# Parent and Family Functioning in a Pediatric Cancer Population

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A Doctoral Project Manuscript Submitted in Partial Fulfillment of the Requirements for the Degree of Doctor of Psychology in the Department of Psychology at Pace University

New York

Fall 2012

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**Acknowledgments**

I want to start off by thanking my advisor, Dr. Michele Zaccario, for her never-ending support throughout this process. Dr. Zaccario, you have always encouraged me to pursue my interest in the field of pediatric oncology and have provided me with the opportunities I needed to immerse myself in this population. I am forever grateful for my experiences at NYU and Hassenfeld Children's Center for Cancer and Blood Disorders. Thank you Dr. David Salsberg and Dr. Laura Tagliareni for welcoming me to Hassenfeld and sharing your very busy office with me during the data collection process. The passion and commitment you both possess to your work has always inspired me. I would also like to thank my consultant, Dr. Alfred Ward, for working with me on this project and patiently guiding me until I understood the statistics associated with my research.

Special thanks to Simone Grazi and Jen Gilbert who volunteered their time to help me collect and enter data associated with this project at Hassenfeld. These findings are as much yours as they are mine.

I would like to extend my gratitude for the support of the faculty of the psychology department at Pace University. Dr. Fernandez, thank you for always helping us get through what seemed like insurmountable obstacles along our journey to become psychologists. I have learned so much watching you genuinely and compassionately relate to others. Dr. Stokes and Dr. Bart, thank you for helping us process our "thoughts and feelings" while gaining valuable experiences in our school placements. Dr. Mowder, thank you for your mentorship and support throughout the years. You have all had such an impact on my education and I thank you.

I would like to thank my best friend and roommate, Anna Weissman, for putting up with me while writing my dissertation. Thank you for letting me take over the dining room table with my books, articles, and laptops, and never asking me to move my stuff. I owe you one.

To my parents, Morad and Manijeh Mottahedeh: I am so grateful for your support during my journey to become a psychologist. Your value of education and hard work has shown me that I have what it takes to reach my goals. I promise I will focus on getting married now! To my older sister, Debbie: you have always been there for me and I have always looked up to the way you so effortlessly balance a career as a physician and raise a family with twins.

To my younger sister Emily, a two-time Leukemia survivor by age 12, who is without a doubt the strongest, most passionate, person I know— I dedicate this dissertation to you. Your resilience and ability to rise above hardship has defined who you are as a person. Your commitment to bettering the lives of children and families facing chronic illness has inspired me to contribute to this field. I am consistently blown away by your dedication to Two By Twelve, the non-profit organization you founded at age 22. I am so proud to be your sister.

And finally, to a dear childhood friend, Brian, who lost his battle with Leukemia at the young age of 30. You are forever in our hearts.

**Abstract**

The construct of quality of life was developed as a means to assess an individual's functioning across a variety of domains, including physical, psychological, and social functioning. Due to the advances made in the medical treatment of childhood cancer, many children are surviving or living longer with the disease; therefore researchers have begun to look at the quality of life of pediatric cancer patients and their families. While studies have shown that caring for a child with cancer can negatively affect parent and family functioning, findings are inconsistent.

The primary goal of the current study was to shift the focus onto the caregivers of pediatric cancer patients by specifically assessing the relationships between parental adjustment, parental stress, and family functioning. An evaluation of the effects of time since diagnosis and treatment intensity was conducted as well. Archival data from 67 caregivers of children receiving outpatient treatment for cancer was examined.

Results indicated that lower parental adjustment predicted poorer family functioning, as did higher parental stress. No significant relationships were found between parental adjustment, parental stress, impact on family, and time since diagnosis. When comparing parents caring for children with brain tumors versus leukemia, no significant differences were found in regard to parent adjustment, stress, and family functioning. However, caregivers of children on active treatment were significantly more likely to be less adjusted (less emotional resources), report higher stress levels (higher parental distress, higher parent-child dysfunctional interactions, higher total stress) and endorse poorer family functioning. Exploratory analyses were conducted to assess the moderating effect of parental adjustment on parenting stress and impact on family. No

significant interaction effects were found. Implications for clinical and school psychology are discussed.

# CHAPTER ONE

## Introduction

Childhood cancer has been widely studied in the literature. Advances in the medical treatment of childhood cancer have resulted in many children surviving or living longer with the disease. A pediatric cancer diagnosis is undoubtedly one of the most stressful situations a child and his/her family can face. There are a myriad of illness-specific stressors that present themselves during and following a child's treatment for cancer. As a result, many researchers are now assessing the quality of life of children with cancer. Treatment protocols are demanding and pose serious disturbances to one's daily life. Due to the chronic nature of this illness, those who are involved in the child's treatment (i.e. caregivers, parents, siblings) are expected to adapt to changes and continue functioning in order to improve the likelihood of the affected child's survival.

