Psychosocial Factors and Health-Related Quality of Life in Pediatric Cancer

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Abstract

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Children with cancer are at risk for poorer health-related quality of life (HRQOL). Prior work indicates that HRQOL may change throughout cancer treatment, and some evidence indicates that psychosocial factors affect overall HRQOL. Additional research is needed to examine the trajectory of domain-specific HRQOL over the first year of pediatric cancer treatment as well as the psychosocial predictors of those trajectories. The current study addresses gaps in the literature by describing the trajectories of domains of HRQOL, examining psychosocial predictors of those trajectories, and examining changes in the association between HRQOL and psychosocial factors over time. Primary caregivers of children newly diagnosed with cancer completed self-report measures of depression, anxiety, PTSS, parent-child conflict, emotion coaching and their child's psychological adjustment and HRQOL at 1-, 6- and 12-months post-diagnosis. Data were analyzed using multi-level models. Child HRQOL increased over the first year of treatment. Child internalizing symptoms at the time of diagnosis were associated with level of general ($\beta = -6.82$), physical ($\beta = -7.80$), social ($\beta = -6.32$), and school ($\beta = -6.86$) HRQOL during the first year of pediatric cancer treatment. Parent-child conflict was associated with level of social HRQOL ($\beta = -2.67$). Changes in psychological adjustment over time were

not associated with changes in HRQOL. On average, children's HRQOL improves over the first year of cancer treatment; however, children with more internalizing problems and more conflict with caregivers at baseline may be at risk for poorer HRQOL over time.

Psychosocial Factors and Health-Related Quality of Life in Pediatric Cancer

In the United States, approximately 16,000 children are diagnosed with cancer every year (Miller et al., 2019). Children diagnosed with and treated for pediatric cancer face many challenges and stressors through the cancer experience (McCaffrey, 2006; Rodriguez et al., 2012). Specifically, children and teens undergoing cancer treatment and their families discuss the primary challenges of needle procedures, chemotherapy, long hospital stays, fear of dying, loss of control, and missing out on activities with family and friends (McCaffrey, 2006). Consequently, children report feeling more depressed, unable to engage in school and extracurricular activities, and a broad impact of cancer treatment on many aspects of their daily functioning (Bemis et al., 2015; McCaffrey, 2006; Rodriguez et al., 2012). It is clear that cancer interferes with children's typical routine and development. The challenges of cancer affect children's wellbeing and put them at risk for poor health-related quality of life (HRQOL; Garas et al., 2019; Momani et al., 2016; Stokke et al., 2015).

HRQOL encompasses a person's perception of their health and functioning, consisting of physical, social, emotional, and role (school/work) functioning (Aaronson, 1991; Varni et al., 2001; Ware, 1984). The concept of HRQOL first emerged as the medical field began to acknowledge the importance of understanding the impact of diseases on people beyond treatment and survival outcomes (Ware, 1984). Medical providers recognized that patient care is more than just keeping people alive, concluding that "health is more than freedom from disease" (Ware, 1984). HRQOL was established as a concept to understand the impact of medical conditions on wellbeing. An emphasis was placed on a patient's subjective view of their capacity to perform everyday tasks in the context of illness and treatment. Early conceptualizations of HRQOL include domains of physical, social, psychological, and role functioning (Aaronson, 1991; Spieth

& Harris, 1996; Ware, 1984). These domains can include a variety of tasks including mobility, self-care, managing relationships, and performing daily activities at work, school, or home. Other researchers consider disease-related symptoms and cognitive functioning as domains of HRQOL (Aaronson, 1991; Varni et al., 1998). More recently, the World Health Organization (WHO; 2007) has identified HRQOL as a critical construct of wellbeing in the context of chronic illness and describes HRQOL as "what people "feel" about their health condition or its consequences; hence it is a construct of subjective well-being." Across literature, there seems to be agreement that HRQOL captures a person's impression of their functioning across various domains in the context of illness.

HRQOL is critical to examine in context of pediatric cancer treatment, as it captures a broad range of children's functioning to assess the impact of cancer across many aspects of their lives. Theoretical and empirical work has identified factors that may impact children's HRQOL while undergoing cancer treatment including diagnosis, treatment-related factors, demographic factors, and psychosocial factors (Ferrans et al., 2005; Momani et al., 2016 Wilson & Cleary, 1995). Much of the empirical work that has been done on HRQOL in pediatric cancer has focused on cancer-related and demographic factors. However, less work has focused on psychosocial factors and HRQOL. The association between psychosocial factors and HRQOL in pediatric cancer is critical to understand modifiable factors that may promote better outcomes for children with cancer. The current paper investigates child-level and caregiver-level psychosocial variables that may impact HRQOL over the course of the first year of pediatric cancer treatment.

HRQOL and Pediatric Cancer

Qualitative work demonstrates that childhood cancer affects children throughout many aspects of their lives (McCaffrey, 2006). Thus, HRQOL is an important outcome to study in childhood cancer because it is a holistic assessment of the effects of cancer beyond physiological outcomes. Various domains of HRQOL assess pain, mobility, personal relationships, social support, school/work performance, affect, and mental health. Multiple cross-sectional comparison studies and reviews of the literature demonstrate that children with cancer report lower HRQOL across functioning domains both during and after their cancer treatment compared to healthy control groups and siblings across ages and diagnoses (An et al., 2011; Dixon et al., 2019; Fardell et al., 2017; Garas et al., 2019; Langeveld et al., 2004; Stam et al., 2006; Yagci-Kupeli et al., 2012). One study of children (N = 31; M_{age} = 9 years) diagnosed with brain tumors found they had lower overall, physical, emotional, social, and school HRQOL compared to healthy peers (An et al., 2011). Similar findings were reported in a literature review focused on children (N =1,245; ages 2-18 years) undergoing treatment for acute lymphoblastic leukemia (ALL), such that children with ALL had lower HRQOL compared to healthy peers (Garas et al., 2019).

Survivors of pediatric cancer also experience lower HRQOL compared to their peers (Langeveld et al., 2004; Yagci-Kupeli et al., 2012; Stam et al., 2006). One study of cancer survivors (N = 302; M_{age} = 13 years) diagnosed with various cancers (e.g., lymphoma, CNS tumors, Wilms tumor, sarcomas, neuroblastoma) demonstrated that children treated for cancer had relatively lower HRQOL in domains of social and physical functioning compared to healthy peers (N = 272; M_{age} = 10 years; Yagci-Kupeli et al., 2012). Additionally, a literature review by Fardell et al. (2017) examining HRQOL in children (N = 2,073; ages 1-18 years) with ALL,

found that some children continue to experience poorer physical and psychological HRQOL long-term. Yet another meta-analysis of survivors of bone tumors found that HRQOL improved over time (Stokke et al., 2015). Theoretical models of HRQOL have been developed to explain factors that might contribute to variation in HRQOL.

Theoretical Views of HRQOL

Researchers have proposed theoretical models as a framework to understand variables that might impact HRQOL (Bakas et al., 2012; Ferrans et al., 2005; Wilson & Cleary, 1995). For example, one theory proposed by Wilson & Cleary (1995; see Figure 1) emphasizes that HRQOL is related to physical health through disease-related characteristics and functional limitations. However, HRQOL is distinct from physical health in the sense that it accounts for subjective perceptions of health and wellbeing. They claim that HRQOL is a combination of perceptions of physical functioning (e.g., pain and mobility), social functioning (e.g., personal relationships, social support), role functioning (e.g., daily living, school/work performance), mental health (e.g., emotions, cognition, executive functioning), and general perceptions of health. Furthermore, they describe four factors that contribute to HRQOL: (1) biological factors, (2) symptoms, (3) functional status, and (4) perception of health. According to Wilson & Cleary, biological and physical factors (e.g., cancer, cancer treatment) impact someone's symptoms (e.g., fatigue). The symptoms consequently impact functional status (e.g., ability to go to school, play), which in turn affect someone's general perceptions of their health (e.g., "I am unwell"). This perception then leads to the concept of overall HRQOL. Wilson & Cleary (1995) also suggest that perceptions of health and functional status may be

impacted by other psychosocial factors of the individual and the environment, such as one's values, personality, amount of social support, or economic support.

Expanding on Wilson & Cleary's (1995) model, Ferrans et al. (2005; see Figure 2) proposed a more detailed conceptual model of HRQOL, identifying specific elements and determinants of HRQOL. Similar to Wilson & Cleary, they suggest that HRQOL is influenced by factors at both the individual level (particular characteristics of a person) and environmental level (characteristics of external factors outside of the individual). According to their model, individual level factors may include demographic, developmental, psychological, and biological characteristics. Environmental level factors include social characteristics (family, friends, providers) and physical characteristics (household, neighborhood, workplace, school). Ferrans et al. (2005) also argue that these individual and environmental level characteristics not only impact HRQOL, but also impact the causal factors of HRQOL as well. For example, an individual's biological function, symptoms, functional status, general health perceptions, and consequently their HRQOL, might be influenced by their age and race as well as their level of social support or access to healthcare in their neighborhood.

Others have developed a model of HRQOL specific to pediatric cancer through qualitative interviews with children ($N = 23$; $M_{age} = 12$ years) undergoing cancer treatment (Hinds et al., 2004). Researchers asked children "What makes a good/bad day for you?" and "Are there some things you like to do that you cannot do now?" Through qualitative analysis of common themes in children's responses, they established that HRQOL in pediatric cancer is "an overall sense of well-being based on being able to participate in usual activities; to interact with others and feel cared about; to cope with uncomfortable physical, emotional, and cognitive reactions; and to find meaning in the illness experience" (Hinds et al., 2004, p. 767). This

conceptualization of HRQOL emphasizes the importance of children's functioning across many aspects of daily life. Additionally, they identified six dimensions contributing to HRQOL: (1) symptoms, (2) usual activities, (3) social and family interactions, (4) health status, (5) mood, and (6) making meaning of being ill. Similar to others, this model describes both illness-related factors and psychosocial factors associated with children's HRQOL.

Furthermore, others argue that in context of pediatric cancer, HRQOL varies over the course of cancer treatment in association with the symptom trajectory (Woodgate & Degner, 2004). Longitudinal empirical work in people who had cancer during adolescence ($N = 61$; $M_{age} = 15$ years) has demonstrated non-linear change in physical and psychological HRQOL between two and ten years post-diagnosis (Ander et al., 2016). Specifically, physical HRQOL increases between two and three years post-diagnosis and then levels off, and psychological HRQOL shows a sharp decrease between two and three years post-diagnosis and then gradually declines. Additional longitudinal research is needed to examine changes in HRQOL while children are undergoing cancer treatment.

Cancer-Related and Demographic Factors Associated with HRQOL

Each of the theoretical models describes suggest that variation in HRQOL may be explained by certain risk factors, such as diagnosis, treatment-related factors, socio-demographic factors, as well as psychosocial factors. Recent reviews of the literature have concluded that empirical research on children's HRQOL during pediatric cancer treatment has primarily focused on the effects of diagnosis, treatment-related factors, and demographic characteristics (Momani et al., 2016). Regarding demographic factors,

research has focused on child age and sex. Various cross-sectional studies of children on treatment and pediatric cancer survivors have found that child sex is associated with HRQOL in pediatric cancer such that female children typically have poorer HRQOL than male children across ages and diagnoses (Nathan et al., 2007; Nolan et al., 2014; Stokke et al., 2015; Sung et al., 2009). One paper conducted a meta-analysis of papers that investigated HRQOL in patients under age 25 treated for bone tumors (e.g., sarcoma; Stokke et al., 2015). Findings demonstrated female sex and older age at diagnosis are associated with poorer overall HRQOL. Another cross-sectional study of children ages 2-18 years old (N = 376) undergoing cancer treatment for various cancers found that age, diagnosis, and type of treatment were associated with children's physical, emotional, and social HRQOL (Sung et al., 2009). Specifically, younger child age and a diagnosis of ALL compared to other diagnoses were associated with better HRQOL, and more intensive chemotherapy treatment was associated with poorer HRQOL. Findings from the Childhood Cancer Survivor Study (N = 2,064) demonstrate that age and sex are associated with physical HRQOL in survivors of pediatric cancer (Nolan et al., 2014). Patients in this sample were approximately 14 years old at the time of diagnosis and 65% were diagnosed with leukemia or lymphoma. Female sex and older current age were associated with poorer concurrent physical HRQOL. In sum, there is evidence that female sex and older age at diagnosis are associated with poorer HRQOL in children on treatment for cancer and survivors of pediatric cancer.

Multiple review papers of children on treatment and survivors of pediatric cancer have focused on cancer-related factors and HRQOL, concluding that diagnosis (Klassen et al., 2011; Momani et al., 2016; Shin et al., 2019), treatment type (Klassen et al., 2011; Zeltzer et al., 2008), and treatment intensity (Momani et al., 2016) are associated with children's HRQOL. Children

with central nervous system (CNS) tumors are more likely to have poorer HRQOL compared to children diagnosed with other cancers (i.e., leukemia, lymphoma; Klassen et al., 2011; Momani et al., 2016; Shin et al., 2019). Furthermore, those who receive cranial radiation as part of their treatment have worse HRQOL than children who do not receive cranial radiation (Klassen et al., 2011; Zeltzer et al., 2008). Finally, children who receive more intense treatment, meaning more frequent, higher doses, and more types (chemotherapy, radiation, bone marrow transplant) of treatment, have poorer HRQOL compared to children with less intense treatment (Momani et al., 2016). These findings are consistent across children of all ages and diagnoses undergoing cancer treatment.

Research has also focused on cancer-related symptoms and symptom distress and their impact on children's HRQOL. For example, pain and fatigue are two most common symptoms experienced by children with cancer and have a negative impact on children's HRQOL (Keener, 2019; Miller et al., 2011). Keener (2019) conducted a qualitative study interviewing 14 caregivers of children ages 1-12 years (M_{age} = 6 years) old undergoing cancer treatment for ALL, neuroblastoma, and Hodgkin lymphoma. Caregivers' perception of fatigue was related to their report of how fatigue had interfered with their child's daily emotional, social, and physical functioning. Specifically, caregivers who perceived their child's fatigue to be more intense and longer-lasting also perceived more impairment in their child's overall functioning. Other work has investigated pain and HRQOL. Calissendorff-Selder and Ljungman (2006) conducted a longitudinal study of the association between pain and HRQOL in eight teens ages 13-18 years (M_{age} = 15 years) diagnosed with various cancers (e.g., lymphoma, osteosarcoma, ALL). Teens reported on pain and HRQOL between 3 months and two years post-diagnosis. Teens

self-reported that variation in pain was associated with changes in HRQOL, such that more pain was associated with poorer HRQOL. Large-scale cross-sectional studies of symptoms and HRQOL in survivors of childhood cancer (i.e., St. Jude Lifetime Cohort Study) have also found associations between symptoms and HRQOL (Huang et al., 2013; Olsson et al., 2021). Survivors who self-report more frequent symptoms have poorer HRQOL (Huang et al., 2013). Specifically, those who experience more pain have worse physical and emotional HRQOL (Olsson et al., 2021). Taken together, this work provides evidence that aspects of the cancer experience, including course of treatment and experience of symptoms, affect children's HRQOL.

Importance of Psychosocial Factors and HRQOL in Pediatric Cancer

Previous work demonstrates that cancer-related factors and demographic factors impact HRQOL. However, these studies have not examined the effect of psychosocial factors on children's HRQOL during cancer treatment. Each of the theoretical models previously discussed highlights the importance of studying the effects of psychosocial variables on HRQOL (Bakas et al., 2012; Ferrans et al., 2005; Hinds et al., 2006; Wilson & Cleary, 1995). Wilson & Cleary (1995) propose that perceptions of health and functional status may be influenced by psychosocial factors of the individual and their environment, such as one's values, personality, amount of social support, and economic support. Ferrans et al. (2005) suggest that HRQOL is influenced by both individual-level and environmental-level factors such as demographic, developmental characteristics, psychological characteristics, social characteristics (e.g., family, friends, providers) and physical characteristics (e.g., household, neighborhood). Hinds et al. (2004; 2006) emphasize family interactions. In pediatric populations, characteristics of the family environment may be particularly relevant to examine in terms of HRQOL as children's functioning and development is influenced by their family. These proposed models highlight

factors beyond physical health and illness that impact HRQOL and identify multiple psychosocial factors that may play a role.

