitive functions, regarding especially memory or concentration or organization, may be impaired by the trauma of the child's illness and they may be associated to parents' Post-traumatic symptoms such as uncontrollable intrusion thoughts, avoidance behaviors and high arousal.

5.3 Longitudinal analyses on Parent's Psychological Health and Adaptation throughout the several time points

5.3.1 Development and stability of Parent's Psychological Health

We have seen that in most pediatric tumors, different phases can be identified: The pre-diagnostic, the acute, the chronic, the remission or off-therapy phase. Each phase requires its own adaptations, yet the first, acute phase is the one which requires

the complete modification, often the upturning, of the previous family life and routines.

The literature about the longitudinal incidences of parental psychological symptoms throughout all the child's treatment mainly identified the acute phase as the most stressful period for parents (LaMontagne et al., 1999; Sawyer et al., 1986; 1997; 2000; Sloper, 1996) with the presence of negative emotions such as anxiety, depression, insomnia or somatic and social dysfunctioning (Sawyer et al., 2000; Pelcovitz, 1996; Van-Dongen Melman et al., 1995). Thereafter, psychological stress tends to decrease (Bracken, 1990; Wijnberg-Williams et al., 2006), but it does not go back to normal values (Hoekstra-Webers et al., 1996). For example, neither mothers nor fathers' mean of marital adjustment scores changed over time (Dahlquist et al., 1996) and self-perceived social support behavior hadn't a unique timing-behavior, being such a controversial concept in the literature (Manne et. Al, 2000; Dockerty et al., 2000).

The specific literature about parental self-reported PTSS shows a high incidence of these symptoms at the beginning of the child's treatment, but also that they are still present approximately 2 years following diagnosis (Phipps et al., 2005). Anxiety is elevated at diagnosis but declines for most parents as treatment begins and the family accommodates to the new "routines" in their lives (Steele et al., 2004). There is long term stability for families' psychosocial risks (as measured here) in the time range from 3 to 6 months after the diagnosis (Kazak et al., 2003).

So we formulated this research question: What type of time trend is related to the parent's psychological health and adaptation along the several time points?

Basing on this literature reviewed, we expected to find a significant decrease along the first year of child's therapies of the parental general symptomatology such as anxiety, arousal, depression with a general better perception of their lives and that parental PTSS would have remained stable and continuous during time as the literature has suggested us. Dealing with parental psycho-social factors we had expected that: Couple connectedness, family routine reorganization and trust in the medical care would

have increased from the diagnosis while social support would have had a significant decrease. For other factors such as parental communication around the child's illness, their emotional coping and their cognitive functioning we presumed that they would have remained stable during the time, without significant changes.

Our findings show that there is a significance increase of parent's current life perception, that becomes exponentially higher by time advancing along the first year of therapy. Also depressive symptoms decrease significantly from the second week of hospitalization to post-one year and the same trend is found for the arousal symptoms and for state anxiety, dampened by time increasing.

So we can conclude that parents' psychological health is really in crisis at the beginning of therapies but it gets better along time, especially when the therapies of the child become less intensive.

Our findings show also that parent's physical symptoms and cognitive problems instead don't significantly differ in the three time points considered and neither parent's PTSS has a significant change along time. We imagine that the cognitive problems just after the diagnosis, if present, can't disappear so fast but they can persist along time because the brain's modifications after trauma don't solve very soon as the literature suggest us (Nakano et al., 2002; Kitayama et al., 2005).

We controlled also parents' PTSS stability throughout the several time-points finding that PTSS are stable during time. Parental post-traumatic symptoms persist along time showing that parents more at risk for PTSD in the second month of child's therapies bring this pathology along time, also when the child is getting better. This finding is innovative in the field because the major part of the studies are retrospective, showing an important incidence of PTSS and PTSD especially in mothers of childhood cancer survivors (Bruce et al., 2006). It would be inappropriate to assume that PTSS indicate psychiatric impairment. They are, for many, part of the process of responding and reacting to one's circumstances and may be adaptive in certain ways. This is an

important clinical information and it become relevant to identify the parents more at risk of elevated PTSS just in the first hospitalization of the child.

