CHILDHOOD CANCER AND BRAIN TUMOR LATE EFFECTS: THE IMPACT ON FAMILIES AND ASSOCIATED SURVIVOR PSYCHOLOGICAL OUTCOMES

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In honor of the survivors and their families who participated in this research, this work is dedicated to all children and families affected by childhood cancer and brain tumors.

Childhood Cancer and Brain Tumor Late Effects: The Impact on Families and Associated Survivor Psychological Outcomes

Abstract
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Objective: The study aimed to examine associations between long-term side effects (i.e., late effects) of childhood cancer/brain tumors and family factors, specifically general family functioning and the impact of childhood cancer survivorship on families. Mediation and moderation models including late effects and family factors as predictors of survivor psychological outcomes were tested. **Methods:** Survivors (N=65) of any childhood cancer or brain tumor who were ≥ 2 years off-treatment and between the ages of 10-17 years and one parent/caregiver completed measures assessing child emotional and behavioral functioning, general family functioning, and illness-specific family burden. Medical providers documented survivors' late effects. **Results:** Number of survivor late effects and illness-specific family/social burden was positively correlated, $r = .29$, $p < .05$. Parent report of more severe survivor late effects also related to greater illness-specific family/social burden, $r = .56$, $p < .01$. Number of late effects was unrelated to general family functioning and to survivor psychological outcomes, although higher number of late effects associated with at-risk or clinical elevations in symptoms of PTSD, $p < .05$. Support for an indirect effect of number of late effects on parent-reported survivor internalizing problems as mediated by illness-specific family burden was demonstrated, $p < .05$, 95% CI [.24, 2.17]. Indirect effects were not found in models predicting PTSD and externalizing problems. **Conclusions:** Illness-specific family

burden is an important family-based intervention target for reducing risk for internalizing problems in survivors of childhood cancer, particularly in those experiencing late effects.

Childhood Cancer and Brain Tumor Late Effects: The Impact on Families and Associated Survivor Psychological Outcomes

Advances in the treatment of childhood cancer have increased the five-year survival rate to nearly 80% (Rowland et al., 2004). These curative successes have contributed to a growing population of childhood cancer survivors (Hewitt, Weiner, & Simone, 2003). The identification and prevention of treatment-related long-term side effects (i.e., late effects) has become central to childhood cancer survivorship research and healthcare delivery (Landier et al., 2004; Oeffinger & Hudson, 2004; Oeffinger & Robison, 2007). Long-term physical late effects, such as endocrinopathy, cardiomyopathy, infertility, and second malignancies, are well documented in this population (Diller et al., 2009; Geenen et al., 2007). Approximately two-thirds of survivors experience at least one medical late effect (Geenen et al., 2007) and nearly one-third of survivors exhibit cognitive and neuropsychological impairments (Brown et al., 1998; Copeland et al., 1996; Moleski, 2000). With regard to psychosocial outcomes, the majority of childhood cancer survivors fare well; however, a subset of survivors experience adverse psychological sequelae (Hobbie et al., 2000; Schultz et al., 2007). Specifically, those exposed to central nervous system (CNS) insults as a result of the cancer or cancer treatment are at increased risk for adverse psychosocial outcomes (Boman & Bodegard, 2000; Schultz et al., 2007; Zeltzer et al., 2008).

Although a great deal of childhood cancer survivorship research has accumulated throughout recent decades, there is still much to be learned about late effects and the impact of late effects on childhood cancer survivors and their families (Patenaude & Kupst, 2005). The *National Action Plan for Childhood Cancer* has called for continued

psychological research involving childhood cancer survivors at risk for late effects (Arceci et al., 2002), and a report from the Institute of Medicine highlights the lack of research regarding survivor and family psychosocial burden relative to late effects (Hewitt et al., 2003). Despite this call for research, a gap in the literature remains (Hocking et al., 2011; Peterson & Drotar, 2006; Vannatta, Salley, & Gerhardt, 2009). In a review by Peterson and Drotar (2006), no studies were identified that assessed family burden specific to cancer late effects.

According to the social ecology model, social systems (e.g., family, peers, health care system) both influence and are influenced by a developing child (Bronfenbrenner, 1977). Extending this framework to childhood illness (Kazak, 1989), all family members are likely to be affected by the childhood cancer experience. Although burdens associated with caring for a child undergoing cancer treatment are likely to decrease once a child enters survivorship, parents continue to report cancer-related distress long after treatment ends (Boman, Lindahl, & Bjork, 2003). New stressors may develop as late effects emerge. Family functioning, in turn, may also influence the psychological adjustment of survivors (e.g., Kazak & Meadows, 1989; Levin Newby, Brown, Pawletko, Gold, & Whitt, 2000; Rait et al., 1992). By providing a greater understanding of the associations between late effects and family functioning through the proposed research, survivor psychological adjustment may be better understood and future family-based interventions better informed (Peterson & Drotar, 2006).

The proposed study was designed to examine associations between survivor late effects, family factors (i.e., illness-specific family burden, general family functioning), and survivor psychological outcomes. A second aim was to examine mediators and

moderators of the relationship between survivor late effects and survivor psychological outcomes. Guided in part by the *Transactional, Stress and Coping Model* (Thompson, Gil, Burbach, Keith, & Kinney, 1993; Thompson, Gustafson, Hamlett, & Spock, 1992; Thompson & Gustafson, 1996), the hypothesized mediating effects of illness-specific family burden on the relationship between late effects and survivor psychological adjustment was examined (see Figure 1). This model, which was recently utilized to explain the role of parenting stress in predicting poorer behavioral functioning in children with cancer (Colletti et al., 2008), provided a conceptual framework for study hypotheses. Specifically, it was hypothesized that parental appraisals of illness-specific family burden would mediate the relationship between late effects and survivor psychological outcomes. For example, greater family burden due to a child's late effects, such as seeing one's family and friends less or family financial strain due to time lost from work to care for child, may place the child at greater psychological risk when compared to a child whose family does not experience significant burden related to the child's late effects.

Additionally, because the *Disability, Stress, and Coping Model* posits that modifiable risk and resilience factors also play an important role in the adjustment of children to pediatric illness (Wallander et al., 1989; Wallander & Varni, 1992), the moderating role of general family functioning was examined (see Figure 2). This analysis was based upon research that has determined healthier family functioning to be associated with fewer child internalizing and externalizing symptoms in youth newly diagnosed with cancer (Varni, Katz, Colegrove, & Dolgin, 1996) and fewer post-traumatic stress symptoms in adolescent survivors (Alderfer et al., 2009). Similarly, investigations of children recovering from traumatic brain injury have demonstrated the

moderating effects of family burden in predicting greater child behavior problems (Taylor et al., 1999). A similar moderating relationship between late effects and psychological functioning has been proposed in childhood cancer survivors, which suggests that healthier family functioning reduces psychological risk for survivors with late effects (Hocking et al., 2011; Peterson & Drotar, 2006); although, this interactive model had yet to be empirically tested. For example, families with greater problem-solving skills may be better equipped to arrange needed services for their child with late effects, such as establishing an Individualized Educational Plan (IEP) at school, which may help to reduce the negative impact of late effects on a child's functioning.

Childhood Cancer/Brain Tumors and Treatment

Over the past two decades there has been an increase in the incidence of childhood cancer. Despite the increase, childhood cancer remains relatively rare. Approximately 1 or 2 children per 10,000 youth are diagnosed with cancer annually in the United States. In 2007, it was estimated that 10,400 American children ages 0-14 years were diagnosed with cancer. Approximately 1,545 children die from the disease annually, making cancer the leading cause of death for children under the age of 15 (American Cancer Society, 2007). Leukemias and brain/CNS cancers account for approximately half of childhood cancer diagnoses (Ries et al., 2007). Acute lymphoblastic leukemia (ALL) is the most common pediatric cancer, accounting for approximately 25% of all pediatric malignancies (Pui & Evans, 2006) with 4 per 100,000 children diagnosed with ALL each year (Brown, 2006). Acute myeloid leukemia (AML), which occurs less frequently, accounts for 15-20% of childhood leukemias (Rowland et al., 2004). Malignant and non-malignant brain and CNS tumors occur at rates of 5.1

diagnoses per 100,000 children, approximating to 4,300 expected pediatric diagnoses in 2013 (CBTRUS, 2012).

Treatment protocols may vary based on diagnosis, risk, and stage of the cancer and/or tumor. The most common treatment modalities include: chemotherapy, radiation therapy, surgery, and bone marrow transplantation (Brown, 2006). Generally, chemotherapy drugs interfere with the division and multiplication of cancer cells. Common immediate side effects of chemotherapy treatment include: hair loss, low blood counts, nausea/vomiting, skin rashes, fatigue, and mouth sores (Keene, Hobbie, & Ruccione, 2007). While side effects are common to all chemotherapies, an intrathecal method of chemotherapy delivery directly impacts the CNS, increasing risk for long-term negative outcomes (Ness & Gurney, 2007). The CNS serves as a safe haven for leukemia cells to grow and multiply when chemotherapy agents are unable to pass the blood-brain barrier. Thus, CNS prophylaxis is critical in terms of maximizing long-term survival for some childhood cancers (Moleski, 2000).

Radiation therapy is often used when a tumor cannot successfully be treated with chemotherapy and/or surgery alone. Radiation therapy is also used when cancer cells have been detected at time of diagnosis in the CNS of children with leukemia. Immediate side effects of radiation therapy include diminished appetite, fatigue, and skin irritation at the radiation site. Cranial and spinal radiation therapies are associated with long-term risks and cognitive toxicities, including permanent damage to the CNS (Brown, 2006). However, until future therapies for preventing the spread of cancer to the CNS are discovered, radiation therapy remains critical to the survival of children with cancer detected in the CNS or at high-risk for relapse in the CNS (Keene et al., 2007).

Surgery is commonly used to remove tumors; although, many times surgery is combined with other therapies (i.e., chemotherapy, radiation) due to risk of metastases. Bone marrow transplantation, which involves intravenously transplanting marrow from a matched donor or extracted marrow from the patient while in remission, is a treatment modality most commonly used for youth with leukemia or solid tumor cancer. Complications associated with bone marrow transplantation include high-risk for infection and graft-versus-host disease. In some instances, these complications may result in death (Brown, 2006).

Fortunately, advances in these treatment modalities have increased the five-year survival rate for all childhood cancers to nearly 80%, a notable improvement from survival rates of 58% during 1975-1977 (Ries et al., 2007). The use of CNS prophylaxis, combination drug regimens, and maintenance intrathecal chemotherapy (i.e., Methotrexate) has contributed to increasing survival rates (Brown, 2006). It is estimated that 1 in every 640 young adults is a childhood cancer survivor (Hewitt et al., 2003), and this population is growing. However, cure can be costly. Treatment can be associated with long-term late effects, which may emerge years after treatment has ended (Oeffinger & Robison, 2007).

Childhood Cancer Late Effects

Medical Late Effects. Approximately two-thirds of survivors experience at least one medical late effect and a quarter of survivors report experiencing a severe and/or life-threatening condition as a result of their cancer (Geenen et al., 2007; Oeffinger et al., 2006). Childhood cancer survivors are at a three to six times increased risk of developing a second malignancy when compared to healthy controls (Ness & Gurney, 2007).

Endocrine disorders (e.g., growth hormone deficiency, insulin resistance) are also commonly reported. For example, one study of children treated in a late effects clinic documented that 62% of the survivors were diagnosed with endocrinopathies (Hameed & Zacharin, 2005). Impairments to cardiac and pulmonary functioning have also been documented (for review, see Ness & Gurney, 2007). Additional systems impacted by childhood cancer and its associated treatments include: orthopedic, reproductive, neurological, dermatological, renal and sensory-motor. Increased risk for obesity is also experienced by some groups of childhood cancer survivors (Geenen et al., 2007; Gurney et al., 2003; Gurney et al., 2006; Ness & Gurney, 2007; Oeffinger et al., 2003). These medical late effects, which have led experts in the field to consider childhood cancer to be a chronic condition given its long-term implications (Oeffinger & Robison, 2007), contribute to an 11 times increased risk of mortality among survivors when compared to the general U.S. population (Mertens et al., 2001).

Neuropsychological Late Effects. In addition to medical late effects, survivors of childhood cancer are also at increased risk of neuropsychological late effects. A number of studies have examined the long-term intellectual and academic functioning of children who received CNS-directed chemotherapy treatment. The adverse effects of CNS-directed therapies on the neuropsychological functioning of childhood cancer survivors are notable. Researchers have reported declines in full scale IQ (Brown et al., 1992; Giralt et al., 1992; Ochs et al., 1991), performance IQ (Giralt et al., 1992; Schlieper, Esseltine, & Tarshis, 1989), and verbal IQ scores (Ochs et al., 1991).

In a study of 24 survivors of ALL treated with both intrathecal chemotherapy drugs and cranial radiation, Rubenstein and colleagues (1990) discovered significant

declines in IQ scores across the sample. Similarly, a meta-analysis of 13 studies by Peterson and colleagues (2008) found that survivors of ALL who received CNS-directed chemotherapy had significantly lower full scale IQ, performance IQ, and verbal IQ scores. Furthermore, results of the meta-analysis revealed significantly poorer academic achievement in ALL survivors when compared to control groups. Researchers concluded that children receiving CNS-directed chemotherapy are susceptible to neuropsychological late effects, specifically in the areas of perceptual reasoning, working memory, processing speed, math, and reading (Peterson et al., 2008).