Caregiver-level and child-level psychosocial factors are particularly critical to investigate in context of children's HRQOL because those variables may have a more proximal impact on many aspects of child functioning (Bronfenbrenner, 1977; Kazak, 1989; Long & Marsland, 2011). According to the bioecological model of development, child functioning occurs within the environment of the family system and is influenced by family functioning (Bronfenbrenner, 1977). Factors within the microsystem, or those within an individual or in the immediate setting containing that individual, have more direct effects on child functioning. For example, intrapersonal factors, such as child's own psychological functioning, influence how they interact with the environment (e.g., manage distress during medical procedures) and consequently impact their wellbeing and functioning. A child who experiences more anxiety or depression may be more avoidant or withdrawn, therefore less able to overcome cancer-related challenges and engage in behaviors that contribute to better HRQOL, such as maintaining relationships, completing schoolwork, or active play (e.g., running and jumping). Primary caregiver-level variables, such as caregiver own psychological adjustment, are also particularly important as caregivers influence how a child interacts with their environment. In fact, reviews of empirical work have found that numerous psychosocial factors, including parent and child psychological adjustment and family functioning, are associated with children's HRQOL during childhood cancer treatment across ages and diagnoses (Klassen et al., 2011; Momani et al., 2016). Finally, psychosocial factors are more amenable to change compared to diagnosis, treatment, and demographic factors; thus, they are critical to

study because may be more useful targets for intervention to promote healthier HRQOL outcomes in children with cancer.

Considering the bioecological model of child functioning, specifically caregiver psychological adjustment, caregiver-child relationships, aspects of parenting, and child's own psychological adjustment, should be more closely examined in context of HRQOL in children with cancer. Each psychosocial risk factor will be discussed below in relation to child HRQOL and pediatric cancer.

Caregiver-Level Variables and Child HRQOL

Caregiver Psychological Adjustment

Caregiver psychological adjustment to the cancer experience may be particularly important to children's adjustment as it can impact how a caregiver manages cancer-related stressors, talks to their child about the cancer experience, help their child manage distress, and subsequently influence the child's HRQOL. For example, caregivers who are more depressed, may be more withdrawn or disengaged from their child and more emotionally distressed. Therefore, they are potentially less able to provide support, manage caregiving responsibilities, and help their children regulate their own emotions in response to the cancer experience. Caregiver psychological adjustment is critical to consider regarding child HRQOL, as the mental wellbeing of a caregiver can impact the wellbeing and adjustment of the child (Kazak, 1989).

Previous work has demonstrated that caregiver overall mental health and HRQOL is associated with child HRQOL during treatment. One study examining HRQOL in children ages 2-16 years old ($N = 87$; $M_{age} = 7$ years), found that mothers' physical, emotional, and social HRQOL was positively correlated with parent-proxy report of children's physical, emotional, and social HRQOL respectively (Eiser et al., 2005). Furthermore, caregiver overall mental health

is also associated with children's HRQOL during cancer treatment (Landolt et al., 2006; Pierce et al., 2017). Pierce et al. (2017) conducted a cross-sectional study with children ($N = 67$; $M_{age} = 9.5$ years) undergoing cancer treatment and less than one year from diagnosis. Caregivers of patients reported on their own emotional distress as well as their child's HRQOL. Caregiver distress was associated with overall HRQOL and physical HRQOL such that higher caregiver distress was related to poorer overall and physical HRQOL. However, caregiver distress was not associated with psychosocial HRQOL. Similarly, Landolt et al. (2006) examined cognitive, physical, social, and emotional HRQOL in children ages 6-15 ($N = 52$; $M_{age} = 11$ years) newly diagnosed with cancer within six weeks of diagnosis and again one year later. They also assessed caregiver symptoms of mental health problems. Results showed that children's cognitive HRQOL around time of diagnosis was higher if their parents reported fewer mental health problems concurrently. Another study examined the association between caregiver emotional functioning and child self-reported HRQOL ($N = 258$; $M_{age} = 10.9$; Rodday et al., 2017). Parent emotional functioning was correlated with children's physical, emotional, and school HRQOL, such that better emotional functioning was associated with better HRQOL across domains. Taken together, this work provides evidence that caregiver mental health and psychological functioning is associated with multiple aspects of children's HRQOL including overall, cognitive, physical, and school functioning. However, there are discrepancies in the literature regarding caregiver mental health and psychosocial HRQOL, as one study found no association between the two constructs. Further, these previous studies only examined concurrent associations between factors, so

additional work is needed to understand the long-term impact of caregiver adjustment on child HRQOL.

Other work has specifically investigated the impact of concurrent caregiver depression and anxiety on children's HRQOL during cancer treatment (Penn et al., 2009; Roddenberry & Renk, 2008). Roddenberry & Renk (2008) examined caregiver (N = 63) psychological depression and anxiety and children's HRQOL in children (N = 19; M_{age} = 8 years) who were actively on cancer treatment for various diagnoses. Caregivers self-reported on their mental health symptoms and children self-reported on their HRQOL. Higher parent depression and anxiety was associated with worse overall HRQOL in children undergoing treatment. Another study focused particularly on children ages 1-16 years old with brain tumors over the first year after diagnosis and found similar results (N = 35; Penn et al., 2009). Specifically, caregiver symptoms of depression and anxiety were concurrently associated with children's overall HRQOL at six- and 12-months post-diagnosis, such that higher caregiver anxiety and depression was related to lower HRQOL in children. In sum, better caregiver psychological adjustment is related to better overall HRQOL in children undergoing cancer treatment. However, additional work is needed to examine the association between caregiver depression and anxiety and specific aspects of HRQOL (e.g., physical, emotional, social, school) to understand how caregiver depression and anxiety might differentially impact children in various domains of life.

These studies provide evidence that better caregiver psychological adjustment overall is associated with better child HRQOL across various domains of functioning in context of pediatric cancer treatment. However, further research is needed to understand changes in caregiver adjustment and relative changes in HRQOL over time. Previous work has found that caregiver depression, anxiety, and PTSS on average decrease over the first year of pediatric

cancer treatment (Katz, Fladeboe, King et al., 2018). Yet, it is unclear if changes in caregiver adjustment relate to changes in child HRQOL. Examining associations between the trajectories of caregiver adjustment and child HRQOL can help to understand how HRQOL changes over time in children with cancer. A correlation between the trajectories of caregiver psychological adjustment and child HRQOL would indicate that not only are baseline levels of adjustment associated with HRQOL, but changes in caregiver adjustment are also related to HRQOL. Such results would have implications for monitoring caregiver adjustment longitudinally to predict variability in child HRQOL.

Parent-Child Relationships

The primary caregiver is typically the family member with the most contact with the child and is responsible for managing cancer-related stressors (Rodriguez et al., 2012). The cancer experience often adds more stress and burden on caregivers, which may lead to more caregiver-child conflict and consequently poorer child outcomes (Ishibashi, 2001). For example, the stress of cancer treatment may lead to more arguing if a child does not want to engage in a medical procedure. Indeed, caregivers and children with cancer report more conflict in their relationships compared to healthy peers (Ishibashi, 2001), and 12-19% of families experience significant parent-child conflict during the first year of pediatric cancer treatment (Katz, Fladeboe, Lavi et al., 2018). High conflict between caregivers and children may impact child outcomes, including HRQOL. Research outside of pediatric cancer has demonstrated that parent-child conflict is related to poorer child adjustment and is a primary predictor of child internalizing and externalizing problems (Cummings et al., 2000; Rutter, 1985). Parent-child conflict can also interfere with healthcare as more family conflict may be associated with poorer

adherence to medical care (Miller-Johnson et al., 1994). Consequently, parent-child conflict may negatively affect children's physical and emotional HRQOL.

In non-cancer samples, high parent-child conflict is associated with increased child internalizing and externalizing problems (Burt et al., 2003; Marmorstein & Iacono, 2004). Burt et al. (2003) specifically examined the association between parent-child conflict and prevalence of conduct disorder (CD), oppositional defiant disorder (ODD), and ADHD in healthy children ages 10-12 years old. They found that parent-child conflict is a vulnerability factor that increases risk for these externalizing problems. Similar associations have been found in adolescents, such that teens (M_{age} = 17 years) who report more parent-child conflict are more likely to meet criteria for CD and major depression disorder (Marmorstein & Iacono, 2004). These studies provide evidence that parent-child conflict impacts children's emotional functioning.

Research focused on pediatric cancer populations has examined how family relationships and functioning affects children's HRQOL during pediatric cancer treatment. Barkat et al. (2010) conducted a cross-sectional study of adolescents (N = 102; M_{age} = 15 years) who were an average of 20 months from diagnosis and currently receiving treatment for leukemia, lymphoma, solid tumors, and brain tumors. Teens self-reported on their HRQOL, family functioning, and parent-child relationships. Two aspects of HRQOL were examined: physical HRQOL and psychosocial HRQOL (i.e., aggregate of emotional, social, and school functioning). Adolescents' reports of family functioning and parent-child relationships were not associated with physical HRQOL. Better family functioning and more parent overprotection was associated with higher psychosocial HRQOL. In contrast, Hullman et al. (2010) found that more parental overprotection was associated with poorer overall HRQOL in children with cancer (N = 89). Of note, this sample was younger (M_{age} = 5.6 years) relative to the participants in Barakat et al. (2010), and

the study utilized parent-proxy report of child HRQOL. Penn et al (2009) also examined family social support in children with brain tumors (N = 35; M_{age} = 9 years) at 1-, 6-, and 12-months post-diagnosis. They found that stronger family social support was associated with better general HRQOL in children at six- and 12-months post-diagnosis when measured concurrently. These studies provide evidence that parent-child relationships and family functioning influence multiple aspects of pediatric HRQOL.

There is minimal work that examines the direct association between parent-child relationships and children's HRQOL while undergoing cancer treatment. However, parent-child conflict has been linked to other adjustment outcomes in children with cancer. Manne and Miller (1998) investigated parent-child conflict in adolescents (N = 50; M_{age} = 16 years) actively on treatment for various cancer diagnoses and on average 6 months post-diagnosis. More parent-child conflict was associated with greater psychological distress in adolescents. One study of childhood cancer survivors (N = 190) investigated the concurrent association between quality of parent-child relationships and HRQOL during survivorship (Orbuch et al., 2005). Survivors in this sample were on average 8 years old at the time of their diagnosis and 11 years from their diagnosis. The measure of parent-child relationship quality included aspects of respect, understanding, and affection. Survivors completed self-report measures of HRQOL and relationship quality. Survivors who reported better quality relationships with their parents also reported better psychological, social, spiritual, and overall HRQOL. Taken together, this work suggests that parent-child relationships impact children' psychological functioning. Given the central role of the primary caregiver, the quality of parent-child relationships

should be further examined, as the interactions between parent and child may have implications for HRQOL.

It is possible that more parent-child conflict interferes with caregivers' ability to provide optimal care to their children or reduces the emotional support between caregivers and children. Thus, children's physical or psychological HRQOL may suffer as a result of conflict. Further research is needed to examine the association between parent-child relationships and specific domains of child HRQOL. It is unclear if more parent-child relationship conflict has a particular impact on children's physical, psychological, social, or school functioning. Clarifying the association between quality parent-child relationships and each individual domain of HRQOL can help to identify the areas of risk in children with cancer and targets where more support and resources are needed.

Emotion Socialization

Another important aspect of the parent-child relationship is communication about emotions surrounding a cancer diagnosis and treatment. The primary caregiver is often the family member helping the child not only manage the tangible and logistical aspects of cancer, but also the person helping to navigate the emotional impact of cancer (Rodriguez et al., 2012). Caregivers are largely responsible for teaching children to regulate their emotions and communicate their emotions with others through emotion socialization (Morris et al., 2017). Emotion socialization is the process of caregivers teaching their children about emotions, how to identify, express, and cope with emotions. The cancer experience engenders negative emotions that may impact children's HRQOL, so emotion socialization should be examined. Indeed, childhood cancer can prompt negative affect, such as fear or sadness, in children, which can lead to more internalizing and externalizing problems and consequently poorer HRQOL (Katz,

Fladeboe, King et al., 2018). Caregivers who teach their children how to appraise and respond to these emotions may impact different domains of child functioning during cancer treatment (Thompson, 2014).

Specifically, parent-meta emotion philosophy (PMEP), or a parent's beliefs and feelings about their own and their child's emotions, may be particularly relevant in how caregivers help their children manage negative emotions (Katz et al., 2012). PMEP can range from "emotion coaching" to "emotion dismissing." Parents who are more emotion coaching are more aware and accepting of their own and their children's emotions, more expressing of emotions, see emotions as learning opportunities, and teach their children how to validate and regulate emotions. Parents who are more emotion-dismissing are more suppressing of emotions, view emotions as negative, dangerous, or unpleasant, and may be invalidating of their children's emotions. Despite the possible implications for children's HRQOL during cancer treatment, emotion socialization has not been closely studied in pediatric cancer samples. However, work outside of pediatric cancer research has provided evidence for the importance of emotion socialization on various aspects of children's functioning.

Research in non-cancer samples has demonstrated that parent emotion socialization is associated with child depression (Shortt et al., 2016). A mixed method study compared parent reactions to children's negative emotions in adolescents (ages 14-18) who met criteria for depression versus adolescents without depression. Self-report questionnaire data as well as observational data demonstrated that parents of children who are depressed compared to parents of children who are not depressed are more punitive and display more anger in response to their child's negative emotions (e.g.,

sadness, anger). Parents of teens who are depressed also engage in less emotion coaching relative to parents of non-depressed teens. Another study with a longitudinal design found that when parents had supportive reactions to their child's negative emotions at age 5 led to better concurrent and future child emotion regulation skills (Perry et al., 2020). Furthermore, better child emotion regulation skills at age 5 and 10 were associated with better social competence at age fifteen. Together these studies provide evidence that emotion socialization has an impact on children's emotional and social functioning, and more emotion coaching is associated with better socio-emotional outcomes in children. Thus, caregivers' responses to their children's emotional distress during cancer treatment may have implications for the emotional and social HRQOL.

Work outside of pediatric cancer has also provided evidence that PMEP is associated with numerous factors of child functioning, including physical, psychological, school, and social functioning (Katz et al., 2012). One study examined both observed and self-reported emotion socialization in parents of preschool children and observed children's prosocial behavior (Denham et al., 1997). Children whose parents were more expressive of emotions and responsive to their child's emotions displayed more positive emotions and more prosocial behavior. Another study investigated PMEP and longitudinal child outcomes, including academic achievement, emotion regulation, peer relationships, and physical health, from ages 5 to 8 years old (Gottman et al., 1996). This study demonstrated that PMEP at age 5 predicted future outcomes at age 8. More emotion coaching PMEP was associated with higher academic achievement, emotion regulation, peer relationships, and physical health. This work suggests that children of caregivers who are more aware and accepting of their child's emotions and teach their children about emotions have better concurrent and long-term physical, emotional, academic, and social functioning.