Other findings are about parental psycho-social factors. Couple connectedness, family routine reorganization, parental communication around the child's illness and trust in the medical care significantly increase from the diagnosis to 1 year post diagnosis. The trend of the couple connectedness is different from how reported by the literature where neither mothers nor fathers' mean of marital adjustment scores changed over time (Dahlquist et al., 1996). In our results we can note how couple connectedness is really low at the diagnosis showing an important couple crisis time, but then it has a significant increase at 6 month post diagnosis and then a stability of this increase at 1 year post diagnosis. The same trend is found for trust in the medical care, whit parent's attachment to the pediatric staff increasing by time, especially from the diagnosis to 6 months post diagnosis: Parent become nearer to the hospital community, feeling sometimes as to be a part of a big new family. Routine and time reorganization become more efficient during time as we have seen above when we had showed the results of parental psychological health at 6 month post diagnosis and at 1 year post diagnosis. At 1 year post diagnosis the child's therapies become less intensive, some children can return to school and some parents restart their jobs: The caring niche of the child formed at the diagnosis time is changing into a new readapted development niche with the building of a new quite stable family routine.

For other psycho-social factors, such as social support and parent's emotional coping, our results show that they remain stable during the time, without significant changes. So we don't confirm our hypothesis about social support trend during time and, particularly, that it would decrease over time. Probably the quantity of the objective social support may decrease over time, but the quality of parent's perceived social support remain stable during time: The parent who has declared that she/he hasn't received social support at the diagnosis have the same opinion also during all the first

year of child's therapies; the parent who instead has declared an important perceived social support at the diagnosis maintains her/his opinion also along time.

Emotional coping of parents is always necessary during the child's therapies timing and this is the probable reason of the maintaining of its level during time.

5.4 Predictive analyses identifying factors associated with Child's Behavioral Adaptation along the several time points

In the literature (Vance & Eiser, 2004) we have seen that parents' behavior may affect the child's reactions to treatment and general adjustment in several ways: Helping children during medical procedures (Jacobsen et al., 1990; Dahlquist et al., 2001), increasing their general compliance with treatment (Manne et al., 1993; LaMontagne et al., 1999) and, finally, using appropriately discipline (Dahlquist et al., 1994). Also more adaptive and cohesive family relationships and parental psychological adjustment are associated with positive psychological adjustment (Drotar, 1997).

Studies have emphasized on the importance of family communication and support (Kupst et al., 1984; Rodrigue et al., 1994) and of general family factors in exacerbating or attenuating the impact of the disease on the child (Ostroff et al., 2000; Stuber et al., 1996). Parental social support may buffer the association between parent and child distress (Cohen & Wills, 1985) even if the quality and the timing of support are not clearly established. Another factor linked to distress in children is the quality of their family environment (Hammen et al., 2004; Varni et al., 1996; Drotar et al., 1997) with cohesive and expressive families more capable of ensuring the adjustment of each family member, and thereby buffering parent and child distress (Hammen et al., 2004).

5.4.1 Factors measured at T1 associated with Child's Behavioral Adaptation at T4

To answer the research question about which family, child and disease factors just after the diagnosis communication were responsible for long-term adaptation of children with leukemia after 1 year of treatments we examined the precedent studies. But we had noted that in the literature there was no study that measured which family factors are responsible for long term child's behavioral adaptation at specific time points of the illness such as the second week after hospitalization and post 1 year. Our related priority was then to develop and test an explicit model of how family processes influence the psychological development of children with chronic disease conditions. So we expected that family factors and disease characteristics would be causal independent variables which impacted upon children's adaptive behaviors post one year of child's therapies. In particular, we thought that a general dimension such as Parenting (comprehensive of all the parental strategies to help children to cope with the illness) assessed at the beginning of the child's hospitalizations and treatments could be an important mediator that impact upon child's early coping to medical procedures and upon child's behavioral adaptation one year post diagnosis.

Our findings confirm the above hypotheses, showing that child's coping to medical procedures at the second week after the diagnosis controlled for parenting effect impacts upon child's behavioral adaptation one year post diagnosis. Parenting is a mediator that increase the effect of child's early coping upon child's adaptive functioning. We can appreciate this result because a specific intervention programme can be implemented to help children more at risk just after the diagnosis for developmental delays. So we can think about two parallel programmes: One to increase child's coping strategies during the first hospitalization, especially for school-aged children, and the other to teach some parenting strategies to parents of children just at the beginning of therapies, specific for the younger children.

5.4.2 Factors measured at T2 associated with Child's Behavioral Adaptation at T4

Examining the literature cited above, we asked which family, child and disease factors after 1 month from the diagnosis communication were responsible for long-term adaptation of children with leukemia after 1 year of treatments.