Attention and executive functioning deficits are also common late effects experienced by survivors (Moleski, 2000; Waber & Mullenix, 2000; Waber et al., 1995). Reddick and colleagues (2006) reported that while neuropsychological deficits across a number of domains (e.g., intelligence, academic achievement) were observed in a sample of ALL survivors treated with chemotherapy alone, problems with attention were found to be the most significant deficit when survivors' scores were compared to population norms. Deficits in the areas of visual-spatial attention, short-term working memory, visual motor integration, processing speed, and memory have also been identified among survivors of various cancers (Brown et al., 1992; Copeland, Moore, Francis, Jaffe, & Culbert, 1996; Hertzberg et al., 1997; Lesnik, Ciesielski, Hart, Benzel, & Sanders, 1998; Moleski, 2000; Schatz, Kramer, Ablin, & Matthay, 2000; Waber & Mullenix, 2000; Waber et al., 1995). Impairments in academic functioning have also been reported. In a large study of 800 survivors ages 6-16 years and matched controls, survivors were more likely to repeat a grade, attend learning disability or special education programs, and experience other school-related problems (e.g., below average grades) (Barrera, Shaw,

Speechley, Maunsell, & Pogany, 2005). Similar adverse educational outcomes have been reported across the literature (Brown et al., 1998; Haupt et al., 1994; Mitby et al., 2003).

Risk Factors for Medical and Neuropsychological Late Effects. The variability in incidence of late effects has led to the investigation of potential risk factors. With regard to medical and neuropsychological late effects, CNS-directed treatments, such as intrathecal chemotherapy and cranial radiation, put survivors at increased risk for long-term problems when compared to treatment protocols that do not include CNS-directed therapies (e.g., Barrera et al., 2005; Geenen et al., 2007). Additionally, child age at diagnosis, gender, and treatment dosage also pose additional risk factors. Younger age at diagnosis has been found to be associated with increased risk for neuropsychological late effects and academic problems (Copeland et al., 1996; Leung et al., 2000). Female sex has been shown to correlate with poorer long-term cognitive outcomes, such as decreased full-scale IQ (Bleyer et al., 1990; Kato et al., 1993). Similar findings were noted in a meta-analytic review of thirteen studies, with girls performing poorer than boys on measures of full-scale IQ, performance IQ, and verbal IQ (Peterson et al., 2008). Other risk factors associated with medical and neuropsychological late effects include dosage amounts, time since treatment, preexisting conditions (e.g., seizures, Down's syndrome), and treatment complications (Moore, 2005).

Psychological Late Effects. When compared to medical and neuropsychological late effects, the long-term psychological consequences of childhood cancer are not as well understood. Despite the wealth of literature in this area, it has been challenging to make strong conclusions due to inconsistent findings (Marsland, Ewing, & Thompson, 2006; Zebrack et al., 2002). A number of studies have documented normative

psychological functioning in survivors of childhood cancer (e.g., Eiser, Hill, & Vance, 2000; Kazak, Christakis, Alderfer, & Coiro, 1994; Noll et al., 1997), while others have reported an increased risk of psychological maladjustment in a subset of survivors (Hobbie et al., 2000; Schultz et al., 2007; Stuber et al., 1997).

With regard to externalizing behavior problems among child and adolescent survivors, Noll and colleagues (1997) concluded that parent and teacher reported problems are within the normative range. However, despite falling within the normative range, adolescent survivors were 1.7 times more likely than siblings to exhibit parent-reported antisocial behaviors (Schultz et al., 2007). Similarly, when compared to age and gender matched school peers, survivors ages 6-16 years were rated by their parents as having significantly more behavior problems (Olson, Boyle, Evans, & Zug, 1993).

Marsland and colleagues (2006) identified 10 studies that measured depression in survivors of childhood cancer. Some studies reported no significant differences between adolescent and young adult survivors of cancer and control groups (Greenberg, Kazak, & Meadows, 1989; Noll, Bukowski, Davies, Koontz, & Kulkarni, 1993; Teta et al., 1986). However, although it has been reported that depressive symptoms often fall within the normative range (Elkin, Phipps, Mulhern, & Fairclough, 1997; Kazak et al., 1994), survivors of childhood cancer report greater depressive symptoms than their siblings (Schultz et al., 2007; Zebrack et al., 2002). In an investigation of 2,979 adolescent survivors of childhood cancer and their siblings, Schultz and colleagues (2007) found that survivors were 1.5 times more likely than siblings to have symptoms of depression/anxiety. Others have reported that young adult survivors are more likely to report negative mood states, depression, tension, anger, and confusion when compared to

siblings (Zeltzer et al., 1997). Overall, survivors may be at increased risk for depressive symptoms; however, there is little evidence to suggest that they are at increased risk of clinically significant depression. Similarly, research to date suggests that survivors of childhood cancer report levels of anxiety that are comparable to controls and/or population norms (Barakat et al., 1997; Pendley, Dahlquist, & Dreyer, 1997; Sloper & Charlton, 1994).

Notably, it has been suggested that measures of depression and anxiety do not fully capture important emotional aspects of surviving childhood cancer (Kazak, 1998); thus, a number of researchers have examined symptoms of posttraumatic stress disorder (PTSD) among survivors. Current PTSD incidence rates range from 4.5-17% (Barakat et al., 1997; Butler, Rizzi, & Handwerger, 1996; Kazak et al., 1997; Pelcovitz et al., 1998). In a sample composed of childhood leukemia survivors (N=64) ages 7-19 years, 12.5% of youth endorsed severe levels of post-traumatic stress (Stuber, Christakis, Houskamp, & Kazak, 1996). Notably, while many studies report incidence rates within the range reported above, there are a few exceptions. For example, Stuber et al. (1991) found that 50% of a small sample (N = 6) of survivors who underwent a bone marrow transplantat met criteria for PTSD one year after treatment ended. Similarly, an early DSM-IV field trial reported that 35% of adolescent survivors met criteria for lifetime PTSD (Pelcovitz et al., 1998). Incidence rates may also be higher when survivors of childhood cancer reach early adulthood. For example, Hobbie and colleagues (2000) found that 20.5% of their sample of young adult survivors of childhood cancer (N=78) met criteria for current PTSD.

Subclinical symptoms of PTSD are also commonly experienced by survivors. In a sample of childhood cancer survivors ages 12-35, 78% of the sample reported at least one symptom of PTSD that was functionally impairing. Stuber et al. (1996) reported that approximately 52% of their pediatric sample reported feeling afraid or upset when thinking about their cancer experience and 59% reported having bad dreams about their cancer. Intrusion/re-experiencing and avoidance have been found to be the most commonly reported symptoms among survivors (Hobbie et al., 2000; Kazak et al., 2001; Stuber et al., 1996). For example, Kazak et al. (2001) reported that 50% of childhood cancer survivors in their sample met criteria for cluster B (i.e., re-experiencing).

Risk for Factors for Psychological Late Effects. Survivors experiencing medical and/or neuropsychological late effects are at increased risk for poorer psychological adjustment (for review, see Marsland, Ewing, & Thompson, 2006; Patenaude & Kupst, 2005). For example, in a study 138 survivors ages 8 to 16 years, those experiencing severe late effects (e.g., learning delays requiring special education, blindness, alterations in appearance) endorsed greater depressive symptomology, poorer self-concept, and greater external locus of control (Greenberg et al., 1989). Similarly, in a large study of adolescent survivors of childhood cancer (N = 2,979), those treated with intrathecal chemotherapy and/or cranial radiation were identified as being at greatest risk for long-term adverse psychological outcomes (Schultz et al., 2007). In a sample of 88 adolescent survivors, those reporting severe post-traumatic stress symptoms were more likely to have late effects that required continued medical attention (Ozono et al., 2007).

Inconsistencies across the literature make it difficult to conclude if type of cancer, treatment intensity, time off treatment, age at diagnosis, and sex moderate the

relationship between childhood cancer and psychological adjustment (Marsland et al., 2006). For example, some have reported that males are at greatest risk for adverse psychosocial outcomes (Kazak et al., 1994; Teta et al., 1986), while others have suggested that females are at greatest risk (Zebrack et al., 2002; Zeltzer et al., 1997). Similar inconsistencies have been reported regarding associations between age at diagnosis and psychological outcomes (e.g., Eiser & Havermans, 1994; Kupst et al., 1995). Lower family income or socioeconomic status has been found to be associated with more negative psychological outcomes (e.g., Barakat et al., 1997; Eiser & Havermans, 1994; Kupst et al., 1995; Zebrack et al., 2002). In a large study of 5,736 young adult survivors of childhood cancer and their siblings (N = 2,565), only socioeconomic variables (i.e., lower income, less education, umemployed) and survivor sex (i.e., female) predicted depressive and somatic symptoms (Zebrack et al., 2002).

Families of Childhood Cancer Survivors

Consistent with the family systems framework that has been applied to childhood chronic conditions (Kazak, 1989), childhood cancer has been referred to as a family disease (Chesler & Barbarin, 1987). Although burdens associated with caring for a child undergoing cancer treatment are likely to decrease once a child enters survivorship, new stressors may develop as late effects emerge. These families are at risk of long-term adverse psychological distress, even after treatment ends (Boman et al., 2003).

A subset of families of survivors struggle to maintain normative family functioning (Alderfer et al., 2009; Cohen, Friedrich, Jaworski, Copeland, & Pendergrass, 1994; Rait et al., 1992). When compared to population norms, 50% of an adolescent survivor population reported their overall family functioning to be poor (e.g., poor

communication, difficulties with problem-solving). Similarly, 35% of mothers' and 38% of fathers' reports of their general family functioning fell in the clinically "unhealthy" range (Alderfer et al., 2009). In a sample of 88 adolescent survivors, 40% of respondents viewed their families as significantly more disengaged and lacking in cohesiveness when compared to a normative sample (Rait et al., 1992). Similarly, a meta-analytic review of the pediatric cancer literature determined that mothers of children with cancer (14 days to 16.4 years since diagnosis) perceive greater family conflict than mothers of healthy children (Pai et al., 2007). With regard to illness-specific family burden, reports of objective caregiver burden was similar among parents of children undergoing active treatment for brain tumors (N = 90) and parents of children off-treatment (N = 43); however, illness-specific total family burden was greater in families of children actively undergoing treatment (Hutchinson, Willard, Hardy, & Bonner, 2009). Overall, Hutchinson and colleagues (2009) proposed that as late effects emerge, family and caregiver burden may increase.

In a recent study, mothers reporting a greater number of medical and psychosocial late effects (i.e., 7 or more late effects) experienced by their child were also more likely to endorse greater family dysfunction when compared to parents of survivors with minimal late effects (Peterson, Cousino, Donohue, Schmidt, & Gurney, 2012). Van Dongen-Melman and colleagues (1995) found that parental distress (e.g., negative feelings and perceived loss of control) was related to invisible late effects (e.g., infertility) and school-related problems in their sample of 133 parents of survivors ages 8 to 12 years. Qualitative research also supports this likely association (e.g., Deatrick, Mullaney, & Mooney-Doyle, 2009; Patterson, Holm, & Gurney, 2004). For example, in

a sample of 26 families of children one or more years off-treatment, 77% of families indicated that fears of relapse, invasive thoughts about cancer, and uncertainties about the future were burdening for their family. Specific to late effects, approximately 23% of families endorsed family strain associated with cancer-related losses (e.g., fertility, functional impairment, limb loss). Nearly 12% of families reported long-term strain as a result of emerging child attention problems (Patterson, Holm, & Gurney, 2004). Thus, researchers have suggested an association of late effects with negative family outcomes, but more definitive study of these possible relationships is needed (Deatrick et al., 2009; Hocking et al., 2011; Hutchinson et al., 2009; Patterson et al., 2004; Peterson et al., 2012; Peterson & Drotar, 2006).

Specifically, Greenburg and colleagues (1989) called for research that investigates family factors associated with psychological adjustment in survivors. According to the family systems perspective (Kazak, 1989), negative effects on family functioning may in turn have adverse effects on survivor psychological adjustment. A number of studies have demonstrated associations between parental distress, family dysfunction, and poorer emotional, behavioral, and social functioning among survivors (Kazak et al., 1997; Levin Newby et al., 2000; Rait et al., 1992; Robinson, Gerhardt, Vannatta, & Noll, 2007; Sloper, Larcombe, & Charlton, 1994). For example, in a longitudinal investigation of 63 children with brain tumors, greater family stressors predicted more child internalizing and externalizing behavior problems approximately 24 months post-baseline (Carlson-Green, Morris, & Krawiecki, 1995). Less family cohesion and adaptability are associated with poorer psychological outcomes in survivors (Kazak & Meadows, 1989; Levin Newby et al., 2000; Rait et al., 1992). Although greater family cohesion is associated with better

survivor psychological outcomes, Rait and colleagues (1992) reported lower mean levels of family cohesion among a group of adolescent survivors and their families when compared to normative samples. Open family communication is associated with fewer internalizing symptoms, and less family conflict is correlated with fewer behavior problems (Phipps & Mulhern, 1995).

Parental reactions and family functioning are also important predictors of child adjustment following trauma exposure (Pfefferbaum, 1997). Across the broader child PTSD literature, family variables, such as less family cohesion and greater family chaos, are associated with higher rates of child PTSD (for review, see Scheeringa & Zeenah, 2001). Some have suggested that parental response to the event and alterations in family functioning better predict child post-traumatic stress symptoms than the child's direct exposure to the trauma (McFarlane, 1987). Relationships between family functioning and post-traumatic stress symptoms have been examined in childhood cancer survivor populations. In a sample of 130 leukemia survivors ages 8-20 years, maternal ratings of poorer general family functioning was associated with greater post-traumatic stress symptoms in survivors (Kazak et al., 1997). Similarly, in a sample of 144 adolescent survivors, 75% of survivors with a diagnosis of PTSD were from families who reported poorer overall family functioning (Alderfer et al., 2009). Others have found similar associations between family functioning and post-traumatic stress symptoms in survivors (Ozono et al., 2007; Pelcovitz et al., 1998).

