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LONGITUDINAL PREDICTORS OF QUALITY OF LIFE IN ADOLESCENT SURVIVORS
OF CHILDHOOD CANCER: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR
STUDY

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of
Philosophy at Virginia Commonwealth University.

by

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Abstract

LONGITUDINAL PREDICTORS OF QUALITY OF LIFE IN ADOLESCENT SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY

By Claire C. Russell, M.S.

A Dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University.

Virginia Commonwealth University, 2013

Major Director: Marilyn Stern
Professor, Department of Psychology

Objective: The impact of childhood cancer on future quality of life (QoL) in survivors is unclear. Current studies focus on comparing outcomes to healthy peers and identifying related treatment and demographic variables, but a shift in our approach is necessary. This study is guided by the Wilson and Cleary Model (WMC) and seeks to identify longitudinal predictors of QoL in adolescent survivors of cancer that explain variance in QoL beyond the impact of treatment and demographic variables. Methods: The Childhood Cancer Survivor Study (CCSS) is a multi-institutional longitudinal study following a cohort of childhood cancer survivors. This study focuses on the CCSS cohort (N = 305) who completed the baseline survey in 1994 and the Teen survey in 2001. The baseline survey assessed parent-report of child's psychological and physical symptoms, functional status, and health perceptions. The Teen survey utilized the Child Health and Illness Profile – Adolescent Edition (CHIP-AE), a self-report measure assessing QoL in six

domains: achievement, resilience, satisfaction, discomfort, disorders, and risk. The primary hypothesis was that psychological and physical symptoms, functional status impairment, and health perceptions as rated by parents at baseline would predict variance in quality of life as rated by adolescents at follow-up after adjusting for demographic and treatment-related variables. Six separate hierarchical regressions were analyzed for each of the QoL domains. Results: The main hypothesis was supported. For each QoL outcome, a significant amount of variance was predicted: achievement, $F(6, 259) = 8.90, p < .001, \text{adjusted } R^2 = .152$, resilience, $F(12, 209) = 3.47, p < .001, \text{adjusted } R^2 = .118$, satisfaction, $F(6, 265) = 8.73, p < .001, \text{adjusted } R^2 = .146$, discomfort, $F(7, 273) = 6.75, p < .001, \text{adjusted } R^2 = .126$, disorders, $F(9, 212) = 6.47, p < .0001, \text{adjusted } R^2 = .182$, and risk, $F(7, 238) = 4.81, p < .001, \text{adjusted } R^2 = .098$. Furthermore, for all outcomes, psychological and physical symptoms, functional status impairment, and health perceptions predicted variance above and beyond the impact of demographic and treatment variables. These factors accounted for an additional 9.5% of the variance in the achievement domain, 6.2% for resilience, 10.8% for satisfaction, 6.5% for discomfort, 12.4% for disorders, and 6.1% for risk. Conclusions: Results suggest that psychological and physical symptoms, functional status and health perceptions should be assessed and targeted in interventions for childhood cancer survivors to promote future positive QoL. Future studies need to continue identifying factors related to positive long-term functioning in diverse samples of childhood cancer survivors.

Longitudinal Predictors of Quality of Life in Adolescent Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study

Each year, approximately 12,400 children are diagnosed with cancer, with one in 300 boys and one in 333 girls being diagnosed. Although childhood cancer remains the number one disease killer of children, recent medical advances have contributed to a higher rate of survivorship, with 80% of children reaching the five year survival mark (Reis, et. al., 2007). As childhood cancer survival rates increase, the focus of psychological research and interventions has shifted from palliative care and grief in the 1970's, to pain management in the 80's and 90's, to issues of survivorship and quality of life in the past fifteen years (Brown, 2006). Current estimates suggest that 1 in 900 adults between the ages of 15 and 45 are childhood cancer survivors, making the study of survivorship and optimal adjustment to both the cancer diagnosis, treatment, and life after cancer necessary (Robison, et. al., 2002). As noted by Schwartz (2003):

“It is not uncommon to speak of curing cancer, but cure is the restoration of health. While cancer can be eradicated, survivors must be restored to health that lasts for decades. Five-year survival is only the beginning, not the end point of successful treatment” (Schwartz, 2003, p. 1641).

Quality Of Life in Childhood Cancer Survivors

Although rates of survivorship have increased, the cost of surviving childhood cancer can be high. Two-thirds of survivors experience medical late effects as a result of treatment, including secondary cancers, heart defects, lung defects, infertility, stunted growth and impaired cognitive ability (Hewitt, Weiner, & Simone, 2003). Therefore, a diagnosis of cancer in childhood often leads to life-long medical complications that must be monitored and treated. Increased morbidity further contributes to a greater risk of mortality for cancer survivors. A study examining death certificates of over 200,000 children diagnosed with cancer who had survived at least five years from diagnosis found that survivors had a significantly greater risk of

mortality, with the leading cause of death being cancer recurrence (67%) followed by secondary cancers, and cardiac and pulmonary problems (Mertens, et. al., 2001). The presence of chronic medical conditions and late-effects has been found to increase risk for lower educational attainment, unemployment, social outcomes such as lower rates of marriage, and psychological impairments (Pang, et. al., 2008; Florin, et. al., 2007; Ness, et. al., 2005; Meeske, Patel, Palmer, Nelson & Parow, 2007; Zebrack, Yi, Peterson, & Ganz, 2008), highlighting the broad affect of these late-effects.

The negative physical impact of being diagnosed and treated for cancer as a child is well-established, but the impact of cancer on future quality of life is less clear. Quality of life is a broad construct defined as a, “multidimensional construct including general health, and physical, emotional, and social functioning (Speechley, Barrera, Shaw, Morrison, & Maunsell, 2006, p. 2536).” Quality of life has been examined as both a general construct in childhood cancer survivors (Wu, et. al., 2007; Shankar, et. al., 2005), and through the examination of physical, psychological or social functioning separately, and findings have varied.

Several studies report negative outcomes for childhood cancer survivors, including higher rates of anxiety (Schultz, et. al., 2007; Hobbie, et. al., 2000), depressive symptomatology (Schultz, et. al., 2007; Zebrack, et. al., 2002), and suicidal ideation (Recklitis, Lockwood, Rothwell, & Dillner, 2006). In adolescent survivors, elevated rates of Posttraumatic Stress Disorder/Symptoms (PTSD/S) have also been reported, with survivors showing rates similar to other children who have experienced traumatic events such as surviving a natural disaster (Kazak, et. al., 2004; Hobbie, et. al., 2000). A study examining several domains of functioning in adolescent survivors found increased risk for problems in many areas when compared to a control group of siblings (Schultz, et. al., 2007). Based on parent report, survivors were more

likely than siblings to have elevated symptoms across all assessed domains, including depression/anxiety, headstrong (e.g. oppositional, stubborn), attention problems, social withdrawal, antisocial behaviors, and social competence. Survivors had particular increased risk for difficulties with depressive/anxiety symptoms (1.5 times higher than siblings), and antisocial behavior (1.7 times higher). Continued impairment in psychological functioning has been reported in adult survivors of childhood cancer as well. One study examined suicidality in adult survivors and found that 12.8% of survivors were classified as having suicidal ideation, defined as indicating current or past suicidal ideation on a questionnaire or reporting previous suicide attempts. This rate of suicidal ideation is higher than rates reported for the general population, suggesting that survivors may be more likely to experience thoughts of suicide (Recklitis, Lockwood, Rothwell, & Dillner, 2006).

In addition to examining the emotional functioning of childhood cancer survivors, other studies have focused on the impact of cancer and its subsequent treatment on social and developmental outcomes. The experience of cancer in childhood interrupts normative development as children are often isolated due to the side-effects of their treatment. Additionally, they spend a significant amount of time at the hospital and generally interact more with adults than other children. With many treatments lasting several months and some lasting as long as three years, this interruption can cross critical developmental time periods which may have a lasting impact on survivors. Studies have shown that particular sub-groups of childhood cancer survivors, such as brain tumor survivors, are more likely to have social difficulties, including having fewer friends (Vannatta, Garstein, Short & Noll, 1998), and long-term social outcomes including lower rates of marriage have also been reported (Gurney, et. al., 2009).

Stam and colleagues (2005) examined the developmental trajectory of survivors by assessing the age at which survivors reportedly met major developmental milestones. Surveyed milestones focused on autonomy development, psycho-sexual development, social development, anti-social behavior, and risk behavior (e.g. tobacco and alcohol use). They found that survivors ($M_{age} = 24.3$), reportedly accomplished fewer milestones in autonomy development (e.g. survivors were less likely to have had a job during high school, or to have gone on vacation without adults), psycho-sexual development (e.g. survivors were older when they had their first boyfriend/girlfriend, had sexual intimacy, and had sexual intercourse), and social development (e.g. survivors were less likely to be involved on a sports team, reported fewer friends, and were less likely to spend free time with peers) when compared to a group of similar-aged peers without a history of cancer. A majority of the assessed milestones typically occur during adolescence, so it is striking that the mean age of diagnosis for this sample of survivors was around 6 years old. These results highlight the long-term impact of cancer in childhood, with implications for development occurring throughout the life-span, not just during the time of treatment.

While many studies report increased risk for cancer survivors in areas including emotional, social, and developmental functioning, many other studies report no increased risk, and some suggest positive growth in survivors. A 2007 study examining health-related quality of life compared adolescents undergoing cancer treatment ($N = 136$) and adolescent survivors of cancer ($N = 226$), with healthy adolescents ($N = 134$). They found that while adolescents on treatment reported lower quality of life and worse physical functioning when compared to healthy controls, adolescent survivors did not significantly differ from the healthy population on overall quality of life or any of the domains assessed, including physical, cognitive,

psychological and social, body image, intimate relations, and outlook on life (Wu, et. al., 2007). Other studies report similar findings, with childhood cancer survivors comparing normally to the general population in regards to depression (Fritz & Williams, 1988) and anxiety (Barakat, et. al., 1997). Shankar and colleagues (2005) examined quality of life in younger survivors between the ages of 8 and 12, and found that some survivors reported significantly better quality of life when compared to healthy controls. However, this difference was only seen in male survivors of non-neurological solid tumors who were diagnosed after the age of six. This suggests that some sub-populations of survivors may have increased functioning and improved adaptation, a finding that has been reported in other studies as well (Shankar, et. al., 2005; Radcliffe, Bennett, Kazak, Foley & Phillips, 1996; Anholt, Fritz, & Keener, 1993).

The variability of findings in regards to the emotional functioning of survivors of childhood cancer, with some studies reporting poorer outcomes, others reporting no increased risk, and some reporting increased functioning, are likely related to the inconsistent methodological approaches to these studies. For example, where some studies focus on adult survivors of cancer (Zebrack, et. al., 2002; Recklitis, Lockwood, Rothwell, & Diller, 2006; Stam, Grootenhuis & Last, 2005; Gurney, et. al., 2009), others focus on survivors who are still in childhood and adolescence (Speechley, Barrera, Shaw, Morrison, & Maunsell, 2006; Schultz, et. al., 2007; Noll, et. al., 1997; Kazak, et. al., 2004). Even within studies examining child and adolescent survivors, there is variability, including those that report parent-report of child symptoms (Speechley, Barrera, Shaw, Morrison, & Maunsell, 2006; Schultz, et. al., 2007; Noll, et. al., 1997), those that discuss self-reported symptoms (Kazak, et. al., 2004; Barakat, et. al., 1997), and those that examine both parent and child report (Reiter-Purtill, Vannatta, Gerhardt, Correll, & Noll, 2003). Moreover, some studies examine only certain diagnoses, such as brain

tumors (Vannatta, Garstein, Short & Noll, 1998; Radcliffe, Bennett, Kazak, Foley & Phillips, 1996) or leukemia (Noll, et. al., 1997; Kazak, et. al., 1997), while others are broad and include several cancer diagnoses (Speechley, Barrera, Shaw, Morrison, & Maunsell, 2006; Schultz, et. al., 2007; Stam, Grootenhuis, & Last, 2005; Gurney, et. al., 2009). Another area of variability is sample size, with some studies reporting large sample sizes across institutions (Schultz, et. al., 2007; Zebrack, et. al., 2002; Barakat, et. al., 1997), and others having a smaller number of subjects within one institution (Vannatta, Garstein, Short & Noll, 1998; Radcliffe, Bennett, Kazak, Foley & Phillips, 1996; Reiter-Purtill, Vannatta, Gerhardt, Correll, & Noll, 2003). Comparison groups also vary, with some studies comparing survivors to established population norms (Noll, et. al., 1997; Recklitis, Lockwood, Rothwell, & Diller, 2006; Hobbie, et. al., 2000), others comparing outcomes to siblings (Schultz, et. al., 2007; Zebrack, et. al., 2002; Gurney, et. al., 2009) and others comparing to groups of individuals who never had cancer (Speechley, Barrera, Shaw, Morrison, & Maunsell, 2006; Stam, Grootenhuis, & Last, 2005; Reiter-Purtill, Vannatta, Gerhardt, Correll, & Noll, 2003). Finally, the wide range of chosen outcomes (e.g. depression, anxiety, posttraumatic stress, quality of life, developmental milestones, social relationships, employment, involvement in romantic relationships, etc.) makes it difficult to reach a general conclusion about the emotional functioning of childhood cancer survivors (Eiser, Hill, & Vance, 2000).

Predictors of Quality Of Life

There is a great deal of disagreement in the literature about the overall psychological status of survivors, but studies agree that there is a wide-variety of functioning in important domains. Therefore, rather than continuing to examine outcomes of childhood cancer survivors in order to create generalized statements about their overall functioning, a shift should be made

to identifying the predictors of such outcomes. While several studies have focused on demographic and treatment-related variables related to quality of life, very few studies have examined constructs that are malleable to change, such as perceptions of health or psychosocial functioning. Treatment-related and demographic variables help clinicians to better understand which populations may be at an increased risk for worse outcomes, but it is important that variables are identified that would allow for interventions designed to increase positive outcomes in all survivors.

Quality of life model. A model to help guide our understanding of quality of life in childhood cancer survivors is now offered. The Wilson and Cleary (1995) model is a guide for the examination of a variety of important variables that may impact quality of life. The model was developed because of a need to better understand how various clinical variables relate to quality of life, as this has become an important outcome in medical treatments. Wilson and Cleary posit that in order to understand quality of life, biological and medical variables along with social and psychological factors must be considered. Specifically, Wilson and Cleary assert that biological variables, physical and psychological symptoms, functional status, health perceptions, and characteristics of the person and environment are important predictors of quality of life. Biological variables are defined as factors that focus on the “function of cells, organs and organ systems,” and also include, “factors whose effects on health are principally mediated by changes in cell, organ, or organ system function” (Wilson & Cleary, 1995, p. 60). Biological variables therefore include information such as medical diagnosis and medical treatments (e.g. chemotherapy, radiation). Symptom status includes physical and psychological symptoms. Physical symptoms are broader than biological variables, with the focus shifting from the cellular and organ system level to the body as a whole. Physical symptoms are defined as, “a perception,

feeling, or even belief about the state of our body” (Wilson & Cleary, 1995, p. 61), and include information such as perceptions of pain. Psychological symptoms focus on a person’s emotional health and assess symptoms of fear, anxiety, sadness, etc. The third primary factor relating to quality of life is functional status, which is an individual’s ability to carry out everyday tasks independently. Finally, health perceptions refer to the person’s views of their health status. All of these symptoms are also impacted by factors of the individual, such as age and socioeconomic status and factors in the environment such as functioning in the school or work environment.

The Wilson and Cleary model has been used to better understand quality of life in a wide-range of populations. Sousa and colleagues (1999) used the Wilson and Cleary model to assess quality of life in adult patients with HIV. They found that the model including biological variables, symptoms, functional status, and health perceptions predicted 32% of the variance in quality of life scores, with symptoms contributing the greatest amount of variance (Sousa, Holzemer, Henry, & Slaughter, 1999). Faulkner (2010) used the Wilson and Cleary model to guide the inclusion of variables to assess the relation between physical fitness and quality of life in children and adolescents with type 1 and type 2 diabetes. Results show that while general fitness was related to both perceptions of health and biological variables including A1C (a measure of blood sugar over time), no significant relations with quality of life were found (Faulkner, 2010).

Wilson and Cleary’s model has been applied to quality of life in a variety of adult populations, including adults with angina (Ulvick, Nygard, Hanestad, Wentzel-Larsen, & Wahl, 2008), heart-failure (Heo, Moser, Riegel, Hall & Christman, 2005), HIV (Sousa, Holzemer, Henry, & Slaughter, 1999), and in older adults (Halvorsrud, Kirkevold, Diseth, & Kalfoss, 2010), but with the exception of the study cited above on diabetes, no known studies have used this

model with children and adolescents or with childhood cancer survivors. For the purposes of this study, the Wilson and Cleary model served as a guide for the inclusion of variables to assess for longitudinal predictors of quality of life in adolescent survivors of childhood cancer. In line with this model, selected predictors will include demographic and disease related variables, physical and psychological symptoms, functional status, and health perceptions. The rationale for choosing these predictors is detailed in the following sections.

Demographics. The reported relations between demographic variables and quality of life in childhood cancer survivors have been mixed. However, some consistent findings have been reported across studies, including those associated with gender, with female survivors being found to be at an increased risk for poorer outcomes (Zebrack, et. al., 2002; Gurney, et. al., 2009; Wu, et. al., 2007). Socioeconomic status has also been examined, with some studies reporting increased risk for lower SES individuals (Zebrack, et. al., 2002; Sung, et. al., 2008), and other studies reporting no relation (Klassen, Anthony, Khan, Sung, & Klaassen, 2011). Several other studies have also examined ethnicity as a predictor of quality of life in survivors and have reported an increased risk for poorer quality of life outcomes in non-white survivors (Wu, et. al., 2007; Shankar, et. al., 2005).

Age at diagnosis has also been examined as a predictor of quality of life outcomes in survivors. Several studies have identified specific risks for children diagnosed with cancer at a younger age, as intensive treatments during these critical developmental years may impact development and future functioning in distinctive ways. Being diagnosed prior to the age of three has consistently shown to significantly increase the likelihood of experiencing severe neurocognitive sequelae (Nathan, et. al., 2007). Exposure to whole-brain radiation during these early developmental years further increases these risks, with one study reporting a mean IQ loss

of 27 points for children treated with whole brain radiation before the age of seven. In this study, children over the age of seven who were treated with whole brain radiation did not show a significant decrease in their IQ, thus highlighting the importance of developmental stages on late-effects (Radcliffe, et. al., 1992). Furthermore, young children (ages 0 -5) treated for CNS tumors are more likely to utilize special education services, with boys being 13.3 times more likely to have used special education services compared to siblings and girls being 30.5 times more likely to utilize such services (Mitby, et. al., 2003). The affect of treatment at a young age extends beyond school, with survivors treated earlier in life showing increased risk for unemployment in adulthood (Gurney, et. al., 2009). Finally, younger age at diagnosis has also been found to be related to lower scores on physical and psychological quality of life in long-term CNS survivors (Sands, et. al., 2001) and increased suicidal ideation in adult survivors (Recklitis, Lockwood, Rothwell, & Diller, 2006).

Despite many studies reporting increased risk for children diagnosed and treated for cancer at a young age, these findings are not conclusive. Other studies report that age at diagnosis is not a significant predictor of future outcomes (Zebrack, et. al., 2002), or that those diagnosed at an older age have increased risk. Specifically, studies have found that older age at diagnosis has been related to lower physical and psychological quality of life (Speechley, Barrera, Shaw, Morrison, & Maunsell, 2006) and increased risk for illness-related worry and worse social functioning (Klassen, Anthony, Khan, Sung, & Klaassen, 2011). Therefore, the impact of age at diagnosis on future outcomes should continue to be examined.