Other studies have focused specifically on the association between PMEP and children's mental health (i.e., internalizing and externalizing problems). Katz et al. (2007) measured PMEP through parent interviews and parent-child interactions. They found that children (ages 12-14) with parents who were less accepting of negative emotions reported more symptoms of depression compared to children whose parents were more emotion coaching. Lunkenheimer et al. (2007) found similar results when observing family interactions between parents and their children ages 8-11 years. They investigated the association between emotion coaching/dismissing behavior and children's behavior problems as reported by parents and teachers. Children of parents who were more emotion dismissing during their interactions had more behavioral problems and poorer emotion regulation skills. Overall, Children of parents who are more emotion coaching have better physical health, academic achievement, social competence, and peer relationships and fewer internalizing and externalizing problems compared to children whose parents are more emotion dismissing (Denham et al., 1997; Gottman et al., 1996; Katz & Hunter, 2007; Lunkenheimer et al., 2007). The association between emotion coaching and numerous child outcomes may have implications across multiple domains of HRQOL, including social and emotional functioning.

In context of pediatric cancer, emotion coaching PMEP may be particularly beneficial in response to the stressors and challenges of cancer treatment. Caregivers who are more accepting, aware, and regulating of their own emotions may be able to handle the distress of cancer caregiving, and therefore able to provide more support for their children. Additionally, caregivers who teach their children strategies to accept and regulate their own emotions may better enable their children to manage cancer-related distress. Subsequently, children who have

caregivers who are more emotion coaching may have better functioning in multiple domains of HRQOL. Emotion coaching should be explored as a potential critical variable that may promote better HRQOL in a pediatric cancer population.

Child Psychological Adjustment and Child HRQOL in Pediatric Cancer

Children's own mental health and psychological functioning may have a strong impact on their HRQOL. A child who experiences more mental health challenges, and is consequently more withdrawn, may be less able to engage in daily routine (e.g., schoolwork, extracurricular activities, socializing) or less able to cope with challenges in a way that would contribute to better HRQOL. Empirical work has provided evidence suggesting that poorer psychological adjustment is associated with worse HRQOL in children who have cancer.

Multiple facets of child psychological adjustment are associated with HRQOL in pediatric cancer. Tremolada et al. (2009) conducted a qualitative study with caregivers of children with leukemia (N = 128; M_{age} = 6 years) to understand the connection between children's HRQOL and other psychosocial factors. Caregivers participated in unstructured interviews within two weeks of a child's cancer diagnosis and were asked about their child's daily routine, functioning, and support. Caregivers described children's HRQOL as their capacity to maintain aspects of their typical, routine life (e.g., keeping contact with peers, engaging in schoolwork, play, homework, participating in pre-cancer activities). They also related their children's HRQOL to the child's own ability to cope and adapt to cancer-related stressors. Caregivers perceived their children as having better HRQOL overall if their children were better able to adapt and cope.

Other work has specifically focused on internalizing problems, externalizing problems, and HRQOL in pediatric cancer. In one cross-sectional study of children actively on cancer

treatment for various diagnoses, children (N = 19; M_{age} = 8 years) self-reported on internalizing and externalizing problems as well as their overall HRQOL (Roddenberry & Renk, 2008). They found that internalizing and externalizing problems were negatively correlated with HRQOL, such that more problems were associated with poorer overall HRQOL. Another study of children with brain tumors (N = 142; M_{age} = 8.5 at start of treatment) examined the association between self-reported behavior problems and general HRQOL (Kuhlthau et al., 2012). They found that children with more behavior problems at the start of treatment had poorer HRQOL concurrently.

Similar associations between child psychological adjustment and HRQOL have been explored in survivors of childhood cancer. One review of survivors of pediatric cancer found that fewer externalizing and internalizing problems and more adaptive behaviors are associated with better HRQOL (Klassen et al., 2011). PTSS is also related to HRQOL in pediatric cancer survivors, such that higher PTSS is associated with poorer physical and psychological HRQOL (Schwartz & Drotar, 2006; Sedmak et al., 2020). In one study, survivors of pediatric cancer (N = 57; M_{age} at diagnosis = 9 years) who were off-treatment for more than one year reported on PTSS, depression, and HRQOL (Schwartz & Drotar, 2006). Survivors who reported more PTSS also reported more symptoms of depression and worse physical and psychosocial HRQOL. Sedmak et al. (2020) also investigated the association between PTSS and general HRQOL in survivors of childhood cancer (N = 83). These survivors were on average 12 years old at the time of diagnosis and 8 months off-treatment at the time of the study. They found a moderate negative correlation between PTSS and HRQOL, such that survivors who reported more PTSS had worse HRQOL. Taken together, previous work illustrates that a child's overall

mental health is associated with their HRQOL during cancer treatment and survivorship. Children with poorer psychological adjustment may experience more difficulty in overall functioning long-term after diagnosis. However, additional research is needed to further examine the association between psychological adjustment and specific aspects of HRQOL.

Changes in children's psychological adjustment may be related to changes in HRQOL. Children's internalizing and externalizing symptoms tend to be highest around the time of diagnosis, decline over the first year of treatment (Katz, Fladeboe, King et al., 2018) and continue to decline years after the end of treatment (Ander et al., 2016; Larsson et al., 2010). In contrast, overall, physical and psychological HRQOL tend to increase a few months after initial diagnosis, and then stabilize through multiple years off treatment (Ander et al., 2016; Landolt et al., 2006; Penn et al., 2009). However, previous research has not directly examined longitudinal associations between changes in child psychological adjustment and changes in child HRQOL. It is possible that as children's psychological adjustment improves, their HRQOL also improves. Understanding the relation between changes in child adjustment and HRQOL is important for developing time-sensitive interventions and preventing potential poorer long-term outcomes in children who have cancer.

When considering the relation between children's own psychological adjustment and their HRQOL, it is important to acknowledge that many conceptualizations and measures of HRQOL include some aspect of children's mood and psychological functioning (Varni et al., 2001; Hinds et al., 2004). The studies that have tested the association between psychological adjustment and HRQOL in pediatric cancer have primarily examined overall HRQOL (Kuhlthau et al., 2012; Roddenberry & Renk, 2008; Sedmak et al., 2020), and none have specifically examined school or social HRQOL. General HRQOL incorporates aspects of children's

emotional functioning, meaning that there may be significant overlap between measured HRQOL and the independent variables tested (e.g., internalizing and externalizing problems). Thus, significant associations between psychological adjustment and HRQOL may really be driven by conceptual overlap between the two constructs. Research is needed to parse apart the association between psychological functioning individual aspects of children's HRQOL separately.

Current Study

Research on HRQOL of children with cancer is limited in that many studies fail to examine the effects of potentially important psychosocial factors (e.g., emotion socialization) and fail to individually investigate specific domains of HRQOL (e.g., physical, psychological, school, social). Much of the research on predictors of HRQOL in pediatric cancer has focused on cancer-related factors and demographic factors. It is critical to examine psychosocial predictors of children's HRQOL, as they are more amenable to change and could be potential critical targets for intervention to promote better HRQOL in children undergoing cancer treatment. Additional work is also needed to determine the impact of psychosocial factors on HRQOL relative to cancer-related and demographic factors to better understand which factors might be most important in shifting children's HRQOL during treatment. Of the studies that have examined psychosocial factors, few have focused on caregiver-level factors such as parent-child conflict and emotion socialization in association with HRQOL in pediatric cancer. Research investigating the impact of caregiver psychosocial factors on HRQOL is needed to identify variables (beyond diagnosis and treatment-related factors) that may promote better HRQOL.

Studying specific domains of HRQOL separately, rather than overall HRQOL, is necessary to clarify the association between psychosocial factors and different domains of HRQOL. Much of the previous work in this area of study has examined overall, physical, or emotional HRQOL (Hullman et al., 2010; Kuhlthau et al., 2012; Pierce et al., 2017; Rodday et al., 2017; Schwartz & Drotar, 2006; Sedmak et al., 2020). However, HRQOL encompasses many aspects of daily functioning, including social and school functioning. Few studies have examined children's social and school HRQOL specifically, thus additional work is needed to examine these other aspects of HRQOL. Further, while some studies have examined changes in HROQL during cancer treatment (Kuhlthau et al., 2012; Penn et al., 2009), only one (Landolt et al., 2006) has investigated changes in individual domains of HRQOL. Thus, research is needed to describe the trajectory of domain-specific HRQOL over the first year of pediatric cancer treatment. Additional work can help to identify the particular areas of functioning that are at risk for poorer outcomes in pediatric cancer as well as determine the individual psychosocial factors that are relevant to a given domain. Identifying more specific psychosocial predictors is also important to guide development of more targeted psychosocial interventions to promote better HRQOL in children with cancer.

Prior studies on HRQOL and psychosocial factors in pediatric cancer have also not accounted for the association between multiple psychosocial variables and their relative impact on HRQOL. Thus, it is unclear if child and caregiver psychological adjustment, parent-child relationship conflict, and emotion socialization have equal or differential effects on HRQOL. Additional work is needed to understand the relative impact of various psychosocial factors on HRQOL in pediatric cancer to better identify which factors contribute to the most variation in children's HRQOL (Fardell et al., 2017). Research outside of pediatric cancer demonstrates that

these psychosocial factors are associated with one another (i.e., emotion coaching is associated with better child psychological adjustment; Katz et al., 2012). Therefore, it is possible that a particular psychosocial variable accounts for majority of the variance in HRQOL in children with cancer above and beyond other variables. Additional research is needed to investigate the collective effect of psychosocial factors on child HRQOL and identify the factors that account for the most variance in HRQOL. It is important to clarify whether there is a single psychosocial factor or multiple psychosocial factors that might impact children's HRQOL. This may aid providers in understanding the breadth of risk factors for poorer HRQOL in children with cancer and identify and target the factors that might have the biggest influence on HRQOL. Thus, healthcare providers can better allocate resources and develop more interventions directed toward a particular psychosocial factor to promote better HRQOL outcomes.

The effect of psychosocial factors around the time of diagnosis should be examined as predictors of the trajectory of children's HRQOL through treatment. There is some evidence that children's HRQOL improves a few months after diagnosis (Kuhlthau et al., 2012; Landolt et al., 2016; Penn et al., 2009); however, there is little research on what factors might predict that trajectory in HRQOL. Previous work has demonstrated that children and their caregivers are particularly distressed and struggle to adjust shorty after diagnosis (Katz, Fladeboe, King et al., 2018; Rodriguez et al., 2012; Vrijmoet-Wiersma et al., 2008). Thus, psychosocial functioning around diagnosis may have implications for HRQOL long-term. Identifying baseline psychosocial factors that affect HRQOL over time can help facilitate early intervention for children in need of more support services to promote better HRQOL long-term. Previous work that has

investigated children's HRQOL over time has only examined concurrent associations with changes in HRQOL. However, identifying early risk factors may help to provide evidence for early intervention and prevent long-term negative effects on HRQOL.

Much of the research on psychosocial factors and HRQOL in children with cancer has utilized cross-sectional and correlational methods. Studies that have examined changes in HRQOL have found that HRQOL improves over the first year of pediatric cancer treatment (Landolt et al., 2006; Tsai et al., 2013). However, additional work is needed to study the trajectories of psychosocial factors in association with the trajectories of specific domains of HRQOL to better understand changes in HRQOL over time. Psychosocial predictors of the trajectories of child HRQOL should be examined to understand what factors contribute to HRQOL over time. Furthermore, changes in psychosocial variables over time may be associated with changes in HRQOL over time. Specifically, caregiver and child psychological adjustment change over the course of the first year of treatment and may vary with HRQOL, thus they should be examined over time with HRQOL (Katz, Fladeboe, King et al., 2018; Katz, Fladeboe, Lavi et al., 2018). Examining concurrent changes in adjustment and HRQOL over time is critical for understanding how and why children's HRQOL changes throughout the course of cancer treatment. Longitudinal work is important for understanding these associations over time and identifying patients at risk for poorer long-term outcomes.

The current study aims to extend previous work by investigating the association between child psychological adjustment, caregiver psychological adjustment, parent-child conflict, emotion socialization and different domains of HRQOL across the first year of pediatric cancer treatment. There are three primary aims: (1) describe the trajectory of overall, physical, psychological, social, and role HRQOL over the first year of pediatric cancer treatment; (2a)

investigate the independent effects of baseline psychosocial factors (caregiver psychological adjustment, child psychological adjustment, emotion socialization, and parent-child conflict) on overall, physical, psychological, social, and role HRQOL, (2b) investigate the combined effects of baseline psychosocial factors (caregiver psychological adjustment, child psychological adjustment, emotion socialization, and parent-child conflict) on overall, physical, psychological, social, and role HRQOL and (3) investigate the association between the changes in child and caregiver psychological adjustment over time and trajectories of overall, physical, psychological, social, and school HRQOL. It is hypothesized that all domains of HRQOL will improve over the first year of pediatric cancer treatment and that all psychosocial factors will be associated with the average level and rate of change of overall child HRQOL. Specifically, better child and caregiver psychological adjustment, less parent-child conflict, and more emotion coaching will be associated with better average levels of child HRQOL and improvement of child HRQOL over time. It is also hypothesized that caregiver psychological adjustment will account for most of the variance in overall child HRQOL above and beyond child's own psychological adjustment and emotion socialization given that caregiver adjustment may account for variance in child adjustment, parent-child conflict, and emotion socialization. Finally, it is predicted that changes in caregiver and child psychological adjustment will be associated with the trajectory of overall child HRQOL. Given the limited evidence on individual domains of HRQOL, specific hypotheses across the three aims about physical, psychological, social, and school functioning domains of HRQOL are not proposed.

Method

Participants

The study utilized secondary data from participants involved in a larger project investigating child and caregiver adjustment during the first year after a pediatric cancer diagnosis (Katz et al., 2018). Participants included families of children recently diagnosed with cancer recruited from two hospitals in urban areas in the Northwest and Southeast United States. Families were eligible to participate if the child had no history of a developmental delay, spoke English, and if the primary caregiver was the same as prior to the cancer diagnosis. Families were excluded if the child had neurofibromatosis type 1 (NF1), relapsed cancer, or secondary malignancy. At initial assessment, primary caregivers were invited to participate, and caregivers self-identified the child's primary caregiver.

Procedures

Families of children newly diagnosed with cancer were approached by their physician or nurse within two weeks of diagnosis. Those who were interested in participating in the study were then approached by a member of the research team who obtained consent and HIPAA authorization. Informed consent was obtained from primary caregivers at the time of enrollment. Primary caregivers reported on their own psychological adjustment, emotion coaching, parent-child conflict, as well as their child's psychological adjustment and HRQOL. They completed questionnaires around the time of diagnosis and 6- and 12-months post-diagnosis. Participants were compensated for their participation. IRB approval was received from the University of Washington, Seattle Children's Hospital, and Vanderbilt University for all study procedures.

Measures

Socio-demographic Characteristics

Primary caregivers self-reported their child's race/ethnicity, age, and sex at the time of diagnosis as part of a baseline survey. Information about child diagnosis and treatment intensity was obtained from medical records. Treatment intensity was coded on a scale of 1 (least intense) to 4 (most intense) based on diagnosis, stage/level of disease, and number or type of treatment modalities using the Intensity of Treatment Rating (ITR-3; Kazak et al., 2012).

Health-Related Quality of Life

Caregivers reported on children's health-related quality of life using the Pediatric Quality of Life Inventory (PedsQL; Varni et al., 2001). The PedsQL has 23 items and measures quality of life in four domains of functioning, including physical functioning (e.g. "Walking more than one block", "Taking a bath or shower by him or herself"), emotional functioning (e.g. "Feeling afraid or scared", "Worrying about what will happen to him or her"), social functioning (e.g. "Getting along with other children", "Not able to do things that other children his or her age can do"), and school functioning (e.g. "Paying attention in class", "Missing school to go to the doctor or hospital"). Primary caregivers responded to the question "In the past month, how much of a problem has this been for your child" on a 5-point Likert scale from 0 "Never" to 4 "Almost Always." Per Varni et al. (2001), raw scores were transformed to a 0-100 scale as follows: 0=100, 1=75, 2=50, 3=25, 4=0. The subscale scores were calculated by averaging the transformed ratings of items within each domain of functioning. Overall HRQOL was calculated by averaging the transformed score of all items. Higher scores indicate better HRQOL. Reliability in our sample was strong with Cronbach's alpha ranging from .90-.93 with an average of .92 across the three time points of assessment.