The importance of family factors with regards to child response to trauma is well-established across the broader PTSD literature. However, research of this nature specific to childhood cancer survivors remains underdeveloped. Additional investigations are

needed (Alderfer et al., 2009). Calls for future studies that examine post-traumatic stress and family functioning in child illness populations have been made to better inform clinical practice (Kahana, Feeny, Youngstrom, & Drotar, 2006).

Significance

Overall, this study was designed to address the call for research to examine family burden associated with survivor late effects (Hewitt et al., 2003) and its relation to psychological adjustment in children who have had cancer. The literature suggests that family functioning and survivor psychological outcomes are related, but possible associations between late effects and family factors are not as well understood (Peterson & Drotar, 2006; Vannatta et al., 2009). Drotar (1997) emphasized the importance of testing mediating and moderating models that include illness-specific assessments to better understand the relationships between family factors and child psychological functioning. To our knowledge, this is the first study to have examined interactive models that included late effects and family functioning (i.e., illness-specific family burden, general family functioning) to predict survivor psychological outcomes. The primary goal of the study was to examine late effects on family functioning and how family outcomes, in turn, influence general child emotional and behavioral functioning and post-traumatic stress symptoms in survivors. In addition to examining how interactions between late effects and family functioning may influence general child emotional and behavioral functioning, the current study specifically examined how family factors are associated to post-traumatic stress symptoms in survivors, a population at increased risk for the development of PTSD (e.g., Stuber et al., 1996 Pelcovitz et al., 1998).

The development of interventions aimed at ameliorating adverse psychosocial outcomes for survivors and their families was named a research priority by the Institute of Medicine (Hewitt et al., 2003). The current research is positioned to provide an improved understanding of family risk and resilience factors, which will consequently lead to the development of more tailored interventions to prevent or minimize risk of psychosocial morbidity in survivors experiencing late effects. Investigations of these factors is consistent with recommendations from researchers who have highlighted the importance of identifying families at greatest risk for poorer psychosocial outcomes and providing targeted interventions for this group (Kazak, 2005). For example, a family that is not highly adaptable may experience greater challenges and distress related to the child's emerging late effects. These families may be less likely to make appropriate adjustments to changes in their child's functioning (e.g., impaired attention, decreased academic achievement). By identifying problems in family functioning, clinicians can work with at-risk families to problem-solve ways to manage late effects and their sequelae with an overarching goal of preventing or reducing long-term adverse psychosocial outcomes.

Aims & Hypotheses

The current study had two main objectives, both of which addressed the need for research on the influence of families on long-term outcomes of childhood cancer (Hewitt et al., 2003; Hocking et al., 2011; Peterson & Drotar, 2006; Vannatta et al., 2009). First, the study aimed to examine associations between survivor late effects, family factors (i.e., illness-specific family burden, general family functioning), and survivor psychological outcomes (Aim 1). It was hypothesized that families of survivors with a greater number

of late effects would experience greater illness-specific family burden (Hypothesis 1a), have poorer general family functioning (Hypothesis 1b), and have poorer psychological outcomes (i.e., greater externalizing, internalizing, and post-traumatic stress symptoms) (Hypothesis 1c).

Second, this study aimed to examine family factors as predictors and moderators of the relationship between survivor late effects and survivor psychological outcomes (Aim 2). It was hypothesized that illness-specific family burden would mediate associations of survivor late effects with survivor psychological outcomes (i.e., greater externalizing, internalizing, and post-traumatic stress symptoms) (Hypothesis 2a). Secondly, it was hypothesized that the relationship between late effects and survivor psychological outcomes would be moderated by general family functioning, such that healthier family functioning would attenuate the relationship between greater number of late effects and adverse survivor psychological outcomes (Hypothesis 2b).

Method

Recruitment and Participants

The University Hospitals Institutional Review Board and Case Comprehensive Cancer Center Protocol Review and Monitoring Committee approved the study. Care providers (i.e., nurses, physicians) in the Center for Childhood Cancer Survivors Long-Term Follow-Up Clinic at Rainbow Babies and Children's Hospital, Cleveland, Ohio, identified potential participants and explained that they were eligible to participate in a study about childhood cancer and brain tumor late effects and their impact on families and survivors. Long-Term Follow-Up Clinic staff first obtained verbal consent from eligible participants to be approached by IRB-approved research staff. Once verbal

consent was obtained, IRB-approved research staff met with eligible participants during their clinic visit and described the study. Questions were answered and families were informed that their participation in the study was voluntary. Written consent was obtained from participating parents/caregivers. Youth participants provided written assent.

The study sample consisted of 65 childhood cancer and brain tumor survivors ages 10-17 years and one parent/caregiver recruited from the Long-Term Follow-Up Clinic at Rainbow Babies and Children's Hospital, which provides care for approximately 250 childhood cancer and brain tumor survivors ranging from infancy to 35 years of age. For the purposes of this study, survivorship was defined as survival for two or more years post-treatment. Due to the small sample of childhood cancer survivors in the general population, survivors of all cancer types and brain tumors were eligible to help insure an adequately powered study. This was consistent with the inclusion criteria employed by previous research in this area (e.g., Alderfer et al., 2009; Phipps & Mulhern, 1995). Eligibility was restricted to English-speaking youth and caregivers due to the lack of psychometric data on the translation of study measures to other languages.

Survivor characteristics, including information on the type and treatment of cancer, are summarized in Table 1. The most common cancer diagnoses were ALL (36.9%) and brain/CNS cancers (26.2%), such as astrocytoma, medulloblastoma, and optic pathway glioma (see Table 1). The majority (86.2%) of participants received chemotherapy as part of their treatment regimen. Approximately half (52.3%) of the sample underwent a major surgery, such as tumor resection or organ removal, and 27.7% of the participants received radiation.

Demographic and socioeconomic characteristics of youth and families are listed in Tables 1 and 2. Youth participants had a mean age of 14.13 years (*SD* = 2.07; Range 10.58-17.93) with 52.3% of the sample being female (see Table 1). Mean age at diagnosis was 6.16 years (*SD* = 3.46; Range 2.59-16.39) and youth participants were on average 6.21 years off-treatment (*SD* = 2.83; Range 2.22-14.57). Parent/caregiver participants were most commonly biological mothers (76.9%). Per parent/caregiver report, approximately 73.8% of the youth sample was White/Caucasian. The majority of the youth participants lived in two-parent (64.6%) or single-parent (18.5%) homes. The sample was socioeconomically diverse with nearly half of the sample reporting annual family incomes of $50,000 or less (48.4%) and approximately 20% of the sample reporting family incomes of greater than $100,000 annually. The majority of mothers completed some college or received a collegiate degree (73.9%). The same was true for many fathers (56.3%).

Of the 82 eligible survivors (i.e., those who attended a clinic visit and met all inclusion criteria), 76 were approached, 74 agreed to participate, and 65 completed the study (86% participation rate). The remaining eligible participants either declined to participate (N = 2) or were not approached due to IRB-research staff being unavailable for recruitment at clinic (N = 5). One additional eligible survivor was not approached, as the patient and family were being presented with news of a possible relapse at the appointment. Of the 74 consenting survivors and their families, nine families did not return their completed packets. There were no significant group differences in cancer or treatment type between those who completed the study and the nine participants whose

packets were not returned. Survivor and family demographic data were not available for non-participants.

Procedures

Upon providing written consent and assent, participants completed a packet of self-administered, paper-pencil questionnaires during or immediately following their outpatient clinic visit. The packets took youth and caregivers approximately 30-50 minutes to complete. IRB-approved research staff answered questions, helped child participants complete the questionnaires, and checked study packets for completeness. All attempts were made for study questionnaire packets to be completed while the family was at the outpatient clinic; however, participants unable to complete all instruments in clinic were offered the opportunity to complete the questionnaires at home and return the completed packets by mail in a pre-stamped envelope. Parent and youth participants each received a $10 gift card for their time upon completing study questionnaires.

Background & Demographic Questionnaire. The investigator-designed demographic questionnaire was used to gather family background and demographic information (e.g., race/ethnicity, family structure, family income, parent educational background). Parents provided demographic information about their child (e.g., age, sex) and reported on their child's educational background (e.g., academic performance, learning problems). Parents also rated how intense they believed their child's cancer treatment was and how severe they perceived their child's current late effects to be on a 4-point Likert scale with higher scores indicating greater intensity/severity. These two items were taken from the parent version of the Health Knowledge Inventory (HKI; Schwartz et al., 2010). Parent report of severity of late effects was used in correlative

analyses to test associations between late effects, family factors, and survivor psychological outcomes.

Family Assessment Device, General Functioning Scale (FAD-GF; Epstein, Baldwin, & Bishop, 1983). The total score from the 12-item parent-reported FAD-GF, a subscale of the Family Assessment Device (FAD), was used to assess general family functioning (e.g., problem-solving, communication). Parents rated the extent to which each statement described their own family along a 4-point Likert scale ranging from "strongly agree" to "strongly disagree." Higher scores indicated "unhealthy" family functioning. Evidence for validity is provided by correlations of the FAD with the Family Adaptability and Cohesion Evaluation Scale (FACES-II; Olsen, Portner, & Lavee, 1985; Miller, Epstein, Bishop, & Keitner, 1985). Factor analysis revealed that the FAD-GF highly correlates with the first principal component of the other six subscales (48 items) of the FAD, demonstrating its appropriateness as a comprehensive measure of overall family functioning (Kabacoff, Miller, Bishop, Epstein, & Keitner, 1990). The FAD-GF has demonstrated high internal consistency with a Cronbach's alpha coefficient of .92 reported (Epstein et al., 1983; Miller et al., 1985). In the current study, the Cronbach's alpha coefficient for the FAD-GF was .88.

Impact-on-Family Scale (IOF; Stein & Riessman, 1980). The 33-item parent-reported IOF was used to assess the impact of the child's health condition on the family system. Instructions were adapted to emphasize the impact of the child's current state (i.e., late effects) on the family. Subscales include Financial Burden, Familial/Social Impact, Personal Strain, and Mastery. A Total score is obtained from summing all subscales. In the current study, the Financial Burden, Familial/Social Impact, and

Personal Strain subscales, as well as the Total score, were used to test associations between late effects and measures of family impact. The Financial Burden subscale measures the extent to which a child's current medical condition causes economic stress on the family (e.g., "Additional income is needed in order to cover medical expenses"). The Family/Social Impact subscale, which was also used as the measure of illness-specific family burden in mediation analyses, assesses the degree to which a child's current medical condition impacts the family and social systems (e.g., "I don't have much time left over for other family members after caring for my child," "We see family and friends less because of the illness"). The Personal Strain subscale measures primary caretaker burden directly related to the child's medical condition (e.g., "Fatigue is a problem for me because of my child's illness"). A Total score is obtained from summing these subscales, along with the Mastery subscale.

Items are scored along a 4-point Likert scale ranging from "strongly agree" to "strongly disagree." Higher scores indicated a greater negative impact of the child's health condition on the family. Internal consistencies of the three subscales used range from .72-.89 (Stein & Jessop, 2003; Stein & Riessman, 1980). The Cronbach's alpha coefficient for the IOF total score in current study was .91 and internal consistencies of the three subscales used were: Financial Burden (α = .84), Familial/Social Impact (α = .86), and Personal Strain (α = .82). Validity of the IOF has been demonstrated via correlations with measures of maternal psychological functioning (e.g., Psychiatric Symptom Index; Ilfeld, 1976) (r = .47), poorer child psychological functioning (e.g., Personal Adjustment and Role Skills Scale; Ellsworth, 1979) (r = -.41), and poorer child heath status (r = -.39) (Stein & Jessop, 2003).

Behavior Assessment System for Children, Second Edition (BASC-2; Reynolds & Kamphaus, 2004). The BASC-2 provided a comprehensive assessment of child behavioral and emotional functioning. Parent scores on the Externalizing Problems scale and both parent and child report on the Internalizing Problems scale were used in the current study to assess survivor psychological adjustment. The child self-reported instrument for ages 8-11 years includes 139 items, and the adolescent version for ages 12-21 includes 176 items. The parent-reported instrument contains 150-160 items depending on the age of the child. Respondents rated behaviors along a 4-point Likert scale ranging from "never" to "almost always." Raw symptom counts were used as the continuous variable. High internal consistencies (.70-.80) and good reliability estimates (.80-.90) have been reported. Validity has been demonstrated via associations with the Achenbach System of Empirically Based Assessment Child Behavior Checklist (Achenbach & Rescorla, 2001; Reynolds & Kamphaus, 2004).

Child PTSD Symptom Scale (CPSS; Foa, Johnson, Feeny, & Treadwell, 2001). The youth-reported CPSS includes 17 items corresponding to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for PTSD. It was adapted to assess symptoms of PTSD specific to the childhood cancer experience. Items are scored along a 4-point Likert scale ranging from "not at all or only at one time" to "5 or more times a week/almost always" to determine how often a child has experienced symptoms of PTSD in the past two weeks. Total scores range from 0-51, and a clinical cut-off score of ≥11 is used to identify children experiencing a significant number of PTSD symptoms. High internal consistency (.70-.89) and good test-retest reliability (.63-.85) have been reported. The Cronbach's alpha coefficient for the current study was .81. Construct

validity has been demonstrated via associations (r = .80) with the Child Posttraumatic Stress Disorder Reaction Index (Pynoos et al., 1987, Foa et al., 2001).