In summary, the large number of studies that have examined the relations between demographic variables and quality of life have reported a wide-range of findings, with few consistent relations being found across studies. However, female gender has consistently been

found to be associated with increased risk for negative outcomes in survivors. Furthermore, many studies indicate that low SES may be a risk factor for negative outcomes. Although not examined as often, some studies also suggest that white survivors have better outcomes when compared to other racial groups. Finally, the relation between age at diagnosis and future outcomes has been mixed, though several unique risk factors for children diagnosed at a young age have been identified, suggesting that understanding the future functioning and quality of life for this subset of survivors is important.

Biological Variables. The relation between disease-related variables, such as diagnosis and treatment-exposures, and quality of life has been examined in many studies (Speechley, Barrera, Shaw, Morrison, & Maunsell, 2006; Schultz, et. al., 2007; Recklitis, Lockwood, Rothwell, & Diller, 2006). While there is range of findings across studies, some consistent relations have been reported. For example, the diagnosis of a CNS tumor has been consistently linked to increased risk for poorer outcomes (Klassen, Anthony, Khan, Sung, & Klaassen, 2011), including lower overall quality of life (Zebrack & Chesler, 2002) poor social functioning (Schultz, et. al., 2007; Vannatta, Gartsein, Short, & Noll, 1998; Zebrack & Chesler, 2002), impairment in functional status and poor health-status (Hudson, et. al., 2003), increased utilization of special education services (Gurney, et. al., 2009), lower psychosocial quality of life (Speechley, et. al., 2006), and higher risk for unemployment (Gurney, et. al., 2009).

Additionally, several studies have reported a higher risk for poor outcomes for survivors of acute lymphoblastic leukemia (ALL). One study found a higher likelihood of ALL survivors reporting suicidal ideation as adults when compared to survivors of lymphoma and solid tumors (Recklitis, Lockwood, Rothwell, & Dillner, 2006). A similar finding has also been reported for a general measure of quality of life, with leukemia survivors reporting significantly lower scores

when compared to solid tumor and lymphoma survivors (Wu, et. al., 2007). Another study reported that leukemia survivors were one subgroup at increased risk for poorer physical quality of life as survivors, though six other diagnostic groups also reported significantly lower scores when compared to controls, suggesting ALL survivors may not have more of a risk than other diagnoses (Speechley, et. al., 2006). However, in contrast, other studies have reported decreased risk for negative outcomes for leukemia survivors, including Hudson and colleagues (2003) who reported that bone tumor and CNS survivors were significantly more likely to report poor health-status when compared to leukemia survivors.

Many studies report different diagnostic groups as being at increased risk for poorer outcomes, with some reporting solid tumors such as neuroblastoma (Schultz, et. al., 2007), and many reporting leukemia (Schultz, et. al., 2007; Recklitis, Lockwood, Rothwell, & Diller, 2006), thus making it difficult to form a consistent understanding of which diagnostic groups are at increased risk for worse adjustment in the future. One way to gain a better understanding of the impact of diagnosis on future functioning is by examining the impact of treatments received. Often treatment exposure and diagnosis assess the same thing since diagnosis dictates treatment, though some forms of treatment cut across diagnostic groups (e.g. the majority of children treated with cranial radiation have a brain tumor but some children with leukemia are also treated with cranial radiation (Speechley, et. al., 2006)).

Therefore, while survivors of leukemia and CNS tumors are often identified as diagnoses with increased risk for poorer quality of life as survivors, this is likely due to the exposure to cranial radiation (CNS tumors) and intrathecal methotrexate (leukemia) that are part of the treatment protocols for these diagnoses. Indeed, two of the most common predictors for worse outcomes in survivors are exposure to cranial radiation and intrathecal methotrexate. Studies

have reported the lowest health-related quality of life scores among survivors treated with cranial radiation (Speechley, et. al., 2006), and other studies have reported increased risk of depression/anxiety symptoms, attention problems, antisocial behaviors, and worse social competence in survivors treated with either intrathecal methotrexate, cranial radiation, or both (Schultz, et. al., 2007). Another study reported no difference in behavior problems for those survivors treated either with just intrathecal methotrexate or with intrathecal methotrexate and cranial radiation, suggesting that perhaps after hitting a certain level of treatment intensity, the additive effects of other treatments do not significantly impair functioning (Noll, et. al., 1997).

In trying to understand the affect of treatment on future outcomes in survivors, one difficulty is the lack of standard approaches to assessing and categorizing treatment. While many studies examine exposure to specific chemotherapy agents or radiation treatment, others assess treatment modality or focus on treatment intensity. Studies examining the impact of receiving different types of treatment, including chemotherapy, radiation, surgery, or a combination of these modalities have reported that survivors who have received all three types of treatment typically report lower quality of life compared to those who received only one or two types of treatment (Speechley, et. al., 2006). Another study found that when treatment included surgery or radiation, the risk of poor health status was greater in adult survivors (Hudson, et. al., 2003).

A wide range of studies has chosen to examine the effects of treatment intensity on future functioning. Zebrack and colleagues (2002) reported that more intense treatment protocols were associated with increased depressive symptoms in leukemia survivors and somatic symptoms in ALL survivors. Similarly, Sung and colleagues found that increased intensity was associated with worse physical, emotional, and social quality of life in patients undergoing active treatment (Sung, et. al., 2009). However, such findings are not conclusive as other studies have found no

relation between treatment intensity and future outcomes (Noll, et. al., 1997). There are several problems with the literature on treatment intensity, including how treatment intensity is measured and defined. Studies have varied in how they assess for treatment intensity, with some studies using parent-perceptions of intensity (Sung, et. al., 2009), and others using physician-ratings or medical record review (Sawyer, Anotoniou, Toogood, & Rice, 1999). Furthermore, several studies categorize treatments as being “intensive” without providing a clear definition for that label (Zebrack, et. al., 2002; Noll, et. al., 1997).

Along with demographic variables, relations between disease-related variables and future outcomes have received the most attention in the literature. However, despite a large number of studies examining these relations, various approaches to assessing disease-related variables make it difficult to generalize findings. Two clear risk factors for negative outcomes have emerged, and these include the diagnosis of a CNS tumor and exposure to cranial radiation and/or intrathecal methotrexate as part of the treatment protocol. Trends have emerged suggesting that leukemia survivors, along with those exposed to more intense treatment protocols or more treatment modalities may also be at increased risk for negative outcomes, though several other studies have disputed these findings, making it difficult to draw clear conclusions. With results being varied, it is important to continue examining relations between treatment exposures and future functioning.

Psychological symptoms. Less information is available about the longitudinal relation between psychological symptoms and quality of life in survivors of childhood cancer. Several studies have concluded that early psychological adjustment in the course of cancer treatment predicts later psychological adjustment in parents (Best, Streisand, Catania, & Kazak, 2002; Hoekstra-Weebers, Jaspers, Kamps, & Klip, 2001) and children (Kupst, et. al., 2002). One study

examined psychological functioning over time in children undergoing hematopoietic stem cell transplant (Kupst, et. al., 2002). In this study, parents completed ratings of their child's internalizing (e.g. anxiety, depression, withdrawn) and externalizing (e.g. attention, rule-breaking) symptoms on the Child Behavior Checklist (CBCL) at three time points: pre-transplant, one year post-transplant and two years post-transplant. They found that initial reports of internalizing and externalizing symptoms predicted future internalizing and externalizing symptoms in these patients, suggesting that psychological adjustment can predict future psychological adjustment. However, this relation has never been examined in survivors of childhood cancer.

Several studies have reported significant relations between psychological symptoms and quality of life in children with cancer (Barrera, Atenafu, & Pinto, 2009) as well as other pediatric chronic illness populations, including diabetes (Grey, Boland, Yu, Sullivan-Bolyai, & Tamborlane, 1998) and asthma (Goldbeck, Koffmane, Lecheler, Thiessen, & Fegert, 2007; Vila, et. al., 2003). Barrera and colleagues (2009) followed children with cancer through stem cell transplant and assessed psychological functioning and quality of life pre-transplant as well as 1-year post-transplant and 2-years post transplant. They found that psychological functioning was related to physical quality of life, with those parents who reported worse physical quality of life for their child also reporting more internalizing and externalizing symptoms. This suggests a strong relation between quality of life and psychological functioning in children going through active treatment and into survivorship.

In a study of children with asthma, 81 children completed a self-report measure of quality of life and their parents completed the CBCL. A negative correlation between emotional symptoms and quality of life was found, with the internalizing subscale of the CBCL and the

CBCL total score being negatively related to child-reported quality of life (Goldbeck, Koffmane, Lecheler, Thiessen, & Fegert, 2007). Vila and colleagues (2003) further found that internalizing symptoms as rated by parents and anxiety as rated by the child accounted for the greatest amount of variance in self-reported quality of life in children with asthma, with 39% of the variance being explained by these measures of psychological functioning. This study suggests that perhaps the presence of emotional problems influences quality of life above and beyond the impact of having a chronic illness.

While several studies report that psychological functioning is related to future psychological functioning and that psychological functioning and quality of life are related, no studies have examined the longitudinal predictive power of psychological functioning on future quality of life. It is important to gain a better understanding of the longitudinal impact of psychological functioning on future quality of life in survivors of pediatric cancer. Assessing for psychological difficulties when a survivor is being followed more consistently in survivorship clinics is important. If psychological screeners could be given to parents and/or children during their survivorship appointments, concerns could be monitored and addressed more immediately when greater access to psychological services is available. Further, it is possible that intervening at an earlier time could not only alleviate current symptoms but also prevent poorer quality of life in the future (Mulhern, Wasserman, Friedman, & Fairclough, 1989).

Physical symptoms. Physical symptoms such as pain, fatigue, and physical disfigurement are also associated with quality of life in adolescent and young-adult cancer survivors (Barrera, Atenafu, & Pinto, 2009). Zebrack and Chesler (2002) examined physical quality of life in a sample of 176 adolescent and young adult cancer survivors between the ages of 16 and 28 and found that the most problematic physical symptoms for survivors included pain

and fatigue. Additionally, despite being done with treatment, 49% of survivors indicated that they were still experiencing noticeable side-effects. Moreover, those survivors reporting medical late-effects reported lower quality of life in the social domain, highlighting the extended affect of physical problems.

Physical disfigurement in childhood cancer survivors can range from limb amputation, scars from surgeries, permanent hair loss, or skin discoloration due to radiation (Ganz, 2006). Punyko and colleagues (2007) found that of the 417 survivors who reported an ongoing medical condition, 71% reported cosmetic problems while 24% reported neurosensory problems (Punyko, et. al., 2007). In one of the first studies examining physical problems with survivors, Mulhern and colleagues (1989) found that 83% of survivors reported experiencing physical symptoms including scars, visual impairments, learning problems, and obesity. Of those, 35% of participants reported having mild cosmetic impairment, defined as physical issues only obvious during physical examination or when wearing a bathing suit, or something on the face that could be covered with cosmetics. Twenty-five percent of participants reported moderate cosmetic impairment, defined as impairment that could be seen when the participant wore street clothes and/or facial disfigurement that was apparent even with the use of cosmetics. Finally, 4.4% of participants reported severe cosmetic impairment, defined as obvious physical deformities.

In examining the relation between physical disfigurement and quality of life, most studies have focused on the impact of limb salvage or limb amputation surgery in survivors of bone cancer. Studies have examined differences in psychological and social outcomes for survivors treated with limb amputation versus limb salvage surgery and have found no significant differences between scores on quality of life and outcomes such as psychosocial functioning, employment, level of education, or marriage (Nagarajan, et al., 2003; Eiser, Darlington, Stride,

& Grimer, 2001; Felder-Puig, et. al., 1998; Zebrack, et. al., 2007). However, when compared to sibling controls, both limb-salvage and limb-amputation participants had significant deficits in educational attainment and employment status (Nagarajan, et. al., 2003). This suggests that perhaps any physical impairment or disfigurement may affect future functioning despite the severity.

Another physical symptom that may continue to impact survivors is pain. Zebrack and Chesler (2002) found that aches and pains were the most endorsed long-term physical symptom in survivors, and pain levels continued to influence perceptions of quality of life. However, other studies have found that ratings of pain in survivors are similar to or lower than population norms (Speechley, et. al., 2006; Zeltzer, et. al., 2008). Several subgroups of survivors are reportedly at increased risk for experiencing pain, including bone tumor survivors (Zeltzer, et. al., 2008; Hudson, et. al., 2003), CNS tumor survivors (Armstrong, et. al., 2009) and survivors of autologous bone marrow transplant (Calaminus & Kiebert, 1999).

The presence of physical symptoms has consistently been linked with increased risk for poorer outcomes in survivors (Klassen, Anthony, Khan, Sung, & Klaassen, 2011; Zeltzer, et. al., 2008). For instance, survivors with disfigurement reported significantly more symptoms of depression and anxiety as well as attention problems and social concerns when compared to survivors without disfigurement (Schultz, et. al. 2007). Another study reported that survivors with PTSD were more likely to report moderate to severe medical late effects, and a relation between poor social functioning and the presence of late effects was also found. In this study, medical late effects were blindly rated by a pediatric oncologist and oncology nurse practitioner through a review of medical records, and areas assessed included restriction in daily activities, cosmetic changes, and the level of required medical attention (Meeske, Ruccione, Globe, &

Stuber, 2001). Finally, the presence of physical symptoms has also been found to be a significant predictor of suicidal ideation in adult survivors of childhood cancer (Recklitis, Lockwood, Rothwell, & Dillner, 2006).

Physical functioning variables have also been found to significantly predict poorer quality of life in survivors (Zebrack, Peterson, & Ganz, 2008). In a sample of child and adolescent survivors of pediatric cancer, those reporting more pain, fatigue, or severe medical late effects were more likely to report lower overall health-related quality of life. In this sample of 86 survivors, fatigue was associated with worse physical and psychological functioning, including worse social, school, and emotional functioning (Meeske, Patel, Palmer, Nelson, & Parow, 2007). This highlights the impact that physical symptoms can have on the various domains of quality of life. Another study of 400 adolescent and adult long-term survivors of childhood cancer found that the presence of more medical late-effects or health problems was associated with worse functioning in areas including mental health and social functioning (Langeveld, Grootenhuis, Voute, de Haan, & Van Den Bos, 2004).

One problem with the literature examining the relation between physical functioning and quality of life is that physical functioning is defined in several different ways. Some studies define physical functioning as including medical late effects (Pemberger, et. al., 2005; Langeveld, Grootenhuis, Voute, de Haan, & Van Den Bos, 2004), others focus on pain and fatigue (Zebrack & Chesler, 2002), others on physical disfigurement (Mulhern, Wasserman, Friedman, & Fairclough, 1989; Felder-Puig, et. al., 1998), and others on perceptions of health and functional status (Langeveld, Stam, Grootenhuis, & Last, 2002). Some studies also combine several outcomes under the umbrella of physical functioning, including perceptions of health, pain, and the presence of medical late-effects, making it difficult to tease apart the individual

impact of these constructs (Punyko, et. al., 2007; Meeske, Ruccione, Globe, & Stuber, 2001). Furthermore, there are more outcome reports on physical functioning since this is often a subscale on quality of life measurements (Zebrack & Chesler, 2002; Mulhern, Wasserman, Friedman, & Fairclough, 1989), so less is known about the predictive power of physical symptoms on future functioning. However, with this in mind, there is a growing body of literature suggesting that physical symptoms are related to quality of life in survivors of childhood cancer.

Functional status. In a sample of 183 survivors ($M_{age} = 12.2$ years), Mulhern and colleagues found that while the majority of their respondents reported no functional impairment (62.8%), a significant percentage reported either mild impairment (15.3%), defined as problems that require daily attention but causes little disruption to normal activities, or moderate impairment (20.8%), defined as requiring, “help with activities of daily living normally performed independently” (Mulhern, Wasserman, Friedman, & Fairclough, 1989, p. 21). Ness and colleagues (2005) reported that approximately 20% of adult survivors of childhood cancer ($M_{age} = 23$ years) reported significant limitations in completing tasks such as lifting objects, carrying groceries, walking uphill, climbing stairs, walking one block, eating, dressing, or bathing, and nearly 8% reported that these impairments affected their ability to attend school or work (Ness, et al., 2005). Punyko further found that rhabdomyosarcoma survivors were six times more likely to report that physical sequelae interfered with their ability to participate in work or school (Punyko, et. al., 2007). Another study found that adult survivors of childhood leukemia were two times more likely than their siblings to report functional impairment (Mody, et. al., 2008). However, not all studies have found that survivors report impairment in functional status. A survey of 90 young survivors of cancer found that survivors did not report significantly more

difficulty in engaging in activities or playing sports, nor did they report levels of fatigue that interfered with functioning when compared to a large group of healthy controls (Shankar, et. al., 2005).

More important than the rates of functional status impairment in childhood cancer survivors is the impact of such impairment on emotional functioning and quality of life. Mulhern and colleagues found that the presence of any functional impairment was significantly related to poor school performance, increased somatic concerns, internalizing, externalizing, and total problems as reported on the CBCL, with those reporting functional impairment being two to four times more likely than other survivors to report problems in these areas (Mulhern, Wasserman, Friedman, & Fairclough, 1989). A study of 37 survivors treated for bone cancer in childhood examined the impact of “everyday competence” on quality of life. Everyday competence assessed the participants’ ability to complete functional tasks such as preparing meals or dressing themselves. They found that everyday competence was a significant independent predictor of quality of life in this sample, with those reporting more difficulties completing everyday tasks also reporting worse quality of life, especially in survivors treated with limb salvage surgery (Eiser, Darlington, Stride, & Grimer, 2001).

Several studies have also found relations between functional status and social outcomes in survivors. Joubert and colleagues examined the affect of functional impairment on relationship styles in 97 adult survivors of childhood cancer. They found that those who reported an onset of functional impairment in adulthood also reported more insecurity in relationships and greater ambivalence in their relationships with their parents (Joubert, et. al., 2001). Generally, they found only negative relational outcomes for those survivors who reported that the onset of their functional impairment was in adulthood. Those who experienced functional impairments

beginning in childhood and adolescence did not report an impact on relational styles, suggesting a developmental component to the impact of functional impairments. Elkin and colleagues (1997) examined the affect of a variety of medical factors on psychological functioning in a sample of adolescent and young adult survivors ($M_{\text{age}} = 19$) of childhood cancer. While the majority of patients did not report functional impairment, 36% had some level of impairment, and functional impairment was found to significantly increase the risk of interpersonal problems. In fact, participants who reported severe functional impairment were 11 times more likely to report interpersonal difficulties (Elkin, Phipps, Mulhern, & Fairclough, 1997).

Although the majority of survivors do not experience severe functional impairment, these studies suggest that those who experience any amount of limitations in their daily activities are at an increased risk for worse adjustment in areas such as psychological functioning and interpersonal relationships. The developmental impact of functional status impairment has been studied and suggests that problems associated with functional impairment may be related to the time of onset. With this developmental model in mind, it is important to understand the predictive power of functional status impairment over time, especially if targeting these individuals earlier on in survivorship could offset the later impact of these impairments.