Child Psychological Adjustment

Children's psychological adjustment was measured using the caregiver-report versions of the Child Behavior Checklist (CBCL; Achenbach, 1991). Caregivers of children who were 2- to 5-years-old completed the preschool form, and caregivers of children who were 6- to 18-years-old completed the school-age form. The CBCL assesses numerous domains of children's psychosocial functioning, including a variety of internalizing symptoms (anxious/depressed symptoms, withdrawn/depressed symptoms, somatic complaints) and externalizing symptoms (rule-breaking behavior, aggressive behavior). *T*-scores for externalizing symptoms and internalizing symptoms were analyzed. Previous work has demonstrated that the somatic complaints score may not be as valid in caregiver report of chronically ill populations (Perrin et al., 1991), thus only the anxious/depressed score was used to assess internalizing symptoms. Higher scores indicate more internalizing and externalizing problems. For internalizing scores, Cronbach's alpha in the current sample ranged from .87-.89, with an average of .88 across the three time points. For externalizing scores, Cronbach's alpha in the current sample ranged from .85-.93, with an average of .87 across the three time points.

Caregiver Psychological Adjustment

Caregiver Depression. Caregiver depression was measured using the short form of the Center for Epidemiological Studies-Depression Scale (CESD-10; Andresen et al., 1994). This 10-item self-report scale asks caregivers to rate the frequency of depression symptoms within the past month (e.g., "I was bothered by things that usually don't bother me."). Caregivers rated each item on a scale from 0 ("Rarely or none of the time") to 3 ("All of the time"). Ratings are summed to yield a total sum score ranging between 0 and 30. Higher scores represent more frequent depressive symptoms. Cronbach's alpha in the current sample ranged from .84-.89, with an average of .86 across the three time points.

Caregiver Anxiety. Anxiety symptoms were measured using the anxiety subscale of the Depression, Anxiety, and Stress Scale (DASS; Lovibond & Lovibond, 1995). This 7-item subscale assesses caregiver-reported frequency of anxiety symptoms in the past month (e.g., "I found it hard to wind down"). Caregivers rated items on a scale of 0 ("Did not apply to me at all") to 3 ("Applied to me very much, or most of the time"). Items were summed to create total scores ranging from 0-21, with higher scores indicating more frequent anxiety symptoms. Cronbach's alpha in the current sample ranged from .81-.86, with an average of .84 across the three time points.

Caregiver Post-Traumatic Stress Symptoms. Post-traumatic stress symptoms (PTSS) were measured using the Impact of Events Scale – Revised (IES-R; Weiss & Marmar, 1997). This is a 22-item self-report measure with 3 subscales of PTSS: (1) Avoidance, (2) Intrusion, (3) Hyperarousal. A total PTSS score was calculated by summing the average score of each subscale. Total scores range from 0-12 with higher scores indicating more PTSS. Reliability was excellent in our sample, with Cronbach's alpha ranging from .93-.95, with an average of .94 across the three time points.

Parent-Child Conflict

The Parenting Questionnaire (Fauchier & Margolin, 2004) is a 6-item, caregiver-report scale that was used to measure conflict between caregivers and their child. Example items include "I easily lose my temper with my child" and "I yell or scream at my child when he/she has done something wrong." Caregivers rated each item on a 5-point scale ranging from 1 ("Not at all descriptive of me and my child") to 5 ("Extremely descriptive of me and my child"). A total conflict score was computed as a sum of the six items with higher scores indicating more

parent-child conflict. Reliability was good, with Cronbach's alpha ranging from .78-.82, with an average of .77 across the three time points.

Emotion Socialization

The Emotion Coaching Questionnaire (ECQ; Lagacé-Séguin & Coplan; 2005) is a 54-item, self-report scale used to assess three domains of caregiver meta-emotion philosophy, including Awareness (e.g. "I can tell when my child is angry"), Acceptance (e.g. "It is okay for my child to be sad"), and Coaching (e.g. "When my child is experiencing an emotion, I try to help them identify what emotion they are experiencing"). Caregivers rated each item on a 5-point Likert scale from 1 "Strongly Disagree" to 5 "Strongly Agree." Higher scores represent more emotion coaching PMEP. Cronbach's alpha ranged from 85-.88 with an average of .86 across the three time points of assessment.

Data Analytic Strategy

Because of the nested within-participant structure of the data, data were analyzed using a Multilevel Modeling (MLM) approach with the Maximum Likelihood estimator in R. The trajectory of HRQOL over time was modeled, psychosocial predictors of that trajectory were examined, and the association between the trajectory of HRQOL and changes in child and caregiver psychological adjustment were tested. Missing data were handled in MLM with fill-information maximum likelihood, which allows family trajectories to be estimated from a different number of observations for each caregiver (Enders, 2010). Data were included in the model if an individual had any HRQOL data after the baseline assessment at the time of cancer diagnosis. The specific data analytic strategy for each aim is described in the subsequent sections.

Aim 1: Describe the trajectory of overall, physical, psychological, social, and role HRQOL.

A linear growth model was estimated to model the average trajectory of each HRQOL domain and variability in that trajectory between children. Time was coded as -2 (baseline), -1 (6-months post-diagnosis), and 0 (12-months post-diagnosis). The intercept parameter represents the end point for HRQOL (12 months post-diagnosis) to examine differences in children's HRQOL a year after diagnosis. This model estimated two fixed effects: an intercept parameter representing the starting point of HRQOL as well as a slope parameter representing the rate of linear change in HRQOL over time. Random effects for the intercept and slope improve model fit were also tested to determine whether there are between-person differences in initial levels or rate of change over time in HRQOL. This model determines if sufficient variance exists between children in their levels of HRQOL or rates of change to test psychosocial predictors that may account for differences in HRQOL over time.

Aim 2: Investigate the independent and combined effects of psychosocial factors on HRQOL.

To assess the independent effect of each psychosocial factor (child psychological adjustment, caregiver psychological adjustment, parent-child conflict, emotion coaching) at the time of diagnosis on the trajectory of HRQOL, the centered baseline score of each psychosocial factor was included in separate models as a predictor of the trajectory (as determined in Aim 1) of each domain of HRQOL (overall, physical, psychological, social, school). Each psychosocial predictor was independently examined in associated with the level of (intercept) or rate of change in (slope) domain-specific and overall HRQOL. The effect of child adjustment on the trajectory of emotional HRQOL was not tested, given the conceptual overlap in constructs. In each tested model, diagnosis. treatment intensity, child age, and sex were included as covariates to determine if psychosocial factors are uniquely associated with HRQOL above and beyond cancer-related and demographic factors. Child diagnosis was categorized into three groups

(leukemia/lymphoma, CNS tumors, and non-CNS tumors) and dummy coded with the leukemia/lymphoma group as the reference group. All predictor variables were standardized for ease of interpretation.

To assess the unique contribution of each psychosocial factor relative to others, baseline scores of all psychosocial variables were included in a single model for each HRQOL outcome. These cumulative models tested the strength and statistical significance of each psychosocial factor on the trajectory of overall and domain-specific HRQOL when accounting for all other psychosocial factors. Child diagnosis, treatment intensity, age, and sex were included as covariates in each model. Variables were standardized for the purpose of directly comparing the relative strengths of each predictor's association with HRQOL.

Aim 3: Longitudinal Associations Between Psychological Adjustment and HRQOL

To examine the association between child and caregiver psychological adjustment and HRQOL over time, the effect of the interaction between adjustment and time on the trajectory of HRQOL was tested. First, the average trajectory and variability of each caregiver and child adjustment variable was modeled using similar methods as described in Aim 1. Next, caregiver and child psychological adjustment variables were centered at the between-person level. To obtain between-person scores, each individual's mean predicted score was subtracted from the estimated grand mean score, or the average adjustment across all three observations for all caregivers and children. The between-person score reflects how much each individual score over time deviated from the sample average, and its effects on each outcome reflects how this deviation in psychological adjustment was associated with differences in trajectories child HRQOL over time. Finally, the individual effect of the between-person adjustment variable and that variable's interaction with time on the trajectories of overall and domain-specific HRQOL

were tested. A significant effect of the interaction between the adjustment variable and time suggests that adjustment and HRQOL vary together over time. Child diagnosis, treatment intensity, age, and sex were included as covariates in each model.

Results

Participant Characteristics

At time of enrollment, children (N = 159) were 52% female and ages 2-17 years (*M* = 6.31, *SD* = 3.54). Pediatric cancer diagnoses of the sample were 36% leukemia, 22% CNS tumors, 11% lymphoma, 11% sarcoma, 8% Wilms tumor, 4% neuroblastoma, 8 % other cancers (e.g., melanoma). Primary caregivers (N = 154) were 86% mothers, 11% fathers, and 3% other (i.e., grandparent, step-parent), on average 36.45 years old (*SD* = 7.98), and 89% White/Caucasian, 5% Black/African American, 3% Asian, and 3% Other. Seventy-eight percent of caregivers reported they were married. The median annual income of the sample was $60,000-$69,000, with 45% of the sample earning less than $60,000 per year and over 25% of the sample earning $100,000 or more per year. The federal poverty line around the time of data collection was between $23,000-$24,000 for a household of four. Approximately 3% of caregivers did not have a high school diploma, 24% completed high school, 61% completed college, and 12% completed graduate education.

Missing Data

There were on average 101 respondents at each timepoint of assessment. Missingness analyses demonstrated the completion rate of the HRQOL measure (i.e., number of completed time points) was not correlated with baseline reports of HRQOL, average parent-child conflict, average emotion coaching, or average child psychological adjustment. There were small, negative correlations between completion rates of the HRQOL measure and average caregiver

depression (r = -0.24, p < .01), average caregiver anxiety (r = -0.30, p < .01), and average caregiver PTSS (r = -0.24, p < .01), suggesting that more distressed caregivers were less likely to complete measures. Descriptive statistics of all measures are presented in Table 1. Correlations between primary variables of interest are presented in Table 2a & 2b.

Aim 1: Trajectory of HRQOL

Estimated trajectories of each domain of HRQOL are presented in Figure 3 and growth model statistics are presented in Table 3. A model that included a fixed effect of slope as well as a random effect of intercept was determined to be the best fitting model for all domains of HRQOL. Including a random effect for slope did not improve model fit. This suggests that there is significant variability between children's average level of HRQOL one year after diagnosis and the rate of change in HRQOL is similar between children.

Trajectory of Overall HRQOL

On average, overall HRQOL was 74.28 units one year after diagnosis, and HRQOL increased by 8.33 units every six months during the first year of treatment (Table 3). Sufficient variance was observed in the intercept to test predictors of these differences, though analyses indicated fixed slope best fit the data. Thus, children experienced similar rates of change in HRQOL over time, yet overall level of HRQOL varied between children. Specifically, random effects suggested that for 68% of children, the average level of HRQOL ranged between 62.73 and 85.83 one year post-diagnosis.

Trajectory of Physical HRQOL

On average, physical HRQOL improved over the first year after a pediatric cancer diagnosis. Specifically, children's physical HRQOL was 73.76 units one year after diagnosis, and physical HRQOL increased by 12.69 units every six months (Table 3). Sufficient variance

was observed in the intercept, though variance was not observed in the slope, meaning the average level of physical HRQOL differs between children, but the rate of change in physical HRQOL over time is similar. Random intercept suggested that for 68% of children, the average level of physical HRQOL is between 54.89 and 92.62 one year post-diagnosis.

Trajectory of Emotional HRQOL

On average, emotional HRQOL improved over the first year after a pediatric cancer diagnosis. Specifically, one year after diagnosis, children's emotional HRQOL was 72.32 units, and emotional HRQOL increased by 9.07 units every six months (Table 3). Sufficient variance was observed in the intercept, though variance was not observed in the slope, meaning the average level of emotional HRQOL differs between children, but the rate of change in physical HRQOL over time is similar. Random intercept suggested that for 68% of children, the average level of emotional HRQOL is between 60.34 and 84.29 one year post-diagnosis.

Trajectory of Social HRQOL

On average, social HRQOL improved over the first year after a pediatric cancer diagnosis. Specifically, one year after diagnosis, children's social HRQOL was 80.14 units, and social HRQOL increased by 4.68 units every six months (Table 3). Sufficient variance was observed in the intercept, though variance was not observed in the slope, meaning the average level of social HRQOL differs between children, but the rate of change in social HRQOL over time is similar. Random intercept suggested that for 68% of children, the average level of social HRQOL is between 68.09 and 92.20 one year post-diagnosis.

Trajectory of School HRQOL

On average, school HRQOL improved over the first year after a pediatric cancer diagnosis. Specifically, one year after diagnosis, children's school HRQOL was 68.33 units, and

social HRQOL increased by 5.16 units every six months (Table 3). Sufficient variance was observed in the intercept, though variance was not observed in the slope, meaning the average level of social HRQOL differs between children, but the rate of change in social HRQOL over time is similar. Random intercept suggested that for 68% of children, the average level of social HRQOL is between 50.56 and 86.10 one year after diagnosis.

Aim 2: Baseline Psychosocial Predictors of Trajectories of HRQOL

The results of each model tested for Aim 2 can be found in Tables 4-8. The individual effects of baseline caregiver adjustment on HRQOL are displayed in Table 4. The individual effects of baseline parent-child conflict are displayed in Table 5. The individual effects of baseline caregiver emotion coaching are displayed in Table 6. The individual effects of baseline child adjustment are displayed in Table 7. The cumulative effects of all baseline psychosocial factors on HRQOL are displayed in Table 8.

Baseline Predictors of Overall HRQOL

Child psychological adjustment was individually associated with overall HRQOL such that children with more internalizing problems experienced lower levels of HRQOL on average across the first year of cancer treatment (see Table 7). Regarding child adjustment, unexpectedly, when both internalizing symptoms and externalizing problems were included as predictors of the trajectory of HRQOL, externalizing problems had a positive association with HRQOL ($\beta = 0.83$), though this association was not statistically significant ($p = 0.60$). Further probing of this counterintuitive result showed high multicollinearity between internalizing and externalizing problems, with the correlation between baseline internalizing and externalizing symptoms raw scores being 0.70 and the correlation between the estimated effects on HRQOL as 0.72. The independent effect of externalizing problems on the trajectory of HRQOL was also examined.

When tested individually, the association is negative ($\beta = -4.51$, $p < .001$), such that more externalizing problems is associated with poorer HRQOL. The change in association between externalizing problems and HRQOL and the multicollinearity between externalizing and internalizing problems is evidence of suppression. In sum, the effect of externalizing problems on HRQOL overlaps with the effect of internalizing problems on HRQOL and it does not contribute to significantly unique variance in HRQOL. Thus, externalizing problems were removed from the model for parsimony. With externalizing problems removed, baseline internalizing problems remain a significant predictor of average level of overall HRQOL ($\beta = -6.82$, $p = 0.0000$; Table 7). Emotion coaching, parent-child conflict, and caregiver psychological adjustment at the time of diagnosis were not individually associated with the trajectory of overall HRQOL.

When examining the cumulative effect of all baseline psychosocial factors (emotion coaching, parent-child conflict, caregiver adjustment, child internalizing problems) on overall HRQOL, internalizing problems is the only significant psychosocial predictor of HRQOL ($\beta = -6.12$, $p = 0.0000$; Table 8). Children who experience more internalizing problems around the time of diagnosis have poorer HRQOL on average when accounting for other psychosocial factors. This suggests that internalizing problems account for the most variance in overall HRQOL above and beyond other psychosocial factors during the first year of pediatric cancer treatment.