Health Knowledge Inventory (HKI) (Schwartz et al., 2010). The provider-completed 35-item HKI measure was used as a comprehensive assessment of survivor late effects. IRB-approved medical providers (i.e., nurse or physician) completed the HKI following a participant's outpatient medical visit, indicating whether or not a participant had or is currently experiencing late effects (i.e., side effects) due to their cancer. Examples of late effects indicated on the HKI include growth problems, infertility, vision impairments (e.g., blindness), and significant scarring. Psychological late effects measured by the HKI were not included due to the overlap with the outcome variables of interest. The provider version of the HKI has been used in previous studies involving childhood cancer survivors (Hocking et al., 2012; Kazak et al., 2010; Schwartz et al., 2010); however, psychometric properties have not been reported.

Data Analysis

To protect confidentiality, all participants were given a study code number and de-identified data were stored in a secured filing cabinet. Study data was managed using Research Electronic Data Capture (REDCap; Harris et al., 2009) tools hosted at Case Western Reserve University, which is a secure, web-based, data capture application. All data were double-checked and validated by two separate coders. Only IRB-approved research staff that underwent a formal background check and completed hospital-based research training had access to paper-based and electronic data.

Descriptive Analyses

Statistical analyses were performed using the Statistical Software Package for the Social Sciences (SPSS, v. 21.0). Within-case mean imputation was used to handle missing data due to non-response (Little & Rubin, 2002), which occurred in <1% of all data. Demographic characteristics were described using summary statistics (e.g., frequencies, percents, mean, standard deviation). Associations between demographic characteristics, family factors, and survivor psychological outcomes were examined using Pearson correlations when variables were continuous. Point biserial correlations were used when one variable was continuous and the other was binary. Phi coefficients were calculated to detect associations between two binary variables. Relationships between cancer characteristics (e.g., age at diagnosis, time since diagnosis, treatment type), family factors, and survivor psychological outcomes were also examined using Pearson correlations, point biserial correlations and Phi coefficients.

Associations Between Late Effects, Family Factors, and Survivor Psychological Outcomes.

Pearson correlations were computed to test the hypothesis that a greater number of survivor late effects would be associated with greater illness-specific family burden (Hypothesis 1a) and poorer general family functioning (Hypothesis 1b). Pearson and point biserial correlations were also used to test the hypothesis that a greater number of survivor late effects would be associated with poorer survivor psychological outcomes (i.e., internalizing problems, externalizing problems, post-traumatic stress) across the continuum of symptom ratings (Hypothesis 1c) and as indicated by presence of at-risk or clinically elevated survivor psychological problems (secondary analyses). These

relationships were also examined using parent rating of late effects severity as an alternative measure of survivor late effects.

Survivor sex, majority racial/ethnic status, and parental education were unrelated to survivor psychological outcomes; therefore, these factors were not controlled for in regression analyses. Survivor age was only correlated with youth-report of internalizing problems, and therefore, was controlled for in models predicting self-reported internalizing problems. Family income was not significantly correlated with parental report of internalizing or externalizing symptoms. However, family income was negatively associated with youth report of internalizing symptoms and PTSD symptoms. Family income was controlled for in regression analyses predicting youth report of internalizing symptoms and PTSD symptoms.

Does Illness-Specific Family Burden Mediate the Relationship Between Number of Late Effects and Survivor Psychological Outcomes?

A non-parametric bootstrapping approach (Preacher & Hayes, 2004; 2008) was used to test the hypothesis that the association between survivor late effects and survivor psychological outcomes, as measured by the BASC-2 and CPSS, is mediated by illness-specific family burden (Hypothesis 2a). Preacher and Hayes (2004) argue that this approach is superior to the commonly used Baron and Kenny (1986) approach for testing mediation, which is reportedly flawed by its (a) criterion of a significant total effect of the independent variable on the dependent variable, (b) requirement that mediation is only indicated if this association is non-significant after including the proposed mediator, and (c) low statistical power (Krause et al., 2010; MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002). The non-parametric bootstrapping approach can be utilized in smaller

samples with greater confidence as this approach examines whether the difference between the c and c' paths (See Figure 1) is statistically significant without requiring a normal distribution of the cross product. Separate significance tests of the a and b paths are not required in this approach (Figure 1; Preacher & Hayes, 2004; 2008). Indirect effects can still be found despite nonsignificant paths and lack of support for complete mediation (Preacher & Hayes, 2004).

The INDIRECT macro (Preacher & Hayes, 2008) for SPSS was used to conduct the non-parametric bootstrapping mediation analyses via ordinary least squares regression. As shown in Figure 1, this method tests the following: (a) the relationship between the independent variable and the proposed mediator (i.e., a coefficient), (b) the relationship between the proposed mediator and the dependent variable (i.e., b coefficient), (c) the relationship between the independent variable and the dependent variable (i.e., c coefficient; direct effect), and (d) the relationship between the independent variable and the dependent variable when controlling for the proposed mediator (i.e., c' coefficient; indirect effect). Indirect effects are evidenced by a statistically significant a*b = c – c' value. Furthermore, when determining mediation, the confidence interval for the indirect effect cannot contain zero (Preacher & Hayes, 2004; 2008; Hayes, 2013). Four mediation models were tested in primary analyses, one for each of the parent- and self-report measures of survivor psychological functioning.

Does General Family Functioning Moderate the Relationship Between Number of Late Effects and Survivor Psychological Outcomes?

Hierarchical linear regression analyses were used to test the hypothesis that the association between survivor late effects and survivor psychological outcomes is

moderated by general family functioning (Hypothesis 2b). Univariate normality of continuous variables was assessed and all variables were determined to be normally distributed (West, Finch, & Curran, 1995). The guidelines outlined by Aiken and West (1991) were used to test the hypothesized moderating model. Independent variables were standardized (i.e., converted to z-scores) to reduce multicollinearity. Covariates (i.e., family income and youth age when appropriate) were entered in the first step. Independent variables (i.e., late effects, general family functioning) were entered in the second step, and interaction terms were entered in the third step. Four regressions were performed to test for moderation. The assumption of multicollinearity for regression analysis was met based upon examination of tolerance, variance inflation factor and correlations among independent variables. No multivariate outliers were found based upon examination of Cook's distances. Investigation of the Normal Probability Plots revealed that all assumptions of homoscedacity, linearity, and multivariate normality were met (Tabachnick & Fidell, 2007). Post-hoc probing of simple slopes was conducted (Aiken & West, 1991; Holmbeck, 2002).

Secondary Analyses

Furthermore, to better understand associations between late effects and family factors and their potential influence on survivor psychological problems, secondary analyses were conducted to examine predictors of rates of at-risk or clinically significant survivor psychological problems (i.e. where psychological outcomes were considered as binary rather than continuous traits). For survivor internalizing and externalizing problems, T-scores on the BASC-2 were dichotomized (i.e., 1 or 0) to indicate clinically at-risk or significantly elevated symptoms (T-scores ≥60) versus no clinical elevations

(T-scores ≤59). For survivor PTSD risk, CPSS scores were dichotomized (i.e., 1 or 0) based upon the clinical cut-off score of ≥11 to identify youth with clinically significant levels of PTSD symptoms (Foa et al., 2001). Previous research supports investigation of family factors in association with clinically significant child psychological outcomes. For example, in a previous study of adolescent survivors of various cancers (Alderfer et al., 2009), the presence of PTSD was used in analyses instead of a continuous measure of symptoms of post-traumatic stress due to lack of consistent associations between family functioning and subthreshold symptom levels (Barakat et al., 1997; Brown, Madan-Swain, & Lambert, 2003). The PROCESS macro for SPSS (Hayes, 2013), which is similar to the INDIRECT macro (Preacher & Hayes, 2008) utilized in primary meditational analyses, allows for the use of dichotomized outcomes and was applied to examine mediating influences on the presence/absence of at-risk or clinically significant youth emotional and behavioral problems.

Secondary regression analyses were conducted to further test the association between number of late effects and illness-specific family burden when controlling for treatment type. Similar regression analyses were conducted to test the association between number of late effects and at-risk or clinically significant PTSD symptoms when controlling for treatment type. The purpose of these analyses were to determine if number of late effects was related to family or child outcomes independent of treatment type.

Results

Sample Description, Variable Associations, and Family and Survivor Outcomes

Survivor Psychological Outcomes and Associations with Demographic Characteristics. Correlations between demographic characteristics and survivor psychological outcome variables are reported in Table 3. Lower family income related to greater survivor-reported internalizing symptoms, $r = -.31$, $p < .05$, and presence of at-risk or clinically significant internalizing problems, $r = -.33$, $p < .01$. Similarly, lower family income was associated with greater survivor reported PTSD symptoms, $r = -.39$, $p < .01$, and presence of at-risk or clinically significant PTSD, $r = -.30$, $p <. 05$. Family income was unrelated to parent report of survivor internalizing and externalizing problems. Youth age was positively correlated with survivor reported internalizing symptoms, $r = .36$, $p < .01$, but unrelated to other survivor psychological outcomes. Racial/ethnic majority status was unrelated to survivor psychological outcomes. Similarly, parental education was unrelated to survivor psychological outcomes, with the exception of paternal education being negatively correlated survivor PTSD symptoms, $r = -.27$, $p < .05$.

Descriptive data on survivor psychological outcomes are provided in Table 4. With regard to outcome measurements, the parent-reported mean T-score on the Internalizing subscale of the BASC-2 was 54.28 ($SD = 12.05$) with 28.1% of the sample having clinically at-risk or significantly elevated internalizing symptoms (T-score ≥ 60). The parent-reported mean T-score on the Externalizing subscale of the BASC-2 was 47.94 ($SD = 8.07$) with only 6.3% of the sample having clinically elevated scores on this subscale. The youth-reported mean T-score on the Internalizing subscale of the BASC-2 was 46.77 ($SD = 9.12$). One-tenth of youth respondents (10.8%) endorsed internalizing symptoms in the clinically at-risk or significant range. The mean score on the youth-

reported CPSS measure, which was utilized to assess symptoms of post-traumatic stress was 8.89 (*SD* = 6.57). Notably, one-third of youth respondents (33.8%) self-endorsed clinically significant levels of PSTD symptoms specific to their cancer experience.

Family Factors and Associations with Demographic Characteristics. Correlations between family factors and demographic characteristics are also presented in Table 3. Older child age positively correlated with more problematic general family functioning, $r = .37$, $p < .01$, and greater illness-specific caregiver burden, $r = .26$, $p < .05$. Lower family income related to greater illness-specific family financial burden, caregiver burden, and total burden. Survivor sex and parental education level were unrelated to family factors. With the exception of greater illness-specific family financial burden, survivor racial/ethnic status was also unrelated to family factors. Descriptive data on family outcomes are provided in Table 5. Based upon one parent/caregiver report, 30.8% of participating families endorsed "unhealthy" family functioning according to the FAD-GF cut-off score (Miller et al., 1985).

Associations of Cancer-Related Characteristics with Late Effects, Family Factors and Child Outcomes. As shown in Table 6, few associations were found between cancer characteristics and survivor psychological outcomes. Greater treatment intensity as reported by parents related to clinically significant survivor-reported PTSD symptoms, $r = .26$, $p < .05$. Presence of cranial radiation treatment correlated with greater survivor-reported PTSD symptoms, $r = .28$, $p < .05$, and parent-reported externalizing symptoms, $r = .34$, $p < .01$. Bone marrow transplant treatment positively related to greater survivor internalizing symptoms, $r = .35$, $p < .01$, and PTSD symptoms, $r = .34$, $p < .01$, as reported by youth participants. Survivor psychological outcomes were

unrelated to age at diagnosis, time since end-of-treatment, surgical treatment, and Methotrexate chemotherapy treatment.

Cancer characteristics, such as treatment type, were also largely unrelated to family factors. Exceptions to this include associations of older age at diagnosis with more problematic general family functioning, $r = .28$, $p < .05$; cranial radiation with greater illness-specific family burden, $r = .30$, $p < .05$, and total burden, $r = .26$, $p < .05$; and Methotrexate chemotherapy treatment with better family functioning and less illness-specific family burden.

Number of Late Effects and Parent Ratings of Severity of Late Effects. On average, participants in the current study experienced 2.08 (*SD* = 3.00) late-effects as a result of their cancer. However, 20% of the sample experienced greater than five late effects, with some having as many as 11 late effects resulting from their cancer experience. The most common late effects experienced by participants included: cognitive late effects (32.3%), scarring (24%), vision problems (15.4%), and hearing problems (13.8%). The mean parent-reported rating of late effects severity was 1.98 (*SD* = 1.10). With regard to parent/caregiver report of late effects severity, 12.3% of survivors had "extremely serious" late effects, 18.5% had "moderately serious" late effects, 24.6% had "somewhat serious" late effects, and 44.6% of survivors had "minimally serious" late effects. Parent-report of late effects severity positively correlated with provider report of number of late effects, $r = .42$, $p < .01$. The mean parent-reported rating of treatment intensity was 2.80 (*SD* = .80). The majority of parent/caregivers described their child's treatment as "moderately intense" (33.8%), "very intense" (43.1%) or "most intense" (20.0%). Only 3.1% of parent/caregivers

reported that their child's treatment was "least intense." Parent report of treatment intensity positively correlated with provider report of number of late effects, $r = .27$, $p < .05$.

Hypotheses Testing

Associations Between Late Effects and Family Factors. Table 7 presents results of analyses testing associations between number of late effects and family and survivor outcomes. In support of hypotheses (Hypothesis 1a), a significant positive association between number of late effects and illness-specific family burden was observed, $r = .29$, $p < .05$, as measured by the Family/Social Subscale of the IOF. Further analyses revealed that when controlling for presence of radiation and Methotrexate chemotherapy treatment, neither these treatment variables, nor the number of late effects significantly predicted illness-specific family burden. Analyses failed to detect an association between number of late effects and illness-specific total family burden (IOF Total Score). Correlative analysis did not support the hypothesized relationship between greater number of late effects and poorer general family functioning.