Health perceptions. Several studies have also examined the relation between perceptions of health and quality of life in adult survivors of cancer and have found that perceptions of poor health are related to outcomes across a variety of domains. Hobbie and colleagues (2000) reported that perceptions of treatment intensity and perceptions of current life threat were significantly related to increased posttraumatic stress symptoms in young adult survivors of childhood cancer. Moreover, treatment intensity ratings as determined through chart reviews were not significantly related to posttraumatic stress symptoms, highlighting the important role

of subjective health beliefs on outcomes such as psychological functioning in survivors (Hobbie, et. al., 2000). Zebrack and colleagues (2007) focused on current perceptions of overall health in a sample of survivors, and they found that those who rated their health as “fair/poor” were more likely to report increased distress across the domains of anxiety, depression, and somatization when compared to survivors who rated their health as “good/very good/excellent” (Zebrack, et. al., 2007). Additionally, many studies include perceptions of health in assessments of physical functioning, and as reviewed above, this area is consistently linked with quality of life outcomes. However, few studies have focused on the role of parental health perceptions on the functioning of children with cancer or child survivors.

When examining the influence of health perceptions in pediatric samples, it is important to consider parental perceptions of their child’s health. Parents of children with cancer report a great deal of worry about the health of their child, often reporting significantly more worry than the child while on treatment (Levi & Drotar, 1999). Parents of survivors also report a great deal of worry about their child relapsing or developing a secondary cancer, while survivors are more likely to report worries about the impact of late effects (Molgaard-Hansen, et al., 2011). Often, parents of childhood cancer survivors continue to perceive their child’s health to be poor, as evidenced by one study of parents of 800 cancer survivors that found that parents rated their child’s health as being significantly more at risk than parents of healthy children (Speechley, et. al., 2006).

A study of 62 parents with children on active treatment for cancer examined the influence of parental perceptions of their child’s health, parental overprotection, and parental stress on social, emotional, and behavioral adjustment in the child. They found that while parental stress was related to behavioral and social adjustment in children, parental perceptions of increased

health vulnerability were significantly related to emotional adjustment in these children (Colletti, et. al., 2008). There is a limitation in the methodology of this study as behavioral, emotional, and social adjustment were rated by the parent, and it is therefore possible that the parental perceptions of their child were also reflected in those scores. Still, this study suggests a relation between psychological functioning in children and parental perceptions of their child's health, but this relation has never been examined in cancer survivors despite information suggesting that negative parental health perceptions continue into survivorship.

The relation between parental views of their child's health and quality of life has been examined in other groups of children with chronic illness. Anthony and Gil studied a sample of 69 parent-child dyads recruited from pediatric rheumatology and pulmonology clinics. They found that parental perceptions of vulnerability were related to child-report of social anxiety, with children reporting increased social avoidance and generalized social distress when their parents reported higher perceptions of vulnerability (Anthony, Gil, & Schanberg, 2005). In children with asthma, Spurrier and colleagues (2000) found that children with parents who reported higher perceptions of vulnerability regarding their child's health had significantly more school absences than children with parents reporting less concern. This finding held after controlling for disease severity, and highlights the impact parental health perceptions can have on children as they develop. Higher parental perceptions of vulnerability have also been associated with adolescent's own feelings of illness uncertainty in adolescents with type 1 diabetes and asthma, highlighting the impact parental health perceptions can have on child health perceptions (Mullins, et. al., 2007).

Several studies indicate that parents of childhood cancer survivors continue to have a great deal of worry about their child's health and may perceive their child's health to be poor.

The effect of these negative health perceptions on future functioning in childhood cancer survivors has not been examined. Parental perceptions of vulnerability have been linked with outcomes such as social anxiety, school absences, and emotional functioning in samples of children with asthma and children on active cancer treatment. These findings suggest that an important relation exists between parental health perceptions and outcomes for the child. An understudied area in this literature is the longitudinal affect of these perceptions on child functioning. However, one study found that parental perceptions of vulnerability predicted internalizing and externalizing symptoms in the child two years later, suggesting that the impact of negative parental health perceptions can be long-lasting (Thomasgard & Metz, 1996). Another study found similar results with parental perceptions of vulnerability in premature infants. It was reported that perceptions of vulnerability at 5-months of age predicted lower mental scores at 32-months, again highlighting the pervasive and long-term influence of these parental perceptions (Stern, Karraker, McIntosh, Moritzen, & Olexa, 2006). These studies suggest that it is important to assess for the long-term impact of parental health perceptions on quality of life outcomes in childhood cancer survivors.

Summary of Predictors. Many studies have examined rates of emotional, physical, and functional status impairments as well as health perceptions of survivors of childhood cancer. Far fewer studies have examined the predictive power of these variables on future functioning. It is important that we begin to shift our focus to identifying those survivors who are at risk for future impairments earlier on in survivorship to properly and effectively target interventions.

Quality of Life Outcome. As previously noted, one difficulty in summarizing the quality of life data available on survivors of childhood cancer is the wide range of outcomes that assess quality of life. While some studies assess unidimensional outcomes of quality of life and focus

on one general quality of life score (e.g. Varni, Burwinkle, Katz, Meeske & Dickinson, 2002), other studies examine several dimensions of quality of life. Multidimensional models of identity and quality of life assert that several constructs, including academics, peer relationships, athletics, and appearances (Harter, Bresnick, Bouchey, & Whitesell, 1997; Masten, Coatsworth, Neemann, Gest, Tellegen, et. al., 1995) are included in one's perception of identity and therefore quality of life. A shift in the developmental literature has been noted, with older developmental models suggesting a unidimensional view of identity, and more recent models understanding that adolescents typically view themselves differently when they are with peers versus family versus school (Harter, 1998). Therefore, functioning and quality of life may vary across these areas. A similar shift in the cancer literature has been noted, with more recent studies examining quality of life across several domains, including psychological symptoms, social functioning, family environment, and vocation (Dolgin, Somer, Buchvald, Zaizov, 1999; Bampoe, Laperriere, Pintilie, Glen, Micallef, & Bernstein, 2000).

The Child Health and Illness Profile – Adolescent Edition (CHIP-AE) is a multidimensional measure of quality of life specifically for adolescents (Starfield, Riley, Green, Ensminger, Ryan, Kelleher, et. al., 1995). The CHIP-AE generates scores on 20 subdomains that map onto six primary domain scores: achievement, discomfort, disorder, resilience, risk, and satisfaction with health. Conceptually, these six domains include three positive quality of life domains: achievement, resilience, and satisfaction with health, and three negative quality of life domains: discomfort, disorder, and risk. More information on the CHIP-AE is included below.

The CHIP-AE has never been used as a quality of life outcome in studies of childhood cancer survivors. However, the multidimensional structure of the CHIP-AE provides a wealth of information about quality of life that would meaningfully contribute to the understanding of this

population. The CHIP-AE has been used in otherwise healthy urban and rural populations to establish population norms (Starfield, et. al., 1995), as well as with adolescents with psychiatric disorders (Riley, Ensminger, Green, & Kang, 1998), and incarcerated male adolescents (Forrest, Tambor, Riley, Ensminger, & Starfield, 2000).

The CHIP-AE has also been used to understand quality of life in adolescents with chronic illness, and relatively consistent findings have been reported. In one study examining acutely ill versus chronically ill adolescents, Starfield and colleagues (1996) found that adolescents with chronic illness reported significantly more limitations in daily activity, more medical disorders, lower satisfaction with their health, and lower physical fitness compared to established population norms. This is similar to findings for children with asthma who reported lower satisfaction with health, more limitations in daily functioning, more medical problems, and more emotional problems than children without asthma (Forrest, Starfield, Riley & Kang, 1997). Adolescents with chronic kidney disease also reported lower satisfaction with health and greater impairment in daily functioning. However, positive findings were also reported, with higher family involvement, better home safety and health, and better social-problem solving skills being reported (Gerson, Riley, Fivush, Pham, Fiorenza, Robertson, et. al., 2005). Taken together, these studies suggest that children with chronic illness may be more likely to report lower scores on the satisfaction with health domain, lower scores on the disorder domain which assesses medical comorbidities, and emotional disorders, lower scores on the discomfort domain which assesses limitations in daily functioning, and higher scores on the resilience domain which assesses home health and safety, family involvement, and social problem solving. However, these constructs need to be examined in childhood cancer survivors.

Adolescent Survivors

In addition to shifting the focus from outcomes of survivors to identifying predictors of such outcomes, attention to specific subsets of childhood cancer survivors is warranted. Fewer studies of childhood cancer survivors have specifically focused on adolescents and adolescent quality of life, with many studies including either adult survivors or a wide age-range of child survivors. Adolescence is a unique developmental time when emotional and physical late effects from cancer treatment can be particularly powerful (Eden, Barr, Bleyer, & Whiteson, 2005), and many adolescent survivors report that their cancer experience affects their self-perceptions (Smith, Ostroff, Tan, & Lesko, 1991). In addition to better understanding the unique experience of being an adolescent cancer survivor, it is important to understand functioning in adolescent survivors because fulfillment of developmental tasks during adolescence is an important predecessor to positive adjustment in adult life (Stam, Grootenhuis, & Last, 2005). Studies have found that functioning in adolescence can be predictive of future functioning in areas such as relationships, education, and productivity in the work-force, thus highlighting the need for positive adjustment during this time (Weissman, et. at., 1999; Trzesniewski, et. al., 2006).

In addition to focusing on this unique developmental period, it is also important to assess quality of life from the adolescent's perspective. Studies consistently suggest that parent reports of their adolescent's symptoms are not always accurate, especially in relation to non-observable symptoms such as psychological functioning (Eiser & Morse, 2001). Furthermore, studies have found that the discrepancy in these ratings is higher for parents of children with chronic illness, such as cancer, when compared to parents of healthy children (Levi & Drotar, 1999). This highlights the need in the literature to increase our understanding of the adolescent with cancer survivor's experience from their own point of view (Theunissen, et. al., 1998).

Finally, long-term adolescent survivors represent a unique group of survivors who were treated for cancer at a younger age. Intensive treatments during these critical developmental years may affect development and future functioning in distinctive ways. Several studies have identified increased risk in this population, including a greater likelihood of experiencing neurocognitive late-effects (Nathan, et. al., 2007), and poorer psychological functioning (Recklitis, Lockwood, Rothwell, & Dillner, 2006; Sands, et. al., 2001), as well as increased utilization of special education services in school and increased risk for unemployment in adulthood (Gurney, et. al., 2009). Given the unique developmental considerations of adolescent survivors, coupled with the unique impact of being treated at a younger age, it is clear that focused attention on long-term adolescent survivors is necessary.

Current Study

The purpose of the current study was to examine the longitudinal impact of psychological and physical symptoms, along with functional status and health perceptions, on quality of life in adolescent survivors of cancer while controlling for demographic and treatment-related variables. This examination allowed for the identification of target variables for future interventions to increase positive quality of life in childhood cancer survivors. Examined variables were chosen based on previous literature and guided by the Wilson and Cleary model which posits that demographic, disease variables, physical and psychological symptoms, perceptions of health, and functional status are related to quality of life. This model has been examined in other populations but has not been used as a theoretical guide in examining outcomes in childhood cancer survivors. This study addressed many of the current gaps in the pediatric cancer literature by focusing on long-term adolescent survivors, utilizing longitudinal data, and focusing on the identification of predictors of quality of life.

The current study used data from the Childhood Cancer Survivor Study, a large national database following a cohort of childhood cancer survivors for more than 15 years. Specifically, this study utilized data collected from the initial Baseline Survey completed in 1994 and the follow-up Teen survey that was completed between 2001 and 2003 by participants between the ages of 14 – 19. Predictors from the Baseline Survey, including child behavior, anxieties/fears, perceptions of health, pain, functional status, diagnosis, cancer therapy, and demographic factors, were used to predict quality of life which was measured with the Teen survey. Specifically, the Teen survey included the Child Health and Illness Profile - Adolescent Edition (CHIP-AE) that examines quality of life across 6 domains (satisfaction with health, discomfort, achievement, risk, resilience, and disorders; Starfield, et. al., 1995). Negative domains (discomfort, disorder, and risk) are reverse coded, so for each domain, a higher score indicates better health (e.g. a higher resilience score indicates more resilience whereas a higher discomfort score indicates less discomfort). Therefore, in the hypotheses, higher quality of life scores always indicates better health, while lower quality of life scores indicate worse health across all domains. More details on the study design are included in the Methods section below.

Specific Aims

1. To compare quality of life outcomes in adolescent cancer survivors to established population norms in six domains assessed by the CHIP-AE, including satisfaction with health, achievement, resilience, discomfort, risk, and disorders.
2. To identify predictors of positive adolescent quality of life (satisfaction with health, achievement, resilience), as rated by survivors on the CHIP-AE, using individual baseline characteristics such as child behavior, anxieties/fears, perceptions of health, pain, functional status, diagnosis, cancer therapy, and demographic factors.

3. To identify predictors of negative adolescent quality of life (discomfort, risk, disorders), as rated by survivors on the CHIP-AE, using individual baseline characteristics such as child behavior, anxieties/fears, perceptions of health, pain, functional status, diagnosis, cancer therapy, and demographic factors.

Hypotheses

1. Based on previous literature showing that adolescents with chronic illnesses are more likely to report significantly lower discomfort, disorder, and satisfaction with health scores and significantly higher resilience scores compared to established population norms (Starfield, et. al., 1996; Forrest, Starfield, Riley & Kang, 1997; Gerson, et. al., 2005), it was hypothesized that:
 - a. Adolescent cancer survivors would report significantly lower quality of life scores on the disorder, discomfort, and satisfaction with health domains of the CHIP-AE compared to established population norms.
 - b. Adolescent cancer survivors would report significantly higher quality of life scores on the resilience domain of the CHIP-AE compared to established population norms.
 - c. Adolescent cancer survivors would not report significantly different scores on the risk or achievement domains of the CHIP-AE compared to established population norms.
2. Given the literature, it was expected that:
 - a. Gender would be significantly related to quality of life outcomes in survivors, with males reporting higher quality of life scores than females across the six domains.

- b. Non-white individuals would report lower quality of life scores across the six assessed domains when compared to white participants.
 - c. Survivors treated with more treatment modalities would report lower quality of life scores across the six domains.
 - d. Survivors exposed to cranial radiation and methotrexate would report lower quality of life scores across the six domains.
3. Psychological and physical symptoms, functional status and health perceptions as rated by parents at baseline would account for a significant amount of variance in quality of life as rated by adolescents at follow-up after adjusting for demographic and treatment-related variables.
4. For each block in the hierarchical regression, given previous literature, it was predicted that the following relations would be found:
 - a. Demographics: Male gender, older age at diagnosis, and higher socioeconomic status at baseline would significantly predict higher quality of life scores as rated by adolescent cancer survivors at follow-up compared to female gender, younger age at diagnosis, and lower socioeconomic status.
 - b. Biological: Exposure to methotrexate and/or cranial radiation would significantly predict lower quality of life scores as rated by adolescent cancer survivors at follow-up compared to those who did not receive high-risk treatment.
 - c. Symptoms: Fewer psychological symptoms and fewer physical symptoms as rated by the parent at baseline would significantly predict positive quality of life outcomes as rated by adolescent cancer survivors at follow-up compared to those reporting more psychological and physical symptoms.

- d. Functional status: Lower functional status as rated by the parent at baseline would significantly predict negative quality of life as rated the adolescent cancer survivors at follow-up compared to those with higher functional status.
- e. Health Perceptions: Negative health perceptions as reported by the parent at baseline would predict lower quality of life scores as rated by adolescent cancer survivors at follow-up, while positive health perceptions would predict higher quality of life scores.

Methods

Participants

Participants for this study were members of the Childhood Cancer Survivor Study (CCSS). The CCSS is a multi-institutional longitudinal study following a cohort of childhood cancer survivors. Eligibility for CCSS participants included: 1) diagnosed between January 1 1970 and December 31, 1986; 2) diagnosed and treated for one the following cancers: leukemia, CNS tumors, Hodgkin disease, non-Hodgkin lymphoma, neuroblastoma, soft tissue sarcoma, kidney cancer, or bone cancer; 3) under the age of 21 at the time of diagnosis, 4) survived five years from the date of diagnosis (next of kin were asked to complete surveys for those participants who died after five year survival); 5) English or Spanish speaking; 6) resident of the United States or Canada at the time of initial contact for the study (Robison, et al 2002). Of the 20,276 survivors found to meet criteria for the CCSS, 17,280 could be contacted for study participation and 14,054 completed the Baseline questionnaire (Robison, et al 2002). Of these, 3,960 were under the age of 18 at baseline.

A follow-up survey of adolescent survivors (the Teen survey) was collected between February 2001 and December 2003 for CCSS cohort members ages 14 – 19 at the time of Teen

survey completion. A total of 702 adolescent survivors in the CCSS were identified as eligible for participation in this sub-survey. Of those, 30 could not complete the questionnaire due to cognitive impairments, and 9 survivors were deceased. Of the remaining eligible survivors, 444 agreed to participate in the study, and 307 completed and returned the questionnaire packet (Klosky, Howell, Li, Foster, Mertens, Robison, & Ness, 2012). This subset of survivors were treated at a very young age, with all participants in the Teen survey being three or younger at the age of diagnosis. The current study focused on the 307 CCSS cohort members who completed the Baseline and Teen surveys. According to Klosky and colleagues, (2012), “survivors who were White, older, female, and from households with incomes greater than or equal to \$60,000 were more likely to participate as compared to survivor nonparticipants (p-values range from <.01 to .03)” (Klosky, Howell, Li, Foster, Mertens, Robison, & Ness, 2012, p. 3). Reasons for not participating (e.g. refusing participation or not returning questionnaires) were not gathered for the Teen survey. See Table 1 for diagnostic information on participants.

Table 1.

Diagnosis information for current CCSS sample

Diagnosis	Baseline <18 yrs (N=3960)	Teen Survey (N=307)	Baseline <18 yrs and Teen Survey (N=307)
Leukemia	1771 (44.7)	95 (30.9)	95 (30.9)
CNS tumor	551 (13.9)	40 (13.0)	40 (13.0)
Hodgkin Lymphoma	50 (1.3)	-	-
NHL	154 (3.9)	4 (1.3)	4 (1.3)
Wilms tumor	585 (14.8)	56 (18.2)	56 (18.2)
Neuroblastoma	538 (13.6)	90 (29.3)	90 (29.3)
Soft tissue sarcoma	255 (6.4)	19 (6.2)	19 (6.2)
Bone tumor	56 (1.4)	3 (1.0)	3 (1.0)
Total	3960	307	307

Procedure

Eligible participants for the CCSS were identified from 26 cancer institutions across the United States. Each institution initially contacted participants from their site to register them in the cohort database using a structured protocol. Recruitment began in August of 1994. After this initial contact, a letter was sent from the coordinating center at the University of Minnesota Cancer Center to confirm participation (the coordinating center has since moved to St. Jude's Research Hospital). The Baseline questionnaire was sent to participants and contained 289 questions assessing areas such as demographics, medical information, late effects, mood, pain, marital status, health habits, etc. (See: <https://ccss.stjude.org/docs/ccss/survey-baseline-under-18.pdf>, for a copy of the Baseline Survey). Parents completed the Baseline questionnaire packet for survivors under the age of 18 at baseline. Two weeks after baseline packets were distributed, a reminder was sent in the mail to participants who had not returned their packets. Two weeks after the mail reminder, participants who did not return their packets were called. During this reminder phone call, it was confirmed that participants received their survey and any questions were addressed. Participants were also given the option of completing the questionnaire over the phone. When completed questionnaire packets were received, they were reviewed and entered into a computer database according to protocol (Robison, et. al., 2002).

Participants who completed the Baseline questionnaire were also asked to consent to the release of their medical records to collect information about their diagnosis and treatment. Of the 14,054 participants who completed the Baseline questionnaire, 91% consented for the release of this information and medical information was gathered from 98% of those cases. In addition to diagnosis and age at diagnosis, information gathered included exposure to 49 specific types of chemotherapy, cumulative dose information on 26 types of chemotherapy, and information about

routes of chemotherapy administration (e.g. intrathecal versus through a port). Radiation exposure was also collected, including dosages and location, and all surgical procedures were also documented (Robison, et. al., 2002).