Baseline Predictors of Physical HRQOL

Child psychological adjustment was individually associated with level of physical HRQOL such that children with more internalizing problems experienced lower levels of physical HRQOL on average across the first year of cancer treatment. Similar to analyses with

overall HRQOL, there was evidence of suppression and multicollinearity between externalizing problems and internalizing problems, so externalizing problems were removed from analyses for parsimony. With externalizing problems removed, baseline internalizing problems are a significant predictor of average level of physical HRQOL ($\beta = -7.80$, $p = 0.0000$; Table 7). Emotion coaching, parent-child conflict, and caregiver psychological adjustment at the time of diagnosis were not individually associated with the trajectory of physical HRQOL.

When examining the cumulative effect of all baseline psychosocial factors (emotion coaching, parent-child conflict, caregiver adjustment, child internalizing problems) on physical HRQOL, baseline internalizing problems is the only significant psychosocial predictor of average level of physical HRQOL ($\beta = -8.83$, $p = 0.0001$; Table 8). Children who experience more internalizing problems around the time of diagnosis have poorer levels of HRQOL on average throughout the first year of cancer treatment when accounting for other psychosocial factors. This suggests that internalizing problems account for the most variance in level of physical HRQOL above and beyond other psychosocial factors during the first year of pediatric cancer treatment.

Baseline Predictors of Emotional HRQOL

Caregiver psychological adjustment was individually associated with children's average level of emotional HRQOL. Specifically, children had poorer average level of emotional HRQOL across the first year of pediatric cancer treatment when their primary caregivers reported more PTSS around the time of diagnosis compared to other caregivers ($\beta = -5.93$, $p = 0.0005$; Table 4). Baseline caregiver depression and anxiety were not associated with children's emotional HRQOL. Emotion coaching and parent-child conflict at the time of diagnosis were not

individually associated with the trajectory of emotional HRQOL. Child adjustment was not tested as a predictor of the trajectory of emotional HRQOL, given construct overlap.

When examining the cumulative effect of all baseline psychosocial factors (emotion coaching, parent-child conflict, caregiver adjustment) on emotional HRQOL, caregiver PTSS is the only significant psychosocial predictor of average level of emotional HRQOL ($\beta = -5.84$, $p = 0.0006$; Table 8). Children of caregivers who report higher PTSS at the time of diagnosis, have poorer levels of emotional HRQOL on average throughout the first year of cancer treatment when accounting for other psychosocial factors. This suggests that baseline caregiver PTSS accounts for the most variance in average level of emotional HRQOL above and beyond other tested psychosocial factors during the first year of pediatric cancer treatment.

Baseline Predictors of Social HRQOL

Parent-child conflict at the time of diagnosis was individually associated with average level of social HRQOL throughout the first year of pediatric cancer treatment ($\beta = -2.67$, $p = 0.0465$; Table 5). Higher conflict at the time of diagnosis is associated with poorer social HRQOL on average. Child psychological adjustment was also individually associated with average level of social HRQOL, such that children with more internalizing problems ($\beta = -6.32$, $p = 0.0008$; Table 7) experienced lower levels of social HRQOL on average across the first year of cancer treatment. Of note, there was no evidence of suppression between internalizing and externalizing symptoms in the model, so externalizing symptoms were included. Emotion coaching and caregiver psychological adjustment at the time of diagnosis were not individually associated with the trajectory of social HRQOL.

When examining the cumulative effect of all baseline psychosocial factors (emotion coaching, parent-child conflict, caregiver psychological adjustment, child psychological

adjustment) on social HRQOL, baseline internalizing problems is the only significant psychosocial predictor of average level of social HRQOL ($\beta = -5.90$, $p = 0.0044$; Table 8). When accounting for other psychosocial factors, children who experience more internalizing problems around the time of diagnosis have poorer levels of social HRQOL on average throughout the first year of cancer treatment. This suggests that internalizing problems account for the most variance in level of social HRQOL above and beyond other psychosocial factors during the first year of pediatric cancer treatment.

Baseline Predictors of School HRQOL

Child psychological adjustment was individually associated with level of school HRQOL such that children with more internalizing problems experienced lower levels of physical HRQOL on average across the first year of cancer treatment. Similar to analyses with overall and physical HRQOL, there was evidence of suppression and multicollinearity between externalizing problems and internalizing problems, so externalizing problems were removed from analyses for parsimony. With externalizing problems removed, baseline internalizing problems remained a significant predictor of average level of school HRQOL ($\beta = -6.86$, $p = 0.0029$; Table 7). Emotion coaching, parent-child conflict, and caregiver psychological adjustment at the time of diagnosis were not individually associated with the trajectory of school HRQOL.

When examining the cumulative effect of all baseline psychosocial factors (emotion coaching, parent-child conflict, caregiver adjustment, child internalizing problems) on school HRQOL, emotion coaching at time of diagnosis was associated with average level of school HRQOL. Unexpectedly, higher emotion coaching around the time of diagnosis was associated with lower levels of school HRQOL on average ($\beta = -5.23$, $p = 0.025$; Table 8). These results

suggests that emotion coaching accounts for the most variance in level of school HRQOL above and beyond other psychosocial factors during the first year of pediatric cancer treatment.

Aim 3: Longitudinal Associations Between Psychological Adjustment and HRQOL

Changes in caregiver depression over the first year of pediatric cancer treatment were associated with the trajectory of children's emotional HRQOL. Specifically, children's emotional HRQOL increases at a slower rate for children whose parents are more depressed relative to other parents ($\beta = -4.11$, $p = 0.0330$; Table 9). Changes in caregiver anxiety and PTSS and changes in child psychological adjustment were not associated with overall, physical, emotional, social, or school HRQOL over the first year of pediatric cancer treatment (see Tables 9 & 10).

Discussion

The current study sought to establish the trajectory of overall and domain-specific HRQOL in children undergoing cancer treatment during the first year after a diagnosis. Furthermore, both child-level and caregiver-level psychosocial factors around the time of diagnosis were explored in association with the trajectories of domain-specific and overall HRQOL. Importantly, both the independent and relative contributions of each of those psychosocial factors were examined. The purpose of the study was to clarify differences between domains of HRQOL and identify psychosocial predictors of HRQOL as effective targets to promote children's HRQOL across domains of functioning.

Aim 1: Trajectories of HRQOL

The results of the current study align with previous research suggesting that children's HRQOL improves over the first year after a pediatric cancer diagnosis (Landolt et al., 2006; Tsai et al., 2013). Furthermore, the results provide evidence that there is similar improvement in HRQOL across all domains, suggesting that children's emotional, physical, social, and school

functioning improve from the time of diagnosis. These changes in HRQOL over the first year after a pediatric cancer diagnosis are clinically significant. Previous work utilizing the PedsQL measure of HRQOL has found that a change of 4.5 points in parent-proxy reported general HRQOL scores is clinically meaningful (Varni et al., 2014). In the current sample, general HRQOL improved by 8.33 points every six months. Similar to other work that has demonstrated improvement in HRQOL the year after diagnosis (Landolt et al., 2006), these results suggest that most children demonstrate some adaptation to a cancer diagnosis.

Of note, there was significant variability between children in average level of HRQOL one-year after diagnosis, suggesting that while all children's functioning improves at a similar rate, there are differences in their average level functioning. Thus, despite increases in HRQOL on average, some children may continue to experience lower HRQOL relative to their peers throughout the first year of cancer treatment. These findings support other work that asserts the importance of regular screening of children's wellbeing and HRQOL throughout treatment (Kazak et al., 2015). Routine assessment of HRQOL during the first year after a cancer diagnosis can help identify children who may have lower HRQOL or those whose HRQOL is not improving so that they may get additional support to reduce risk of poorer outcomes.

Interestingly, school HRQOL was lowest on average compared to other domains of functioning and had a smaller rate of change relative to overall, physical, and emotional HRQOL. This builds on previous work that has found children experience difficulty with school functioning throughout treatment (Thompson et al., 2015) and two other studies that also demonstrated school HRQOL is lower relative to other domains of HRQOL in children with cancer (Houtrow et al., 2012; Kuhlthau et al., 2012). One explanation for why school HRQOL may be lower compared to other domains of functioning is the impact of cancer treatment and

side-effects on cognitive functioning and school attendance. Many children miss a significant amount of school during cancer treatment, especially during the first year after diagnosis (French et al., 2013; Vance & Eiser, 2002). In fact, parents of children with cancer report absenteeism due to treatment as the primary disruptor to school functioning (Tsimicalis et al., 2017). The PedsQL items about school functioning assess both attendance (e.g., "Missing school because of not feeling well") and cognitive functioning (e.g., "Paying attention at work or school"). When examining item-level scores in the current sample, items about attendance were on average rated as more of a problem compared to items about attention and cognitive functioning (Table 11). This suggests that cancer-related appointments or long hospital stays that interfere with attendance may drive lower school HRQOL.

The current study provides additional evidence that children undergoing cancer treatment need additional school support, especially regarding disruptions to school attendance (Thompson et al., 2015). Interventions, such as school liaison programs that increase effective communication between families, medical professionals, and education staff, may promote better HRQOL by assessing and addressing a child's specific educational needs while they are on treatment and unable to attend school (Bruce et al., 2012; Northman et al., 2015). Other technological interventions that help children attend school virtually or thought interactive robots may increase children's virtual attendance when they are unable to physically attend school and improve school HRQOL (Weibel et al., 2020). For example, Newhart et al. (2016) tested the feasibility of utilizing a "telepresence robot" to help five children with chronic illnesses in grades 2-9 attend school. The robot allowed children to see and be seen by their classmates, talk, interact, as well as move around the school environment remotely. The children expressed that the robot allowed them to connect with their peers as well as increased their school attendance.

Attending school via the telepresence robot was preferred by the children and their parents compared to at-home instruction. Children also reported higher engagement in school and hope for their academic futures after attending school via the robot. Furthermore, recent research in non-cancer samples on remote learning during the COVID-19 pandemic has demonstrated that remote teaching methods do result in academic improvement and are feasible for families (Maggio et al., 2021), however they require interaction and increased flexibility and support from both teachers and caregivers (Garbe et al., 2020). Technologies that allow for remote learning might help to boost children's school HRQOL by not only increasing attendance, but also by allowing for more natural communication and interaction with teachers and peers.

Social HRQOL was the highest domain of HRQOL through the first year of pediatric cancer treatment. One reason for this may be because of children and teens' use of technology and social media to stay connected with peers. Thus, despite potentially missing school, extracurricular activities, or playdates, children may still feel engaged and involved through connecting with friends via technology (i.e., Instagram, text messaging, video chat). Indeed, recent qualitative work has demonstrated that adolescents with cancer utilize social media to maintain a sense of normalcy with their peers (Daniels et al., 2021). For example, one teen described video-chatting a friend while in the hospital noting: "It's like I was there, but I wasn't there […]. Even though I couldn't really talk to 'em […] I could see all of them and I got some good laughs out of it."

Aim 2: Baseline Psychosocial Predictors of Trajectories of HRQOL

Psychosocial factors around time of diagnosis were differently associated with the trajectories of general and domain-specific HRQOL over the first year of pediatric cancer treatment. Importantly, baseline psychosocial factors (i.e., children's internalizing symptoms,

parent-child conflict) were significant predictors of HRQOL when accounting for diagnosis, treatment intensity, child age, and sex. Furthermore, psychosocial factors accounted for a similar magnitude of change in HRQOL relative to demographic and cancer-related factors. This provides evidence that the impact of psychosocial adjustment on HRQOL is critical to understand in addition to the influence of cancer-related and demographic factors. To best identify children at risk for poorer HRQOL and provide targeted support, healthcare providers should consider psychosocial factors as well as cancer-related and demographic risk factors.

There were differences between domains of HRQOL in their associations with the multiple psychosocial variables that were tested. For example, baseline parent-child conflict was significantly associated with the level of social HRQOL but not the level of general, physical, or emotional HRQOL. As such, children may need more or less support in a particular domain of HRQOL throughout cancer treatment, depending on other supports or risk factors present. A child who has good psychological adjustment, but more parent-child conflict, may be at higher risk for lower social functioning, but not physical function, and as such should receive more social support.

Given the differences between domains of HRQOL in their trajectories and psychosocial predictors, the current study provides support for the importance of examining each domain of HRQOL individually and not only as an average or general concept of overall functioning. By assessing each domain individually, researchers may identify areas particularly and risk and providers can better identify the specific areas of functioning with which an individual child may benefit from additional support. Consider a child who's general HRQOL score appears high. The high overall score may be driven by higher emotional, physical, and social functioning, while school functioning is lower. By only looking at general scores, providers may miss areas of

functioning (e.g., school) in which a child may need more support. Health care providers should screen each aspect of HRQOL individually in addition to psychosocial factors that may impact HRQOL, such as children's psychological adjustment. By examining each specific domain, providers may better understand risk factors and more accurately provide interventions directed toward a particular area of functioning (e.g., academic tutor vs. occupational therapy, vs. psychotherapy).

Child Psychological Adjustment & HRQOL

Consistently across all domains of HRQOL, one of the predictors of children's functioning during the first year of cancer treatment was children's own internalizing symptoms around the time of diagnosis. Fewer internalizing symptoms at baseline was associated with higher levels of overall, physical, social, and school HRQOL throughout treatment. This supports other work that has found that better child adjustment is associated with better child general HRQOL during pediatric cancer treatment (Roddenberry & Renk, 2008). Child psychological adjustment around time of diagnosis also accounted for most variance in general, physical, and social HRQOL, above and beyond caregiver psychological adjustment, parent-child conflict, emotion coaching as well as diagnosis and treatment intensity. Thus, children with fewer internalizing symptoms have better HRQOL.

This work demonstrates that internalizing symptoms are critical in children's functioning in context of pediatric cancer treatment, as they have a significant impact on many aspects of children's HRQOL. Previous work has demonstrated that about 7% of children experience clinically significant levels of internalizing symptoms at the time of diagnosis (Katz, Fladeboe, King et al., 2018), and clinical levels of depression may persist through the first year after diagnosis (Myers et al., 2014). While previous work has found that child psychological

adjustment improves on average over the first year after a pediatric cancer diagnosis, there is also evidence that adjustment varies significantly between children (Katz, Fladeboe, King, et al., 2018). Children expecting more depression and anxiety around the time of diagnosis and those whose adjustment does not improve over time may be at particularly high risk for poorer physical, social, and overall HRQOL. Overall, the current study aligns with other work that emphasizes the importance of regularly screening children's mental health throughout treatment to promote better outcomes in children with cancer (Kazak et al., 2015; Wiener et al., 2015).

Of note, there was evidence of suppression between the effects of internalizing and externalizing symptoms on HRQOL in the current sample, meaning that these predictor variables were highly collinear with one another. The effect of externalizing problems on HRQOL was primarily accounted for by the effect of internalizing problems on HRQOL. Externalizing problems may occur through children's internalizing symptoms. Indeed, previous work demonstrates that more internalizing symptoms in younger children may manifest as externalized behavior (Bhatia & Bhatia, 2007). For example, a child who is more depressed or anxious, may appear more irritable and act out. It is possible that in the current sample, externalizing problems were representative of a child's internal state. Thus, the effect of externalizing problems on HRQOL is primarily accounted for by the effect of internalizing problems.

It is unsurprising that children's own psychological adjustment accounts for the most variance across many domains of HRQOL given that it is the most proximal factor to child functioning that was tested in the current study and as such may have a more direct effect on HRQOL (Bronfenbrenner, 1977). When children feel more anxious or depressed, they tend to avoid and withdraw (Rubin et al., 2009). Specifically, children with cancer who are more depression/anxious might believe that activities (e.g., playing sports, going for walks) are too

hard or too draining to participate in, or they might worry about getting sick or keeping up with schoolwork, and thus disengage from school or physical activities impacting their HRQOL.