To further examine the potential role of late effects, secondary analyses were conducted to include parent-report of severity late effects. Parent report of more severe late effects related to "unhealthy" family functioning, $r = .36$ $p < .01$, as determined by the cut-off score of the FAD-GF (Miller et al., 1985). With regard to illness-specific family burden, parent report of more severe late effects related to greater illness-specific total family burden, $r = .51$, $p < .01$. Parent report of more severe late effects was also positively correlated with greater illness-specific family financial burden, $r = .42$, $p < .01$,

greater illness-specific family/social burden, $r = .56$, $p < .01$, and greater illness-specific caregiver burden, $r = .49$, $p < .01$. Notably, these correlations are moderately high, indicating strong relationships between parental perceptions of late effects severity and illness-specific family burden.

Associations Between Late Effects and Survivor Psychological Outcomes. Generally, results failed to demonstrate hypothesized associations between number of late effects and survivor psychological outcomes (Hypothesis 1c). Survivor-reported internalizing problems, parent-reported internalizing problems and parent-reported externalizing problems were unrelated to number of late effects. Similarly, secondary analyses failed to reveal associations of parent-report of severity of late effects with survivor psychological outcomes. However, as shown in Table 7, a positive correlation was detected in secondary analyses examining associations of the number of late effects with rates of at-risk or clinically elevated symptoms of PTSD, $r = .25$, $p < .05$. Further analyses revealed that when controlling for treatment intensity and presence of bone marrow transplant treatment, neither these variables, nor number of late effects significantly predicted at-risk or clinically elevated symptoms of PTSD.

Does Illness-Specific Family Burden Mediate the Relationship Between Number of Late Effects and Survivor Psychological Outcomes? Results are presented in Table 8. Generally, it was hypothesized that illness-specific family burden would mediate the relationship between number of late effects and survivor psychological outcomes (Hypothesis 2a). The overall F-test indicated a good fit for the model predicting parent-reported survivor internalizing symptoms, $p < .01$. Number of late effects significantly predicted illness-specific family burden, $\beta = .50$, $SE = .21$, $p = .02$.

Illness-specific family burden significantly predicted parent-reported survivor internalizing symptoms, $\beta = 1.98$, $SE = .71$, $p = .01$. Direct effects were nonsignificant; however, findings supported an indirect effect, $p < .05$, 95% CI [.24, 2.17], which suggests that illness-specific family burden serves as a factor through which number of late effects contributes to greater parent-reported survivor internalizing symptoms. The overall model predicting parent-reported externalizing symptoms did not indicate a good fit.

Overall F-tests indicated a good fit for models predicting survivor-reported internalizing symptoms, $p < .05$, and survivor-reported PTSD symptoms, $p < .01$. The number of late effects significantly predicted illness-specific family burden in both models. Illness-specific family burden did not significantly predict survivor-reported internalizing or PTSD symptoms. Direct and indirect effects were nonsignificant for both models as shown in Table 8.

In secondary analyses, meditational models were tested to predict presence of at-risk or clinically elevated survivor psychological outcomes (Table 9). Similarly to primary findings, the overall F-test indicated a good fit for the model predicting presence of parent-reported at-risk or clinically elevated survivor internalizing problems, $p < .05$. Number of late effects significantly predicted illness-specific family burden, $\beta = .50$, $SE = .21$, $p = .02$. Illness-specific family burden significantly predicted presence of parent-reported at-risk or clinically elevated survivor internalizing problems, $\beta = .13$, $SE = .06$, $p = .04$. The direct effect was nonsignificant; however, support was obtained for an indirect effect, $p < .05$, 95% CI [.01, .18]. This further supports the notion that illness-specific family burden is a pathway by which number of late effects may contribute to

greater parent-reported at-risk or clinically elevated survivor internalizing problems. While the model predicting parent-reported at-risk or clinically elevated survivor externalizing problems demonstrated good fit, $p < .05$; direct and indirect effects were nonsignificant (see Table 9).

Model indices demonstrated good fit in mediation analyses predicting survivor-reported at-risk or clinically elevated internalizing problems, $p < .05$, and PTSD, $p < .05$. Number of late effects significantly predicted illness-specific family burden in both models (see Table 9). Illness-specific family burden did not significantly predict survivor-reported at-risk or clinically elevated internalizing problems or PTSD. Direct and indirect effects were nonsignificant in both models.

Does General Family Functioning Moderate the Relationship Between Number of Late Effects and Survivor Psychological Outcomes? Results of moderation analyses are displayed in Table 10. It was hypothesized that general family functioning would interact with number of late effects to influence survivor psychological outcomes across the continuum of symptom ratings (Hypothesis 2b). Overall, analyses failed to reveal interaction effects in each of the four models tested. However, the number of late effects significantly accounted for a portion of the variance in predicting parent-reported survivor externalizing symptoms, $\beta = .26$, $SE = 2.70$, $p = .04$. Although nonsignificant, a similar trend for a main effect was found in models predicting parent-reported survivor internalizing symptoms, $\beta = .24$, $SE = 3.74$, $p = .06$, and survivor reported PTSD symptoms, $\beta = .23$, $SE = .79$, $p = .07$.

Secondary analyses examining rates of at-risk or clinically significant survivor psychological outcomes were also performed (Table 11). As shown in Table 7, general

family functioning as measured by the FAD-GF and number of late effects were unrelated to parent report of presence of at-risk or clinically elevated survivor internalizing problems. However, the interaction of family functioning and number of late effects trended towards significance in predicting parent-reported at-risk or clinically elevated survivor internalizing problems, $R^2 = .10$, $\Delta R^2 = .04$, $\Delta F(1, 60) = 2.95$, $p = .091$ (see Table 11). Overall, the model accounted for 10.2% of the variance in parent-reported survivor internalizing problems, with number of late effects ($\beta = .27$, $p = .04$) and the interaction between late effects and family functioning ($\beta = .23$, $p = .09$) making the largest contributions. Although the interaction effect was not significant, post-hoc probing was conducted to better understand this trend. Post-hoc probing indicated that the simple slope was significantly different from zero at high levels of the proposed moderator (i.e., FAD-GF; more problematic general family functioning), but not at low levels of the proposed moderator. The trend-level interaction suggests that risk for parent-reported youth internalizing problems may be exacerbated when a survivor has more late effects in combination with more problematic general family functioning.

As shown in Table 7, general family functioning was unrelated to clinically meaningful survivor PTSD symptoms, while number of late effects positively correlated with clinically meaningful survivor PTSD symptoms. In moderation analyses (see Table 11), the interaction of family functioning and number of late effects trended towards significance in predicting youth-reported clinically meaningful PTSD symptoms, $R^2 = .18$, $\Delta R^2 = .04$, $\Delta F(1, 57) = 2.88$, $p = .095$. The final model accounted for 18.4% of the variance in youth-reported PTSD symptoms. Predictors of elevated PTSD symptoms included family income ($\beta = -.31$, $p = .012$), number of late effects ($\beta = .27$, $p = .034$),

and the interaction between late effects and family functioning (β = .22, p = .095). Although the interaction effect was not significant, post-hoc was conducted to better understand the trend. Probing revealed that the slope for high levels of the proposed moderator (i.e., FAD-GF; more problematic family functioning) was significantly different from zero; however, the slope for low levels of the proposed moderator was not. The trend-level interaction suggests that risk for clinically significant PTSD symptoms may be greatest in survivors with a higher number of late effects in combination with more problematic general family functioning.

Secondary analyses failed to reveal interaction effects between family functioning and number of late effects in models predicting parent-reported presence of at-risk or clinically elevated survivor externalizing problems and youth-reported presence of at-risk or clinically elevated internalizing problems. Additionally, no significant main effects were detected in either model, with the exception of family income, which significantly contributed to variance in rates of elevated youth-reported internalizing symptoms.

Discussion

Late effects resulting from cancer and its associated treatments are common among the growing population of childhood cancer survivors (Brown et al., 1998; Copeland et al., 1996; Geenan et al., 2007; Moleski, 2000). This has contributed to the growing notion of childhood cancer as a chronic illness (Oeffinger & Robison, 2007). This study aimed to investigate relationships between family factors and childhood cancer late effects. In addition, the interactive effects of late effects and family factors, such as general family functioning and illness-specific family burden, on survivor psychological outcomes were examined. To our knowledge, this was the first study to

test the interplay between late effects, family factors, and survivor psychological outcomes.

Consistent with previous research, on average, externalizing and internalizing problems among the sample of survivors were minimal (e.g., Eiser, Hill, & Vance, 2000; Kazak, Christakis, Alderfer, & Coiro, 1994; Noll et al., 1997) with mean T-scores on broad-based emotional and behavioral functioning measures across parent and youth report falling within normal limits (T-score <59). However, approximately 1/3 of the sample fell in the clinically at-risk or clinically significant range on parent-reported internalizing problems.

Similarly, one-third of survivors in the current sample reported clinically significant PTSD symptomology specific to their cancer experience. Rates of current PTSD were higher in the study sample as compared to previous research, which has generally reported current incidence rates of 4.5-17% (e.g., Barakat et al., 1997; Butler, Rizzi, & Handwerger, 1996; Kazak et al., 1997; Pelcovitz et al., 1998, Stuber et al., 1996). Results were more in line with lifetime PTSD rates in adolescent survivors of childhood cancer reported in the DSM-IV field trials (Pelcovitz et al., 1998). Differences in findings may be related to variations in PTSD measurement. For example, some studies used general measures of PTSD without any adaptations specific to the cancer experiences (e.g., Stuber et al., 1996) whereas the current study specifically assessed PTSD symptoms specific to the cancer experience (i.e., "Having upsetting thoughts or images about cancer/treatment that come into my head when you didn't want them to"). Sample differences may also account for variations in findings. For example, Kazak and colleagues (1997) reported no group differences in post-traumatic stress symptoms

among survivors and peers. However, Kazak et al.'s (1997) sample was comprised solely of childhood leukemia survivors. The current study included children of all cancer types and had a large portion of participants with CNS malignancies, which often require more intense treatment, such as CNS radiation. This is supported by the positive association between treatment intensity and presence of clinically significant PTSD symptoms demonstrated in the current study, as well as in other studies (e.g., Hobbie et al., 2000). Consistent with previous research, results indicate that while many childhood cancer survivors fare well psychologically, a subset of survivors are at risk for adverse psychological sequelae.

With regard to family outcomes, approximately one third of the current study sample fell in the "unhealthy" or problematic range of family functioning based upon parent-caregiver report. Generally, the high rates of problematic family functioning found in the current study are consistent with other studies of families of childhood cancer survivors (Alderfer et al., 2009; Peterson et al., 2012). While rates of problematic functioning are generally comparable to those expected in families of healthy children (Miller et al., 1985), a significant portion of families of childhood cancer survivors experience problematic functioning, particularly in the areas of communication and problem-solving.

Late Effects and Survivor Psychological Outcomes

Previous researchers have suggested that survivors experiencing late effects are at greatest risk for adverse psychological outcomes (e.g., Greenberg et al., 1989; Ozono et al., 2007). However, results of the current study did not conclusively support an association between late effects and psychological risk. Only survivor-report of clinically

significant PTSD symptoms was associated with greater number of late effects. For some children, it may be that the long-term and lasting side effects from cancer and treatment serve as constant reminders of their traumatic cancer experience. This is consistent with the general trauma literature, which has demonstrated associations between physical impairments resulting from a trauma and risk for PTSD (Martz & Cook, 2001). Alternatively, it may be that the memory of more intense cancer treatment, such as undergoing a bone marrow transplant, may contribute to persisting psychological effects of cancer. Moreover, parent report of treatment intensity, cranial radiation treatment, and surgical treatment correlated with provider report of number of late effects in the current study. Thus, the fact that the association between number of late effects and clinically significant PTSD symptoms did not remain significant when controlling for treatment intensity and treatment type raises the possibility that aspects of cancer treatment may have long-term effects on family and child outcomes and that the late effects themselves may play a lesser role.

The non-significant relationships between number of provider-reported late effects and survivor internalizing and externalizing problems may be due to the small number of study participants endorsing psychological problems in these areas. Furthermore, study participants experienced, on average, two late effects. Thus, the current study may have been statistically underpowered for detecting such relationships.

Alternatively, the study's emphasis on number of late effects, as compared to kind or impact of late effects on survivors functioning may account for the lack of conclusive findings. For example, while medical providers reported on presence of neuropsychological late effects, this single item indicator likely fails to capture the range

of cognitive, learning and executive functioning impairments that may result from childhood cancer. It also fails to weigh late effects in accordance with their psychological effects on survivors. For survivors, newly emerging cognitive and learning impairments may be particularly distressing, especially for those who were previously performing at higher levels pre-cancer. Research in adults has demonstrated that deficits in executive functioning, such as difficulties with cognitive control (e.g., inhibiting or switching mental sets), may also impose significant challenges for psychological functioning (Joormann, Levens, & Gotlib, 2011); however, the current study did not have a large enough sample to compare differences in psychological functioning among groups of survivors (e.g., those with only medical late effects vs. those with only cognitive late effects).

Late Effects and Family Outcomes

To our knowledge, this was the first study to quantitatively measure general family functioning and illness-specific family burden related to childhood cancer survivorship and late effects. As expected, higher number of provider-reported survivor late effects was associated with greater illness-specific family burden. Specifically, parent/caregivers of survivors with more late effects reported that their child's current condition causes greater burden on the family system, such as seeing family and friends less and having less time for other family members. This finding is consistent with results from a qualitative study documenting family strain and burden related to medical/physical late effects (i.e., infertility, limbs) and cognitive late effects (Patterson, Holm, & Gurney, 2004). As a secondary measure of late effects, parent-report of late effects severity was examined in relation to illness-specific family burden and general

family functioning. Consistent with hypothesized findings, parental perceptions of their child's late effects severity was related to greater illness-specific family and social burden, financial burden and caregiver burden. These findings are similar to those found by Peterson et al. (2012).