The CCSS cohort has been followed longitudinally since the initial Baseline questionnaire, with two main follow-ups of the whole cohort occurring in 2003 and 2007. Additionally, smaller sub-samples of the cohort have been contacted to participate in specific surveys including Women's Health, Men's Health, and the Teen survey. The 208-item Teen survey included the Child Health and Illness Profile – Adolescent Edition (CHIP-AE; see below for a detailed description). Participants who completed the Teen survey were able to identify an organization to which a donation on their behalf would be given as incentive for completion.

Measures at Baseline

Demographics/environment. Demographic information, including sex, age, and race of the child, and annual household income, was collected in the Baseline questionnaire completed by parents. Upon examining the data, household income was dropped as a variable of interest due to lack of variance. Only 7% of all participants reported household incomes under \$20,000, and previous literature suggests that quality of life outcomes often vary between those children living in households making under \$20,000 and those making over \$20,000. With race, the sample was overwhelmingly white, not Hispanic (88%). In order to examine relations between race and the predictors and outcomes, the race category was created as a dichotomous variable with White and Non-white individuals as the two categories.

Educational information about the child was also collected, with parents identifying if their child received special education services in grades Kindergarten through 12th grade (<https://ccss.stjude.org/docs/ccss/survey-baseline-under-18.pdf>, page 14, O.4). In order to

meaningfully capture differences between children who required special education services versus those who did not, a dichotomous variable was created, with those who never used special education services as one of the categories and those who used special education services at any time in school at the time of the baseline survey as the other category.

Biological. Biological and treatment-related information was ascertained through information collected in participant's medical charts. The present study utilized the following data:

Diagnosis. Diagnostic information, including the number of participants in the sample diagnosed with Leukemia, CNS tumors, Hodgkin Disease, Non-Hodgkin Lymphoma, Wilms tumor, Neuroblastoma, Soft tissue sarcoma, and Bone tumor.

Treatment modalities.

Chemotherapy. Two types of information were utilized in relation to chemotherapy. First, dichotomous (yes/no) information regarding exposure to chemotherapy was gathered from treatment information. In addition, exposure to methotrexate was assessed (yes/no).

Radiation. Dichotomous information on exposure to either cranial radiation (yes/no) or other bodily radiation (yes/no) was gathered from treatment-related information.

Surgery. Dichotomous information about whether or not participants underwent surgery for their treatment (yes/no) was also gathered from the treatment-related data.

Treatment information was used to create two treatment variables: 1) exposure to high-risk treatment and 2) the number of treatment modalities received. Exposure to high-risk treatment assessed if the child received methotrexate or cranial radiation, with three possible responses: neither methotrexate nor cranial radiation, either methotrexate or cranial radiation, or both methotrexate and cranial radiation. For treatment modalities, data were aggregated to assess

if patients received one, two, or three types of treatment, including chemotherapy, radiation, and/or surgery.

Psychological Symptoms.

Behavior Problems Index. Information about psychological symptoms was ascertained from the Behavioral Problems Index (BPI) which was included in the Baseline questionnaire for participants under the age of 18 (<https://ccss.stjude.org/docs/ccss/survey-baseline-under-18.pdf>, p. 10, J. 16 – 21). The BPI consists of 32-items adapted from the Child Behavior Checklist which assess parent-report of child psychological symptoms across several domains: anxious/depressed, headstrong (e.g. oppositional), hyperactive, antisocial, peer problems, and dependent (Zill & Peterson, 1986). On the BPI, the parent is asked to rate 32 symptoms as “often true,” “sometimes true,” or “not true.” Sample symptoms include, “My child is ... too fearful or anxious/is stubborn, sullen, or irritable.” The BPI was initially created and utilized for the 1981 National Health Survey, Child Health Supplement. Subscales have shown good reliability in cancer survivors, with Cronbach’s alpha ranging from .80 (attention) - .89 (headstrong; Schultz, et. al., 2007).

The initial plan for the current project was to generate three scores from the BPI, including internalizing, externalizing and a total score. However, upon review of the data, several problems with the BPI data were found. To begin, a previous study completed a factor analysis of the BPI for CCSS participants between 12 – 18 years old and revealed slightly different subscales than the original subscales (Schultz, et. al., 2007). This suggests that subscales of the BPI may be different for childhood cancer survivors. Therefore, using established methods of calculating internalizing and externalizing scores based on the original subscales was not appropriate for this sample. Also, while four subscales (23 questions) were the

same for children of all ages, one subscale was different for children under 12 years old and children 12 and older. For children under the age of 12, items were completed for a dependency scale, and for children 12 and older, items were completed for a peer conflict scale (Zill & Peterson, 1986). Therefore, in order to use the defined subscales, the sample would need to be split by age for all analyses. Moreover, many of the subscales were skewed, kurtotic, and highly correlated with one another, indicating that issues with normality and multicollinearity would have arisen with the scales moving forward.

For the purpose of the current project, a factor analysis was completed to identify subscales of the BPI specific to this study's sample. A principal component factor analysis using a varimax rotation of the 23 BPI items common to all participants was conducted. Four factors had Eigenvalues greater than 1.00 and explained 58.9% of the variance. The first factor included the following items: being disobedient at home, cheating or telling lies, having a bad temper, being a bully, being disobedient at school, arguing, being stubborn, being impulsive, and not being sorry. For the purpose of the current study, this factor was labeled "externalizing symptoms" because the items generally describe a broad pattern of symptoms that are outwardly expressed and may include temper tantrums, disobedience, and fighting (Weisz, 2008). The next factor included: being withdrawn, not being liked by other children, feelings of depression, difficulty getting along with other children, difficulty getting along with teachers, feeling inferior and experiencing obsessions. This factor was labeled "internalizing symptoms" because the items encompass a broad pattern of symptoms that are typically internally experienced and include feelings of sadness and anxiety (Weisz, 2008). The third factor included: hyperactivity, difficulty concentrating, being high strung, being fearful or anxious, and being confused. This factor was labeled attention/hyperactivity symptoms because they generally describe symptoms

common for individuals with Attention Deficit Hyperactivity Disorder (ADHD). Finally, the fourth factor included two items: sudden changes in mood, and feeling like no one loves him/her.

Special consideration was given to the fourth subscale since it only had two items. Several options were considered for the fourth subscale, including keeping it as a separate subscale, not using the two items on the fourth subscale in further analyses, and combining the two items on the fourth subscale with the internalizing subscale because they are conceptually similar as they both assess internal thoughts and feelings (Weisz, 2008). Initial analyses were run with the fourth subscale kept separate, added into the internalizing subscale, and dropped from the analyses, and results did were not significantly different. Therefore, a decision was made to add the two items from the fourth subscale to the internalizing subscale. This approach prevented loss of information which would have resulted from discarding the items and also increased clinical relevance that would have been compromised with an independent two-item subscale. See Table 2 for factor loadings.

Because factor scores are not clinically significant, subscales were created based on factor loadings, with each item included on the subscale on which it loaded the highest. Therefore, three subscales were used in subsequent analyses: 1) externalizing symptoms, 2) internalizing symptoms, and 3) attention/hyperactivity symptoms. These three factors were normally distributed and not highly correlated with one another. The mean score for each subscale was calculated and used in all further analyses.

Table 2.

Factor Loadings and Scale Construction for the Behavior Problems Index

Item	Factor 1	Factor 2	Factor 3	Factor 4
Disobedient at home	78*	2	12	14
Cheats or tell lies	73*	9	13	15
Has a strong temper	68*	15	25	34
Bullies or is cruel to others	65*	26	5	28
Disobedient at school	65*	45	4	-19
Argues too much	65*	11	14	36
Is stubborn, sullen, or irritable	62*	18	31	29
Is impulsive or acts without thinking	58*	22	53	3
Does not seem to feel sorry after misbehaving	52*	22	19	9
Is withdrawn	6	70*	31	9
Is not liked by other children	22	67*	25	29
Is unhappy, sad, or depressed	16	66*	11	38
Trouble getting along with other kids	31	65*	24	19
Trouble getting along with teachers	49	61*	9	-16
Feels worthless or inferior	12	57*	21	49
Has obsessions	15	50*	44	13
Restless or overactive	37	13	68*	-1
Difficulty concentrating	31	32	67*	-4
High strung/tense/nervous	12	12	63*	40
Is too fearful or anxious	1	29	59*	33
Easily confused	10	47	53*	-2
Complains that no one loves him/her	34	11	4	67*
Sudden changes in moods	23	20	12	63*

Note. Values are multiplied by 100 and rounded to the nearest integer.

Social competence. Information about social competence was derived from three primary questions on the Baseline questionnaire. These questions included: “About how many close friends does your child have?” with answers ranging from “0” to “4 or more.” The next question asked, “About how many times a week does your child do things with close friends?” with answers ranging from “less than 1” to “3 or more.” The final question is a series of questions where parents were asked to answer, “Compared to other children his/her age, how well does your child...” get along with his/her brothers and sisters, get along with other children, behave with his/her parents, and play and work by himself/herself. These questions were ranked as “worse,” “about the same,” and “better.” A total score was derived by adding responses to these items, with higher scores indicating better social competence. These questions have been used in previous CCSS studies to assess social competence (Schultz, et. al., 2007; <https://ccss.stjude.org/docs/ccss/survey-baseline-under-18.pdf>, p. 10, J. 16 – 18).

Anxieties/Fears. To assess for parent’s perceptions of the anxieties and fears that their child had that were directly related to their cancer experience, parents were asked to answer the question, “Does your child currently have anxieties/fears as a result of his/her cancer, leukemia, tumor, or similar illness, or its treatment?” There were five possible answers including, no anxiety/fears, small amount of anxiety/fears, medium amount of anxiety/fears, a lot of anxiety/fear, and very many/extreme anxiety/fears (<https://ccss.stjude.org/docs/ccss/survey-baseline-under-18.pdf>, p. 11, J.24). This question has previously been used to assess for cancer-specific anxiety and worries in adult survivors in the CCSS cohort (Hudson, et. al., 2003).

For this sample, 61% of parents reported that their child experienced no cancer specific anxiety, 30% reported small amounts of anxiety, and the remaining 10% reported medium to extreme amounts of anxiety. Because relatively few reported anything for the top three

categories -- medium, a lot, and, extreme –these categories were collapsed into one for subsequent analyses. The final derived variable had three levels: no anxiety, some anxiety, and medium to extreme anxiety.

Physical Symptoms.

Physical disfigurement. Physical disfigurement was assessed by a series of yes/no questions asking about persistent hair loss, scarring or disfigurement on the body, walking with a limp, and the loss of a limb or eye (<https://ccss.stjude.org/docs/ccss/survey-baseline-under-18.pdf>, p. 5, B.9). These questions have previously been used to assess for physical disfigurement in children in the CCSS cohort (Schultz, et. al., 2007). The majority of participants (39%) reported one area of physical disfigurement followed by no physical disfigurement (29%), and two areas of physical disfigurement (18%). Because very few participants reported more than two areas of disfigurement, the categories were collapsed from up to five areas of disfigurement into three categories: no disfigurement, one area of disfigurement, and two or more areas of disfigurement.

Pain. Parental perceptions of the level of pain their child experienced was assessed with the question, “Does your child currently have pain as a result of his/her cancer, leukemia, tumor, or other similar illness or its treatment?” Possible responses ranged from no pain to very bad/excruciating pain (<https://ccss.stjude.org/docs/ccss/survey-baseline-under-18.pdf>, p. 11, J.23). A similar self-report version of this question has been used to assess pain in samples of adult survivors in the CCSS cohort (Mertens, et. al., 2003). Few parents reported that their child experienced pain as a result of cancer or its treatment. 89% reported no pain in their child, so a dichotomous variable with “no pain” or “any pain” was created.

Functional status. To assess for functional status, parents were asked to complete a series of questions included in the Baseline questionnaire that assessed for functional status and limitations in activity. These questions were derived from the National Health Interview Survey and the Behavioral Risk Factor Surveillance System Survey Questionnaire (Hudson, et. al., 2003).

The first two questions assessed their child's ability to independently meet their needs, and asked parents if their child needed help with personal care or routine needs (yes/no; see <https://ccss.stjude.org/docs/ccss/survey-baseline-under-18.pdf>, p. 13, N. 6,7). Next, parents were asked if their child had any impairment that prevented them from going to school or holding a job (answered yes/no; <https://ccss.stjude.org/docs/ccss/survey-baseline-under-18.pdf>, p. 13, N.8). Finally, parents were asked to answer a series of questions with the prompt, "Over the last 2 years, how long (if at all) has your child's health limited them in each of the following activities." Assessed activities include vigorous activities (e.g. lifting heavy objects, running), moderate activities (e.g. carrying groceries), walking uphill/climbing stairs, bending/lifting, walking one block, and eating/dressing/bathing/toileting. Parents ranked their child's limitations on a three-point scale from "not limited at all" to "limited for more than three months" (<https://ccss.stjude.org/docs/ccss/survey-baseline-under-18.pdf>, p. 13, N.10). These questions have previously been used to assess for functional status in adult survivors in the CCSS cohort (Hudson, et. al., 2003).

Very few parents reported functional status impairments, with 83% reporting no impairment on the list of activities. Ninety-four to ninety-eight percent of parents indicated that their child did not need any help with personal care, meeting routine needs, or not being able to go to school. The continuous variable was highly skewed and kurtotic and therefore violated the

assumption of normality. Therefore, a dichotomous variable with no impairment or some impairment as the categories was created for the purposes of the current study.

General Health Perceptions. Parental perceptions of survivors' health were gathered through a series of questions. Parents were asked to answer a general question about their child's overall health: "Would you say your child's health is:" with five options ranging from "poor" to "excellent." This question has been used to assess for health perceptions in adults in the CCSS cohort (Zebrack, et. al., 2007; Hudson, et. al., 2003; <https://ccss.stjude.org/docs/ccss/survey-baseline-under-18.pdf>, p. 14, N.11). Parental perceptions of vulnerability were assessed with two questions. Parents were asked to "Please rate how concerned you are about the following issues," which include, "Your child's future health," and, "Your child developing cancer." Both of these items are rated on a 5-point scale from "not at all concerned" to "very concerned" (<https://ccss.stjude.org/docs/ccss/survey-baseline-under-18.pdf>, p. 19, R.1,3).

While the initial plan for the current project was to combine these two questions into one overall score of health perceptions, it became clear upon examining the data that perceptions of health and perceptions of vulnerability were measuring two separate constructs. While most parents reported positive perceptions of their child's current health ($M = 1.64$, $SD = .81$, with 1 being "excellent" and 5 being "poor"), they also reported a great deal of anxiety about their child's future health. On a scale of 1 – 5, with 1 being "very concerned" and 5 being "not at all concerned," the mean score for future health concerns was 2.04 ($SD = 1.16$), and for concerns about developing cancer in the future, the mean was 2.27 ($SD = 1.24$). Therefore, a decision was made to separate these two constructs. One question assessed current health perceptions, which was recoded so higher scores were equated to better health perceptions, and perceptions of

vulnerability which combined the two questions about future health, so that higher scores were equated with lowered levels of perceived vulnerability.

Measures from Teen Survey

Quality of life. Quality of life is the primary outcome of interest and was measured with the Child Health and Illness Profile – Adolescent Edition (CHIP-AE; Starfield, et. al., 1995). The CHIP-AE is a 108-item self-report measure of quality of life that assesses 20 subdomains of quality of life that map onto six primary domains: satisfaction with health, discomfort, achievement, risk, resilience, and disorders. (See: <https://ccss.stjude.org/docs/ccss/survey-teen-health.pdf>, for a copy of the full survey). The achievement domain assesses functioning in school and work (when applicable) with the academic performance and work performance subdomains. The subdomains in the resilience domain include: physical activity, social problem-solving, home safety and health, and family involvement, while the satisfaction with health subdomains include: satisfaction with health and self-esteem. The discomfort domain includes the physical discomfort, emotional discomfort, and limitations of activity subdomains that assess functional limitation as well as psychological and physical symptoms. The disorder domain includes several subdomains: acute minor disorders, acute major disorders, recurrent disorders, long-term medical disorders, long-term surgical disorders, and psychosocial disorders and examines specific conditions, injuries, or impairments (e.g. speech problems, disordered eating, learning disability, ear infections, acute medical diagnoses). Finally, the risk domain assesses risk-taking behavior with the individual risks, threats to achievement, and peer influences subdomains (Starfield, et. al., 1995).

The CHIP-AE has been normed in the general population, and each domain and subdomain has a standard score of 20 and a standard deviation of 5. Reliability and criterion,

convergent, and discriminant validity were established in a series of studies of 11 – 17 year olds in urban and rural schools (Starfield, et. al., 1995). Good reliability has been reported across each of the twenty subdomains, with Cronbach alphas ranging from .70 to .93 (Starfield, et. al., 1995).

Statistical Analyses

IBM SPSS Statistics 20.0 was used to analyze the data. Prior to hypothesis testing, all data was inspected for conformance to the assumptions of the General Linear Model (GLM; Tabachnick & Fidell, 2007). Details of assumption checking are reviewed in the results section. Descriptive statistics, including means, standard deviations, ranges, medians, and frequencies, were calculated for the primary outcome of interest as well as the selected predictors. Unpaired t-tests were used to determine if significant differences were present between the mean quality of life sub-domain scores and the established population norms (hypothesis 1a, 1b, and 1c). Independent sample t-tests were used to examine differences in quality of life scores between male and female participants (hypothesis 2a), and white and non-white participants (hypothesis 2b). Analysis of Variance (ANOVA) was used to assess for differences in quality of life outcomes based on treatment variables, including number of treatment modalities and level of exposure to high-risk treatment (hypothesis 2d).

Hierarchical regression was used to test whether psychological and physical symptoms, along with functional status and health perceptions, would account for additional variance in quality of life over and above the variance accounted for by demographic and treatment-related variables (hypothesis 3). With hierarchical regression, independent variables are entered into the regression model in a pre-specified order based on theoretical grounds. Variables are entered in blocks, with each independent variable being assessed for how much variance it adds to the model after controlling for the previous variables (Tabachnick & Fidell, 2007).

Six separate hierarchical regressions were created for each of the six quality of life domains. As guided by the Wilson and Cleary (1995) model, the blocks entered into each of the six regressions included demographics/environment, biological (treatment) variables, psychological and physical symptoms, functional status, and health perceptions. Because demographic and treatment-related variables have been examined more often in the literature and are consistently linked with quality of life outcomes in cross-sectional studies, these blocks were entered first, with block 1 defined by the demographic variables and block 2 made up of the treatment variables. Thus, the first blocks entered into the model assessed for the impact of factors that are not malleable to change and were controlled for moving forward. Next, in line with previous literature (Recklitis, Lockwood, Rothwell, & Diller, 2006), the symptom blocks of predictors were added. Although the Wilson and Cleary model combines psychological and physical symptoms into one construct, they were split into two separate blocks for the current study because they were deemed to be conceptually different. This split is consistent with previous studies, as was the decision to add psychological symptoms first, followed by physical symptoms (Recklitis, Lockwood, Rothwell, & Diller, 2006). Therefore, psychological symptoms were added in the third block, followed by physical symptoms in the fourth block. The final two blocks of predictors were functional status and perceptions of health. See Figure 1 for a sample of the variables entered for each block of the hierarchical regression. Details of the model building process are included in the results section as are the relations between the individual predictors and outcome variables (hypothesis 4).