We expected that children's use of coping strategies to front medical procedures and hospitalization in the first month impacted on their adaptive functioning one year later. In particular we thought that cognitive strategies could impact positively on their use of adaptive behavior while the emotional strategies could be related negatively as the literature on child's coping and adaptation has suggested us (Aldrige & Roesch, 2006).

We also supposed that the parental perceptions about children's control on their health could positively impact on child's adaptive functioning, due to the believe that they have the power and the possibility to work on the situation to cope in the best way.

Our results don't confirm totally these hypotheses showing that several parental and child predictors assessed in the second month of hospitalization impact upon child's adaptive functioning at 1 year post diagnosis. For parental predictors our results identify three type of parental locus of control strategies on child's health, all of external type: Fate influence, Divine influence and Child influence. The first is associated negatively while the other two are related positively: The more parents believe that Fate influences their child's health the more child's adaptive functioning will become worse at 1 year post diagnosis while more they believe that God and the same child control her/his health more child's adaptive functioning will be better. For child's factors our results find problem solving and social support strategies as the best predictors, with the first positively associated, while the second negatively related. Social support strategy is an emotional strategy that doesn't help children to have a good adaptive functioning post 1 year of treatment, while problem solving is a cognitive strategy that contributes to a long-term child's adaptive functioning. We have to take into consideration this

information to implement specific psycho-educational programmes to help children to cope with this delicate first hospitalization time so to prevent their possible long term developmental delays.

5.4.3 Factors measured at T3 associated with Child's Behavioral Adaptation at T4

We examined which family and disease factors after 6 months from the diagnosis communication were responsible for long-term adaptation of children with leukemia after 1 year of treatments. At this purpose, we expected that family capacity to communicate with their children and with the other persons about the child's illness can be a positive reinforcement for the child so that her/his adaptive functioning can be continuously active and can develop a good adaptation until the first year of treatment (Kupst et al., 1984; Rodrigue et al., 1994), when then the child will re-start school and some social activities.

Our findings confirm our hypothesis but also a new factor is found: Parent's current life perceptions and communication about the child's illness at six month post diagnosis impact upon the child's adaptive functioning post 1 year of treatment. Communication about the child's illness to the same child and to all the social community is an important resource activity of parents and can be implemented by specific psycho-social programmes to help parents. Parent's current life perception questionnaire can be an important screening instrument to identify the parents more in difficulty in their educational role during the illness phases. This measure can be an explanation on how much parents trust their parenting capacities of caring their ill child, so it give us an important and easy tool to device for parents more at risk specific helping programmes. In this way also child's adaptive functioning can be consequently better.

5.5 Predictive analyses identifying factors associated with Parent's Psychological Health and Adaptation along the several time points

The model presented in chapter 2 (Figure 2.2) is used as a framework in our study to explain the variability in parental psychological functioning by identifying concurrent and prospective predictors of maladjustment (Hoekstra-Weebers et al., 2000). Childhood cancer is viewed as an ongoing stressor to which each parent has to adapt. Three basic components and their interactions influence parents' adaptation outcomes. The first is the type of child leukemia, the duration and outcomes of the therapy – all considered as <u>main stressors</u>. The second component is made by the stable variables which can influence parental adjustment outcomes: SES, life and parents' personality traits, such anxiety. They are called <u>stable moderators</u>. The third component is made of more flexible variables such as parental coping strategies, available social support, and marital satisfaction (Ruccione et al., 1991; Brown et al., 1993). These are called <u>modifiable moderators</u>. Stable moderators influence modifiable moderators which in turn impact upon stress and adjustment outcomes.

5.5.1 Factors measured at T1 associated with Parent's Psychological Health and Adaptation at T2

We have seen above the possible factors associated with parental PTSS at concurrent time. Here the question is if there are just some family and child factors at the post diagnosis (T1) predictive of PTSS one month after (T2).

Considering the several parental psycho-social factors we presumed that emotional coping and support received by parents could be key resources dampening parents' symptomatology assessed at the diagnosis and indicative of less future PTSS problems.

Our findings partially confirm our hypotheses. The path model performed to test

whether family and illness factors were related to PTSS at 6 months post diagnosis shows that emotional coping and support assessed at the diagnosis are key elements impacting, the first, on their memory abilities, and, the second, on their perceptions of their current lives. Then all these family factors are also related to parents' BSI-18 global score assessed at the diagnosis and indicative of short-term PTSS problems.