In addition, parent perceived late effects severity related to unhealthy general family functioning, while provider report of number of late effects was unrelated to general family functioning. General family functioning, particularly in the context of family problem-solving and communication skills, is likely established prior to a child's cancer diagnosis. It may be that families with poorer functioning are more likely to perceive late effects as severe due to their lack of family-based resources for managing the long-term side effects. For example, families with poorer communication skills may perceive a child's hearing deficits as being more severe than a family with better-developed communication skills. Conversely, families with good problem-solving and communication skills are likely to maintain these skills even in the context of long-term cancer late effects.

Overall, results underscore the importance of considering parent perceived severity of survivor late effects in predicting the familial impact of childhood cancer survivorship. Particularly, results suggest that parental perception of severity of late effects may be more important than the actual number of late effects present. For example, although blindness is likely considered by many to be an impactful and severe late effect, some parents may not view blindness resulting from cancer as a severe long-term problem in the context of all that their child has been through and overcome. This

finding has important clinical implications, particularly in the context of early identification of families at greatest risk for adverse family outcomes.

The Role of General Family Functioning

Although general family functioning was unrelated to number of provider-reported late effects and survivor psychological outcomes as hypothesized, moderation models examining the interactive effects of general family functioning in combination with number of late effects approached significance when predicting parent-reported at-risk or clinically elevated survivor internalizing problems and survivor reported clinically elevated PTSD symptoms. Specifically, post-hoc probing of the trend-level interaction effect revealed that the negative effects of number of late effects on clinically significant survivor psychological functioning may be exacerbated at high levels of problematic family functioning. Findings correspond with previous research by Alderfer et al. (2009), which indicated that adolescent cancer survivors with PTSD were more than five times as likely to be members of families reporting problematic general family functioning. Current findings build upon the work of Alderfer et al. (2009) by also investigating the role of late effects. Although based on trend-level findings, thus limiting the interpretation, results suggest that for youth experiencing a greater number of late effects, poorer general family functioning may contribute to increased risk for at-risk or clinically elevated internalizing problems and PTSD symptoms.

Neither significant nor trend-level findings were found in models predicting survivor psychological outcomes along the continuum of symptoms. These null results may be related to the lack of significant associations between problematic general family functioning and non-clinically elevated survivor psychological symptoms, such as PTSD,

as demonstrated by current research as well as by others (Barakat et al., 1997; Brown et al., 2003). The fact that survivors in healthy functioning families rarely meet criteria for lifetime PTSD (Alderfer et al., 2009) is another relevant consideration. Thus, the study's focus on survivor psychological outcomes along the continuum of symptoms among a sample of youth who were generally functioning well may help to account for general lack of associations of number of late effects with adverse survivor outcomes. Samples that include larger numbers of children meeting criteria for psychological disorders may be needed to demonstrate these relationships.

The Role of Illness-Specific Family Burden

Illness-specific family burden was also investigated to further examine the role of family factors in survivor psychological outcomes. Notably, results of the current study demonstrated support for illness-specific family burden as a mediator of the association between late effects and parent-reported survivor internalizing problems. In support of our hypotheses, findings demonstrated a chain of associations by which more late effects are associated with greater illness-specific family burden, with family burden in turn related to increased parent report of survivor internalizing symptoms. This indirect effect was further supported by a model predicting rates of at-risk or clinically elevated parent-reported survivor internalizing symptoms. To our knowledge, this is the first study to demonstrate this clinically informative chain of associations, highlighting illness-specific family burden as an important target for intervention. It is important to note that direct effects were not found between late effects and survivor psychological outcomes, such as internalizing problems; thus, results suggest that negative effects of late effects on the child is likely most apparent in the context of families that experience more burden or are

less able to cope adaptively. Decreasing illness-specific family burden related to late effects may reduce risk for internalizing problems in survivors. Although efforts are being made to develop and test less invasive and compromising treatments for childhood cancer, the current study advances intervention efforts by identifying factors that can be intervened upon in the interim.

The findings failed to demonstrate a significant indirect, or mediating, effect of illness-specific family burden on the relationship between number of late effects and survivor-reported internalizing problems. In the current study, parents reported greater rates of internalizing symptoms than survivors, which may account for the difference in findings. Differences in findings between parent and survivor reports of internalizing problems may be related to parental psychological functioning. While parent psychological functioning was not assessed in the current study, parents who are more distressed may report both greater family burden and perceive their child's psychological functioning to be poorer. Alternatively, the validity of reporter ratings may explain differences in findings. Some have found that parents report greater child internalizing and externalizing symptoms, while others have found the opposite (Holmbeck, Li, Shurman, Friedman, & Coakley, 2002; Stanger & Lewis, 1993). Therefore, it is difficult to discern who is the more accurate reporter of youth psychological functioning. However, it has been suggested that parents may be more accurate reporters of psychosocial functioning in pediatric illness populations with impaired cognitive functioning, such as those with neurofibromatosis (Krab et al., 2009), and in developmentally limited pediatric cancer populations (Chang & Yeh, 2005). Given that one third of the study sample experienced cognitive late effects, parent-report of

internalizing problems may have provided a more valid indicator of psychological functioning for this sample.

Limitations and Strengths

Results must be considered in light of study limitations. Despite the high participation rate, the study sample is limited in size, as well as in the proportion of youth with a high number of late effects and psychological problems. The sample limits the study's power to detect statistical findings. The small sample is due to a number of factors. First, recruitment was limited to one site. Given the small number of childhood cancer survivors in the general population, multi-site collaborations should be considered by future investigators to insure an adequately powered study in this area. Additionally, the age range of the current study was restricted to 10-17 year-olds. This age range was selected in an effort to have the largest sample possible, while being cognizant of developmental differences across childhood and adolescence that would limit the interpretability of results. Future studies in this area should seek to recruit a larger sample of childhood cancer survivors to allow for the examination of associations between late effects and family factors among various age groups and cancer types.

While including survivors of all cancer types and brain tumors increased generalizability of study findings, there are differences among the various cancer diagnoses with regard to medical and psychosocial long-term risks. For example, survivors of leukemia, CNS tumors and neuroblastoma have been found to be at greater risk for internalizing and externalizing problems than survivors of other cancers, such as bone cancers and soft tissue sarcomas (Schultz et al., 2007). The study sample size did

not allow us to control for cancer type or make comparisons across diagnoses or treatment type.

With regard to measurement limitations, the HKI (Schwartz et al., 2010) is a novel tool that has not been previously validated. Additionally, due to time constraints and concerns about participant burden, the HKI was only completed by the survivor's medical provider. Parent and patient versions of the HKI are available. Use of these measures may have yielded important information. For example, comparisons between all reporters could have been made to understand what parents and patients view as "late effects" as compared to medical professionals. Continued use of the HKI measure in future investigations will be helpful in bolstering psychometric support of this late effects measure and improving understanding of relationships between late effects and variables of interest, especially when all versions of the HKI (i.e., provider-, parent-, and self-report) are used.

Moreover, the HKI only assesses the total number of late effects and does not weigh these effects in accordance with their severity or psychological consequences for children and families. As results of the current study suggested, the sheer number of late effects may not be as important to understanding survivor and family psychosocial outcomes as is the nature and severity of the late effects. For example, blindness as a single late effect may impose greater subjective burden than a greater number of less consequential late effects (e.g., obscured scarring). The impact of late effects should thus be considered when designing and/or improving measures of survivor late effects. Furthermore, while the study did include a single-item measure of parental rating of late effects severity, medical providers' and survivors' ratings of late effects severity were not

obtained. This prevented comparison between reporters and limits understanding about parental perceptions of late effects severity. In other words, the current study was unable to examine whether or not parent report of late effects severity was consistent with actual late effects severity or overestimates of severity. Examining the relation of provider and caregiver ratings of late effects severity would further inform parent-directed cognitive and problem-solving based interventions.

An additional limitation of the current study is that youth externalizing problems, survivor PTSD, general family functioning, and illness-specific family burden were based upon the report of only one reporter. Future studies should include both parent and youth report of survivor psychological functioning, such as PTSD. Parent/caregiver respondents were most often mothers, which is common in pediatric psychology research (Phares, Lopez, Fields, Kamboukos, & Duhig, 2005), albeit a limitation of the current study. For example, Peterson et al. (2012) found that 32% of mother-father dyads participating in a study of pediatric neuroblastoma survivors disagreed in their reports of whether or not family functioning was "healthy" vs. "unhealthy." Similarly, in survivor populations (Alderfer et al., 2009), community samples, and mental health clinic referred families (Sawyer, Sarris, Baghurst, Cross, & Kalucy, 1988) adolescents have been found to rate family functioning more poorly than parents. Thus, future investigations that include both mother and father report, along with youth report of family functioning, would advance our understanding of the familial impact of childhood cancer survivorship.

The study's cross-sectional design also limits our understanding of causal relationships. Although quite prevalent across psychological research, some researchers

have argued that meditational analyses should not be conducted on cross-sectional data as it may result in biased under- or overestimates of causal effects (Maxwell & Cole, 2007). Longitudinal research designs aimed at examining relationships between late effects and family factors over time will improve our understanding of causal pathways and better inform the development of interventions for survivors and their families. Lastly, although participation rates were high, the findings represent childhood cancer survivors who attended a long-term follow-up clinic appointment, and therefore, cannot be generalized to all survivors.

Notwithstanding these limitations, the current study has a number of strengths. The diverse sample is a notable strength of the study as the dearth of studies involving ethnic minority groups is a significant weakness of childhood cancer survivorship research overall (Kazak, 2005). In the current study, nearly 11% of the sample was Black/African American; whereas only 2% of the >20,000 participants in the Childhood Cancer Survivor Study identified as Black/African American (Robison et al., 2002). The range of cancer diagnoses present in the study allows for greater generalization of study results. An illness-specific measure of family burden was utilized and adapted to assess family burden related specifically to childhood cancer and brain tumor late effects. Illness-specific measurements can help to better inform the development of interventions through the identification of more specific risk factors (Thompson & Gustafson, 1996). The current study was guided by family risk and resource models specific to pediatric populations, which are largely based on social-ecological (Bronfenbrenner, 1977) and stress and coping theories (Lazarus & Folkman, 1984). As Varni et al. (1996) noted, a limitation of the pediatric cancer literature was the lack of theory-guided research.

Clinical Implications

Consistent with previous research (e.g., Schultz et al., 2007), the current study identified a subset of survivors at risk for adverse psychological outcomes. Specifically, results suggest that survivors who received cranial radiation, underwent a bone marrow transplant, or experienced a higher number of late effects are at increased risk for clinically elevated PTSD symptoms. Similarly, those who underwent a bone marrow transplant were also identified as being at risk for internalizing problems, while those who received cranial radiation were found to have greater externalizing symptoms. Early interventions targeting this subgroup of survivors are important. Kazak and colleagues (1999) successfully developed the 1-day *Surviving Cancer Competently Intervention Program (SCIPP)* for adolescent cancer survivors and their families, which combined cognitive-behavioral and family therapy interventions in an effort to reduce post-traumatic stress symptoms in survivors and family members, reduce anxiety and negative beliefs about cancer, and improve social support and family communication. Follow-up study found reduced post-traumatic stress and anxiety symptoms in survivors, siblings and parents 6-months post-intervention; however, improvements in family functioning were minimal. Findings from a randomized clinical trial further supported the positive effects of *SCIPP* in reducing post-traumatic stress in survivors and fathers (Kazak et al., 2004).

To build upon the intervention work of Kazak et al. (1999, 2004), study findings highlight the importance of targeting general family functioning and illness-specific family burden via family-based childhood cancer survivorship interventions. Specifically, to reduce risk of at-risk or clinically elevated PTSD symptoms and

internalizing problems, results highlight the importance of intervening upon family problem-solving and communication skills. A web-based, 12-session family problem-solving intervention for youth with traumatic brain injury (TBI), which included psychoeducation and exercises targeting family problem-solving, communication and behavioral management strategies, successfully decreased injury-specific family burden in participating families (Wade, Wolfe, Brown & Pestian, 2005). As demonstrated by the work of Wade et al. (2005), intervening upon family problem-solving and communication may also decrease illness-specific family burden, which is significant given demonstrated findings that illness-specific family burden predicts greater survivor internalizing problems in youth with more late effects. This successful intervention can be modified and applied to families of survivors of childhood cancer, especially given some of the overlap between long-term effects of TBI and childhood cancer, such as cognitive impairments, and demonstrated support for the effectiveness of problem-solving therapy for mothers of children currently undergoing cancer treatment (Sahler et al., 2005). By participating in an intervention of this nature, families may learn ways to more successfully manage emerging late effects and associated problems. Furthermore, as shown across the pediatric chronic illness literature, youth within families that have better problem-solving and communication skills are often more adherent to their treatment regimen and have better medical and psychosocial outcomes (e.g., Drotar, 1997).

As highlighted previously, results also suggest that parental perception of severity of late effects may be more important than the actual number of late effects present. These findings have important clinical implications and underscore areas for future

research. Parental perceptions of medical severity have been found to predict child psychological functioning in other pediatric populations. For example, maternal perceptions of medical severity in children with congenital heart disease accounted for 33% of variability in predicting child psychological adjustment whereas actual medical severity accounted for only 3% (DeMaso et al., 1991). Furthermore, greater parent perceived child vulnerability is associated with poorer emotional adjustment in children currently undergoing treatment for cancer (Colletti et al., 2008). Therefore, cognitive-behavioral interventions targeting parental perceptions of medical severity, such as severity of cancer late effects, may prove advantageous. Research is needed that compares parent and physician reports of late effects severity to inform interventions of this nature. Additional research is also needed to better understand the interplay between parental perceptions of the severity of their child's late effects and survivor psychological outcomes. Moreover, it will also be important that future research assess child and adolescent perceptions of late effects severity. The testing of interactive models that includes parental and youth perceptions of late effects severity, in combination with other known risk factors, such as general family functioning, will be important for identifying additional intervention targets for decreasing risk of negative psychological sequelae in childhood cancer survivors.