The term "quality of life" has been adopted in the field of pediatric oncology to embody an individual's physical functioning, psychological well-being, social functioning, and physical discomfort (Ivan & Glazer, 1994). Children with cancer undergo many physical changes during treatment and are exposed to anxiety-provoking medical situations on an on-going basis. The need to assess biological, psychological, and social adjustment in children diagnosed with cancer is clear, as dealing with this disease is not a common experience for most children. However, it is also essential to assess the caregivers of these children. Research thus far has demonstrated inconsistencies regarding the functioning of parents caring for a child with cancer. Several studies have demonstrated clearly that having a child with cancer can negatively affect parent well-being (Kazak & Barakat, 1997; Kazak et al., 1997).

A key aspect of systems theory focuses on the relationships and interrelatedness among family members, therefore it would be expected that typical family functioning will be disrupted by the illness-specific stressors that families of children with cancer experience (Streisand, Kazak, & Tercyak, 2003). While studies on childhood chronic illness have been shown to have an effect on the family environment (Sawyer, Antoniou, Toogood, Rice, & Baghurst, 1999), less is known about how the factors related to the child's disease impacts the family as a whole. Studying parent and family functioning simultaneously is likely to yield a more thorough conceptualization of family functioning within pediatric cancer populations. Measures that are specific to the daily life and experiences of a parent caring for a child with cancer are essential in assessing levels of adjustment and stress, which in turn, affect family functioning. The focus of the current study lies in the assessment of caregiver functioning, by examining caregiver adjustment, stress, and the overall impact of the child's illness on family functioning.

# CHAPTER TWO

## Literature Review

This chapter includes a review of the existing literature relevant to pediatric cancer and parent and family functioning. This review includes eight major sections, the first of which focuses on general statistics, incidence, prevalence, mortality, etiology, and classification of pediatric cancer. The next sections summarize the etiology, symptomatology, diagnosis, treatment, and prognosis of the two most common pediatric malignancies, leukemia and central nervous system (CNS) tumors. The following section summarizes the etiology, incidence, diagnosis, and treatment of neurofibromatosis as it relates to pediatric cancer. The paper then examines potential late effects of pediatric cancer, with a focus on neurocognitive effects. The section following highlights the process of adapting to chronic illness. The paper then moves to a discussion of the psychosocial impact among children with cancer, followed by the current literature on parent and family functioning within a pediatric cancer population, paying special attention to quality of life, parent adjustment, illness-specific stressors, stress reactions according to disease phase, the parent-child reciprocal relationship, treatment type, and overall family functioning. This chapter concludes with a description of the rationale and purpose of the current study along with the hypotheses proposed by this research.



### PEDIATRIC CANCER OVERVIEW

#### *Incidence, Prevalence, & Survival Rates*

Each year, one or two children per 10,000 are diagnosed with cancer in the United States (Butler & Haser, 2006). Thus, in 2012, approximately 12,060 children under the age of 15 will be diagnosed with cancer in the United States, and an estimated 1,340

children will die from the disease (American Cancer Society, 2012). Although cancer in children is rare, it is still the leading cause of death by disease in children under the age of 15 (Moore, 2005). Following death by accident, cancer is the second leading cause of death in children (American Cancer Society, 2012). On average, pediatric cancer rates have been increasing by 0.5% per year from 2004 to 2008, an ongoing trend since 1975 (American Cancer Society, 2012).

The incidence rates for pediatric cancer vary significantly according to type of cancer, age, gender, and race. From 1973 to 2008, Caucasian males and females evidenced higher pediatric cancer incidence rates than African American males and females. Caucasian males generally had higher rates than Caucasian females, however no such pattern was seen between African American males and females. Overall incidence rates in 2008 for Caucasian males and females less than 20 years of age were 19.1 and 16.3 cases per 100,000, respectively while rates for African American males and females were 15.1 and 14.1 cases per 100,000, respectively. The incidence rate of leukemia, 4.2 cases per 100,000, makes it the most common pediatric malignancy in children younger than 20 years of age, followed by cancer of the central nervous system, with 3 cases per 100,000 (American Cancer Society, 2012).