<p>Block 1 Demographic Sex Race Age at diagnosis Special Education</p> <hr/>	<p>Block 4 cont Physical Symptoms Physical disfigurement Pain from cancer</p> <hr/>
<p>Block 2 <i>Demographic</i> <i>Sex</i> <i>Race</i> <i>Age at diagnosis</i> <i>Special Education</i> Biological High risk treatment Treatment modalities</p> <hr/>	<p>Block 5 <i>Demographic</i> <i>Sex</i> <i>Race</i> <i>Age at diagnosis</i> <i>Special Education</i> <i>Biological</i> <i>High risk treatment</i> <i>Treatment modalities</i> <i>Psychological Symptoms</i> <i>Internalizing symptoms</i> <i>Externalizing symptoms</i> <i>Attention/Hyperactivity symptoms</i> <i>Social Competence</i> <i>Cancer Specific Anxieties/Fears</i> <i>Physical Symptoms</i> <i>Physical disfigurement</i> <i>Pain from cancer</i> Functional status impairment</p> <hr/>
<p>Block 3 <i>Demographic</i> <i>Sex</i> <i>Race</i> <i>Age at diagnosis</i> <i>Special Education</i> <i>Biological</i> <i>High risk treatment</i> <i>Treatment modalities</i> Psychological Symptoms Internalizing symptoms Externalizing symptoms Attention/Hyperactivity symptoms Social Competence Cancer Specific Anxieties/Fears</p> <hr/>	<p>Block 6 <i>Demographic</i> <i>Sex</i> <i>Race</i> <i>Age at diagnosis</i> <i>Special Education</i> <i>Biological</i> <i>High risk treatment</i> <i>Treatment modalities</i> <i>Psychological Symptoms</i> <i>Internalizing symptoms</i> <i>Externalizing symptoms</i> <i>Attention/Hyperactivity symptoms</i> <i>Social Competence</i> <i>Cancer Specific Anxieties/Fears</i> <i>Physical Symptoms</i> <i>Physical disfigurement</i> <i>Pain from cancer</i> <i>Functional status impairment</i> Health perceptions Current health perceptions Perceptions of vulnerability</p>

Figure 1. Variables entered for each block of the hierarchical regression analyses
Notes. Italicized variables represent variables entered in previous blocks.

Results

Assumption checking

IBM SPSS Statistics 20.0 was used to analyze the data. To begin, all data was inspected for conformance to the assumptions of the General Linear Model (GLM; Tabachnick & Fidell, 2007). First, the normality of the continuous variables was examined by checking skewness and kurtosis values. All predictor values had good skewness and kurtosis values (e.g. no greater than +/-1) aside from the BPI subscale and total functional status impairment variable, which have been previously discussed.

For the outcome variables, the disorder and discomfort domains of the CHIP-AE showed evidence of skewness or kurtosis using the +/- 1 criterion. To inform decisions about transformations, histograms of the outcomes were examined along with the residual scatterplot. The normal probability plot of residuals was also examined to assure that the expected normal values for residuals and the actual values had a linear relation. Finally, the P-P plots were examined to compare the distribution of the outcome with a normal distribution. Based on this information, the only outcome that clearly violated the assumption of normality was the discomfort domain.

Transformations were attempted, including log transformations and square root transformations, but these only increased the skewness and kurtosis values. Because domain scores on the CHIP-AE are scaled scores, they actually can be conceptualized as having already been transformed. Therefore, it was decided to not transform the discomfort domain score, and results would be interpreted with caution.

Univariate outliers were also examined using standardized values, with standardized values greater than 3.29 being deleted. Two cases that were consistent outliers across variables

were deleted from the data set. Finally, to reduce redundancy and inflated standard errors, multicollinearity was examined. All continuous predictors and outcomes were entered into a correlation matrix. None of the variables were too highly correlated ($r > .70$), so no items were dropped during this phase of assumption checking.

Tests of normality continued to be examined during model building. Primarily, the variance inflation factor (VIF) was examined for each of the variables in the final models to identify possible multicollinearity and Mahalanobis distances were observed to determine the presence of multivariate outliers. All models met these assumptions.

Demographics

The current sample was mostly female (59.7%), white (87.8%), leukemia survivors (31%), and from households with incomes over \$60,000 (36.6%). Over one-fourth of respondent's fathers completed high school (25.4%) and another one-fourth were college graduates (25.4%), and one-third of respondent's mothers were college graduates (33.3%). The average age at diagnosis was 18.3 months (SD = 11.9 months), the average age at the baseline survey was 11 years old (SD = 1.37 years), and the average age at the Teen survey completion was 18 years (SD = 1.04 years). The average grade of participants completing the Teen survey was 11th grade. See Table 3 for more detailed demographic information.

Table 3

Sample Demographics (N =305)

	N	%
Age of Diagnosis (M, SD)	18.34 months	11.9
Age at Baseline survey (M, SD)	11.08 years	1.4
Age at Teen survey (M, SD)	18.13 years	1.0
Gender		
Male	123	40.3
Female	182	59.7
Race		
White, not Hispanic	267	87.8
White, Hispanic	6	2.0
Black	11	3.7
Biracial	10	3.2
Other	10	3.2
Household Income		
Less than \$9,999	6	2.0
\$10,000 – 19,999	15	5.1
\$20,000 – 39,999	82	27.8
\$40,000 – 59,999	84	28.5
Over \$60,000	108	36.6
Grade at Teen survey		
Seventh	1	0.4
Tenth	20	7.6
Eleventh	60	22.7
Twelfth	95	36.0
Thirteen	88	33.3
Highest Grade Completed, Father		
Did not finish high school	21	6.9
Diploma/GED	77	25.4
Some college	60	19.8
College graduate	77	25.4
Graduate/Law/Med school	50	16.5
Don't know	18	5.9
Highest Grade Completed, Mother		
Did not finish high school	22	7.3
Diploma/GED	69	22.8
Some college	66	21.8
College graduate	101	33.3
Graduate/Law/Med school	33	10.9
Don't know	12	4.0

Hypothesis One

Hypotheses 1a, 1b, and 1c stated: “*Compared to population norms, adolescent cancer survivors would report significantly lower quality of life on the disorder, discomfort, and satisfaction with health domains, significantly higher quality of life scores on the resilience domain, and would not report significantly different scores on the achievement, discomfort, or risk domains of the CHIP-AE.*” This hypothesis was tested with six unpaired t-tests. The original sample of children from the Baltimore area ($N = 865$) that was used to establish norms for the CHIP-AE was used for comparison. Significant differences were found between the established population norms with the satisfaction, $t(1168) = 1.96, p = .049$, resilience, $t(1168) = 6.90, p = .0001$, and disorder domains, $t(1168) = 7.49, p = .0001$. The subdomains of these domains were also examined, so a conservative Bonferroni correction to account for multiple analyses was implemented, with significance being $p < .003$. With this correction, the satisfaction domain was no longer significantly different from the established population norms.

Adolescent cancer survivors in the current study reported significantly lower disorder scores ($M_{CCSS} = 17.61, SD = 4.14$) compared to the established population norms ($M = 20, SD = 5$). Significant differences between survivors and established norms were present on the acute minor, $t(1168) = 5.05, p < .0001$, long-term medical, $t(1165) = 2.75, p < .0001$, long-term surgical, $t(1168) = 14.98, p < .0001$, and psychosocial subdomains, $t(1165) = 7.67, p < .0001$. Adolescent cancer survivors also reported significantly higher resilience domain scores ($M_{CCSS} = 22.26, SD = 4.69$), indicating a greater amount of resilience compared to the established norms. Significant differences were found on the social problem solving, $t(1166) = 8.27, p < .0001$, and home health and safety, $t(1168) = 13.18, p < .0001$, subdomains. There were no significant

differences between the established population norms and the discomfort, $t(1168) = .846, p = .398$, risk, $t(1168) = 1.78, p = .075$, or achievement domains, $t(1161) = 1.08, p = .279$.

Hypothesis Two

Hypothesis 2a was that, “*Gender would be significantly related to quality of life outcomes in survivors, with males reporting higher quality of life scores than females across the six domains.*” This hypothesis was tested with independent samples t-tests. Gender was significantly related to the satisfaction domain, $t(303) = 2.69, p = .008$, and the discomfort domain, $t(295.4) = 4.88, p < .0001$. These differences remained significant with a conservative Bonferroni correction to account for multiple analyses, with significance being $p < .008$. With both of these domains, males ($M_{\text{satisfaction}} = 20.26, SD = 4.75; M_{\text{discomfort}} = 21.46, SD = 4.61$), scored significantly higher than females ($M_{\text{satisfaction}} = 18.74, SD = 4.90; M_{\text{discomfort}} = 18.53, SD = 5.82$), which is consistent with the hypothesized relations between gender and outcome variables. However, gender was not significantly related to the achievement domain, $t(296) = -1.167, p = .245$, the resilience domain, $t(303) = .790, p = .430$, the disorder domain, $t(303) = 1.26, p = .208$, or the risk domain, $t(303) = .255, p = .799$.

Hypothesis 2b stated, “*Non-white individuals would report lower quality of life scores across the six assessed domains when compared to white participants.*” For this hypothesis, independent samples t-tests were used to examine the relations between race and the outcome variables. Race was significantly related to the resilience domain, $t(303) = 2.53, p = .012$, with white individuals reporting higher resilience domain scores ($M = 22.5, SD = 4.67$) than non-white individuals ($M = 20.39, SD = 4.48$). Race was also marginally related with the achievement domain, $t(296) = 1.82, p = .067$, with white individuals reporting slightly higher scores on the achievement domain when compared to non-white individuals. While these are

significant at the $p < .05$ level, when using the Bonferroni correction, these differences would not remain significant. Race was also not significantly related to the satisfaction, $t(303) = .765, p = .445$, discomfort, $t(303) = .207, p = .836$, disorder, $t(303) = -.007, p = .994$, or risk domains, $t(303) = .337, p = .737$.

Hypothesis 2c was that, “*Survivors treated with more treatment modalities would report lower quality of life scores across the six domains.*” This hypothesis was examined with an ANOVA. The number of treatment modalities received was only significantly related to the risk domain score, $F(2, 290) = 5.37, p = .005$. Post hoc tests using the Bonferroni correction revealed significant differences between participants who received one treatment modality and those who received three treatment modalities (unadjusted $p = .004$). Treatment modality was not significantly related to any other domains, including achievement, $F(2, 283) = .610, p = .54$, resilience, $F(2, 290) = 1.97, p = .141$, satisfaction, $F(2, 290) = 2.09, p = .126$, discomfort, $F(2, 290) = .523, p = .593$, or disorder, $F(2, 290) = .727, p = .484$.

Finally, hypothesis 2d stated, “*Survivors exposed to cranial radiation and methotrexate would report lower quality of life scores across the six domains.*” This hypothesis was examined with ANOVAs. Exposure to high-risk treatment, including cranial radiation and/or methotrexate, was significantly related to the achievement, $F(2, 283) = 5.98, p = .003$, resilience, $F(2, 290) = 4.51, p = .012$, and satisfaction domains, $F(2, 290) = 3.92, p = .021$. For all of these domains, post hoc tests using the Bonferroni correction revealed significant differences between participants receiving no high-risk treatment versus those who received both methotrexate and cranial radiation. Results also show that high-risk treatment was significantly related to the disorder outcome, $F(2, 290) = 3.41, p = .034$, but post hoc tests using the Bonferroni correction revealed significant differences between participants reporting no high-risk treatment and those

reporting receiving either methotrexate or cranial radiation (unadjusted $p = .030$). High-risk treatment was not significantly related to the discomfort domain, $F(2, 290) = 1.78, p = .171$, or the risk domain, $F(2, 290) = 1.24, p = .292$.

Prior to model building, relations among all of the potential predictors and the outcome variables were examined with independent samples t-tests, ANOVAs, and correlations. The purpose of running these analyses was to inform model building for hypotheses three and four. See Table 4 for a summary of the univariate relations between the predictors and outcomes.

Hypothesis Three

Psychological and physical symptoms, functional status and health perceptions as rated by parents at baseline would account for a significant amount of variance in quality of life as rated by adolescents at follow-up after adjusting for demographic and treatment-related variables.

This hypothesis was tested with six separate hierarchical regressions for each quality of life domain.

For each outcome, three guiding principles guided model building: 1) variance; 2) theory and 3) parsimony. One of the primary goals in the development of these models was to find the models that explained the most variance in the outcome. To determine this, the adjusted R^2 was examined. The adjusted R^2 was used because it shows the amount of variance accounted for by the model, while controlling for the number of variables in the model (Tabachnick & Fidell, 2007). This is better to use than the traditional R^2 which is inflated based on the number of items in the model, so that more predictors explains more variance. In addition to trying to create the model that accounts for the most variance, the Wilson and Cleary model served as the theoretical foundation guiding model development. Hierarchical regression is theory-driven, so decisions

Table 4.

P-value of Univariate Relations between Predictor and Outcome Variables

	Achievement	Resilience	Satisfaction	Discomfort	Disorder	Risk
Age at Diagnosis	$p = .002^{**}$	$p = .004^{**}$	$p = .810$	$p = .765$	$p = .607$	$p = .708$
Special Education Utilization	$p < .0001^{**}$	$p = .033^{**}$	$p = .064^*$	$p = .684$	$p = .003^{**}$	$p = .012^{**}$
Race	$p = .067^*$	$p = .012^{**}$	$p = .445$	$p = .836$	$p = .994$	$p = .737$
Gender	$p = .245$	$p = .430$	$p = .008^{**}$	$p < .0001^{**}$	$p = .208$	$p = .799$
Treatment Modalities	$p = .540$	$p = .141$	$p = .126$	$p = .593$	$p = .484$	$p = .005^{**}$
High Risk Treatment	$p = .003^{**}$	$p = .012^{**}$	$p = .021^{**}$	$p = .171$	$p = .034^{**}$	$p = .292$
Internalizing Symptoms	$p < .0001^{**}$	$p = .006^{**}$	$p = .155$	$p = .003^{**}$	$p < .0001^{**}$	$p = .710$
Externalizing Symptoms	$p < .0001^{**}$	$p = .001^{**}$	$p = .061^*$	$p = .086^*$	$p = .001^{**}$	$p = .014^{**}$
Attention/Hyperactivity Symptoms	$p < .0001^{**}$	$p = .048^{**}$	$p < .0001^{**}$	$p = .196$	$p < .0001^{**}$	$p = .160$
Cancer Anxieties/Fears	$p = .142$	$p = .323$	$p = .019^{**}$	$p = .011^{**}$	$p = .002^{**}$	$p = .614$
Social Competence	$p = .030^{**}$	$p < .0001^{**}$	$p = .003^{**}$	$p = .358$	$p = .057^*$	$p = .628$
Physical Disfigurement	$p = .251$	$p = .144$	$p < .0001^{**}$	$p = .076^*$	$p < .0001^{**}$	$p = .014^{**}$
Cancer Related Pain	$p = .979$	$p = .634$	$p = .595$	$p = .558$	$p = .339$	$p = .170$
Functional Status Impairment	$p = .004^{**}$	$p = .011^{**}$	$p < .0001^{**}$	$p = .002^{**}$	$p < .0001^{**}$	$p = .008^{**}$
Current Health Perceptions	$p < .0001^{**}$	$p = .680$				
Perceptions of Vulnerability	$p = .103$	$p = .155$	$p = .185$	$p = .228$	$p = .161$	$p = .020^{**}$

Note. Two asterisks (**) indicate significance at the $p < .05$ and one asterisk (*) indicates that the relation is approaching significance

about including and excluding variables were made with the goal of fitting the models with the Wilson and Cleary theory. Finally, the third guiding principle in model development was parsimony. The goal was to create models that predicted the outcome with as few variables as possible. This increases clinical relevance of the findings and leads to a clearer understanding of the impact of variables on the outcome. Therefore, for each model created, the goal was to find the most parsimonious model that explained the greatest variance in the quality of life outcome and that was most consistent with the Wilson and Cleary model.

For each of the six quality of life outcomes, the same process for model building was followed. Decisions in model building were both data and theory driven. The process was data driven to start and began with backwards elimination. All 16 predictors were initially added into the model. In the next step, variables that were not significant in the original model or in the univariate analyses (see Table 4) were removed. Following this step, items that were not significant in the model were removed. At this point, model building shifted to being theory driven and forward selection was used as items were added back into the model to be consistent with the Wilson and Cleary model and to explain the largest amount of variance in the outcome. The model building approach is reviewed in detail for the achievement outcome. However, for the other five quality of life domains, the process of model building will not be reviewed in detail as the same procedures are followed as described for the achievement outcome. Only the final models will be presented for these outcomes.

To begin model testing with the **achievement** outcome, all variables were initially entered into the model. While the model was significant, $F(16, 194) = 2.17, p = .007$, the adjusted R^2 was only .082, indicating that all sixteen factors in the model only explained about eight percent of the variance in achievement scores after controlling for the number of variables

in the model. Furthermore, only the first block with demographic variables, $F\Delta (4, 206) = 4.30, p = .002$, and third block with psychological symptoms, $F\Delta (5, 199) = 2.32, p = .045$, added significant change to the model. The significant individual predictors in the final block (e.g. block 6 with all items included in the model) of this model included race, $t(209) = -2.73, p = .007$, and internalizing symptoms, $t(209) = -2.58, p = .011$. Special education utilization was significant in earlier blocks but was no longer significant in the final block.

For the next model, the predictors that were found to be significantly related to the achievement score with the univariate analyses (see Table 4), along with the significant individual variables from the initial model were entered. Therefore, the blocks included: block 1) special education utilization, race, and age of diagnosis; 2) high-risk treatment exposure; 3) internalizing, externalizing, and attention/hyperactivity symptoms, and social competence; 4) functional status impairment; and 5) current health perceptions. This model was also significant $F (10, 218) = 3.07, p = .001$ but the adjusted R^2 remained .083. Again, only the first block with demographic variables, $F\Delta (3, 225) = 5.66, p = .001$, and the third block with psychological variables, $F\Delta (4, 220) = 2.47, p = .046$, added significant change to the model, though the final block began approaching significance, $F\Delta (1, 218) = 2.75, p = .099$. In the final block of this model, significant individual items included race, $t(225) = -2.60, p = .01$, special education utilization, $t(227) = -2.70, p = .007$, and internalizing symptoms $t(227) = -2.45, p = .015$. Special education was initially significant but fell out by the final block of the model, and current health perceptions was trending towards significance, $t(227) = 1.66, p = .099$.

Therefore, the next model examined only the individual predictors that were significant or trending towards significance from the previous model: block 1) special education utilization, race; 2) internalizing symptoms; and 3) current health perceptions. This model was significant,

$F(4, 265) = 12.09, p < .001$, and adjusted $R^2 = .142$. Each block added significant change to the model: block 1) $F\Delta(2, 267) = 10.41, p < .001$; block 2) $F\Delta(1, 266) = 19.13, p < .001$; and block 3) $F\Delta(1, 265) = 6.20, p = .013$. Each individual predictor also remained significant in the final model. While this model increased the amount of variance accounted for in achievement domain, it was not in line with the guiding theory behind the development of the model. Because hierarchical regression is theory driven, some variables were added back into the model to examine the impact of the amount of variance accounted for by the predictors. High-risk treatment, physical disfigurement, and functional status impairment were added back into the model. These were chosen because they each represent a factor outlined by Wilson and Cleary as contributing factors to quality of life and they had significant individual relations with the achievement domain in the univariate analyses.