Future Directions

In addition to longitudinal investigation of the associations between late effects, family factors and survivor psychological outcomes with a larger sample of survivors and among survivors of certain cancer types, findings highlight important directions for future research and intervention. First, building upon the work of Schwartz et al. (2010), future

research in the area of childhood cancer survivorship would benefit from the development and validation of a measure that assesses whether or not a late effect is present, and further measures the degree to which the presence of the late effect impacts or burdens the survivor and/or family, as well as reports on the severity of each late effect. This approach has been used with TBI populations to better understand the impact of TBI late effects on families through the development and use of the Family Burden of Injury Interview (Burgess et al., 1999). A measure of this nature specific to childhood cancer survivors would promote greater understanding of the impact of late effects on both survivors and families. Moreover, information of this nature will identify which late effects cause greatest impact on survivors and their families, which will further inform clinical prevention and intervention efforts.

Another important direction for future research is to examine parents' understanding of the significance of late effects. A recent study found that parents of children with cancer were more pessimistic about their child's chances for physical and intellectual late effects than their physicians (Mack et al, 2007). Therefore, given what is known about the potential negative effects of parental perceptions of greater medical severity, future research that aims to measure parent and youth understanding of late effects is needed. In the midst of a re-energized patient-centered care movement, the measurement of understanding and perceptions regarding late effects will promote more effective patient/parent–physician communication, encourage patients/parents to take a more active role in their medical care, and inform health education efforts. Additionally, by identifying families who overestimate the severity of their late effects, those at

greatest risk for adverse family outcomes, such as increased burden, may be intervened upon sooner.

Furthermore, research should seek to more fully examine associations between cognitive late effects, family factors, and survivor psychological outcomes. The single-item measure used in the current study did not fully capture the complexity of cognitive late effects. As demonstrated by current findings, as well as previous literature (e.g., Brown et al., 1998; Copeland et al., 1996; Moleski, 2000), approximately 1/3 of survivors experience cognitive impairments as a result of their cancer/treatment. Thus, given both the prevalence and nature of cognitive late effects, it will be important that future research examine associations between cognitive late effects and family factors, as well as the interplay of these two variables in predicting survivor psychological outcomes. A case-based study elucidated the clinical significance of the interactive effects of cognitive late effects and family functioning (Hocking et al., 2011); however, quantitative research is needed to realize the role of cognitive late effects, independent of medical late effects, in understanding psychological risk in survivors.

The current study only investigated survivor internalizing symptoms, externalizing symptoms and PTSD. Future studies can expand on the current work by examining associations between late effects, family factors, and other psychosocial outcomes. For example, a subset of childhood cancer survivors experience deficits in social functioning (e.g., Levin Newby et al., 2000; Schultz et al., 2007). Similar to current findings, family factors may be identified that can reduce risk of social impairments in survivors. Moreover, while the current study emphasized survivor psychological outcomes, parents of survivors are also at increased risk of adverse

psychological outcomes. To our knowledge, no study has examined the relationships between childhood cancer late effects and parent psychological outcomes, such as depression, anxiety and PTSD. Future research on this topic is needed to identify potential risk factors for psychological problems in parents.

Lastly, the current study highlights the importance of not only identifying survivors at greatest risk for adverse outcomes, but also screening families to identify those in need of intervention. Brief psychosocial screening tools have successfully been used in families of children recently diagnosed with cancer to detect those at greatest risk (Kazak et al., 2003). Similarly, parents of childhood cancer survivors could complete measures that assess family functioning and illness-specific burden, as utilized in the current study, during annual visits to outpatient survivorship clinics. Those families identified as being at moderate-high risk of adverse family functioning could then be referred for further intervention. This screening approach promotes prevention efforts, identifies level of need, allows for the tailoring of interventions based upon need, and takes into account cost and time considerations by providing treatment only to those requiring intervention.

Conclusion

This is one of the first studies to respond to the Institute of Medicine's call for family-based research related to survivor late effects (Hewitt et al., 2003). Findings demonstrated associations of more late effects with greater illness-specific family burden. Notably, results also demonstrated that illness-specific family burden is a factor by which number of late effects leads to greater survivor internalizing problems. Results further underscore the clinical importance of family-based research specific to late effects.

Identification of family-level factors related to longer-term consequences of childhood cancer is of special importance as these factors may be subject to interventions capable of reducing family burden and promoting more positive survivor psychological outcomes. These findings will help to advance the psychosocial care of the growing population of survivors of childhood cancer and their families.

Table 1

Survivor Characteristics

Characteristic	N = 65	
Mean Youth Age in Years (SD)	14.13	(2.07)
Mean Youth Age at Diagnosis in Years (SD)	6.16	(3.46)
Mean Years Since End of Treatment (SD)	6.21	(2.83)
Youth Sex (%)		
Female	34	(52.3)
Male	31	(47.7)
Youth Race/Ethnicity (%)		
White/Caucasian	48	(73.8)
Black/African American	7	(10.8)
Hispanic/Latino	4	(6.2)
Asian/Asian American	1	(1.5)
Bi/Multi-Racial	5	(7.7)
Cancer Type (%)		
Acute Lymphoblastic Leukemia (ALL)	24	(36.9)
Acute Myeloid Leukemia (AML)	4	(6.2)
Brain/Central Nervous System Cancer	17	(26.2)
Neuroblastoma	3	(4.6)
Hodgkin Lymphoma	2	(3.1)
Non-Hodgkin Lymphoma	1	(1.5)
Soft Tissue Cancer	4	(6.2)
Bone Cancer	2	(3.1)
Brain Tumor (Non-Malignant)	8	(12.3)
Treatment Type (%)		
Major Surgery	34	(52.3)
Chemotherapy	56	(86.2)
Radiation	18	(27.7)
Chemotherapy Type[a] (%)		
Methotrexate	25	(38.5)
Anthracyclines	35	(53.8)
No Chemotherapy	9	

[a] N = 56

Table 2

Family Characteristics

Characteristic	N = 65	
Parent/Caregiver Respondent (%)		
Mother	50	(76.9)
Father	12	(18.5)
Other[a]	3	(4.6)
Family Income[b] (%)		
<$25,000	15	(24.2)
$25,000-$50,000	15	(24.2)
$50,000-$75,000	14	(22.6)
$75,000-$100,000	6	(9.7)
>$100,000	12	(19.4)
Mother's Education (%)		
Some High School	2	(3.1)
High School	15	(23.1)
Some College	28	(43.1)
Bachelor's Degree	15	(23.1)
Professional Degree (Masters, Doctoral)	5	(7.7)
Father's Education[c] (%)		
Some High School	6	(9.4)
High School	22	(34.4)
Some College	19	(29.7)
Bachelor's Degree	9	(14.1)
Professional Degree (Masters, Doctoral)	8	(12.5)
Family Structure (%)		
Single-Parent Home	12	(18.5)
Married, Both Parents Live at Home	42	(64.6)
Mixed Family	8	(12.3)
Other	3	(4.6)

[a] Other includes grandparents, non-parent legal guardians.
[b] 3 families did not respond. N = 62.
[c] 1 family did not respond. N=64.

Table 3

Correlations between Demographic Characteristics, Family Outcomes, and Survivor Psychological Outcome Variables

Variable	Youth Age	Youth Sex	Youth Majority Race	Family Income	Mother Education	Father Education
FAD-GF	.37**	.02	-.06	-.12	-.20	-.04
IOF Financial Subscale	.05	-.09	-.27*	-.35**	-.13	-.13
IOF Family/Social Subscale	.14	-.22	-.23	-.20	-.13	-.16
IOF Personal Subscale	.26*	-.09	-.17	-.34**	-.11	-.11
IOF Total Score	.18	-.16	-.22	-.29*	-.09	-.10
Internalizing Symptoms (SRP)	.36**	-.05	.08	-.31*	-.05	-.09
Internalizing Problems (SRP)	.11	-.13	-.02	-.33**	-.09	-.13
Youth PTSD Symptoms (CPSS)	-.04	-.10	-.00	-.39**	-.14	-.27*
Youth PTSD (CPSS)	-.05	-.10	-.02	-.30*	-.04	-.20
Internalizing Symptoms (PRS)	.15	-.20	-.05	-.02	.00	.04
Internalizing Problems (PRS)	.14	-.03	-.40	.05	.05	.05
Externalizing Symptoms (PRS)	.03	.12	-.13	-.13	-.01	-.04
Externalizing Problems (PRS)	-.09	-.11	.00	.04	-.09	-.08

Note. FAD-GF – Family Assessment Device, General Functioning; IOF – Impact on Family Scale; (SRP) = Behavior Assessment System for Children, Second Edition, Self-Report; CPSS = Child PTSD Symptom Scale; (PRS) = Behavior Assessment System for Children, Second Edition, Parent Rating Scales.

* $p < .05$

** $p < .01$

Table 4

Summary of Survivor Psychological Outcomes

BASC-2 Subscale Scores (Self-Report)	**Mean T-Score**	**SD**
Internalizing Problems	46.77	9.12
Anxiety	47.54	9.92
Depression	45.98	6.94
Somatization	50.30	11.03
Attention Problems	48.98	10.86
Hyperactivity Problems	48.68	9.50
Social Stress	45.77	7.99
School Problems	44.49	8.93
CPSS Total Score (Self-Report)	8.89	6.57
BASC-2 Subscale Scores (Parent Report)	**Mean T-Score**	**SD**
Internalizing Problems	54.28	12.05
Anxiety	53.22	11.74
Depression	53.38	11.42
Somatization	53.95	12.23
Externalizing Problems	47.94	8.07
Attention Problems	51.61	9.62
Hyperactivity Problems	50.61	10.62
Conduct Problems	46.64	6.30
Aggressive Behaviors	47.20	8.64
Social Skills	51.33	10.41

Table 5

Summary of Family Outcomes

Family Assessment Device, General Functioning (FAD-GF)	**Mean T-Score**	**SD**
FAD-GF, Total Score	20.32	6.35
Impact on Family Scale (IOF)	**Mean T-Score**	**SD**
IOF Financial Subscale	8.34	3.07
IOF Family/Social Subscale	16.38	5.12
IOF Personal Subscale	12.25	4.03
IOF Total Score	46.08	11.91

Table 6

Correlations between Cancer Characteristics, Late Effects, Family Outcomes and Survivor Psychological Outcomes

Variable	Tx Intensity	Age at Dx	Time Since EOT	Surgical Tx	Cranial Radiation Tx	Methotrexate Chemo Tx	Bone Marrow Transplant
Severity of Late Effects (Parent)	.25*	.07	.05	.19	.32**	-.38**	.39**
Number of Late Effects (HKI)	.27*	-.10	.20	.51**	.77**	-.40**	.09
FAD-GF	-.02	.28*	-.01	.16	.11	-.29*	.07
IOF Financial Subscale	-.00	.17	-.08	.18	.14	-.42**	-.01
IOF Family/Social Subscale	.21	.18	-.08	.13	.30*	-.25*	.18
IOF Personal Subscale	.07	.16	.03	.15	.20	-.32**	.22
IOF Total Score	.11	.18	-.04	.17	.26*	-.31*	.16
Internalizing Symptoms (SRP)	.11	.15	.07	-.09	.22	.13	.35**
Internalizing Problems (SRP)	.15	.11	-.00	-.07	.05	.03	.27*
Youth PTSD Symptoms (CPSS)	.20	.04	-.06	.13	.28*	-.08	.34**
Youth PTSD Problems (CPSS)	.26*	.01	-.08	.10	.23	-.03	.28*
Internalizing Symptoms (PRS)	.24	.04	.06	-.03	.23	.00	.09
Internalizing Problems (PRS)	.19	-.01	.05	-.04	.23	.02	-.05
Externalizing Symptoms (PRS)	.16	-.14	.16	.14	.34**	.03	-.14
Externalizing Problems (PRS)	.23	-.17	.19	.11	.16	-.07	-.08

Note. (HKI) = Health Knowledge Inventory; FAD-GF – Family Assessment Device, General Functioning; IOF – Impact on Family Scale; (SRP) = Behavior Assessment System for Children, Second Edition, Self-Report; CPSS = Child PTSD Symptom Scale; (PRS) = Behavior Assessment System for Children, Second Edition, Parent Rating Scales; Tx = Treatment; Dx = Diagnosis; EOT = End of Treatment.