Childhood cancer deaths have decreased by 66% over the past 40 years, from 6.5 per 100,000 in 1969 to 2.2 per 100,000 in 2008 (American Cancer Society, 2012). Advancements in pediatric oncology treatment protocols have increased survival rates but it is important to note that survival rates vary considerably according to cancer type, patient age, and other factors. Between 2001 and 2007, the five-year survival rate for children less than 15 years of age diagnosed with Hodgkin lymphoma is 95%; Wilms

tumor, 88%; non-Hodgkin lymphoma, 86%; leukemia, 83%; neuroblastoma, 74%; brain and other nervous system tumors, 71%; osteosarcoma, 70%; and rhabdomyosarcoma, 68% (American Cancer Society, 2012).

***Etiology***

The etiology of pediatric cancer is largely unknown. A small percentage of cancers can be traced back to specific chromosomal or genetic abnormalities and exposure to ionizing radiation. It is believed that childhood cancer is likely the result of multiple factors involving the interaction between various aspects originating from the environment as well as human genetics (Buffler, Kwan, Reynolds, & Urayama, 2005). Researchers continue to examine potential environmental influences to developing pediatric cancer, as they have long been suspected of increasing risk of certain pediatric malignancies. Information related to specific etiology will be further elaborated according to cancer type in the section that follows.

***Classification***

Childhood cancers are classified according to histologic cell type. This differs from adult cancers, which are classified according to site of cancer. The system used to categorize childhood cancers is known as the International Classification of Childhood Cancer (ICCC-3) and allows for international epidemiological comparison. The histological classification for childhood cancers is useful for the purposes of understanding the origins of the cancer and for identifying the best treatment. The ICCC-3 is based on the International Classification of Diseases for Oncology (ICD-O) and categorizes pediatric cancer into 12 main diagnostic groups (level 1) and 47 subgroups (level 2). There is a third level of classification in which select subgroups are further

differentiated. An illustration of the ICCC-3 can be found in Appendix A (Steliarova-Foucher, Stiller, Lacour, & Kaatsch, 2005).

## LEUKEMIA

Leukemia is the most common pediatric malignancy, comprising approximately one-third of childhood cancers. There are several different types of childhood leukemias, including Acute Lymphoblastic Leukemia (ALL), Acute Myelogenous Leukemia (AML), Chronic Myelogenous Leukemia (CML), and Juvenile Myelomonocytic Leukemia (JMML). Of these, the most common type is ALL, accounting for approximately 75% of all pediatric leukemia cases (Butler & Haser, 2006). AML comprises almost 20% of pediatric leukemia cases, while CML (2-3%) and JMML make up the remaining 5% (Aplenc & Lange, 2003).

### Acute Lymphoblastic Leukemia (ALL)

#### *Etiology*

Childhood Acute Lymphoblastic Leukemia (ALL) is a type of blood and bone marrow cancer that affects the white blood cells. Lymphocytes are a type of white blood cell that the body normally uses to fight against infection. ALL is caused by the malignant transformation of a single lymphoid progenitor cell and its subsequent proliferation. The immature lymphocytic blasts (or lymphoblasts) exhibit exaggerated and uncontrolled growth, an inability to defend against infection, and a disruption in the production of bone marrow cells (Leukemia and Lymphoma Society, 2012). A decrease in the production of normal bone marrow cells leads to a deficiency in the circulation of the following: red blood cells, which carry oxygen to tissues throughout the body; platelets, which help form blood clots that control bleeding; and white blood cells other

than lymphocytes, such as neutrophils. The overcrowding of leukemic cells in the bone marrow inhibits normal red and white blood cells and platelets from properly functioning (Landier, 2001). Established evidence for increased risk of ALL includes sex, age, race, prenatal exposure to x-rays, therapeutic radiation, and certain genetic syndromes (Buffler et al., 2005). Incidence rates for ALL are higher among males than in females. Childhood leukemia rates are higher among whites than among other races and ethnicities. ALL incidence is higher in children from 0 to 14 years of age than it is in individuals ages 15 through young adulthood (Leukemia and Lymphoma Society, 2012).

***Symptomatology***

Prior to diagnosis, children with ALL have been found to exhibit bruising, fatigue, a pale complexion, fever, abdominal swelling, mucous membrane bleeding, and bone or joint pain (Leukemia and Lymphoma Society, 2012). These symptoms are usually displayed two to six weeks prior to diagnosis. When Leukemia is suspected, a full assessment of the child is conducted which typically includes a complete blood count, chemistry panel, chest x-ray, lumbar puncture, and bone marrow sample (Landier, 2001). It is interesting to note that in more than half of ALL cases, the initial white blood count is within normal limits for the child's age. However, a thorough examination of the white blood cells reveals decreased neutrophils (neutropenia) and the presence of lymphoblasts. Thrombocytopenia, evidenced by a platelet count of less than 100,000, is seen in 75% of children at diagnosis and results in easy bruising and the slow healing of cuts. Anemia (hemoglobin < 10) is present in 80% of cases and underlies the child's fatigue and pallor (Landier, 2001).