Children's psychological adjustment may also mediate or moderate the association between other risk factors and HRQOL. Other psychosocial factors, such as emotion socialization or parent-child conflict, may not have a direct impact on HRQOL, but may have more indirect effects on child HRQOL through child psychological adjustment (Katz & Hunter, 2007; Kay et al., 2019). For example, a child may become more depressed or anxious after experiencing more conflict with their caregiver, and consequently the lower mood affects their HRQOL. Thus, child internalization may act as a mediator. Similarly, child psychological adjustment may moderate the impact of symptoms on HRQOL. For instance, pain may have more of an impact on HRQOL for children who are more anxious. Future work should examine the role of internalizing problems as a mediator between other psychosocial factors and children's HRQOL.

It will also be important for future research to disentangle child psychological adjustment from the domains of HRQOL (e.g., emotional HRQOL and child internalizing symptoms). There may be significant overlap between emotional HRQOL and psychological adjustment as both assess emotional intensity and distress, which is why that association was not tested in the current study. Additional longitudinal research may be helpful to examine bidirectionality between child HRQOL and psychological adjustment. For example, it is unclear if a child has good emotional HRQOL because they are happy and well-adjusted, or if they are happy and well-adjusted because they have good HRQOL (Aaronson, 1991). More longitudinal work is needed to understand the direction of effects between child HRQOL and psychological adjustment.

Interventions that help children address symptoms of anxiety and depression around the time of diagnosis may be critical for improving functioning across multiple domains of HRQOL long-term. One study demonstrated that families prefer early psychosocial intervention around the time of diagnosis, providing support for addressing children's psychological adjustment at baseline (Hocking et al., 2014). Cognitive-behavioral interventions that assist children in identifying negative beliefs or worries about their cancer experience (e.g., "I'm too weak to play," "I'm scared of going out and getting sick"), adapting to limitations or avoidance due to cancer (e.g., not being able to see friends or go to school because of immunosuppression), and establishing behaviors that are potentially more feasible (e.g., cheering on school team if unable to play in a game) may improve children's social, physical, and overall HRQOL. In fact, recent reviews of the literature have found that psychological interventions such as cognitive-behavioral therapy improve both psychological adjustment and HRQOL in children on treatment for cancer and pediatric cancer survivors (Coughtrey et al., 2018; Peikert et al., 2018; Zhang et al., 2021). For example, a brief psychosocial intervention, Promoting Resilience in Stress Management (PRISM), has been developed to target stress management, cognitive reframing, and goal setting in adolescents and young adults with cancer (Rosenberg et al., 2018). A randomized control trial comparing PRISM to usual care found that patients who participated in PRISM reported less psychological distress and better HRQOL compared to those who received usual care. Future work should further examine the effectiveness of psychosocial interventions on children's adjustment and HRQOL while undergoing treatment.

Parent-Child Conflict & HRQOL

Although not associated with general, physical, emotional or school HRQOL, parent-child conflict at diagnosis was associated with social HRQOL. More conflict at baseline was

associated with lower levels of social HRQOL throughout the first year of pediatric cancer treatment. Parent-child conflict may be particularly important to children's social functioning as caregivers often facilitate children's interactions with peers (Ladd & Pettit, 2002). If a child experiences more conflict with their caregiver, they may be less likely to communicate their social needs with parents, and in fact, parent-child communication worsens after a pediatric cancer diagnosis (Cowfer et al., 2021). Thus, higher conflict resulting in poorer communication may lead to lower social and school HRQOL. This supports other work that has suggested that poorer parent-child attachment and communication is associated with poorer social functioning (Tillery et al., 2020). It is also possible that the parent-child relationship sets the blueprint for children's other relationships, as parent-child conflict is associated with poorer quality peer relationships in other samples (Boele et al., 2019; Ostrov & Bishop, 2008). Therefore, children who have more negative interactions with their caregivers may consequently have poorer social skills and poorer interactions with their peers (Boele et al., 2019; Liable & Thompson, 2007), affecting their social HRQOL.

Reducing parent-child conflict and improving communication between caregivers and children might be a beneficial intervention to improve children's social functioning. Family-based interventions may be ideal to address these needs. For example, the Surviving Cancer Competently Intervention Program (SCCIP) was designed to reduce family distress and improve family functioning through cognitive-behavioral and family therapy techniques (Kazak et al., 1999). SCCIP specifically targets increasing social support and family communication, and research has demonstrated that family cohesion and boundaries improve after the intervention. These positive changes in family functioning may subsequently lead to improvements in children's social HRQOL.

Emotion Coaching & HRQOL

More emotion coaching at time of diagnosis was associated with poorer school HRQOL when accounting for other variables, though was unrelated to all other aspects of HRQOL. This contrasts with other literature that demonstrates more emotion coaching is associated with better academic functioning (Gottman et al., 1996; Katz et al., 2012). It is possible this is a spurious effect, given that emotion coaching was not associated with any other aspects of HRQOL and was not independently associated with school HRQOL. Spurious effects are more likely to occur when the sample size is small relative to the number of parameters being estimated and the number of models being estimated (Anderson et al., 2001). In the current study, the model that tested cumulative predictors of the trajectory of school HRQOL included twelve parameters, and this was one of 10 models that included emotion coaching.

Another potential explanation for the negative association between emotion coaching and school HRQOL may involve caregiver response style. Caregivers who are more emotion coaching typically demonstrate more awareness and insight into their child's emotions (Denham et al., 1997; Shortt et al., 2015). Therefore, it may be that caregivers who are more emotion coaching are more aware of their child's functioning and are better able to detect their child's difficulty with school functioning. It is also possible that the negative association is explained by children's starting levels of HRQOL. Those who have lower school HRQOL around the time of diagnosis may need more support from their caregivers. Thus, caregivers utilize more emotion coaching when school HRQOL is low. This supports work in other samples that show parents are more emotion coaching when children's functioning is worse (Shortt et al., 2015). Future work should examine the function of emotion coaching in a pediatric cancer context to better

understand how communication about emotions might impact children's HRQOL during treatment.

Aim 3: Longitudinal Associations Between Psychological Adjustment and HRQOL

Unexpectedly, changes in caregiver psychological adjustment and child psychological adjustment were not associated with children's HRQOL over the first year of cancer treatment. Specifically, changes in caregiver anxiety and PTSS were not related to changes in any domains of child HRQOL. Of note, differences in caregiver depression were associated with the trajectory of children's emotional HRQOL, such that children's emotional HRQOL improved at a slower rate when their caregivers were more depressed compared to other caregivers. Thus, caregivers who are more depressed, may be more withdrawn and less able to provide emotional support to their children. However, these findings should be interpreted with caution given that changes in other aspects of caregiver psychological adjustment (anxiety and PTSS) were not significantly associated with HRQOL. Furthermore, changes in child's own internalizing and externalizing problems across the first year of cancer treatment were not associated with changes in their HRQOL.

One potential implication of these findings is that screening psychosocial factors particularly at the time of diagnosis is critical to understanding a child's risk for poorer HRQOL throughout treatment. How a family reacts and adjusts around the time of diagnosis, rather than changes in adjustment throughout treatment, may have more of an effect on the trajectory of HRQOL. This supports previous work that demonstrates child and caregiver psychological adjustment is poorest around the time of diagnosis (Katz, Fladeboe, King et al., 2018; Vrijmoet-Wiersma et al., 2008). However, these results should be regarded with caution, given that they contradict other work that has demonstrated that changes in caregiver and child psychological

adjustment over time are related to other child outcomes in pediatric cancer samples (Van Schoors et al., 2017). One explanation for the lack of significant associations in the current study is that the sample did have enough data at each timepoint to test interactions with time. Furthermore, the current design only included three points of measurement, and it is possible that more frequent measurement might capture more nuance in the associations between psychological adjustment and HRQOL over time. Future work should continue more longitudinal work with large samples to have more power to conduct full parallel process models to understand whether child HRQOL varies with their own and their caregivers' psychological adjustment over time.

Strengths

There are numerous strengths of the current study. First, this paper examined modifiable psychosocial risk factors (e.g., psychological adjustment) for poorer HRQOL, as opposed to more fixed cancer-related factors (e.g., diagnosis, treatment). This allows providers to understand more potential points for intervention (e.g., child mental health, parent-child relationships) to promote better HRQOL in children undergoing cancer treatment. Second, individual domains of HRQOL were examined separately to clarify differences in particular areas of child functioning. Children experience varying levels of difficulty in functioning across domains of HRQOL, and school functioning is relatively weaker compared to other domains of HRQOL. Finally, the study utilized longitudinal data which allowed the investigation of both baseline predictors of HRQOL and associations over time to better understand the nuance of how psychological adjustment and HRQOL vary with one another over the first year of pediatric cancer treatment.

Limitations and Future Directions

There are several limitations to the current study. First, single-reported bias may be a concern, given that all measures were completed by caregivers. Caregivers who experience more distress may be more likely to have a poorer perception of their child's functioning. However, in the current sample there was not an association between caregiver psychological adjustment and their report of their child's HRQOL, mitigating this concern. Second, caregiver proxy report of child functioning (both psychological adjustment and HRQOL) may not be an accurate reflection of child's own perception of their functioning. Previous work has demonstrated discrepancies between child self-report and parent-proxy report of children's HRQOL and psychological functioning, especially as children enter adolescence (al Ghriwati et al., 2021; Eiser & Varni, 2013; Varni et al., 2015). Caregivers tend to underestimate their children's HRQOL relative to child's own report (Levi & Drotar, 1999; Parsons et al., 1999), thus HRQOL in this sample might truly be higher than what was estimated. Recent work in pediatric cancer is trending toward more research and clinical efforts that involves patient self-reported outcomes to fully capture children's own experiences more accurately (Hinds et al., 2013; Freyer et al., 2022). Future studies should include child self-report of HRQOL, when possible, to better understand children's perception of their own functioning, especially more internal states (i.e., emotional HRQOL) that their caregivers may not be fully aware of. Indeed, previous work demonstrates high discrepancies between caregiver proxy report and child self-report on internalized symptoms of psychological distress as well as physical states such as pain and fatigue (Freyer et al., 2022; Mack et al., 2020).

A third limitation is lack of racial, economic, and gender diversity of the sample, which limits the generalizability of findings. Given the importance of social determinates of health, it is critical to examine HRQOL across multiple samples, including children from a wider range of

racial/ethnic backgrounds and incomes. Recent work has demonstrated that socio-demographic factors are associated with mortality rates of children with cancer. Black and Hispanic children with ALL have lower overall survival rates compared to White and non-Hispanic children with ALL (Acharya et al., 2016; Eche & Aronowitz, 2020). Lower socio-economic status, experiencing poverty, and poorer insurance coverage is also associated with lower survival rates in pediatric cancer (Acharya et al., 2016; Tran et al., 2022). Further, HRQOL is lower in Hispanic survivors of childhood cancer relative to non-Hispanic White survivors (Dixon et al., 2019). Considering the association between survival, HRQOL, and race/ethnicity and economic status, it is critical to include diverse socio-demographic samples when investigating variability in HRQOL in pediatric cancer samples. Given the demographic characteristics of the sample, findings from the current study maybe limited to primarily White and higher income families.

A fourth limitation to the current study is we did not collect data on other factors that may influence children's HRQOL during pediatric cancer treatment. For example, symptom management and distress have been found to be closely associated with HRQOL in pediatric cancer (Hinds et al., 2006; Huang et al., 2013; Rosenberg et al., 2016). Previous work has demonstrated that children with advanced cancer experience more symptoms related to treatment and higher subjective symptom distress (i.e., how much a child is bothered by symptoms) have poorer HRQOL (Rosenberg et al., 2016). Specifically, pain and fatigue are two of the most frequent physical symptoms that negatively impact children's HRQOL. Symptom distress and management have also been found to be primary factors that account for variation in children's HRQOL relative to demographic and treatment-related variables in survivors of pediatric cancer and children with advanced cancer (Huang et al., 2013; Macartney et al., 2014; Rosenberg et al., 2016).

Future work should investigate the effect of the interaction between physical experience of symptom management and distress and psychosocial factors (e.g., child psychological adjustment) on children's HRQOL during cancer treatment. Symptom distress is often measured by assessing both objective frequency of a symptom (e.g., did you experience pain, how much of the time did you experience pain) as well as subjective distress of that symptom (e.g., how much pain did you feel, how much did the pain bother you; Collins et al., 2002). In fact, Miller et al. (2011) found that prevalence of symptoms is not always related to symptom distress. Symptoms rated as most frequent by patients ages 10-17, were not rated as the most severe or distressing.

Given the somewhat subjective nature of symptom management, how much someone is *bothered* by symptoms might be influenced by their psychological adjustment. For example, people who are more depressed tend to interpret the world through a more negative lens, and thus may perceive their symptoms to be more burdensome or distressing relative to people who are less depressed. However, the association between children's psychological adjustment (e.g., coping, depression) and symptom distress is understudied in pediatric cancer (Hinds et al., 2006). It is possible that a child who is more depressed or has fewer coping skills may be less able to handle more frequent symptoms compared to someone with less depression and better coping skills. In contrast, it may be that certain symptoms (e.g., pain, fatigue) are so distressing or impairing, that HRQOL is affected by those symptoms regardless of a child's psychological functioning. Research is needed to better understand the association between symptom management and children's psychological adjustment to clarify how they contribute to variation in HRQOL and subsequently what interventions might be more appropriate to promote children's HRQOL in context of pediatric cancer. Indeed, recent work on the conceptualization

of the symptom experience in pediatric cancer has called for more empirical work to understand relations between symptoms, psychosocial adjustment, and HRQOL (Jibb et al., 2022).

It may also be beneficial for future work to study other psychosocial factors in relation to HRQOL in pediatric cancer. For example, children's coping and resilience may moderate the effects of their internalizing symptoms and distress on HRQOL, and thus should be examined. Prior work demonstrated that children who report more confidence coping with cancer and utilize more coping skills report better HRQOL (Chirico et al., 2017; Fisher et al., 2021). Additionally, survivors of childhood cancer who indicate more resilience report better HRQOL (Vetsch et al., 2018). Interestingly, one study of adolescents with cancer found that resilience mediated the association between symptom distress and HRQOL, such that distress had less of an impact on patients' HRQOL for those who demonstrated more resilience (Wu et al., 2015). Given the current study's findings of the importance of internalizing symptoms on HRQOL, it may be important to examine other psychosocial factors not included in this paper to better understand how coping and resilience interact with children's mental health to mediate or moderate the effects on HRQOL.

The current study contributes to growing literature that suggests HRQOL is an important outcome for children of cancer and also provides clarity into the trajectory of HRQOL and psychosocial factors that might impact HRQOL during the first year of treatment. Specifically, given that HRQOL changes during the year, ongoing assessment of HRQOL is critical to identify children whose functioning is not improving. Furthermore, the findings suggest that children may need more support with school functioning, given that children's school HRQOL is lower compared to other functional domains and does not improve as much throughout the first year of treatment. Finally, interventions that target children's psychological adjustment and

parent-child conflict may be important to improve HRQOL across multiple domains. A critical next step is to examine the effect of interactions between psychosocial factors (e.g., psychological adjustment) and treatment related factors (e.g., symptom management) on children's HRQOL.