So we can note how emotional coping and support received don't impact directly to PTSS but by the mediation of memory abilities, for the first element, and by the mediation of current life perception, for the second one. There is a double via that impact upon PTSS. The first via is the following: Emotional coping strategies of parents help them to have less memory malfunctioning associated with less psychological symptoms that, in turn, are predictive of less PTSS at the second month of hospitalization. The second via is that: Social support received by parents help them to have a good perceptions about their lives associated with less psychological symptoms, always predictive of PTSS.

In only ALL children we also had supposed that another illness element, such as the communication of blastos at day +8, could be an important moderator of the increase of parental psychological symptoms predicting the PTSS incidence one month post diagnosis. No study in the literature has examined the possible consequences of this specific communication by medical staff on parent's mental health.

Our findings confirm this hypothesis: Number of blastos communicated at day +8 is the moderator of parent's physical symptoms that impact on PTSS at one month post diagnosis. So the quantity of blastos communicated increases parents' physical symptoms which in turn positively influence the post-traumatic stress symptoms incidence.

5.5.2 Factors measured at T1 and T2 associated with Parent's Psychological Health and Adaptation at T3

We also wanted to know which family and child factors are responsible for psychological functioning of parents of children with leukemia 6 months post-diagnosis.

We supposed that family factors such as routine reorganization and social support received at the time of the diagnosis (T1) could be related to the parental perception of their current lives post 6 months of therapies (T3). For the demographic factors we had thought that older age of parents and of children could be an important factor for a better parental psychological functioning. In fact, older parents can have more caring instruments and parenting experiences that help them to cope better with the illness difficult situation.

Our findings show that Child's Age, Parent's Mean Job hours/a week, family routine and time reorganization and support impact upon the parental current life perception at T3. Particularly the parental current life perception gets better at 6 month post diagnosis by the increase of child's age, family reorganization and perceived social support and by the decrease of parent's job hours assessed at the second week after hospitalization. The possible explanation of this last information about parents' job activity is that parents can take from this job activity a sort of distraction that can help them to consider their lives in a more hopeful way.

We also presumed that PTSS symptoms assessed at one month (T2) could be strongly associated also to the other symptomatology (such as depression, arousal, cognitive dysfunctioning) measured at 6 month post diagnosis (T3).

Our findings identify as predictors of a worse parents' global psychological functioning at 6 months post diagnosis the younger parent's age, the low family routine and time reorganization and the higher PTSS incidence. Unexpectedly, PTSS incidence increases also the possibility for parents to have cognitive problems. Post-traumatic symptomatolgy, that we have seen remained stable during time, influences the rising of

other symptoms affections (such as depression, arousal and psycho-somatic dysfunctions) and of cognitive problems, i.e. in memory and concentration functions.

5.6 Limits and future directions

This is a very complex study that involves several aspects of psycho-social reactions and effects of cancer on ill child and her/his family. This population of children with cancer and their families is very difficult to study and it requires also a good clinical preparation both to collect data and to give them support. For this reason some limits can be individuated, however most of them w will try to solve with future work.

From a developmental perspective the first limit is that we have such a wide age range in a population of such children. The developmental needs, activities and rules are different along the several ages: Infants need to be cured totally by parents and don't have comprehension of the illness; pre-school-aged children can suffer for loss of social and play activities; school-aged children can feel isolated from their peers and from all the school activities; pre-adolescents and adolescents can complain for hair loss and for all their body modifications due to the illness. The comprehension of the illness is really very different along the several ages, with pre-adolescents and adolescents that, having more cognitive abilities, can comprehend globally their illness and the therapies' effects.

In order to solve this problem, we utilized in this study a battery of instruments that can correct this child's age variability. Firstly, in-depth interview to parents such EFI-C and the creation of a specific codebook ad hoc containing specific items for only children aged 0-3 or 0-5 allow us to have a valid picture of children of different ages and of their family systems. Secondly, the choice of questionnaires such as PPCI divided into age ranges and of semi-structured interviews to parents about child's

development state can minimize the problem of different ages. Thirdly, for a double control through the use of statistics, child's age was always included as independent variable in our regression and path models. However we must admit that in most of our analysis age still played an important role (explaining a good part of the variance); consequently creating groups of children with smaller age ranges and further replicating the analyses would be recommended with a future ampler sample size.