***Diagnosis***

A diagnosis of ALL cannot be made unless the bone marrow sample is positive for at least 25% lymphoblasts. Once diagnosed, ALL is classified as either B-cell precursor, which makes up 83% of cases; mature B-cell, which accounts for only 2% of cases; or T-cell precursor, which represents the remaining 15% of cases. While B-cells are lymphocytes that regulate the humoral immune response, T-cells are lymphocytes that play a role in cell-mediated immunity. These classifications indicate the stage at which lymphoid cell differentiation is blocked in the malignant clone (Landier, 2001). For example, T-cell ALL is classified as so because these cells are stuck in the late thymocyte stage, the second to last maturational stage (Landier, 2001). Essentially, this means that these cells have not reached (and will not reach) mature T-cell development due to their characteristic abnormality and thus will not function properly.

Morphology and cytochemistry is conducted as a part of diagnostic classification. Morphologic evaluation classifies leukemic cells based on physical features such as size, shape, chromatin pattern, and amount of cytoplasm (Landier, 2001). Three morphologic subtypes of ALL have been identified (L1, L2, and L3), the most common of which is L1. Approximately 80% of childhood ALL is L1 morphology and is characterized by small, uniform cells with little cytoplasm and unclear nucleoli (Landier, 2001). In order to distinguish ALL from AML, cytochemical stains are used. Generally, an enzyme called myeloperoxidase is found only in myeloid leukemias (Landier, 2001).

Cytogenetics, by way of karyotyping, has increased our knowledge about the biology of ALL by focusing on the chromosomal abnormalities found in leukemic cells. The abnormalities in chromosome number (ploidy) and structure (translocations,

deletions, and rearrangements) are found in 90% of childhood ALL cases and a number of them are of prognostic significance. For example, a chromosomal abnormality of more than 50 chromosomes (hyperploidy) has been linked to a more promising prognosis, whereas having 46 chromosomes with numeric or structural rearrangements (pseudodiploidy) or having less than 46 chromosomes (hypoploidy) are associated with less favorable outcomes and thus more intensive treatment protocols. Karyotyping has identified translocations as the most common and major changes seen in leukemic cells. Locating a translocation informs the medical team how to proceed. The common t(12;21) translocation is linked to a positive prognosis and is associated with survival rates of more than 90% (Landier, 2001).

***Treatment***

Proper treatment is dependent on a child's specific risk factors and prognosis. Treatment of ALL includes four phases: induction, consolidation/intensification, maintenance of remission, and prevention of disease in the CNS. Each of these will be discussed separately so as to limit confusion. It is important to note that the goal of treatment for leukemia is to destroy leukemic cells and allow normal cells to form in the bone marrow. Treatment decisions are based on the type and stage of leukemia diagnosed, therefore patients will progress through the phases described below differently.

***Induction Chemotherapy***

The first step in treating ALL, which lasts, approximately one month, is to induce a complete remission. This means that leukemic cells are reduced to an undetectable level so as to erase clinical signs of the disease via chemotherapy. This phase also

includes the restoration of normal blood counts and bone marrow that contains less than 5% lymphoblasts. Treatment, based on the Goldie-Coldman hypothesis, proposes that a cocktail of effective drugs used frequently early in treatment will heighten malignant cell death while simultaneously inhibiting the development and growth of drug-resistant malignant copies. Treatment in the induction phase includes a glucocorticoid (prednisone or dexamethasone), vincristine and asparaginase, with the addition of an anthracycline for children who are high-risk. Also, part of this phase involves intrathecal chemotherapy, which all children need to receive spinal taps. Chemotherapy is injected into the cerebrospinal fluid (CSF) to kill any leukemia cells that may have spread to the central nervous system (CNS). The drug that is injected is called methotrexate, however additional drugs like hydrocortisone and cytarabine (ara-C) may be added in high-risk cases (Landier, 2001).

Children with ALL who are high-risk and children who possess leukemic cells in their CSF upon diagnosis may be given radiation therapy to the brain (and possibly to the spinal cord) (Landier, 2001). Radiation therapy works by destroying the DNA within cells, which subsequently prevents the cells from growing and reproducing (Eiser & Tillman, 2001). Although the goal of radiation is to protect healthy cells as much as possible so that the advantage (damaging the leukemic cells) outweighs the risk (damaging healthy cells), the truth of the matter is that healthy cells located near the cancer cells have a high probability of becoming damaged as well. As a result, doctors have tried their best to avoid administering this type of therapy because regardless of the dose, future problems have been associated with cognition, growth, and development and administration is significantly less frequent than in the past.