When these factors were added back in, the model was significant, $F(7, 239) = 7.27, p < .001$, and adjusted $R^2 = .151$. Blocks one with demographic information, $F\Delta(2, 244) = 9.77, p < .001$, two with treatment information, $F\Delta(1, 243) = 5.31, p = .002$, three with psychological symptom, $F\Delta(1, 242) = 16.95, p < .001$, and six with current health perceptions, $F\Delta(1, 239) = 4.29, p = .039$, all added significant change to the overall model. Individual predictors that were significant in the final block included, race, $t(245) = -2.33, p = .020$, high-risk treatment, $t(245) = -1.94.31, p = .054$, internalizing symptoms, $t(245) = -3.18, p = .002$, and current health perceptions, $t(245) = 2.07, p = .039$. Special education utilization was initially significant but later dropped out.

Next, only the significant variables from the previous model were included, but while the model was significant, the amount of variance accounted for by the model dropped (adjusted $R^2 = .131$). Finally, physical disfigurement and functional status impairment were added back in and

special education utilization was dropped. Therefore, this model included: block 1) race; block 2) exposure to high-risk treatment; block 3) internalizing symptoms; block 4) physical disfigurement; block 5) functional status impairment; and block 6) current health perceptions. This model was significant, $F(6, 259) = 8.90, p < .001$, accounted for the most variance (adjusted $R^2 = .152$), and was consistent with the Wilson and Cleary model, so it was the final model for the achievement outcome. Demographic and treatment variables accounted for a total of 5.7% of the variance in the achievement outcome, and psychological and physical symptoms, functional status impairment and current health perceptions added an additional 9.5% of variance in achievement scores. Block 1 with demographic variables, $F\Delta(1, 264) = 5.40, p = .021$, block 2 with treatment variables, $F\Delta(1, 263) = 12.50, p < .001$, block 3 with psychological symptoms, $F\Delta(1, 262) = 25.39, p < .001$, and block 6 with current health perceptions, $F\Delta(1, 259) = 5.03, p = .026$, added significant change to the overall model. See Table 5 for a summary of change statistics for each quality of life domain. The individual predictors that remained significant included race, $t(264) = -2.29, p = .023$, high-risk treatment, $t(264) = -2.40, p = .017$, internalizing symptoms, $t(264) = -3.77, p < .001$, and current health perceptions, $t(264) = 2.24, p = .026$.

Next, similar steps were used to arrive at the final model for the **resilience** quality of life domain. For the resilience domain, the initial model with all the variables accounted for a great deal of variance, and adjusted R^2 significantly dropped as items were removed. Therefore, the final model for resilience had more predictors than other models. The final model included: block 1) special education utilization, race, age at diagnosis, and gender; 2) high-risk treatment, 3) internalizing, externalizing, and attention/hyperactivity symptoms, and social competence, 4) physical disfigurement, 5) functional status impairment, and 6) current health perceptions. This model was significant and accounted for the greatest amount of variance in resilience outcome

score, $F(12, 209) = 3.47, p < .001$, adjusted $R^2 = .118$. Demographic and treatment-related variables accounted for 5.6% of the variance in the resilience outcome, and psychological and physical symptoms along with functional status and current health perceptions added an additional 6.2% of variance. Block 1 with demographic variables, $F\Delta(4, 217) = 4.34, p = .002$, and block 3 with psychological symptoms, $F\Delta(4, 212) = 4.75, p = .001$, added significant change to the model. The individual predictors that remained significant in the final block of the final model included, race, $t(220) = -2.43, p = .016$, and social competence, $t(220) = 2.99, p = .003$. Age at diagnosis, $t(220) = -1.89, p = .06$, and attention/hyperactive symptoms, $t(220) = 1.89, p = .06$, were trending towards significance.

Next, the final positive quality of life model for the **satisfaction** domain was constructed and included: block 1) gender; block 2) high-risk treatment; block 3) internalizing symptoms; block 4) physical disfigurement; block 5) functional status impairment; and block 6) current health perceptions. The final satisfaction domain model was significant, $F(6, 265) = 8.73, p < .001$, accounted for the greatest amount of variance in the satisfaction outcome (adjusted $R^2 = .146$), and was consistent with the Wilson and Cleary model. Demographic and treatment variables accounted for 3.8% of the variance in the satisfaction domain score while psychological and physical symptoms, functional status, and current health perceptions accounted for an additional 10.8% of the variance. Block 1 with demographic variables, $F\Delta(1, 270) = 4.05, p = .045$, block 2 with treatment variables, $F\Delta(1, 269) = 8.61, p = .004$, block 3 with psychological symptoms, $F\Delta(1, 268) = 21.16, p < .001$, block 4 with physical symptoms, $F\Delta(1, 267) = 8.00, p = .005$, and block 5 with functional status impairment, $F\Delta(1, 266) = 4.65, p = .032$, all added significant change to the final model. Additionally, block 6 with current health perceptions, $F\Delta(1, 265) = 2.99, p = .085$, was approaching significance. The individual

predictors that remained significant in the final block of the final model included, gender, $t(270) = -2.64, p = .009$, high-risk treatment, $t(270) = -1.98, p = .049$, internalizing symptoms, $t(270) = -3.23, p = .001$, and physical disfigurement, $t(270) = -2.15, p = .032$. Functional status impairment, $t(270) = -1.72, p = .086$, and current health perceptions, $t(270) = 1.73, p = .085$, were both trending towards significance.

Next, models predicting negative quality of life outcomes were examined, beginning with the **discomfort** domain. The final model included: block 1) gender; block 2) high-risk treatment; block 3) cancer specific anxieties/fears, internalizing and externalizing symptoms; block 4) functional status impairment, and block 5) current health perceptions. This model was significant, $F(7, 273) = 6.75, p < .001$, accounted for the greatest amount of variance in the discomfort domain (adjusted $R^2 = .126$), and was consistent with the Wilson and Cleary model. Demographic and treatment variables accounted for 6.1% of the variance in the discomfort domain scores, and psychological symptoms, functional status impairment, and current health perceptions added an additional 6.5% of variance in the discomfort outcome. Block 1 with demographic variables, $F\Delta(1, 279) = 19.36, p < .0001$, block 3 with psychological symptoms, $F\Delta(3, 275) = 3.97, p = .009$, and block 4 with functional status impairment, $F\Delta(1, 274) = 10.01, p = .002$, added significant change to the overall model. Block 5 with current health perceptions, $F\Delta(1, 273) = 2.92, p = .089$, was trending towards significance. Significant individual predictors in the final block of the final discomfort model included, gender, $t(279) = -4.77, p < .0001$, and functional status impairment, $t(279) = -2.65, p = .008$. Current health perceptions was trending towards significance, $t(279) = 1.71, p = .089$.

The model for the **disorder** domain was constructed next, and the final model included: block 1) special education utilization, gender; block 2) high-risk treatment; block 3)

internalizing, externalizing, and attention/hyperactive symptoms, and social competence; block 4) physical disfigurement; and block 5) functional status impairment. This model was significant, $F(9, 212) = 6.47, p < .0001$, accounted for the greatest amount of variance (adjusted $R^2 = .182$), and was the most consistent with the Wilson and Cleary model. Demographic and treatment variables accounted for a total of 5.8% of the variance in the disorder outcome, and psychological and physical symptoms and functional status impairment added an additional 12.4% of variance in disorder scores. Demographic variables in block 1, $F(2, 219) = 8.27, p < .0001$, psychological symptoms in block 3, $F(4, 214) = 2.73, p = .030$, physical symptoms in block 4, $F(1, 213) = 8.62, p = .004$, and functional status impairment in block 5, $F(1, 212) = 17.69, p < .0001$, added significant change to the disorder outcome. Individual predictors that remained significant in the final block of the final model included, special education utilization, $t(220) = -2.0431, p = .043$, physical disfigurement, $t(220) = -2.21, p = .028$, and functional status impairment, $t(220) = -4.21, p < .0001$. Gender, $t(220) = -1.91, p = .058$, and social competence, $t(220) = -1.91, p = .057$, were marginally significant.

Finally, the model for the **risk** domain was created, with the final model including: block 1) special education utilization; block 2) treatment modalities; block 3) externalizing and attention/hyperactivity symptoms; block 4) physical disfigurement; block 5) functional status impairment; block 6) perceptions of vulnerability. The model was significant, $F(7, 238) = 4.81, p < .001$, accounted for the most variance (adjusted $R^2 = .098$), and was consistent with the Wilson and Cleary model, thus meeting the criteria for model development. Demographic and treatment variables accounted for a total of 3.7% of the variance in the achievement outcome, and psychological and physical symptoms, functional status impairment and health perceptions added an additional 6.1% of variance. Block 1 with demographic variables, $F(1, 244) = 5.28, p$

= .022, block 2 with treatment variables, $F\Delta(1,243) = 6.00, p = .015$, and block 3 with psychological symptoms, $F\Delta(2,241) = 7.06, p = .001$, added significant change to the overall model. Block 4 with physical symptoms, $F\Delta(1, 240) = 3.25, p = .073$, and block 6 with health perceptions, $F\Delta(1, 238) = 2.91, p = .090$, were trending towards significance. The individual predictors that remained significant in the final block of the final model included: externalizing symptoms, $t(244) = -3.81, p < .0001$, and attention/hyperactivity symptoms, $t(244) = 2.18, p = .031$. The number of treatment modalities received was marginally significant, $t(244) = 1.95, p = .053$. See Table 5 for a summary of the final model.

Hypothesis Four

Hypothesis four examined the relations between the individual variables and the quality of life domain scores. The results from the final block of the final models are reported. To understand these relations within the final models, the beta value (b) was examined. Beta shows the affect of an increase of one in the predictor variable on the outcome variable (Tabachnick & Fidell, 2007). See Table 6 for a summary the relations between the individual variables and the quality of life domain scores.

For the demographic blocks, it was hypothesized that, “*Male gender, older age at diagnosis, and higher socioeconomic status at baseline would significantly predict higher quality of life scores as rated by adolescent cancer survivors at follow-up compared to female gender, younger age at diagnosis, and lower socioeconomic status.*” As previously noted, due to the lack of variance in the income variable, SES was dropped as a variable of interest for this study.

Gender emerged as a significant predictor for the satisfaction domain, $b = -.149 (p = .009)$, and the discomfort domain, $b = -.270 (p < .0001)$. It was also marginally significant with the disorder domain, $b = -.118 (p = .058)$. In all cases, female gender was a risk factor for lower quality of life

Table 5. Summary of Change Statistics for Final Models

Domain	Block	R ²	Adj R ²	Δ R ²	Δ F	P-value
Achievement	Block 1: Race	.020	.016	.020	5.40	.021
	Block 2: High-risk treatment	.065	.057	.044	12.5	< .0001
	Block 3: Internalizing	.147	.137	.083	25.4	< .0001
	Block 4: Physical disfigurement	.149	.136	.002	.599	.439
	Block 5: Functional status impairment	.155	.139	.006	1.76	.186
	Block 6: Health perceptions	.171	.152	.016	5.03	.026
Resilience	Block 1: Special education, race, age, gender	.074	.057	.074	4.34	.002
	Block 2: High-risk treatment	.078	.056	.004	.836	.361
	Block 3: Internalizing, attention, externalizing, social	.154	.118	.076	4.75	.001
	Block 4: Physical disfigurement	.155	.115	.001	.381	.574
	Block 5: Functional status impairment	.161	.117	.007	1.65	.201
	Block 6: Health perceptions	.166	.118	.005	1.15	.286
Satisfaction	Block 1: Gender	.015	.011	.015	4.05	.045
	Block 2: High-risk treatment	.045	.038	.031	8.61	.004
	Block 3: Internalizing	.115	.105	.070	21.2	< .0001
	Block 4: Physical disfigurement	.141	.128	.026	8.00	.005
	Block 5: Functional status impairment	.156	.140	.015	4.65	.032
	Block 6: Health perceptions	.165	.146	.009	2.99	.085
Discomfort	Block 1: Gender	.065	.062	.065	19.4	< .0001
	Block 2: High-risk treatment	.068	.061	.003	.925	.337
	Block 3: Internalizing, cancer anxiety, externalizing	.107	.090	.039	3.97	.009
	Block 4: Functional status impairment	.138	.120	.032	10.1	.002
	Block 5: Health perceptions	.165	.126	.009	2.92	.089
Disorders	Block 1: Gender, special education	.070	.062	.070	8.27	< .0001
	Block 2: High-risk treatment	.070	.058	.000	.049	.824
	Block 3: Internalizing, social, externalizing, attention	.116	.087	.045	2.73	.030
	Block 4: Physical disfigurement	.150	.118	.034	8.62	.004
	Block 5: Functional status impairment	.215	.182	.065	17.7	< .0001
Risk	Block 1: Special education	.021	.017	.021	5.28	.022
	Block 2: Treatment modalities	.045	.037	.024	6.00	.015
	Block 3: Externalizing, attention/hyperactivity	.098	.083	.053	7.06	.001
	Block 4: Physical disfigurement	.110	.091	.012	3.25	.073
	Block 5: Functional status impairment	.113	.091	.004	.955	.329
	Block 6: Perceptions of vulnerability	.124	.098	.011	2.91	.090

scores, because as gender rose from 0 (male) to 1 (female), the quality of life scores lowered according to the b values. Therefore, while gender was not a significant predictor for all of the quality of life outcomes, when it was significant, male gender was related to more positive quality of life. Age of diagnosis only emerged as a marginally significant predictor for resilience domain score, $b = -.143$ ($p = .06$), with older age at diagnosis predicting lower resilience domain scores, which did not support the hypothesis.

For the treatment block, it was hypothesized that, “*Exposure to methotrexate and/or cranial radiation would significantly predict lower quality of life scores as rated by adolescent cancer survivors at follow-up compared to those who did not receive high-risk treatment.*” High-risk treatment was a significant predictor for the achievement, $b = -.141$ ($p = .017$), and satisfaction domains, $b = -.116$ ($p = .049$). For both outcomes, increased exposure to high-risk treatments was related to a significant decrease in the achievement and satisfaction outcomes, thus supporting the initial hypothesis.

For the psychological symptoms block, it was hypothesized that, “*Fewer psychological symptoms as rated by the parent at baseline would significantly predict higher quality of life scores as rated by adolescent cancer survivors at follow-up compared to those reporting more psychological and physical symptoms.*” Internalizing symptoms were significantly related to the achievement, $b = -.234$ ($p < .0001$), and the satisfaction domain scores, $b = -.197$ ($p = .001$). Externalizing symptoms were significantly related to the risk domain, $b = -.271$ ($p < .0001$), while attention/hyperactivity symptoms were significantly related to the risk domain, $b = .173$ ($p = .031$), and marginally related to the resilience domain, $b = .172$ ($p = .06$). Finally, social competence was significantly related to the resilience domain, $b = .241$ ($p = .003$), and marginally related to the disorder domain, $b = -.147$ ($p = .057$). An increase in internalizing and

externalizing symptoms consistently predicted lower quality of life scores across domains, while attention/hyperactivity scores consistently predicted higher quality of life scores. The relations with social competence varied; whereas an increase in social competence predicted higher resilience scores, it also predicted lower disorder scores. Cancer specific anxieties and fears were not significantly related to any of the quality of life outcomes.

A similar hypothesis for the physical symptoms block was tested, “*Fewer physical symptoms as rated by the parent at baseline would significantly predict higher quality of life scores as rated by adolescent cancer survivors at follow-up compared to those with more physical symptoms.*” Physical disfigurement was a significant predictor for the satisfaction domain, $b = -.126$ ($p = .032$), and the disorder domain, $b = -.143$ ($p = .028$). The relation went in the hypothesized direction, with an increase in physical disfigurement being related to lower quality of life scores across these domains. Cancer pain was not significantly related to any of the quality of life domains.

For the functional status block, it was hypothesized that, “*Lower functional status as rated by the parent at baseline would significantly predict lower quality of life scores as rated by the adolescent cancer survivors at follow-up compared to those with higher functional status.*” Functional status impairment was significantly related to the discomfort, $b = -.158$ ($p = .008$), and disorder domains, $b = -.269$ ($p < .0001$), and was trending towards significance with the satisfaction domain, $b = -.104$ ($p = .086$). As hypothesized, for all domains, an increase in functional status impairment predicted lower quality of life scores.

For the final health perceptions block, it was hypothesized that, “*Negative health perceptions as reported by the parent at baseline would predict lower quality of life scores as rated by adolescent cancer survivors at follow-up, while positive health perceptions would*

predict higher quality of life scores.” The affect of two health perceptions variables was examined, including perceptions of vulnerability and current health perceptions. While perceptions of vulnerability never emerged as a significant individual predictor, the current health perceptions variable was significantly related to the achievement domain, $b = .142$ ($p = .026$), and was trending towards significance with the satisfaction, $b = .108$ ($p = .085$), and discomfort domains, $b = .109$ ($p = .089$). As predicted, across these domains, more positive health perceptions predicted increases in the quality of life domain scores.

Table 6.

Relations between individual predictors and quality of life domain scores

Domain	Variables in final block	Beta	t	p-value
Achievement	Race	-.131	-2.29	.023
	High-risk treatment	-.141	-.240	.017
	Internalizing symptoms	-.234	-3.77	< .0001
	Physical disfigurement	-.018	-.307	.759
	Functional status impairment	-.046	-.760	.448
	Health perceptions	.142	2.24	.026
Resilience	Age at diagnosis	-.143	-1.89	.060
	Gender	-.088	-1.37	.172
	Race	-.156	-2.43	.016
	Special education utilization	-.007	-.085	.932
	High-risk treatment	-.074	-.947	.345
	Social competence	.241	2.99	.003
	Internalizing symptoms	.003	.031	.975
	Externalizing symptoms	-.128	-1.45	.148
	Attention/hyperactivity	.172	1.89	.060
	Physical disfigurement	-.016	-.228	.820
	Functional status impairment	-.070	-1.04	.302
	Health Perceptions	.077	1.07	.286
Satisfaction	Gender	-.149	-2.64	.009
	High-risk treatment	-.116	-1.98	.049
	Internalizing	-.197	-3.23	.001
	Physical disfigurement	-.126	-2.15	.032
	Functional status impairment	-.104	-1.72	.086
	Health perceptions	.108	1.73	.085

Discomfort				
	Gender	-.270	-4.77	.000
	High-risk treatment	.008	.128	.898
	Cancer anxieties	-.073	-1.21	.226
	Internalizing symptoms	-.047	-.628	.531
	Externalizing symptoms	-.062	-.864	.389
	Functional status impairment	-.158	-2.65	.008
	Health perceptions	.109	1.71	.089
Disorders				
	Gender	-.118	-1.91	.058
	Special education utilization	-.152	-2.04	.043
	High-risk treatment	-.007	-.113	.910
	Social competence	-.147	-1.91	.057
	Attention/hyperactivity	-.051	-.583	.560
	Internalizing symptoms	-.096	-1.03	.305
	Externalizing symptoms	-.127	-1.53	.129
	Physical disfigurement	-.143	-2.21	.028
	Functional status impairment	-.269	-4.21	.000
Risk				
	Special education utilization	.051	.727	.468
	Treatment modalities	.124	1.95	.053
	Externalizing symptoms	-.271	-3.81	.000
	Attention/hyperactivity	.173	2.18	.031
	Physical disfigurement	.098	1.30	.134
	Functional status impairment	.058	.915	.361
	Perceptions of vulnerability	-.107	-1.71	.090

Discussion

The purpose of the current study was to examine quality of life in adolescent survivors of childhood cancer, with a focus on identifying longitudinal predictors of quality of life that account for variance above and beyond the influence of demographic and treatment factors. To begin, quality of life domain scores from the current sample were compared to established population norms. Although quality of life in cancer survivors has previously been compared to population norms (Noll, et. al., 1997; Recklitis, Lockwood, Rothwell, & Diller, 2006; Hobbie, et. al., 2000), this has never been examined with the CHIP-AE.