The second problem is more methodological: The instruments used are all indirect measures of child's development and emotional state. The child was not assessed directly, but only proxy by parent's perceptions. We have seen that parents are valid in judging the child's quality of life, but it can be always a sort of filter of the real state of the child. The present study, in order to solve this problem, will include as future direction the investigation also of child's illness experience by EFI-C to the school-aged child at the end of the therapies, at two years from the diagnosis. We have already been collecting these data on 29 children with leukemia at the stop-therapy time, but we did not include these data in this dissertation due to the little sample size. Our future investigation will take into more account also child's direct perspectives analyzing these new data. Some ethical reasons have guided our choice of not assessing directly child during the illness: The child is fatigued by the therapies and by the illness and she/he is really very involved in medical activities. Only some questionnaires about emotional problems were administered to children up to 7 years old but not included in this dissertation for the same reason of little sample size.

The third limit is that the distribution of children with ALL and with AML is not proportional, with the first sample really more numerous than the second one. This is due to an epidemiological reason of the distribution of leukemias in pediatric age, but it doesn't allow us to make sophisticated inter-group analysis between the two groups because the cell sizes remain quite small for children with AML. For this reason in our study we have decided to make separate analyses only on children with ALL to include

more illness parameters. An enlargement of sample size will allow us to make more specific analyses and reflections on the impact of illness variables on child and her/his family.

Another limit deals with the problem of medical variables that should be taken under consideration when making research in this field. To control this problem we worked with pediatric oncologists and with them we built medical variables, which are considered most important. Also the choice of our project to focus only on a cancer type such as leukemia had helped us to reduce illness variables as much as possible. This is innovative in the present literature where the studies of only a cancer pathology are really a few and not adopting this multi-method and longitudinal approach. The enlargement of the sample will help us, in the long term, to better control these illness variables. Although, a more immediate further work could be that of considering individually cases that have particularly singular characteristics. This is a method that is frequently used in medical research and that could give some interesting improvements also to this type of our work.

A final consideration is that this type of sample size was been longitudinally reduced for several reasons: I.e., 11 had deceased, 4 had changed health center, 5 were relapsed or in grave illness situation and only 5 families drop out from the study (3.9%). This aspect is also strictly related to the long time and huge amount of energy and work need to collect these data. Five years of one researcher full time work, everyday visits at the onco-hematologic unit, which could last two to five hours, in order to interact and built relations with parents and children, support and help them, gave us the chance to collect these data. Several more years are needed to have a larger sample of children and their families followed longitudinally.

Finally, future directions would be those of publishing this work and planning a clinical and educative intervention for children and their parents (see clinical suggestions paragraph).

5.7 Clinical suggestions

One of the major aims of this study is that of being able to plan an intervention for parents, children and hospital staff that could improve their psycho-social functioning. So we can advance here some clinical suggestions on how informative, clinical and practical interventions could be planned on the basis of our empirical findings just presented and discussed.

Some clinical suggestions can be given here to support three types of populations: Parents in their parenting role and in their psychological health; children in their coping and behavioral adaptive functioning to the illness; medical doctors in their role of communication and of giving information. Let's consider them separately.

Clinical suggestions for the work with parents

- The diagnosis time and the period immediately following is very critical for parents' psychological health and for their coping efforts and resources. Parents more at risk for psychological symptoms are that: Younger aged, with children younger and with the diagnosis of AML. Specific psychological supportive programmes can be proposed for parents more at risk, helping them in recognizing also their internal resources, their parenting activities in the hospital and their availability of social support.

- Parents in difficulty for cognitive functioning are those who have to work more hours a week and those who have lower couple connectedness resources at the diagnosis. Specific social assistance interventions can be implemented so that job can be less intensive and couple spaces and times can be stimulated when possible during child's hospitalization.

- Parenting rules have to be sustained, in order to help children's coping, adaptability and their quality of life, especially for parents of younger children where the tasks are more difficult.

- Parental PTSS can be predicted and reduced following two parallel intervention strategies at the diagnosis time: Improving their emotional coping and their memory abilities on one side; increasing their support network and their current life perceptions. Cognitive problems were found as predictors of PTSS at one year post diagnosis, underling again the relationship between trauma and memory dysfunctions. These parental symptoms had resulted stable during time so more these psychological interventions can be preventive more the PTSS quantity during time will not remain during time.

- We had seen how parental PTSS post 6 months of therapies was significantly sustained directly by family routine and time reorganization, by also the mediation effect of parental cognitive and anxiety problems. This is a delicate time in child's treatment and in parents' role so that specific interventions can be built to help parents to cope with this difficult time in the best possible way, dampening also their anxiety state by relaxing and breathing strategies.