* $p < .05$

** $p < .01$

Table 7

Correlations Between Number of Late Effects and Family and Survivor Outcomes (Hypotheses 1a-c)

Variable	1	2	3	4	5	6	7	8
1. Severity of Late Effects (Parent)	-----							
2. Number of Late Effects (HKI)	.42**	-----						
3. FAD-GF	.17	-.08	-----					
4. Unhealthy Functioning (FAD-GF)	.36**	-.07	.70**	-----				
5. IOF Financial Subscale	.42**	.22	.17	.30*	-----			
6. IOF Family/Social Subscale	.56**	.29*	.24	.31*	.70**	-----		
7. IOF Personal Subscale	.49**	.19	.39**	.48**	.71**	.82**	-----	
8. IOF Total Score	.51**	.23	.32*	.40**	.83**	.94**	.91**	-----
9. Internalizing Symptoms (SRP)	.21	.15	.19	.14	.04	.16	.29*	.18
10. Internalizing Problems (SRP)	.15	.06	.14	.09	.11	.03	.18	.10
11. Youth PTSD Symptoms (CPSS)	.22	.21	.12	.04	.03	.19	.24	.17
12. Youth PTSD Problems (CPSS)	.13	.25*	.02	-.05	-.03	.17	.19	.12
12. Internalizing Symptoms (PRS)	.23	.20	.07	.08	.16	.37**	.33**	.33**
13. Internalizing Problems (PRS)	.07	.22	.06	.03	.16	.32*	.26*	.27*
14. Externalizing Symptoms (PRS)	-.00	.21	.19	.16	.01	.20	.22	.21
15. Externalizing Problems (PRS)	.06	.16	.04	-.04	-.14	.11	.02	.01

Note. HKI = Health Knowledge Inventory; FAD-GF = Family Assessment Device, General Functioning Scale; IOF = Impact on Family Scale; (SRP) = Behavior Assessment System for Children, Second Edition, Self-Report; CPSS = Child PTSD Symptom Scale; (PRS) = Behavior Assessment System for Children, Second Edition, Parent Rating Scales.

* $p < .05$

** $p < .01$

Table 8

Regression Coefficients and Bootstrapped Point Estimates Examining Illness-Specific Family Burden as a Mediator of Late Effects and Survivor Psychological Outcomes (Hypothesis 2a)

		Normal Theory Tests			Bootstrapping Results for Indirect Effects (95% CI)			
Dependent Var (Independent Var)	Path	B	*SE*	*T*	Point Estimate	*SE*	Lower	Upper
Youth Self-Report of	a	.43	.21	2.10*				
Int. Symptoms	b	.46	1.39	.33				
(# of Late Effects)	c	1.26	2.16	.58				
	c’	1.06	2.26	.47				
	a*b				.20	.69	-.79	2.05
Youth Self-Report of	a	.45	.20	2.20*				
PTSD Symptoms	b	.10	.17	.60				
(# of Late Effects)	c	.42	.26	1.62				
	c’	.38	.27	1.39				
	a*b				.05	.10	-.06	.35
Parent Report of	a	.50	.21	2.40*				
Int. Symptoms	b	1.98	.71	2.78**				
(# of Late Effects)	c	1.99	1.22	1.64				
	c’	1.01	1.21	.84				
	a*b				.98*	.49	.24	2.17
Parent Report of	a	.50	.21	2.40*				
Ext. Symptoms	b	.65	.55	1.18				
(# of Late Effects)	c	1.51	.90	1.68				
	c’	1.19	.94	1.27				
	a*b				.32	.35	-.17	1.28

Note. 5,000 bootstrap samples; Indirect effect is significant at $p < .05$ if the confidence interval (CI) does not contain zero. See Figure 1 for path descriptions.

* $p < .05$

**$p < .01$

Table 9

Regression Coefficients and Bootstrapped Point Estimates Examining Illness-Specific Family Burden as a Mediator of Late Effects and At-Risk or Clinically Elevated Survivor Psychological Outcomes (Secondary Analyses for Hypothesis 2a)

		Normal Theory Tests			Bootstrapping Results for Indirect Effects (95% CI)			
Dependent Var (Independent Var)	Path	B	*SE*	*t* (Z)	Point Estimate	*SE*	Lower	Upper
Youth Self-Report of Internalizing Symptoms (# of Late Effects)	a	.45	.20	2.20*				
	b	-.05	.10	(-.48)				
	c	.08	.15	(.55)				
	c’	.08	.15	(.51)				
	a*b				-.02	.10	-.21	.11
Youth Self-Report of PTSD Symptoms (# of Late Effects)	a	.45	.20	2.20*				
	b	.02	.06	(.27)				
	c	.16	.09	(1.76)				
	c’	.16	.09	(1.64)				
	a*b				.01	.03	-.04	.10
Parent Report of Internalizing Symptoms (# of Late Effects)	a	.50	.21	2.40*				
	b	.13	.06	(2.09)*				
	c	.15	.09	(1.71)				
	c’	.10	.09	(1.06)				
	a*b				.07*	.04	.01	.18
Parent Report of Externalizing Symptoms (# of Late Effects)	a	.50	.21	2.40*				
	b	.06	.11	(.55)				
	c	.17	.14	(1.24)				
	c’	.15	.15	(1.01)				
	a*b				.03	.25	-.25	.42

Note. 5,000 bootstrap samples; Indirect effect is significant at $p < .05$ if the *CI* does not contain zero. See Figure 1 for path descriptions.

* $p < .05$

**$p < .01$

Table 10

Interaction of Late Effects and Family Functioning to Predict Survivor Psychological Outcomes (Hypothesis 2b)

Model	Predictor	R^2	F	ΔR^2	ΔF	B (SE)	β	t	95% CI for B
[a]Youth Internalizing Problems (Self-Report)	Step 1	.24	9.55**	.24	9.55**				
	Family Income					-13.11 (4.70)**	-.33	-2.80	(-22.52, -3.71)
	Age					9.84 (3.49)*	.36	2.82	(2.84, 16.83)
	Step 2	.25	4.78**	.01	.26				
	Late Effects					4.75 (6.80)	.08	.70	(-8.88, 18.37)
	FAD-GF					2.11 (7.28)	.04	.29	(-12.48, 16.69)
	Step 3	.25	3.76**	.00	.01				
	Late Effects x FAD-GF					.58 (4.90)	.02	.12	(-9.23, 10.39)
[a]Youth PTSD (Self-Report)	Step 1	.15	10.96**	.15	10.96**				
	Family Income					-1.80 (.56)**	-.39	-3.24	(-2.92, -.69)
	Step 2	.20		.05	1.71				
	Late Effects		4.88**			1.50 (.79)†	.23	1.89	(-.09, 3.09)
	FAD-GF					.47 (.81)	.07	.58	(-.1.16, 2.10)
	Step 3	.22		.01	.96				
	Late Effects x FAD-GF		3.90**			.57 (.58)	.12	.98	(-.59, 1.73)
[b]Youth Internalizing Problems (Parent)	Step 1	.05	1.61	.05	1.61				
	Late Effects					7.05 (3.74)†	.24	1.89	(-.42, 14.53)
	FAD-GF					1.49 (4.22)	.05	.35	(-6.96, 9.93)
	Step 2	.07	1.53	.02	1.36				
	Late Effects x FAD-GF					3.33 (2.85)	.16	1.17	(-2.37, 9.03)
[b]Youth Externalizing Problems (Parent)	Step 1	.09	3.12*	.09	3.12*				
	Late Effects					5.69 (2.70)*	.26	2.11	(.30, 11.09)
	FAD-GF					4.15 (3.04)	.18	1.37	(-1.94, 10.24)
	Step 2	.12	2.60†	.02	1.51				
	Late Effects x FAD-GF					2.52 (2.06)	.16	1.23	(-1.59, 6.63)

Note. [a]N = 62. [b]N = 64. All regression coefficients are from the final step. FAD-GF = Family Assessment Device, General Functioning Scale. *p < .05 **p <. 01 †p < .10

Table 11

Interaction of Late Effects and Family Functioning to Predict At-Risk or Clinically Elevated Survivor Psychological Outcomes (Secondary Analyses for Hypothesis 2b)

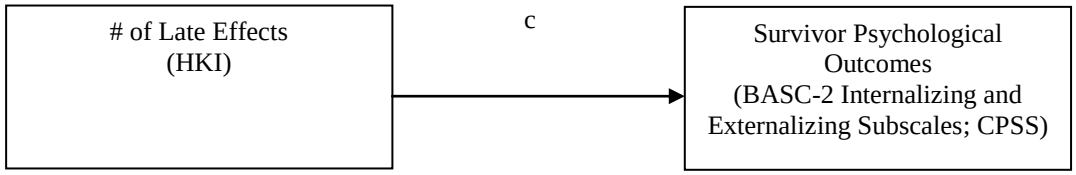
Model	Predictor	R^2	F	ΔR^2	ΔF	B (SE)	β	t	95% CI for B
[a]Youth Internalizing Symptoms (Self)	Step 1	.13	4.36*	.13	4.36*				
	Family Income					-.07 (.03)**	-.33	-2.58	(-.13, -.02)
	Age					.02 (.02)	.12	.89	(-.02, .06)
	Step 2	.13	2.17†	.00	.11				
	Late Effects					.00 (.04)	.01	.05	(-.08, .09)
	FAD-GF					.03 (.04)	.08	.57	(-.06, .11)
	Step 3	.14	1.86	.01	.66				
	Late Effects x FAD-GF					-.02 (.03)	-.11	-.81	(-.08, .04)
[a]Youth PTSD Symptoms (Self)	Step 1	.09	5.96*	.09	5.96*				
	Family Income					-.11 (.04)**	-.31	-2.58	(-.19, -.02)
	Step 2	.14	3.22*	.05	1.77				
	Late Effects					.13 (.06)*	.27	2.17	(.01, .24)
	FAD-GF					-.03 (.06)	-.06	-.49	(-.15, .09)
	Step 3	.18	3.21*	.04	2.88t				
	Late Effects x FAD-GF					.07 (.04)†	.21	1.70	(-.01, .16)
[b]Youth Internalizing Symptoms (Parent)	Step 1	.06	1.86	.06	1.86				
	Late Effects					.12 (.06)*	.27	2.14	(.01, .23)
	FAD-GF					.01 (.06)	.02	.18	(-.12, .14)
	Step 2	.10	2.26†	.04	2.95t				
	Late Effects x FAD-GF					.07 (.04)†	.23	1.72	(-.01, .16)
[b]Youth Externalizing Symptoms (Parent)	Step 1	.03	.95	.03	.95				
	Late Effects					.04 (.03)	.18	1.40	(-.02, .11)
	FAD-GF					.01 (.04)	.04	.30	(-.06, .08)
	Step 2	.03	.70	.00	.22				
	Late Effects x FAD-GF					.01 (.02)	.06	.47	(-.04, .06)

Note. [a]N = 62. [b]N = 64. All regression coefficients are from the final step. FAD-GF = Family Assessment Device, General Functioning Scale. *p < .05 **p <. 01 †p < .10

Figure 1

Conceptual Model: Examining Illness-Specific Family Burden as a Mediator of Late Effects and Survivor Psychological Outcomes (Hypothesis 2a)

A. Direct Effect:



B. Indirect Effect:

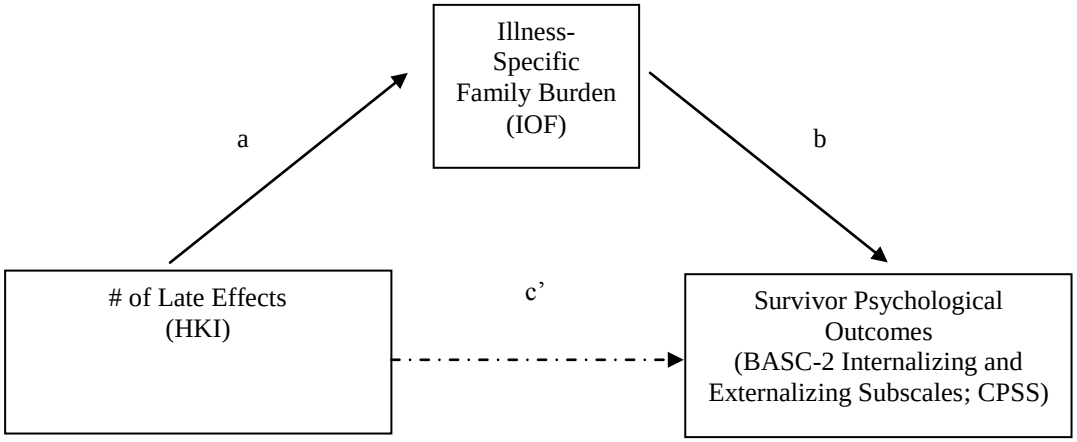
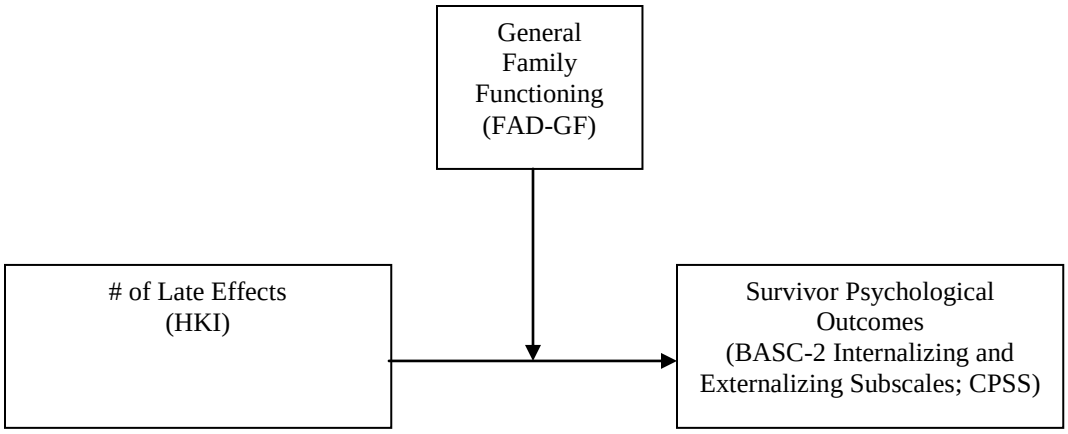


Figure 1. Adapted from Preacher & Hayes (2004). When c – c' (i.e., a*b) is significant, there is evidence of an indirect effect.

Figure 2

Conceptual Model: Examining the Interaction of Late Effects and Family Functioning to Predict Survivor Psychological Outcomes (Hypothesis 2b)



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