Hypothesis One

Results of the comparison between established population norms and this sample of adolescent cancer survivors show that in some areas, survivors are doing better, in some areas survivors are doing worse, and in some areas they are doing the same. This is consistent with the current literature that shows varied quality of life outcomes for survivors of childhood cancer. For the current sample, survivors had significantly higher resilience domain scores, significantly lower disorder domain scores, and were not significantly different on the achievement, satisfaction, discomfort, or risk domains.

These findings are generally consistent with previous literature examining quality of life with the CHIP-AE in adolescents with chronic illness, which have found lower scores on the disorder domain, and higher scores on the resilience domain (Gerson, Riley, Fivush, Pham, Fiorenza, Robertson, et. al., 2005; Forrest, Starfield, Riley & Kang, 1997; Starfield, et. al., 1996). The similarities in CHIP-AE scores across these populations is striking and further supports the conceptualization of childhood cancer as a chronic illness, even after active treatment has ended. However, unlike previous samples, survivors in the current study did not report significantly lower scores on the discomfort or satisfaction with health domains.

While the satisfaction with health domain approached significance in the current study, with the conservative Bonferonni correction, it was no longer significant. This suggests that perhaps childhood cancer survivors continue to face impairments and difficulties, but they adapt and no longer experience frustrations with their health status over time. Previous studies have found that adolescent and young adult survivors of cancer report significantly fewer positive health beliefs compared to controls (Kazak, DeRosa, Schwartz, Carlson, Ittenbach, Mao, et. al., 2010). However, in this study, age of diagnosis was an important variable, as those diagnosed in

adolescence were more likely to report negative health beliefs compared to those diagnosed earlier. Interestingly, this same study found that time since diagnosis was not related to health perceptions, thus suggesting that the developmental time of diagnosis has a greater impact on health perceptions than the amount of time that has passed since diagnosis (Kazak, et. al., 2010). Therefore, it is possible that the very young age of diagnosis in the current sample contributed to higher satisfaction with health domain scores.

For the discomfort domain, no significant differences were found between the current sample and established population norms, suggesting that survivors do not experience significantly more physical discomfort, emotional discomfort, or limitations in activity. These findings are not surprising given that relatively few parents reported pain from their cancer treatment and functional status impairment in the survivor at baseline. Further, these findings are more in line with previous studies reporting that generally survivors are not at increased risk for more psychological problems than the general population (Fritz & Williams, 1988; Barakat, et. al., 1997). It is also important to keep in mind that the discomfort domain was not normally distributed so interpretations of findings from this domain must be made with caution.

Findings from the current study support previous literature showing increased areas of functioning in some cancer survivors (Radcliffe, Bennett, Kazak, Foley & Phillips, 1996; Anholt, Fritz, & Keener, 1993). When examining the subdomain scores of resilience, significant differences between population norms and survivors are present with the social problem solving and home health and safety subdomains.

The social problem solving domain includes the prompt, “You have had a big fight with a close friend and you think that he or she did not understand you and would not listen to what you were saying.” Participants were then asked to rate how likely they would be to engage in various

problem-solving strategies (e.g. talk to others for advice, see the good that could come out of the situation; <https://ccss.stjude.org/docs/ccss/survey-teen-health.pdf>, p.16). Significantly higher scores from survivors suggest that they may be particularly adept in problem solving in social situations. This is interesting in light of research findings that survivors of childhood cancer are more likely to have social difficulties, including having fewer friends, spending less time with peers, and engaging in fewer peer activities (Vannatta, Garstein, Short & Noll, 1998; Stam & Grootenhuis, 2005).

The current findings suggest that a more nuanced approach to understanding social strengths and deficits in survivors is warranted. Despite the fact that some survivors may have fewer friends or experience more social isolation, it is possible that some survivors have well-developed social skills. Other studies have found that the further examination of social deficits in survivors reveals that social functioning may not be globally worse. In one study, low social competence was reported, but only on the communication scale which also assessed academic skills as it focused on use of age-appropriate written and oral communication (Olson, Boyle, Evans, & Zug, 1993). The findings from the current study highlight the need to continue to broadly examine social skills and social development to better understand what social strengths and weaknesses survivors may have.

Survivors in the current study also reported significantly higher scores on the home safety subdomain of the resilience domain. The home health and safety subdomain included items on nutrition, wearing seatbelts, and the presence of smoke detectors and fire extinguishers in the home. It also assessed feelings of safety in school and participants' neighborhoods, along with access to firearms, regulation of the television in the home, and being supported and challenged by parents (<https://ccss.stjude.org/docs/ccss/survey-teen-health.pdf>, p.15). The wide-range of

items assessed on this subdomain make it difficult to interpret the findings, which is a weakness of the CHIP-AE.

If scores are elevated due to good nutrition compared to established norms, this would be inconsistent with the literature that reports increased risk for obesity and poor nutrition in childhood cancer survivors (Oeffinger, et. al., 2003). There is no known research about home environments and safety for childhood cancer survivors. However, these results could indicate that the home environment is safer than average for childhood cancer survivors. Though more information is needed, it is possible that parents who are more overprotective, as some parents of children with a chronic illness are, do more to ensure safe home environments (Holmbeck, Johnson, Wills, et. al., 2002). The role of perceptions of vulnerability in parenting behaviors such as overprotection, and how parents of survivors in the current sample rated perceptions of vulnerability, is discussed in more detail below.

While survivors in the current sample reported higher resilience scores, they also reported significantly lower scores on the disorder domain, which assessed the presence of mental and physical illnesses. However, the disorder domain differs from other scales in that morbidity is not taken into account; rather, the presence or absence of an illness in one's lifetime and in the past 12 months is assessed (<https://ccss.stjude.org/docs/ccss/survey-teen-health.pdf>, p. 17). Survivors scored significantly lower than established norms on the acute minor, long-term medical, long-term surgical, and psychosocial subdomains of the disorder domain.

For several of these subdomains, lower scores can be attributed to common late effects from childhood cancer treatment. For example, the long-term medical disorders subdomain assessed issues such as arthritis or joint problems and heart disease/conditions, both of which are common late effects of childhood cancer treatment (Hewitt, Weiner, & Simone, 2003). Similarly,

the long-term surgical disorders subdomain assessed problems with hearing, vision, and conditions affecting the bone or muscle and disfigurement of an extremity, all of which are common late-effects (Mulhern, Wasserman, Friedman, & Fairclough, 1989; Hewitt, Weiner, & Simone, 2003). Finally, the psychosocial subdomain asked if a doctor had ever told them that they had an “emotional, mental, or behavior problem,” including learning disorders, eating disorders, or speech problems. Again, several previous studies have established increased risk for learning disorders in childhood cancer survivors (Mitby, et. al., 2003), and some have also reported an increase in psychological disorders, though the literature is mixed (e.g. Schultz, et. al., 2007; Zebrack, et. al., 2002). Therefore, the significantly lower score on the disorder subdomain does not add to our understanding of quality of life in childhood cancer survivors, but confirms the presence of continued late effects well after treatment for childhood cancer is complete.

More generally, this portion of the study finds that while survivors are more likely to continue experiencing long-term medical complications as a result of their diagnosis and treatment, they are also more likely to report growth and increased resilience. This is consistent with previous studies showing that while survivors report worse physical functioning compared to the general population, they do not report significantly lower quality of life scores (Wu, et. al., 2007). With the current study’s sample, adolescents rated some areas of quality of life as normal, some as lower than average, and some as higher than average. This suggests that lower functioning in one area of quality of life does not necessarily impact all areas of functioning, and further supports a multidimensional view of identity, self-concept, and quality of life (Harter, Bresnick, Bouchey, & Whitesell, 1997; Masten, Coatsworth, Neemann, Gest, Tellegen, et. al., 1995).

Findings from the current study again highlight the need to move away from a focused attempt to dichotomize the impact of childhood cancer as either “good” or “bad” for survivors. Rather, more data is supporting the notion that the experience of childhood cancer will lead to some areas of decreased functioning, while also bolstering quality of life in other dimensions. These findings thus support the shift away from trying to find generalizations about quality of life and functioning in survivors and moving towards gaining an understanding of what individual factors beyond having cancer may contribute to better or worse quality of life. An increased understanding of these contributing factors is discussed in more detail below as well as other constructs to consider in future studies.

Hypothesis Two

In the univariate analyses examining the relations between the demographic and treatment factors with the quality of life outcomes, hypotheses were generally supported. Consistent with previous literature, when gender was a significant predictor, males reported better quality of life (Zebrack, et. al., 2002; Gurney, et. al., 2009; Wu, et. al., 2007). Similarly, higher treatment intensity, as assessed by the number of treatment modalities received and exposure to high-risk treatment, generally predicted lower quality of life scores (Speechley, et. al.; Schultz, et. al., 2007). Across analyses, it was found that while some predictors were related to certain outcomes, no single predictor was significantly related to all six quality of life domains. This again highlights the importance of examining quality of life as a multidimensional construct as different variables are related to various quality of life domains (Harter, Bresnick, Bouchey, & Whitesell, 1997; Masten, et. al., 1995).

While some of the univariate hypotheses were supported, others were not. Although race has been found to be significantly related to quality of life outcomes in some childhood cancer

studies (Wu, et. al., 2007; Shankar, et. al., 2005), this study did not find any significant differences after controlling for the number of analyses completed. Several relations were approaching significance, so it is possible that the lack of significance was related to the underrepresentation of minorities in this sample. The low representation of minority participants is a problem in the overall CCSS cohort (Robison, et. al., 2002) as well as in pediatric psychology research as a whole (Clay, Mordhorst, & Lehn, 2002). This is a severe limitation of this study that is discussed in more detail below. Future studies need to focus on understanding the relation between race and quality of life in childhood cancer survivors in more representative populations from which stronger conclusions can be drawn.

Age of diagnosis was also examined but was related to few outcomes. It was significantly related to the achievement and resilience domains in univariate analyses, but was only a marginally significant predictor in the final resilience model. With the resilience outcome, increases in age at diagnosis significantly lowered quality of life scores, which is inconsistent with the literature that suggests younger age of diagnosis is related to worse outcomes (Nathan, et. al., 2007; Mitby, et. al., 2003; Gurney, et. al., 2009).

As with race, the lack of significant findings in relation to age of diagnosis is likely due to the small amount of variance within this sample, since all participants were diagnosed prior to the age of three. This suggests that more valuable information could be gained by comparing outcomes across a wide-range of ages that cut across developmental periods. For example, some studies have reported significantly worse outcomes for those survivors treated with cranial radiation before the age of seven, compared to those treated after the age of seven (Nathan, et. al., 2007). The findings from the current study propose that variance in age of diagnosis when examining those diagnosed between zero and three does not greatly influence outcomes. Rather,

in regard to age of diagnosis, this study more generally shows the impact of cancer treatment on quality of life for those treated at a very young age.

Hypothesis Three

The current study contributes the most to the existing literature with the identification of longitudinal predictors of quality of life above and beyond demographic and treatment variables. The process of model building began with the achievement domain, and the final model accounted for a total of 15.2% of the variance in achievement scores. When examining the impact of each block on the overall change in the adjusted R^2 , the demographic and treatment blocks, which include race and exposure to high-risk treatment, accounted for a total of 5.7% of the change in the achievement outcome. Notably, the addition of internalizing symptoms in the third block added an additional 8.3% of variance to achievement score, which was the largest change in R^2 for the model. Current health perceptions also added significant change but only accounted for 1.6% of the total variance.

These findings show that internalizing symptoms at a young age significantly predict achievement outcomes later in life. Other studies have examined the longitudinal relation between psychological symptoms and academic performance in healthy children. One study found that internalizing, externalizing, and attention symptoms were all independently related to reading and math academic skills. However, when examined together, attention symptoms accounted for most of the variance in the academic outcomes (Breslau, Miller, Breslau, Bohnert, Lucia, & Schweitzer, 2009). This suggests that the affect of psychological symptoms on academic performance in childhood cancer survivors may vary from the relations found in healthy children, and future studies should continue to examine these important relations.

With the resilience domain, the final model accounted for 11.8% of the total variance in resilience scores. In addition to demographic factors including special education, race, age, and gender, the only other block that added significant change to the model was the psychological symptoms block. The psychological symptoms block added a total of 7.6% of the variance to the resilience scores. Included in the block were internalizing, externalizing, and attention/hyperactivity symptoms as well as social competence. The most significant individual contributor was social competence, but externalizing symptoms also approached significance. This link is not surprising given that one of the resilience subdomains is social problem solving. What is interesting is the strength of this relation over time; this study suggests that difficulties with social interactions at a very early age predict continued social difficulties into adolescence. Interestingly, this finding is in contrast to much of the published developmental literature that reports little consistency in social development over time, aside from antisocial behavior which has been found to be relatively stable from early childhood through adolescence (Crick, 1996; Morison & Masten, 1991). Masten and colleagues (1995) found that social development constructs such as peer acceptability in school-aged children was only modestly related to social skills and social development in late adolescence. In fact, across the major developmental areas examined, including academic/job, behavior, and social competence, they noted that social competence had the weakest longitudinal relation (Masten, Coatsworth, Neemann, Gest, Tellegen, & Garmezy, 1995). The current study suggests that there may be a stronger longitudinal relation with social skills and social competence in childhood cancer survivors compared to healthy children, and future studies should examine the underlying factors contributing to this stability over time.

Other subdomains within the resilience domain included physical activity, nutrition, and family involvement. Current findings suggest that intervening to ameliorate psychological symptoms at an early age may have an impact on future physical and mental health in childhood cancer survivors, a particularly at-risk group for worse health outcomes, including obesity (Baranowski, Mendlein, Resnicow, Frank, Cullen, & Baranowski, 2000). Finally, family factors are also in the resilience domain, including home safety and family involvement. Kazak and colleagues (1997) examined the relations between psychological symptoms and family functioning in survivors of childhood leukemia and found that child anger and anxiety were related to parent reports of family satisfaction. The current study suggests that a similar relation is found with adolescent-reported family functioning. Although the details of the family functioning literature are beyond the scope of this project, the present study findings are generally consistent with previous literature (Kazak, et. al., 1997; Drotar, 1997; Stern & Zevon, 1990) and support a strong link between a child's psychological symptoms and immediate and future family functioning.

The final satisfaction model accounted for 14.6% of the variance in satisfaction scores. In addition to the demographic and treatment blocks, psychological and physical symptoms and functional status contributed significant variance to the satisfaction domain and current health perceptions was approaching significance. When examining the change in R^2 , the psychological symptoms block added the most variance to the model, with 7% of the variance in satisfaction scores being explained by internalizing symptoms. The satisfaction domain is made up of the self-esteem and satisfaction with health subdomains, and both of these constructs have been found to be related to psychological symptoms. The relation between self-esteem and internalizing symptoms, including anxiety and depression, has been found cross-sectionally in

children with cancer and cancer survivors (Essen, Enskär, Kreuger, Larsson, & Sjöden, 2000). Moreover, previous studies have reported relations between poor health perceptions and low satisfaction with health with increased depressive symptomatology and anxiety in childhood cancer survivors (Pemberger, et. al., 2005). The current study adds to our understanding of these relations over time and highlights the importance of early monitoring of psychological symptoms in order to intervene and prevent long-term negative effects on self-esteem and satisfaction with health from psychological symptoms.

Physical disfigurement and functional status also added significantly to the satisfaction model. A meta-analysis examining the relation between minor and major physical disabilities and self-esteem found that the effect size for the negative relation between minor disabilities (e.g. clumsiness, coordination difficulties, etc) and self-esteem was larger than the effect size for those with major disabilities (e.g. cerebral palsy). This suggests a stronger relation between minor disabilities and lower self-esteem when compared to the association between major disabilities and lower self-esteem. The authors postulate that when a child appears otherwise normal, peers may be more likely to tease them for their impairments which in turn harms their self-esteem. However, it is possible children with more obvious physical impairments receive more empathy and therefore do not experience the same decrease in self-esteem as a result of their impairments (Miyahara, & Piek, 2006). This would be an interesting hypothesis to explore in childhood cancer survivors as most people in the general population do not understand the long-term affect of treatment on the child's functioning. Often childhood cancer survivors do not look sick or continue to have visible signs of cancer treatment, so others expect the once sick child to return to "normal."

For the discomfort domain, the final model included demographic and treatment factors, psychological symptoms, functional status impairment, and health perceptions and accounted for 12.6% of the variance. While the demographic block with gender added the most variance (6.5%), the psychological symptoms block with internalizing and externalizing symptoms and cancer specific anxieties/fears added 3.9% of variance. Additionally, the functional status block added variance 3.2% of variance. These relations are expected given that the subdomains of the discomfort domain were physical discomfort (e.g. feeling sick, experiencing low energy; <https://ccss.stjude.org/docs/ccss/survey-teen-health.pdf>, p. 7), emotional discomfort (e.g. difficulty sleeping, days depressed, days afraid of things; <https://ccss.stjude.org/docs/ccss/survey-teen-health.pdf>, p. 8), and limitations of activities (days missed school, days had trouble running, days had trouble with hands; <https://ccss.stjude.org/docs/ccss/survey-teen-health.pdf>, p. 9) and therefore assess similar things. This again highlights that the presence of psychological symptoms and difficulty with independence/completing daily activities at a young age predicts the presence of more physical and emotional disorders many years later. Moreover, these findings indicate that impairments in daily functioning may not resolve as the survivor gets further away from treatment, and this is perhaps an area that needs more attention during the transition from active treatment to survivorship to prevent long-term impairment. Such interventions could include referrals to physical therapy or including occupational therapy in survivorship care. Increased assessment of functional status impairment would also be encouraged to ensure that any issues with daily functioning are being monitored by the medical team.

For the disorders domain, demographic and treatment variables along with psychological and physical symptoms and functional status impairment accounted for 18.2% of the variance in

disorder domain scores. Psychological symptoms, physical symptoms, and functional status impairment all added significant change to the model, with psychological symptoms accounting for 4.5% of the variance, physical disfigurement with 3.4%, and functional status impairment with the most at 6.5%. Many of these predictors directly map onto the items assessed in the subdomains of the disorders domain. For example, physical disfigurement and the surgical subdomain both assess conditions affecting the bone/muscle and disabled or deformed extremity. Similarly, the psychological symptoms at baseline are similar to the items assessed in the emotional disorders subdomain. Therefore, the important finding from this study is that the presence of these symptoms at a young age will likely lead to continued difficulty in these areas of functioning if proper interventions are not received.

Finally, for the risk domain, demographic and treatment factors along with psychological symptoms, physical symptoms, functional status, and health perceptions accounted for 9.8% of the variance. Interestingly, this was the only model where treatment modalities was the significant treatment factor related to risk outcome, with more modalities of treatment lowering risk scores which is consistent with the literature (Speechley, et. al., 2006). In addition to the demographic and treatment blocks, the psychological symptoms block with externalizing and attention/hyperactivity symptoms was the only other block to add significant change to the model, and each individual variable was also significantly related to risk. Overall, the psychological symptom block contributed over half of the total variance in the risk outcome (5.3%). This finding is consistent with literature that reports a strong relation between mental health factors and risk behavior (Klosky, et. al., 2012). However, while externalizing symptoms predicted lower quality of life risk scores, which is consistent with previous literature,

attention/hyperactivity symptoms predicted higher risk scores (which indicate better health and therefore less risk), which is not consistent with the literature.