- We had seen the parental psychological health behavior during time and we can suggest that the first six months of therapies are very intensive and put parents in difficulty both practical (family and time reorganization, social support availability and activation, communication towards the child's illness) and emotional (intense activation of coping resources, couple crisis, adaptation to the new medical setting and to hospital staff). When the therapies of the child become less intensive, at 1 year post diagnosis, the situation gets better but not for all: Parent's physical symptoms and cognitive problems don't significantly different and neither parent's PTSS has a significant change along time. A psychological intervention to solve cognitive problems and PTSS is necessary along all the therapies' protocol.

Clinical suggestions for the work with children
- We have to take into important consideration child's age for the possible

psychological interventions because we had seen how it influenced both child's coping and adaptability and, consequently, the quality of life. Younger patients are more at risk for coping with pain problems because they use less problem solving and cognitive self-instructions than older children. Specific interventions can be applied to children taking into consideration their age and their best coping strategy used. Other coping strategies can be taught to children and their best coping strategy can be implemented, particularly for older children. For younger children, it is necessary to advance more educational interventions to increase parents' capacity of caring of their child, basing also on understanding of child's possible psychological reactions to the illness and to its treatments.

- Children's coping and adaptability measured at the first hospitalization identify, at short-term, the children more at risk both in catastrophizing strategy using in front of pain, and, at long-term, the children more subjected at developmental delays in their adaptive functioning. A screening instrument, built on our interview items referred to coping and adaptability, can be administered to parents just at the first hospitalization to identify children more at risk and to, consequently, implement a specific psychological programme for dampen the possibility of child's catastrophizing and her/his developmental delays. These programmes can be then taught also to nurses of the Clinic so to have more instruments to sustain children during hospitalizations or in preparation of medical procedures.

- Our findings on the situation of child's developmental delays of almost three months at 1 year post diagnosis can guide specific interventions to parents and to children to fill this gap. Particularly, it is to consider that children with AML and with more days of hospitalization are more at risk for motor delays and to have a low temperamental score in motor activities. At this purpose specific physiotherapic and psycho-motor programmes can be implemented also during hospitalization. Also socialization and educational programmes can be proposed both during hospitalization

and in occasion of day-hospital follow-ups and some social plays and educative guidelines can be taught to parents to stimulate their child also at home.

- We had found how parenting effect impacted upon child's behavioral adaptation one year post diagnosis and controlled also child's coping at the diagnosis time. Basing on this result specific intervention programmes can be implemented to help children more at risk just after the diagnosis for developmental delays. So we can think about two parallel programmes: One to increase child's coping strategies during their first hospitalization, especially for school-aged children (as suggested above), and the other to teach parents some strategies in their caring of children just at the beginning of therapies, in particular for infants and for scholar children.

Clinical suggestions for the work with medical doctors and hospital pediatric staff

- Giving information on our findings through informative seminars and presentations would be useful to improve also medical doctors and nurses interactions and work with children and their parents. Particularly, some specific communication strategies can be taught to health professionals not only at diagnosis time, but in the several illness statuses; communication such as number of blastos at day +8, or the phase of illness risk, or the collateral effects of therapies such as cortisone.

- Promoting collaboration with the medical staff, with the hospital teachers, with the volunteers and the social workers would help exchanging information on patients, improving the quality of the service.

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APPENDIX

Appendix 1: EFI-C dimensions with their respective items

Dimensions	Items
Parental emotional coping	- velocity in activation of a first strategy of coping - search of figures that can give sense of safety - level of the acceptance of the community (friends, neighbours, church, school) involvement - verbal/metaphorical expression of depressive feelings (an unexpected emptiness, like a mourning or a lost) than can be associated to cry/desperation - level of emotional coping (acceptance of illness as bad life experience vs sense of guilty, comprehension of real causes of the illness vs obsessive searching of an explanation) - level of focusing on child's needs - presence of cognitive adaptive strategies (to know the therapy protocol, the stages, think positive) - presence of adaptive strategies for the emotional control (to talk, to give to herself/himself courage, to accept crises of crying). To intend inside a matured and elaborated strategy.. - level of acceptance of negative emotions (pain, anxiety, anger) - realistic search of information (from the doctors and staff of the clinic, from the other parents, from the parental web sites) - level of focusing on sane family members and/or on relaxing activities to feel "the normality" - level of worry and acceptance towards the imminent child's physical modifications due to the therapies - verbal expression of anxious feelings/body reactions (heart rate increase, tremors, agitation)