***Consolidation/Intensification***

Almost all children with ALL achieve remission after approximately 4 weeks of treatment. The consolidation phase, lasting four to eight months, entails intensified treatment for all patients (low risk, average risk, high risk, and very high risk), with the goal of strengthening remission and further eradicating residual or resistant leukemic cells (Eiser & Tillman, 2001). It also attempts to eliminate leukemia from sanctuary sites, especially in the CNS. Intrathecal chemotherapy is continued during this phase. Low-dose short-term maintenance precedes subsequent "spikes" of intensification therapy. Administration of these spikes, which is based on the Norton-Simon hypothesis, is similar to the type of treatment administered during induction and consolidation, but differ in that they aim to abolish the small, but significant number of leftover leukemic cells (Landier, 2001). Agents commonly used during this phase include cytarabine, high-dose methotrexate, asparaginase, cyclophosphamide, epipodophyllotoxins, mercaptopurine, thioguanine, vincristine, glucocorticoids, and doxorubicin (Landier, 2001).

***Maintenance***

Maintenance therapy can begin once the leukemia remains in remission, and lasts somewhere between two and three years. The goal here is to maintain the remission through daily administration of mercaptopurine and weekly doses of methotrexate (both given as pills). Vincristine (given intravenously) and a steroid (either prednisone or dexamethasone) are also administered intermittently. The management of these medications has been associated with reduced incidence of relapse (Eiser & Tillman, 2001).

***Central Nervous System Prophylaxis***

CNS prophylactic treatment is primarily used to reduce the risk of meningeal relapse due to the invasion of the CNS by leukemic cells (Moleski, 2000). Its goal is to maximize survival rates while minimizing potential effects. Before CNS prophylactic therapy was introduced into ALL treatment regimens, more than 40% of children suffered CNS relapses. This is due to the nature of the blood-brain barrier that blocks most systemic agents from reaching the CSF, which is where leukemic cells are located in the CNS. In the 1960s, when prophylactic CNS therapy with craniospinal radiation was implemented, rates of CNS relapse suddenly dropped (Espy, Moore, Kaufmann, Kramer, Matthay, & Hutter, 2001). However, children who had survived ALL exhibited late effects including serious neuropsychological deficits, including learning disabilities and growth failure (Spiegler, Kennedy, Maze, Greenberg, Weitzman, Hitzler, & Nathan, 2006). "CNS prophylactic treatment is largely responsible for the marked increase in long-term survival of children with ALL because the CNS is a sanctuary for leukemic cells, and therefore, CNS preventative therapy reduces the probability of relapse" (Butler & Haser, 2006, pp. 184).



Currently, CNS therapy has been tailored to risk factors. This means that only children with ALL who have CNS disease at diagnosis are given therapeutic doses (2,400 cGy) of cranial radiation. However, it is important to note that all children with ALL receive preventive CNS therapy, which consists of either intermittent intrathecal methotrexate or intrathecal triple therapy (methotrexate, cytarabine, and hydrocortisone) (Buizer, de Sonneville, & Veerman, 2009). Children who are high-risk often receive prophylactic cranial radiation, although at lower doses (1,200 to 1,800 cGy), in addition

to the above-mentioned required standard intrathecal chemotherapy (Espy et al., 2001). Due to the negative effects of cranial radiation therapy (CRT), the current primary therapeutic modality for ALL is a combination of chemotherapy and intrathecal chemotherapy (ITC). ITC has largely been substituted for CRT. As a result of these advances in treatment, overall childhood ALL survival rates have increased to approximately 80%.

***Prognosis***

Due to the heterogeneous nature of childhood ALL, attempts have been made to separate children into homogenous groups according to risk of relapse. Individuals who are classified as high-risk and very-high risk require more intensive treatments with the intent of improving chances of survival, whereas children in low-risk groups are given less intense therapy with the goal of limiting toxicities and reducing late effects of treatment (Landier, 2001).

The most significant prognostic factor is the white blood cell (WBC) count at the time of diagnosis. Children with the highest WBC counts (WBC > 50,000) have the bleakest prognosis and are classified as high-risk and require the most intensive treatment. It has also been found that children under the age of one or older the age of nine have poorer outcomes than children between those ages. Infants younger than 12 months are the least responsive to treatment and have lower survival rates than any other age group (Landier, 2001).

Children who attain remission rapidly, within the first week of treatment have a significantly better prognosis than those who attain remission later in induction therapy (Landier, 2001). Finally, previously mentioned features of leukemic blasts have