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Table 1

Descriptive Statistics of HRQOL and Psychosocial Variables

	Month 1 Mean (SD)	Month 6 Mean (SD)	Month 12 Mean (SD)
Overall HRQOL	N = 136 58.03 (16.43)	N = 104 64.88 (19.10)	N = 63 75.15 (16.70)
Physical HRQOL	N = 135 48.81 (26.53)	N = 104 59.47 (29.13)	N = 62 75.09 (22.92)
Emotional HRQOL	N = 136 54.54 (19.08)	N = 104 62.55 (19.08)	N = 51 72.43 (16.44)
Social HRQOL	N = 135 71.15 (18.51)	N = 104 74.52 (19.15)	N = 51 81.47 (19.53)
School HRQOL	N = 85 57.92 (25.40)	N = 104 61.87 (27.50)	N = 40 71.50 (20.60)
Caregiver Depression	N = 132 13.84 (5.76)	N = 108 10.78 (6.64)	N = 84 8.82 (5.98)
Caregiver Anxiety	N = 131 3.87 (3.85)	N = 108 2.56 (3.52)	N = 83 2.05 (3.20)
Caregiver PTSS	N = 134 30.87 (16.38)	N = 107 22.02 (15.04)	N = 83 18.47 (15.13)
Parent-Child Conflict	N = 139 8.71 (2.97)	N = 108 9.42 (3.01)	N = 84 8.79 (2.93)
Emotion Coaching	N = 139 3.74 (0.28)	N = 107 3.69 (0.30)	N = 83 3.68 (0.29)
Child Internalizing Symptoms	N = 130 57.66 (11.43)	N = 105 52.69 (11.88)	N = 84 48.42 (12.18)
Child Externalizing Symptoms	N = 130 49.15 (11.32)	N = 105 47.44 (11.93)	N = 84 44.64 (10.95)

Table 2a

Pearson's r Correlations Between HRQOL and Psychosocial Factors at Months 1, 6, and 12

		Month 1					Month 6					Month 12				
		Overall HRQOL	Physical HRQOL	Emotional HRQOL	Social HRQOL	School HRQOL	Overall HRQOL	Physical HRQOL	Emotional HRQOL	Social HRQOL	School HRQOL	Overall HRQOL	Physical HRQOL	Emotional HRQOL	Social HRQOL	School HRQOL
Month 1	Caregiver Depression	-0.23**	-0.06	-0.29**	-0.19*	-0.17	-0.19	-0.15	-0.23*	-0.17	-0.10	-0.02	0.10	-0.13	-0.22	-0.09
	Caregiver Anxiety	-0.18*	-0.03	-0.25**	-0.17	-0.09	-0.26*	-0.17	-0.37**	-0.26*	-0.12	-0.08	0.00	-0.05	-0.12	-0.19
	Caregiver PTSS	-0.30**	-0.10	-0.41**	-0.18*	-0.29**	-0.21*	-0.19	-0.25*	-0.21*	-0.14	-0.10	-0.06	-0.29	-0.31*	-0.05
	Parent-Child Conflict	-0.02	0.11	0.02	-0.16	-0.10	-0.14	-0.06	-0.10	-0.18	-0.15	-0.15	-0.02	-0.04	0.01	-0.07
	Caregiver Emotion Coaching	-0.15	-0.10	-0.18*	-0.02	-0.13	-0.80	-0.8	0.03	-0.05	-0.09	-0.01	0.08	-0.31*	-0.14	-0.10
	Child Internalizing	-0.44**	-0.27**	-0.38**	-0.38**	-0.33**	-0.41**	-0.36**	-0.49**	-0.41**	-0.16	-0.08	-0.11	-0.27	-0.15	-0.14
	Child Externalizing	-0.24**	0.00	-0.28**	-0.30**	-0.29**	-0.28**	-0.17	-0.44**	-0.32**	-0.07	-0.08	-0.08	-0.24	-0.05	0.02
Month 6	Caregiver Depression	-0.19	-0.12	-0.18	-0.23*	0.05	-0.43**	-0.32**	-0.53**	-0.43**	-0.21	-0.30*	-0.18	-0.46**	-0.42**	-0.40*
	Caregiver Anxiety	-0.15	-0.07	-0.13	-0.22*	-0.06	-0.32**	-0.15	-0.45**	-0.37**	-0.20	-0.17	-0.08	-0.21	-0.23	-0.25
	Caregiver PTSS	-0.21*	-0.11	-0.26**	-0.17	-0.09	-0.27**	-0.16	-0.38**	-0.33**	-0.12	-0.14	-0.04	-0.32*	-0.26	-0.20
	Parent-Child Conflict	-0.11	0.00	0.01	-0.30**	-0.09	-0.34**	-0.19	-0.43**	-0.40**	-0.18	-0.26*	-0.19	-0.06	-0.24	-0.22
	Caregiver Emotion Coaching	-0.04	-0.04	-0.11	0.05	0.02	0.01	-0.05	0.19	0.04	-0.08	-0.09	-0.10	-0.10	-0.12	-0.13
	Child Internalizing	-0.30**	-0.13	-0.26*	-0.38**	-0.23	-0.58**	-0.42**	-0.64**	-0.59**	-0.34**	-0.32*	-0.19	-0.31*	-0.37**	-0.41**
	Child Externalizing	-0.17	0.06	-0.16	-0.35**	-0.11	-0.34**	-0.14	-0.47**	-0.45**	-0.15	-0.17	-0.03	-0.25	-0.07	-0.26

	Caregiver Depression	-0.22*	-0.15	-0.25*	-0.19	-0.02	-0.34**	-0.27*	-0.47**	-0.39**	-0.06	-026*	-0.17	-0.35*	-0.35*	-0.27
	Caregiver Anxiety	-0.21	-0.05	-0.30**	-0.09	-0.23	-0.32**	-0.16	-0.43**	-0.35**	-0.23	-0.23	-0.13	-0.24	-0.25	-0.15
	Caregiver PTSS	-0.24*	-0.14	-0.32**	-0.13	-0.14	-0.24*	-0.21	-0.33**	-0.24*	-0.09	-0.23	-0.15	-0.30*	-0.23	-0.06
Month 12	Parent-Child Conflict	-0.17	0.00	-0.19	-0.19	-0.23	-0.19	0.00	-.38**	-0.26*	-0.14	-0.30*	-0.13	-0.26	-0.17	-0.33*
	Caregiver Emotion Coaching	-0.24*	-0.20	-0.21	-0.12	-0.17	0.02	-0.01	0.16	0.01	-0.11	0.15	0.16	0.00	-0.06	-0.03
	Child Internalizing	-0.34**	-0.23*	-0.21	-0.42**	-0.23	-0.37**	-0.28*	-0.40**	-0.41**	-0.14	-0.44**	-0.35**	-0.47**	-0.28	-0.42**
	Child Externalizing	-0.25*	-0.06	-0.23*	-0.37**	-0.08	-0.29**	-0.17	-0.42**	-0.42**	0.01	-0.16	-0.11	-0.31*	-0.02	-0.30

Table 2b

Pearson's r Correlations Between Average Scores of Psychosocial Factors

	2	3	4	5	6	7
1. Average Caregiver Depression	0.74**	0.76**	0.28**	0.06	0.58**	0.51**
2. Average Caregiver Anxiety		0.71**	0.23**	0.06	0.60**	0.52**
3. Average Caregiver PTSS			0.16	0.22**	0.50**	0.49**
4. Average Parent-Child Conflict				-0.39**	0.35**	0.44**
5. Average Caregiver Emotion Coaching					0.01	-0.07
6. Average Child Interanlizing						0.74**
7. Average Child Externalizing						

Note. * = $p < .05$; ** = $p < .01$

Table 3

Aim 1: Growth Models of HRQOL

		Fixed Effects		Variance Components	
Model	AIC	Intercept b (SE)	Slope b (SE)	Intercept (σ^2)	Slope (σ^2)
Overall HRQOL					
1	2589.97	74.27 (1.90)	8.32 (1.30)		
2	2557.03***	74.28 (1.84)	8.33 (1.03)	133.45	
3	2560.18	74.16 (1.94)	8.25 (1.07)	179.23	16.06
Physical HRQOL					
1	2827.04	73.80 (2.92)	12.79 (2.00)		
2	2782.80***	73.76 (2.80)	12.69 (1.50)	355.72	
3					ERROR
Emotional HRQOL					
1	2523.16	71.87 (2.18)	8.77 (1.46)		
2	2502.10***	72.32 (2.11)	9.07 (1.20)	143.35	
3					ERROR
Social HRQOL					
1	2523.18	80.40 (2.22)	4.83 (1.49)		
2	2498.23***	80.14 (2.13)	4.68 (1.21)	145.39	
3	2498.65	79.84 (2.31)	4.49 (1.32)	256.76	51.99
School HRQOL					
1	18.53.83	69.92 (3.40)	6.37 (2.36)		
2	1842.98**	68.33 (3.27)	5.16 (1.91)	315.87	
3					ERROR

Note. ** = $p < .01$; *** = $p < .001$. AIC = Akaike Information Criteria; Model 1 = Fixed intercept & fixed slope, Model 2 = Random intercept & fixed slope; Model 3 = Random intercept & random slope.

Table 4

Aim 2: Trajectories of HRQOL Predicted by Baseline Caregiver Adjustment

	Overall HRQOL	**Physical HRQOL**	**Emotional HRQOL**	**Social HRQOL**	**School HRQOL**
Intercept β *(SE)*	103.99 (7.99)***	111.68 (12.74)***	96.46 (8.19)***	97.59 (9.18)***	112.97 (13.36)***
Time β *(SE)*	8.90 (1.09)***	13.40 (1.64)***	8.82 (1.27)***	4.92 (1.31)***	6.44 (2.02)**
Caregiver Depression β *(SE)*	-0.47 (1.89)	-0.41 (3.01)	0.25 (1.92)	-0.34 (2.16)	-2.67 (3.26)
Caregiver Anxiety β *(SE)*	-.158 (1.69)	0.85 (2.69)	-1.98 (1.71)	-2.59 (1.93)	-1.02 (2.83)
Caregiver PTSS β *(SE)*	-3.26 (1.63)	-3.66 (2.61)	-5.93 (1.66)***	-2.85 (1.87)	-2.66 (2.90)
Child Age β *(SE)*	-0.50 (0.38)	-0.89 (0.61)	0.33 (0.38)	-0.72 (0.44)	-0.98 (0.66)
Child Sex β *(SE)*	-2.43 (2.58)	-0.26 (4.12)	-3.71 (2.62)	-2.29 (2.96)	-2.76 (4.38)
Child Diagnosis β *(SE)*	-6.44 (2.52)*	-7.41 (4.03)	-4.72 (2.56)	-2.18 (2.89)	13.42 (4.34)**
Child Treatment Intensity β *(SE)*	-4.91 (1.85)**	-7.55 (2.97)**	-5.32 (1.87)**	-2.39 (2.12)	-5.21 (3.15)

Note. * = $p < .05$; ** = $p < .01$; *** = $p < .001$. For child diagnosis 1 = Leukemia/lymphoma, 2 = CNS tumors, 3 = Non-CNS tumors; For child sex 1 = Male, 2 = Female; All trajectories of HRQOL include random intercept and fixed slope. Intercept for HRQOL was set at 12 months post-diagnosis.

Table 5

Aim 2: Trajectories of HRQOL Predicted by Baseline Parent-Child Conflict

	Overall HRQOL	**Physical HRQOL**	**Emotional HRQOL**	**Social HRQOL**	**School HRQOL**
Intercept β *(SE)*	103.14 (7.69)***	113.89 (12.03)***	98.10 (8.30)***	98.30 (8.63)***	103.60 (12.94)***
Time β *(SE)*	8.17 (1.05)***	12.34 (1.53)***	9.28 (1.22)***	4.67 (1.24)***	4.67 (1.96)*
Parent-Child Conflict β *(SE)*	-1.87 (1.24)	0.68 (1.95)	-1.48 (1.33)	-2.67 (1.39)*	-3.98 (2.18)
Child Age β *(SE)*	-0.44 (0.36)	-1.29 (0.57)*	0.37 (0.39)	-0.50 (0.40)	-0.50 (0.64)
Child Sex β *(SE)*	-2.09 (2.45)	-1.05 (3.84)	4.72 (2.63)	-1.80 (2.74)	0.28 (4.20)
Child Diagnosis β *(SE)*	-6.56 (2.43)**	-7.28 (3.80)	-4.93 (2.60)	-3.04 (2.72)	-13.65 (3.02)**
Child Treatment Intensity β *(SE)*	-5.13 (1.75)**	-7.78 (2.76)**	-4.90 (1.87)**	-2.96 (1.95)	-4.92 (3.03)

Note. * = $p < .05$; ** = $p < .01$; *** = $p < .001$. For child diagnosis 1 = Leukemia/lymphoma, 2 = CNS tumors, 3 = Non-CNS tumors; For child sex 1 = Male, 2 = Female; All trajectories of HRQOL include random intercept and fixed slope. Intercept for HRQOL was set at 12 months post-diagnosis.

Table 6

Aim 2: Trajectories of HRQOL Predicted by Baseline Caregiver Emotion Coaching

	Overall HRQOL	**Physical HRQOL**	**Emotional HRQOL**	**Social HRQOL**	**School HRQOL**
Intercept β *(SE)*	101.78 (7.73)***	113.54 (12.05)***	96.52 (8.31)***	96.61 (8.74)***	101.18 (13.09)***
Time β *(SE)*	8.21 (1.05)***	12.33 (1.53)***	9.29 (1.22)***	4.70 (1.24)***	4.67 (1.95)*
Caregiver Emotion Coaching β *(SE)*	-1.20 (1.21)	-1.08 (1.90)	-1.68 (1.29)	-1.03 (1.36)	-2.74 (2.08)
Child Age β *(SE)*	-0.57 (0.36)	-1.28 (0.56)*	0.25 (0.38)	-0.66 (0.40)	-0.95 (0.64)
Child Sex β *(SE)*	-1.95 (2.46)	-1.15 (3.84)	-4.63 (2.63)	-1.60 (2.77)	0.93 (4.24)
Child Diagnosis β *(SE)*	-5.90 (2.45)*	-7.08 (3.83)	-4.14 (2.62)	-2.23 (2.76)	-11.28 (4.28)**
Child Treatment Intensity β *(SE)*	-4.73 (1.76)**	-7.72 (2.76)**	-4.51 (1.87)*	-2.50 (1.98)	-4.44 (3.07)

Note. * = $p < .05$; ** = $p < .01$; *** = $p < .001$. For child diagnosis 1 = Leukemia/lymphoma, 2 = CNS tumors, 3 = Non-CNS tumors; For child sex 1 = Male, 2 = Female; All trajectories of HRQOL include random intercept and fixed slope. Intercept for HRQOL was set at 12 months post-diagnosis.