Levels of communication on the child illness	- level of clearness about the diagnosis perceived by parent - level of clearness about the diagnosis to the child (all the truth, the things that child can understand, information given gradually about sickness) - preparation of child to loose hair or to any other physical change) (codification not possible for age 0/3) - level of clearness about the diagnosis to the siblings (codification not possible without siblings) - level of clearness about the diagnosis to the siblings (codification not possible without siblings) - level of clearness about the diagnosis to the other family members - level of clearness about the diagnosis to the broader social network - level of communication and relationship with the other parents in the Clinic - facility of communication with the pediatric staff

Parenting the child in the hospital	- creation of links between home and hospital - use of strategies to help child cope with daily medical procedures - level of trust about leaving the child with others during the day - importance given by the parent about being next to the child during his/her sleep - level of parent-child empathy - perceived parental self-efficacy - perceived ability in soothing child cry/desperation - proximity to the child while soothing him/her - perceived difficulties while taking care of the child during hospitalizations

Trust in the medical care and in the hospital community	- level of trust in the hospital - search for specific members of pediatric staff - feelings of belonging to a community ("this is not a hospital, this is a family!") - level of the appreciation for what is offered - perceived emotional/psychological support from the Clinic's staff - importance of the other support figures in the Clinic (psychologists, teachers, volunteers)

Routine and time reorganization	- level of maintaining of the family routines after the diagnosis - level of re-adaptation between the two settings home-hospital - expressed fear in returning home with the child - level of family activity currently focused on arranging and sustaining childcare for the child. (Number of tasks; number of helpers; time or effort expended) - family arranges family time or schedules around the child - current degree of complexity/elaborateness of domestic and hospital workload and schedule (number and difficulty level of chores, time availability of mother, and amount of help received) - reorganization of the rules of the family members - flexibility of father's current work and schedule - time length of the father's stoppage of work - time availability of father for child (before the illness) - flexibility of mother's current work and schedule - time length of the mother's stoppage of work - time availability of mother for child (before the illness) - turns and times organization of familiars - time availability for recovery for parents - amount of time for social activities

Social support	- emotional support perceived by mother - emotional support perceived by father - amount of help parents receive with childcare in the hospital from siblings, or other relatives - amount of help/support parents receive from friends and social community - amount of support family receive from religion, spirituality

Connectedness of the parental couple	- parental perception of family union and cohesion (i.e., close knit family with feelings of togetherness, support, and shared participation in activities and decision making) - current role of husband in the mother's life (give support) - amount of time dedicated to the couple - facility of couple communication about the illness - stability of couple/marriage relationship - level of parent's understanding about the possible differences in their coping styles - level of partner's acceptance of the emotions and despair reactions - level of trust in the strength of the other parent and in his/her availability for the child and for the family - agreement between parents' routine for the childcare

Sibling involvement	- siblings' involvement in the diagnosis, in the therapy (i.e., bone marrow transplantation) and in the daily work related to the illness - level of participation and worry of siblings for the ill child - level of involvement of the ill child to the everyday life of his/ her siblings - level of parent's worry for other children - level of parent's focusing on siblings

Child coping with procedures and hospitalization	- acceptance/understanding of the explanations before medical procedures - use of different strategies during medical procedures - monitoring medical procedures - need for parents before, during, or after medical procedures - need for parents during daily life in the hospital - level of adaptation to the hospital routines - level of adaptation to daily restrictions related to illness - requests for information/reassurance from doctors - coping with painful procedures - tolerance to movement restrictions - level of acceptance of the possible physical changes - coping with emotional stress

Child quality of life in the hospital	- level of child's maintaining of contacts with peers, friends, schoolmates - physical reaction to therapies - level of participation to the play activities in the hospital - level of child's maintaining of some previous routines (sport and play activities) (codification not possible for age 0/3) - tolerance of possible collateral effects of therapies (nausea, vomit, headache, fatigue) with associated fears and feelings (codification not possible for age 0/3) - child's activities of maintaining some previous routines (ask for phone, to do homework) (codification not possible for age 0/3) - level of participation to the school activities in the hospital (codification not possible for age 0/5)