This model explained the least amount of variance among the examined domains, indicating that more information is needed to understand the factors that influence risky behavior in adolescent cancer survivors. The identification of such factors is particularly important in light of recent information published about risky behavior in childhood cancer survivors (Klosky, et. al., 2012). The current study found no significant differences in risky behavior with the established population norms which is generally consistent with other studies which have found that survivors tend to engage in risky behavior as much as their siblings (Klosky, et. al., 2012). However, given the increased health risks adolescent survivors face as a result of their treatment (Hewitt, Weiner, & Simone, 2003; Mertens, et. al., 2001), engagement in normative adolescent risk behavior could have more negative consequences. Therefore, identifying factors that predict risk taking to allow for the development of interventions to reduce risky behavior is extremely important.

Hypothesis Four

While it is important to examine individual relations between predictors and outcomes, it is also important to look at the patterns emerging from this data. First, each of the models only explained 9 – 19% of the variance in the quality of life domains. While this is similar to some studies (Brown, Madan-Swain, & Lambert, 2003), it is lower than a number of studies, including those using the Wilson and Cleary model which report ranges in R^2 from 29 – 32% (Sousa, Holzemer, Henry, & Slaughter, 1999; Heo, Moser, Riegel, Hall & Christman, 2005), and in studies on childhood cancer survivors with 66.2% of the variance being accounted for (Recklitis, et. al., 2007). It is difficult to draw strong comparisons because these studies report R^2 rather than

adjusted R^2 , so the percentages might be slightly elevated. However, R^2 values for the current study range from 12 – 22% and are therefore still significantly lower than the values reported in these other studies.

Of note, for each quality of life outcome, psychological symptoms added significant change to the model, and for most models (all but disorders), this block added the most variance of the examined factors. Therefore, while the focus of the literature has been on demographic and treatment factors, results of this study show that psychological symptoms are providing more information about long-term functioning in most of the models. This suggests that the presence of a variety of psychological symptoms at a young age has a great deal of influence on quality of life in the future. Across most domains, an increase in psychological symptoms predicted lower quality of life scores. All psychological symptoms that were examined, including internalizing, externalizing, and attention/hyperactivity symptoms, along with social competence and cancer specific anxieties/fears, were included in at least one domain model. Internalizing and externalizing symptoms were the most common psychological symptoms to have an individual significant relation with the domain scores. Previous studies have reported higher rates of internalizing symptoms compared to externalizing symptoms in survivors (Mabbott, Spiegler, Greenberg, Rutka, Hyder, & Bouffet, 2005) and suggest more focus on internalizing symptoms, but this study finds that both are important in the long-term functioning of survivors. The impact of psychological symptoms on future functioning has received very little attention in the literature and highlights an enormous gap in our understanding of factors impacting quality of life in survivors. In order to find variables that explain a greater amount of variance in quality of life, studies need to focus on identifying the most important psychological symptoms related to quality of life. Several areas of future investigation are discussed below.

The current study also adds to our understanding of the affect of physical symptoms on future quality of life. Consistent with previous studies, the current sample reported very little pain as a result of their cancer or its treatment (Speechley, et. al., 2006; Zeltzer, et. al., 2008), indicating that this is not the best predictor of future quality of life. With physical disfigurement, most of the studies that have examined relations between disfigurement and quality of life have focused on those with extensive surgical histories, including limb amputation or limb salvage surgery (Nagarajan, et al., 2003; Eiser, Darlington, Stride, & Grimer, 2001; Felder-Puig, et. al., 1998; Zebrack, et. al., 2007). This study included these items in the measure of physical disfigurement, but also included questions about visible scars and permanent hair loss.

Physical disfigurement was included in all of the domain models other than the discomfort domain, and was a significant predictor of lower quality of life scores in the satisfaction and disorder models. Although separate analyses based on the type of physical disfigurement endorsed were not completed, only three participants reported the loss of a limb or eye in the current sample, so the majority of respondents only endorsed the presence of more cosmetic disfigurements (e.g. permanent hair loss, scarring on head/ neck, arms/legs, walking with a limp). Therefore, these findings indicate that cosmetic disfigurement could also impact future functioning, which is in contrast to other studies that have reported no significant relations between more cosmetic physical impairments and quality of life (Mulhern, Wasserman, Friedman, & Fairclough, 1989). Given the importance of appearances for adolescents and the desire to fit in, it is logical that visible signs of any previous illness could affect functioning. However, it is interesting that these symptoms were present during the baseline survey and may or may not have still been an issue in adolescence. Perhaps the developmental impact of having outward signs of their cancer diagnosis and treatment has a lasting effect. The relation between

the variables examined in the current study and the impact of developmental time period of diagnosis and time since diagnosis would be an interesting area for future work and could provide a better understanding of the underlying factors impacting these relations. The importance of examining these relations in future studies is discussed in more detail below.

Functional status also emerged as an important predictor of quality of life scores across domains. Though the current sample reported relatively few functional status impairments compared to other studies (Mulhern, Wasserman, Friedman, & Fairclough, 1989), the effect of any functional impairment was significant. Functional status was included in all six domain models, added significant change to the satisfaction, discomfort, and disorder domains, and was a significant individual predictor for discomfort and the disorders domains. In all cases, increased impairment predicted lower quality of life scores. This indicates that functional status impairment continues to have a great deal of influence on quality of life, particularly in areas related to physical health and functioning. Previous studies have found an interaction with age of onset and functional status impairment on quality of life, with functional status impairments with an onset in adulthood impacting quality of life more negatively than those with an onset in childhood (Joubert, et. al., 2001). However, the current study finds that functional status impairment at a young age can negatively affect future quality of life in several areas and should continue to be monitored.

Finally, this study contributes to our understanding of the impact of parental health perceptions on future quality of life in childhood cancer survivors, a generally understudied area in the literature. Examining parental health perceptions rather than personal health perceptions was an adaptation from the Wilson and Cleary model, but one that makes sense given this was an application of the model to a pediatric sample. For the current study, parent perceptions of their

child's current health at baseline were generally positive, which is in contrast to much of the published literature reporting that parent's often continue to have negative health perceptions for their children even after cancer treatment has ended (Speechley, et. al., 2006). Current health perceptions were included in the final models for resilience, achievement, satisfaction, and discomfort, and had an individually significant relation with the achievement outcome. In all cases, positive health perceptions predicted increases in quality of life scores. This finding is consistent with previous studies which have shown a strong relation between parental health perceptions and child's emotional functioning and quality of life (Colletti, et. al., 2008; Anthony, Gil, & Schanberg, 2005; Spurrier, et. al., 2000), and indicates that parental health perceptions should continue to be examined as they have direct implications for the child's future functioning. Moreover, as future studies examine these constructs in children treated at older ages, perceptions of health and vulnerability should be examined with self-report measures as some studies have found that adolescent and young adult survivors may report increased perceptions of health vulnerability compared to their parents (Foster, Stern, Russell, Shivy, Bitsko, Dillon, et. al., 2011).

It is also interesting that in univariate analyses, perceptions of vulnerability were significantly related to the risk outcome. It also remained in the final risk model, with higher perceptions of vulnerability in the parent predicting more risk behaviors reported by adolescents, though it was not an individually significant variable in the model. The mechanisms through which these perceptions affect the child are unclear. There is an established link between health perceptions with parenting styles, including increased levels of over-protection in parents with perceptions of vulnerability (Thomasgard, Shonkoff, Metz, & Edelbrock, 1995). While most of the published literature shows a decrease in risky behavior in adolescence as parental monitoring

increases (DiClemente, Wingood, Crosby, Sionean, Cobb, Harrington, et. al., 2001; Li, Stanton, & Feigelman, 2000), it is possible that this relation is different in chronically ill children such as childhood cancer survivors. More information about this relation is needed in future studies.

Generally, the results of this study support the use of the Wilson and Cleary model. Each block of the Wilson and Cleary model was significant for at least one of the quality of life domains. As discussed before, the benefit of the CHIP-AE is a more nuanced examination and understanding of quality of life as consisting of multiple areas of functioning. As such, a variety of predictors are necessary to understand these various quality of life domains. With each block being important for different quality of life outcomes, it is important to consider to utility of the whole model.

Clinical Implications

As survivorship increases in the childhood cancer population, and as the long-term impact of childhood cancer and its treatment continues to be better understood, a new model of long-term follow-up care for childhood cancer survivors is being implemented across the country. In 2003, the Institute of Medicine published a report, “Childhood Cancer Survivorship: Improving Care and Quality of Life,” and proposed five recommendations for survivorship care. These recommendations included increased focus on evidence-based practice and the development of practice guidelines in survivorship care. Furthermore, the use of multidisciplinary teams was emphasized (Hewitt, Weiner, & Simone, 2003). They also identified important next steps, including developing minimum standards of care for survivorship clinics, evaluating various models to understand the best system of delivery of care, and building long-term follow-up clinics in all pediatric oncology institutes (Aziz, Oeffinger, Brooks, & Turoff, 2006). Following the Institute of Medicine’s 2003 report, the Children’s Oncology Group

developed a series of standards of care for survivorship care. This report includes guidelines for transition to survivorship and adult care, information about developing appropriate parameters for starting a survivorship clinic, and parameters for building a multidisciplinary team. The importance of including psychology on such teams is discussed and sample screeners used to gather important information on survivor functioning are included (Landier, 2007).

The role of psychology in such clinics has also been discussed. In one study, directors of survivorship clinics expressed a need for more psychological services (Aziz, Oeffinger, Brooks, & Turoff, 2006). Other studies have echoed the need for multidisciplinary care, along with the importance of continuity of care, and the longitudinal approach to survivorship follow-up (Oeffinger, & Hudson, 2004). As standards of care in survivorship clinics are implemented, and as the role of psychology in these clinics is established, studies such as the current one can help to inform evidence-based practice in survivorship care.

Although more information is needed before decisions about specific screeners that should be used for best-practice in childhood cancer survivorship follow-up, several general conclusions from the current study can be used to guide survivorship care. The current study finds that data from five years of cancer survivorship can predict functioning in childhood cancer survivors several years later and across developmental periods. This is important information as survivors are typically followed more closely in the initial years of survivorship and have more access to multidisciplinary care. This study suggests that screeners should be given to survivors during their appointments to identify and intervene with current problems, as current difficulties could lead to impairments in functioning later in life as well.

Broad conclusions drawn from the current study further suggest that it is particularly important that survivors receive screeners of psychological symptoms, as these were important

predictors for all of the examined quality of life domains. A broad measure of psychological symptoms is important, since internalizing symptoms were significantly related to the achievement and satisfaction domains, while externalizing symptoms were related to the resilience and risk domains, social competence was related to the resilience and disorders domains, and attention/hyperactivity symptoms were significantly related to the risk domain scores. Interestingly, parent perceptions of cancer specific anxieties and fears were only included in one model (discomfort) and did not have a unique significant relation with the outcome. This suggests that anxieties and fears about cancer may not be as important to measure and identify as more global psychological concerns.

General screeners assessing various areas of psychological functioning, including internalizing, externalizing, and attention symptoms, would be best. Moreover, including self-report questionnaires from the patients when age-appropriate would be preferred. Ideal measures to use would include the more extended version of the BPI, the CBCL (Achenbach, 1991) and the self-report version of the same measures, the Youth Self Report (YSR; Achenbach, 1991). The CBCL has often been used in childhood cancer research to assess for psychological symptoms (Kupst, et. al., 2002; Goldbeck, Koffmane, Lecheler, Thiessen, & Fegert, 2007; Mulhern, Wasserman, Friedman, & Fairclough, 1989). However, because these instruments are longer and cost money, they may not be the best options for clinics. A more cost-efficient and targeted screening system could also be implemented with a brief screener such as the BPI being used initially and then targeted follow-up assessments being given based on the results of the BPI. For example, if the BPI is showing elevation on internalizing symptoms, then screeners for depression (e.g. the Children's Depression Inventory; Kovacs, 1992) or anxiety (e.g. the Multidimensional Anxiety Scale for Children (MASC); March, Parker, Sullivan, Stallings, &

Conners, 1997), could be given, and if elevations are present on the externalizing subscale, assessments such as the Vanderbilt ADHD parent diagnostic scale (Wolraich, Lambert, Doffing, Bickman, Simmons, & Worley, 2003) could be completed. This screening system would be both cost and time efficient. As future research continues to identify factors important to the long-term functioning of survivors, brief screeners can continue to be shaped.

Limitations and Future Directions

The current study is one of the first known studies to examine longitudinal predictors of quality of life in adolescent survivors of childhood cancer. As reported, factors were identified in young survivors that were able to predict future functioning in adolescent survivors. More importantly, this study showed that factors other than demographics and treatment variables predict long-term quality of life. This lays an important foundation upon which future studies can be developed.

Several areas for future research have already been discussed, including the need to examine social functioning in more depth in survivors, as well as the longitudinal stability of these skills. Other identified areas for future research include examining the role of perceptions of vulnerability on parenting practices, such as monitoring and controlling the home environment, and the subsequent effect on adolescent behavior, and a greater understanding of the relation between psychological functioning and school performance in survivors. In addition to these specific areas for future investigation, there are several limitations in the current study that can be improved upon in future studies. Limitations of the current study generally fall into two categories, including limited generalizability from the current sample and limited variance being accounted for in quality of life from the models.

To begin, the current sample represents a very small group of cancer survivors, which limits the generalizability of the findings. First, the group of survivors examined were diagnosed and treated for cancer at a very young age. Interestingly, this study finds that despite being diagnosed at an age when most adolescents would not remember their treatment, long-term implications are still found in quality of life outcomes. While this study has allowed for a greater understanding of the long-term impact of cancer for children diagnosed very young, it also means that caution must be used in generalizing these findings to other survivors of childhood cancer.

The larger issue with the current sample that limits generalizability is that the sample is comprised of primarily White, middle class individuals. The influence of income on the quality of life domains could not even be examined due to the low variance in income reported by participants, and meaningful conclusions about the impact of race were also impeded. Some studies show differences in outcomes based on race and household income (Wu, et. al., 2007; Shankar, et. al., 2005; Zebrack, et. al., 2002; Sung, et. al., 2008), and these differences must be better understood to inform culturally sensitive, effective interventions for all cancer survivors. To address limitations of the current study, future studies including more representative samples need to be completed in order to generalize the most accurate findings for survivors.

Another important consideration when interpreting the quality of life outcome data in comparison to the established population norms is age of participants at the time of the Teen survey. The CHIP-AE was normed on children in Baltimore between the ages of 11 and 17 (Starfield, et. al., 1995), however, the Teen survey included participants between the ages of 14 – 19, and most participants (75%) were 18 and 19 years old. While an increased understanding can

be gained by knowing how the current sample compares to other adolescents who are generally healthy, these interpretations must also be made with caution.

Another limitation in the current study was the lack of variance in quality of life explained by the proposed models. While each model that was built was significant and predicted some amount of variance in the outcome, the examined factors still only accounted for 10 – 20% of variance, leaving a majority of the variance in quality of life to still be accounted for. One contributing factor to this problem could be that there was limited variance in the many of the predictor variables. In general, most parents reported few symptoms in their childhood cancer survivor. While this suggests that impairment was generally low in this group, which is a positive finding, it made it more difficult to meaningfully understand the impact of some of the predictors on quality of life. This could have contributed to the overall low amount of variance that this study was able to account for in the quality of life outcomes. This also highlights another limitation in the study, which was the use of parent-report measures at baseline, despite the mean age of children at baseline being 11 years old. There is a great deal of literature suggesting that parent-report of child functioning is not always accurate, especially as the child grows older, and with internalizing symptoms (Eiser & Morse, 2001; Foster, Stern, Russell, Shivy, Bitsko, Dillon, et. al., 2011, Levi & Drotar, 1999). In addition to increasing accuracy of symptoms report, it is possible that more variance could have been explained if child-report measures were used, and future studies should address this limitation.

Because a low amount of variance was accounted for with each outcome, future studies first need to examine other longitudinal factors that may explain more variance in future quality of life scores. One approach to this examination would be to continue using the Wilson and Cleary model as a guide, since this study supports the overall utility of the model, and examining

other ways of measuring the constructs in the model. For example, with psychological symptoms, studies in other pediatric populations explained a large amount of variance (39%) using more thorough measures of depression and anxiety, so perhaps these symptoms should be more thoroughly examined in childhood cancer survivors (Vila and colleagues, 2003). Moreover, health perceptions and perceptions of vulnerability could be examined with more thorough measures such as the Vulnerable Child Scale (Perrin, West, & Culley, 1989).

Alternative quality of life models that would allow for the exploration of other constructs of importance in the quality of life for survivors could also guide future studies. For example, Wyatt and Friedman (1996) developed a quality of life model for adult survivors of cancer and postulate that in addition to social, psychological and physical functioning, spiritual beliefs should be assessed (Wyatt & Friedman, 1996). Ferrell and colleagues (1995) also emphasize the importance of examining future outlook and sexuality and fertility perceptions in quality of life in cancer survivors (Ferrell, Dow, & Grant, 1995).

As important factors are identified, more information about timing of such questionnaires and when the predictive power of these variables begins should be examined. Future studies could seek to understand if screeners within the first year or two of treatment predict long-term functioning or if more time from treatment ending is necessary to understand the long-term implications of the cancer diagnosis on the child. Such studies could continue to inform best practices and have direct implications on the follow-up care of childhood cancer survivors.

These research questions also need to be examined in children currently being treated for cancer. The CCSS has many advantages, including the ability to examine longitudinal relations in large samples of childhood cancer survivors, but it also has limitations. The primary limitation is that survivors in the CCSS were treated in the 1970's and early 1980's, and treatment for

childhood cancer has changed a great deal since that time. For example, the total amount of cranial radiation children are exposed to has lowered (Ris, Packer, Goldwein, Jones-Wallace, & Boyett, 2001). Studies have established dose-response relations with cranial radiation and negative outcomes (Nathan, et. al., 2007), so it is possible that this sample reported worse outcomes from treatment than what would be reported from a current sample of children with cancer. This may not be as much of an issue with methotrexate, because a relation between cumulative dose of methotrexate and negative outcomes has not been established. Rather, the negative effect of methotrexate seems to result from a combination of dose, delivery method, and when methotrexate is given (Nathan, et. al., 2007). Because the focus of this study was on controlling treatment variables and identifying other factors that influence quality of life, this is not as much of a limitation for this study as it could be for other studies. However, future studies should examine these relations and continue to identify important predictors for quality of life in children treated on more recent treatment protocols.

Finally, when a clearer understanding of the factors important in predicting quality of life develops, future studies should focus on creating and disseminating interventions to promote positive quality of life across dimensions in survivors of childhood cancer. Such interventions could include referrals to necessary resources such as physical or occupational therapy for functional status impairments, to referrals to a psychologist for help with psychological symptoms or negative health perceptions. Along with increasing access to services, more interventions designed to improve adjustment and positive outcomes in childhood cancer survivors is warranted. Some interventions have already been developed, such as the Surviving Cancer Competently Intervention Program (SCCIP) which combines cognitive behavioral and family therapy to ameliorate PTSS symptoms in patients and their families (Kazak, Simms,

Barakat, Hobbie, Foley, Golomb, & Best, 1999; Kazak, Alderfer, Streisand, Simms, Rourke, Barakat, Gallagher, & Cnann, 2004). More interventions of this nature are needed, but first more research is needed to identify important factors for predicting quality of life to inform the development of such interventions.

Conclusion

The purpose of the current study was to examine quality of life in adolescent survivors of childhood cancer, with a focus on identifying longitudinal predictors of quality of life that account for variance above and beyond the influence of demographic and treatment factors. Factors contributing to future functioning, including psychological and physical symptoms, functional status, and health perceptions were found to predict future quality of life in survivors across important domains. This is an important first step in a new direction of survivorship research that focuses less on identifying patterns of outcomes in survivors and begins to focus more on identifying factors that contribute to worse outcomes in survivors and intervening early to promote positive quality of life.

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Vita

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