Table 7

Aim 2: Trajectories of HRQOL Predicted by Baseline Child Adjustment

		Overall HRQOL	Physical HRQOL	Social HRQOL	School HRQOL
Internalizing & Externalizing	**Intercept β *(SE)***	104.10 (7.09)***	111.68 (11.36)***	99.59 (8.23)***	106.88 (13.37)***
	Time β *(SE)*	8.76 (1.08)***	13.43 (1.59)***	4.94 (1.30)***	5.89 (2.11)**
	Child Internalizing β *(SE)*	-7.41 (1.58)***	-12.20 (2.53)***	-6.32 (1.83)***	-7.54 (3.05)*
	Child Externalizing β *(SE)*	0.83 (1.58)	6.19 (2.55)*	-1.88 (1.84)	1.10 (3.34)
	Child Age β *(SE)*	-0.79 (0.34)*	-1.04 (0.55)	-1.13 (0.39)**	-1.39 (0.67)*
	Child Sex β *(SE)*	-3.47 (2.25)	-1.81 (3.62)	-3.77 (2.60)	-2.28 (4.36)
	Child Diagnosis β *(SE)*	-7.35 (2.22)**	-9.47 (3.57)**	-2.71 (2.57)	-14.27 (4.38)**
	Child Treatment Intensity β *(SE)*	-3.27 (1.62)*	-5.25 (2.61)*	-0.98 (1.87)	-1.86 (3.15)
Internalizing Only	**Intercept β *(SE)***	104.39 (7.06)***	113.96 (11.56)***	99.01 (8.22)***	107.06 (13.33)***
	Time β *(SE)*	8.74 (1.08)***	13.37 (1.59)***	5.02 (1.30)***	5.81 (2.09)**
	Child Internalizing β *(SE)*	-6.82 (1.10)***	-7.80 (1.80)***	-7.65 (1.29)***	-6.86 (2.25)**
	Child Age β *(SE)*	-0.82 (0.33)*	-1.24 (0.55)*	-1.07 (0.39)**	-1.43 (0.66)*
	Child Sex β *(SE)*	-3.53 (2.25)	-2.31 (3.69)	-3.64 (2.61)	-2.42 (4.33)
	Child Diagnosis β *(SE)*	-7.20 (2.20)**	-8.35 (3.61)*	-3.04 (2.55)	-14.00 (4.29)**
	Child Treatment Intensity β *(SE)*	-3.37 (1.61)*	-6.02 (2.65)*	-0.76 (1.86)	-1.94 (3.14)

	Intercept β *(SE)*	104.80 (7.64)***	113.01 (12.32)***	100.08 (8.57)***	107.83 (13.68)***
	Time β *(SE)*	8.69 (1.09)***	13.34 (1.60)***	4.83 (1.31)***	5.48 (2.12)*
	Child Externalizing β *(SE)*	-4.51 (1.19)***	-2.60 (1.93)	-6.43 (1.35)***	-4.47 (2.52)
Externalizing Only	**Child Age β *(SE)***	-0.83 (0.37)*	-1.11 (0.59)	-1.16 (0.41)**	-1.41 (0.69)*
	Child Sex β *(SE)*	-3.31 (2.43)	-1.58 (3.93)	-3.55 (2.72)	-2.06 (4.47)
	Child Diagnosis β *(SE)*	-6.15 (2.38)*	-7.55 (3.86)	-1.77 (2.66)	-12.87 (4.44)**
	Child Treatment Intensity β *(SE)*	-4.23 (1.74)*	-6.82 (2.83)*	-1.81 (1.94)	-3.26 (3.18)

Note. * = $p < .05$; ** = $p < .01$; *** = $p < .001$. For child diagnosis 1 = Leukemia/lymphoma, 2 = CNS tumors, 3 = Non-CNS tumors; For child sex 1 = Male, 2 = Female; All trajectories of HRQOL include random intercept and fixed slope. Intercept for HRQOL was set at 12 months post-diagnosis. Effect of basedline child psychologial adjustment on emotional HRQOL was not tested.

Table 8

Aim 2: Cumulative Effects of Baseline Psychosocial Predictors on Trajectories of HRQOL

	Overall HRQOL	**Physical HRQOL**	**Emotional HRQOL**	**Social HRQOL**	**School HRQOL**
Intercept β *(SE)*	103.75 (7.24)***	110.78 (11.99)***	95.83 (8.19)***	98.29 (8.67)***	112.16 (13.02)***
Time β *(SE)*	8.97 (1.13)***	13.72 (1.70)***	8.83 (1.28)***	4.88 (1.35)***	6.77 (2.14)**
Caregiver Depression β *(SE)*	0.18 (1.69)	0.33 (2.80)	0.15 (1.93)	0.43 (2.02)	-2.62 (3.15)
Caregiver Anxiety β *(SE)*	1.35 (1.56)	4.71 (2.60)	-1.53 (1.74)	0.65 (1.89)	1.97 (2.80)
Caregiver PTSS β *(SE)*	-2.91 (1.45)	-3.09 (2.41)	-5.84 (1.65)***	-2.29 (1.75)	-2.52 (2.83)
Parent-Child Conflict β *(SE)*	-1.37 (1.25)	0.74 (2.06)	-1.79 (1.41)	-1.86 (1.50)	-4.39 (2.41)
Caregiver Emotion Coaching β *(SE)*	-2.33 (1.25)	-2.65 (2.08)	-1.77 (1.43)	-2.02 (1.49)	-5.23 (2.30)*
Child Internalizing β *(SE)*	-6.12 (1.27)***	-8.83 (2.11)***	-	-5.90 (2.03)**	-4.42 (2.40)
Child Externalizing β *(SE)*	-	-	-	-1.42 (2.05)	-
Child Age β *(SE)*	-0.85 (0.35)*	-1.49 (0.58)*	0.41 (0.39)	-1.10 (0.42)*	-1.11 (0.67)
Child Sex β *(SE)*	-3.93 (2.31)	-2.07 (3.84)	-3.70 (2.61)	-3.97 (2.75)	-4.48 (4.25)
Child Diagnosis β *(SE)*	-6.47 (2.27)**	-6.90 (3.76)	-4.65 (2.57)	-2.03 (2.72)	-14.71 (4.25)***
Child Treatment Intensity β *(SE)*	-3.09 (1.69)	-4.88 (2.82)	-5.25 (1.87)**	-0.85 (2.03)	-2.82 (3.14)

Note. * = $p < .05$; ** = $p < .01$; *** = $p < .001$. For child diagnosis 1 = Leukemia/lymphoma, 2 = CNS tumors, 3 = Non-CNS tumors; For child sex 1 = Male, 2 = Female; All trajectories of HRQOL include random intercept and fixed slope. Intercept for HRQOL was set at 12 months post-diagnosis. Effect of basedline child psychologial adjustment on emotional HRQOL was not tested.

Table 9

Aim 3: Changes in Caregiver Adjustment Predicting Changes in HRQOL During the First Year of Treatment

	Overall HRQOL	**Physical HRQOL**	**Emotional HRQOL**	**Social HRQOL**	**School HRQOL**
Intercept β *(SE)*	94.94 (7.59)***	105.24 (12.34)***	89.18 (7.83)***	86.58 (8.48)***	97.77 (13.60)***
Time β *(SE)*	7.88 (1.05)***	12.30 (1.55)***	8.54 (1.20)***	4.19 (1.23)***	4.27 (1.98)*
Caregiver Depression GMC β *(SE)*	-5.43 (2.74)*	-6.26 (4.26)	-7.88 (3.17)*	-6.95 (3.34)*	-6.38 (5.36)
Caregiver Anxiety GMC β *(SE)*	-2.30 (2.91)	0.23 (4.47)	-1.18 (3.22)	-0.52 (3.39)	-3.49 (5.50)
Caregiver PTSS GMC β *(SE)*	1.36 (2.64)	1.21 (4.10)	-0.18 (2.99)	-1.82 (3.15)	4.59 (5.52)
Caregiver Depression GMC x Time β *(SE)*	-2.06 (1.60)	-1.76 (2.36)	-4.11 (1.91)*	-1.96 (1.97)	-4.86 (3.22)
Caregiver Anxiety GMC x Time β *(SE)*	-0.94 (1.71)	-1.30 (2.52)	-0.29 (1.93)	0.93 (1.99)	-0.76 (3.27)
Caregiver PTSS GMC x Time β *(SE)*	2.21 (1.54)	2.21 (2.27)	3.23 (1.79)	-1.23 (1.84)	4.52 (3.22)
Child Age β *(SE)*	-0.58 (0.34)	-1.31 (0.56)*	0.23 (0.35)	-0.66 (0.38)	-0.90 (0.63)
Child Sex β *(SE)*	-0.14 (2.36)	1.19 (3.85)	-2.72 (2.42)	0.49 (2.63)	1.01 (4.31)
Child Diagnosis β *(SE)*	-5.39 (2.30)*	-6.66 (3.74)	-3.23 (2.34)	-1.23 (2.55)	-11.44 (4.24)**
Child Treatment Intensity β *(SE)*	-3.77 (1.71)*	-6.22 (2.79)*	-3.96 (1.74)*	-0.88 (1.89)	-3.59 (3.17)

Note. * = $p < .05$; ** = $p < .01$; *** = $p < .001$. GMC = grand mean centered; For child diagnosis 1 = Leukemia/lymphoma, 2 = CNS tumors, 3 = Non-CNS tumors; For child sex 1 = Male, 2 = Female; All trajectories of HRQOL include random intercept and fixed slope. Intercept for HRQOL was set at 12 months post-diagnosis.

Table 10

Aim 3: Changes in Child Adjustment Predicting Changes in HRQOL During the First Year of Treatment

	Overall HRQOL	**Physical HRQOL**	**Social HRQOL**	**School HRQOL**
Intercept β *(SE)*	98.37 (6.51)***	110.03 (11.15)***	92.45 (7.25)***	98.51 (12.51)***
Time β *(SE)*	8.11 (1.01)***	12.41 (1.51)***	4.49 (1.20)***	4.58 (1.91)*
Child Internalizing GMC β *(SE)*	-8.30 (1.69)***	-9.23 (2.68)***	-8.52 (2.00)***	-7.46 (3.35)*
Child Internalizing GMC x Time β *(SE)*	-0.61 (1.04)	-1.06 (1.54)	0.11 (1.23)	-0.44 (2.03)
Child Age β *(SE)*	-0.60 (0.30)*	-1.31 (0.52)*	-0.77 (0.34)*	-0.93 (0.60)
Child Sex β *(SE)*	-2.33 (2.06)	-1.34 (3.54)	-2.14 (2.28)	-0.88 (4.02)
Child Diagnosis β *(SE)*	-4.98 (2.03)*	-6.27 (3.52)	-0.89 (2.26)	-11.02 (4.03)**
Child Treatment Intensity β *(SE)*	-3.79 (1.48)*	-6.66 (2.56)*	-1.26 (1.63)	-2.73 (2.97)

Note. * = $p < .05$; ** = $p < .01$; *** = $p < .001$. GMC = grand mean centered; For child diagnosis 1 = Leukemia/lymphoma, 2 = CNS tumors, 3 = Non-CNS tumors; For child sex 1 = Male, 2 = Female; All trajectories of HRQOL include random intercept and fixed slope. Intercept for HRQOL was set at 12 months post-diagnosis. Effect of basedline child psychologial adjustment on emotional HRQOL was not tested.

Table 11

Average Scores of the Physical HRQOL Subscale

Item	Month 1 Mean (SD)	Month 6 Mean (SD)	Month 12 Mean (SD)
Paying attention in class	70.08 (25.75)	65.16 (29.32)	69.77 (26.48)
Forgetting things	67.69 (27.14)	66.02 (27.23)	71.51 (24.75)
Keeping up with schoolwork	67.28 (31.29)	64.86 (33.60)	79.41 (26.32)
Missing school because of not feeling well	46.87 (36.54)	58.56 (36.61)	73.00 (32.28)
Missing school to go to the doctor or hospital	41.56 (35.34)	51.71 (33.42)	63.00 (29.12)

Figure 1

Model of HRQOL proposed by Wilson & Cleary (1995)

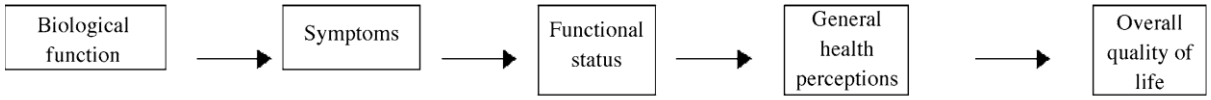


Figure 2

Model of HRQOL proposed by Ferrans et al. (2005)

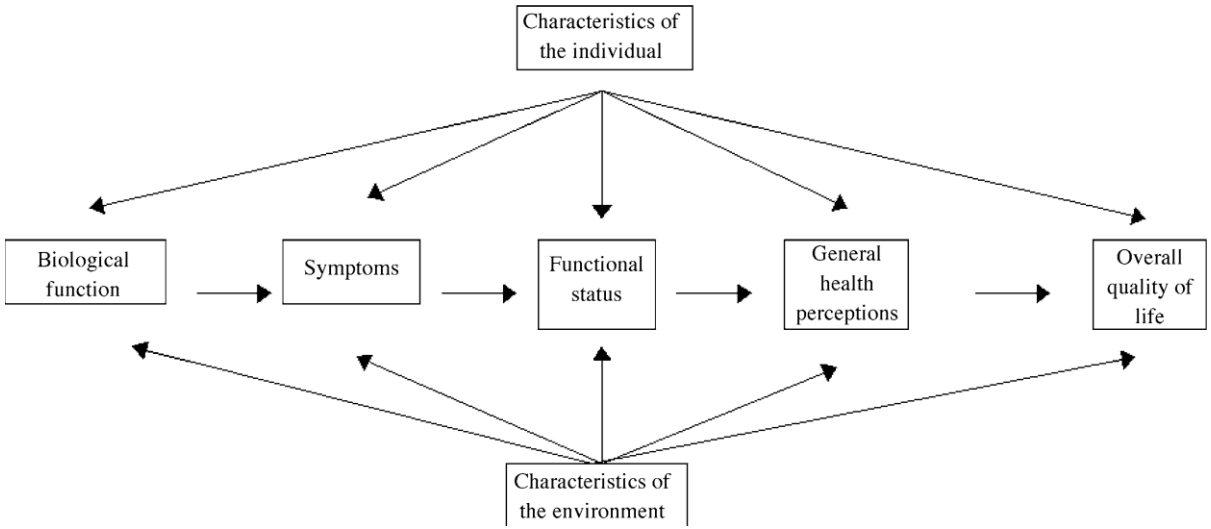
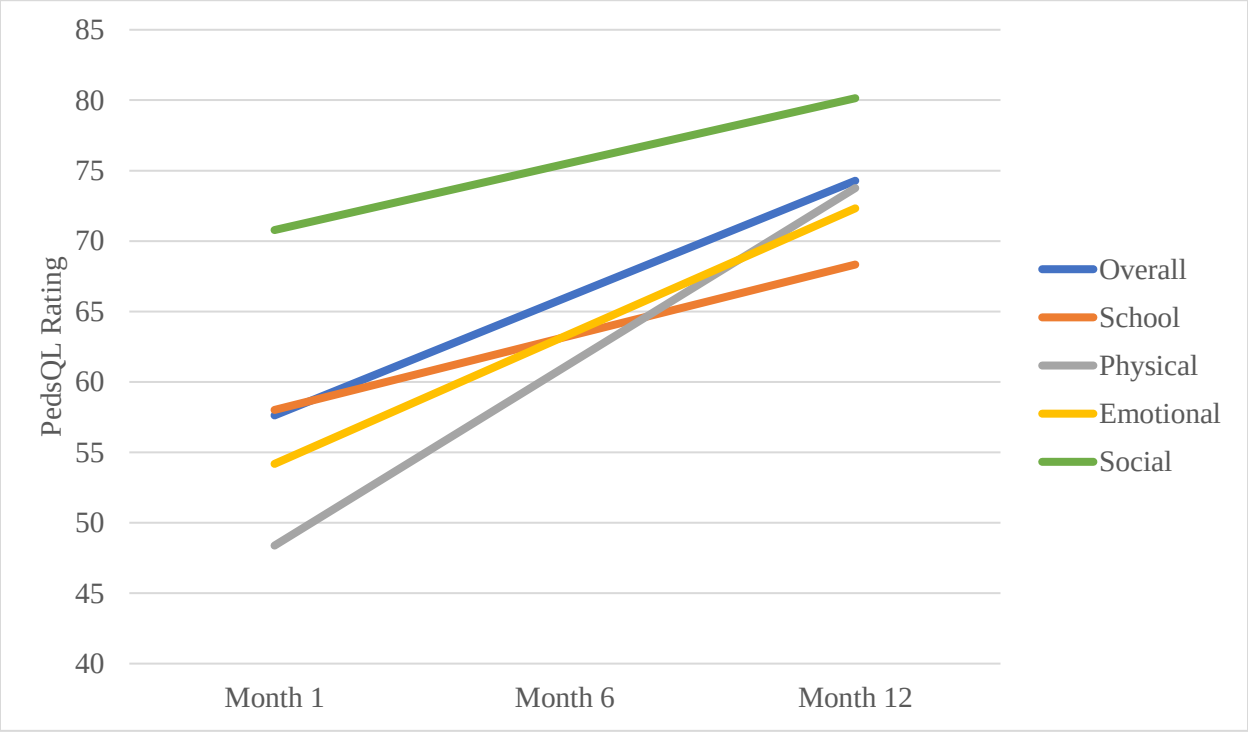


Figure 3

Estimated Trajectories of Overall and Domain-Specific HRQOL During the First Year of Pediatric Cancer Treatment



Note. Higher PedsQL scores indicate better HRQOL.