Child adaptability	- level of child's emotional intensity (crying, anger episodes) associated with specific causes (medical procedures) - sleeping problems - level of child's general curiosity and attention about the hospital environment related with games and play - level of child's consolable capacity - capacity of the child to become serene just after medical interventions - parent's perception about the quality of change in child's relations with doctors and white coats - parent's perception of a stability in child's characteristics - level of parent's perception of sane aspects of the child in spite of the illness

Appendix 2: Child's medical chart

FAMILY NAME /_____/

NAME /_____/

DATE OF BIRTH /_/_/ /_/_/ /_/_/ GENDER ⏐M⏐ ⏐F⏐

NATIONALITY /_____/

CITY /_____/

DATE OF DIAGNOSIS /_/_/ /_/_/ /_/_/ DIAGNOSIS /_____/

CEREBRAL INTERSET AT DIAGNOSIS ⏐YES⏐ ⏐NO⏐

THERAPEUTIC PROTOCOL /_____/

DATE THERAPIES START /_/_/ /_/_/ /_/_/ DATE END THERAPIES /_/_/ /_/_/ /_/_/

1st COMPLETE REMISSION DATE   DATE RELAPSE/PROGRESSION
/_/_/ /_/_/ /_/_/   /_/_/ /_/_/ /_/_/

CRT ⏐YES⏐ ⏐NO⏐   TOTAL CRT DOSES /_____/cGy

STEM CELL TRANSPLANTATION   TYPE OF SCT: /_____/
⏐YES⏐ ⏐NO⏐

   DATE TRANSPLANT /_/_/ /_/_/ /_/_/

PERIPHERIC BLOOD TEST DAY +8 (ALL) n° blastos/ul: /_____/⏐PGR⏐ ⏐PPR HR⏐

BONE MARROW DAY + 33 (ALL) n° blastos/ul: /_____/⏐M1⏐ ⏐HR M2⏐ ⏐HR M3⏐

BONE MARROW DAY + 78 (ALL) n° blastos/ul: /____/⏐SR1 2⏐ ⏐MR1 2⏐ ⏐HR1 2⏐

BONE MARROW DAY + 21 (AML) post 1st ICE:
⏐M1⏐ ⏐HR M2⏐ ⏐HR M3⏐ n° blastos/ul: /_____/
post 2nd ICE
⏐M1⏐ ⏐HR M2⏐ ⏐HR M3⏐ n° blastos/ul: /_____/

N DAYS OF HOSPITALIZATION
AT DAY +33 /_____/
AT +6 MONTHS /_____/
AT +1 YEAR /_____/
AT +2 YEARS /_____/

Legend: PGR = Prednisone Good Response; PPR = Prednisone Poor Response
MR1 = 2nd Re-induction + 1 ad interim Maintenance; MR2 = 1st Re-induction + 1 Maintenance

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Appendix 3: Cortisone psycho-social effects questionnaire

Name of the child…………………………………………………………………...

Name of the parent……………………………………………………………….

Which of these behaviors you have observed in your child in the cortisone treatment phase?

1. calm plays (drawn, listen to the music…)

2. violent plays (fight videogames or fight plays)

3. object thrown

4. anger outbursts

5. sudden cry

6. nervousness, restlessness

7. fatigue

8. motor agitation

9. sleepiness

10. to get easily exhausted

11. to get easily tired of a play after some minutes

12. reading for a long time

13. to complete the drawn, the homework

14. to speak with herself/himself

15. to make nonsense discourses

16. other behaviors not described

……………………………………………………………………………………

……………………………………………………………………………………

Appendix 4: Problem scale dimensions

Dimensions	Items
Impulsivity	"I get upset easily" "I don't think of consequences before acting" "I am impulsive" "I blurt things out"
Labile mood	"I get frustrated easily" "My mood changes frequently" "I am easily overwhelmed"
Disorganization	"I am disorganized" "I have difficulty coming up with different ways of solving a problem" "I have problems getting started on my own" "I am a underachiever" "I have trouble doing more than one thing" "I have problems prioritizing activities" "I have problems solving math problems in my head" "I don't work well under pressure"
Concentration problems	"It takes me longer to complete my work" "I have problems completing my work" "My desk/workspace" is a mess" "I read slowly" "I am slower than others in completing my work"
Memory problems	"I forget instructions easily" "I have difficulty recalling things I have previously learned (e.g., names, places, events, activities)" "I have trouble finding things in my bedroom, closet or desk" "I forget what I am doing in the middle of things" "I have trouble remembering things, even for a few minutes (such as directions, phone numbers, etc.)