THE RELATIONSHIP BETWEEN CAREGIVER STRESS AND PEDIATRIC CANCER PATIENT ANXIETY AND PAIN: TESTING FAMILY BELIEFS AS A MODERATOR

By

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A thesis submitted to the

Graduate School-Camden

Rutgers, The State University of New Jersey

In partial fulfillment of the requirements

For the degree of

Master of Arts

Graduate Program in Psychology

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Camden, New Jersey

May 2022
THESIS ABSTRACT

The Relationship between Caregiver Stress and Pediatric Cancer Patient Anxiety and Pain: Testing Family Beliefs as a Moderator

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Pediatric cancer patients and their families undergo significant stress throughout diagnosis and treatment. The functioning of the family unit has substantial impact on psychological wellbeing and cancer-related quality of life outcomes for children with pediatric cancer (Neugebauer & Mastergeorge, 2021; Van Schoors et al., 2017; Gurtovenko et al., 2021). Increased caregiver stress has been found to lead to declines in psychosocial functioning for both caregiver and child (Sulkers et al., 2014) and the caregiver’s emotional state has been found to strongly influence child outcomes (Platt et al., 2016; Jobe-Sheilds et al., 2009). Additionally, prior research has found that caregivers’ beliefs about their family’s ability to cope with a cancer diagnosis is associated with caregiver stress levels (Quine & Pahl, 1991; Fotiadou et al., 2008). Previously conducted interventions for the cancer population have been successful in reducing negative psychosocial outcomes for families when specific stressors were targeted (Li et al., 2011; Lapid et al., 2015). This study evaluated the relationship between caregiver stress and child report as well as caregiver-proxy report of treatment/procedural anxiety and pain interference with family beliefs as the moderator of this relationship. The aim of this study was to contribute to the development of
targeted interventions which could lead to improved cancer-related quality of life for both the caregiver and child during cancer treatment. The participants were caregiver-child dyads with 101 caregiver participants (of children ages 5-17) and 59 child participants undergoing cancer treatment (ages 8-17). Participants completed self-report questionnaires, specifically the Psychosocial Assessment Tool Oncology (PAT2.0), the Pediatric Quality of Life Inventory—Cancer Module and the Patient-Reported Outcomes Measurement Information System (PROMIS) Pain Interference Scale. Results showed that family beliefs are not a moderator of the relationship between caregiver stress and child treatment/procedural anxiety and pain interference. However, significant relationships were found between caregiver stress and family beliefs. Caregiver-proxy report of child pain interference was significantly associated with caregiver stress level, family beliefs, child pain interference as well as caregiver-proxy and child reports of treatment/procedural anxiety. Potential clinical implications related to the findings are discussed as well. Future research directions are also suggested.
Acknowledgements

I would like to deeply thank my mentor, Dr. Lauren Daniel, for her dedication to my education as a student, researcher, and future clinical psychologist. Her supportive guidance has helped me greatly through the process of developing this thesis and in achieving my goals of attending a clinical psychology doctoral program. I have admired her thoughtful insights and commitment to her role as both a teacher and researcher. I also appreciate the many opportunities she has given me to grow and develop my psychology interests and experiences.

Thank you to my thesis committee, Dr. Rufan Luo and Dr. Kristin August for their sharing important feedback as well as pushing my own development as a researcher.

Thank you to the faculty of the MA in psychology program that have provided a supportive and intellectually stimulating environment that encouraged me to explore my interests as a student while also guiding me towards my professional goals.

Finally, thank you to my family, friends and partner for their tireless support, love and encouragement during every step of my journey to become a clinical psychologist.
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Introduction

In 2022, approximately 10,470 children were diagnosed with cancer (American Cancer Society, 2022). Due to advancements in medical research and care, pediatric cancer patients now have an 85%, 5-year survival rate with the mortality rate in children declining 68% since 1970 (Siegal, Miller & Jemal, 2020). Caregiver and child reactions to the diagnosis and treatment of pediatric cancer can be understood through the theoretical framework, Pediatric Psychosocial Preventative Health Model (PPPHM) (Appendix A). This model assesses family psychosocial risk and pairs the assigned risk level of a family with appropriate interventions (Kazak et al., 2015). The PPPHM was developed for use in pediatric cancer and serves as a helpful reference for pediatric cancer providers to evaluate the risk factors for families entering treatment. The Psychosocial Assessment Tool Oncology (PAT 2.0) measure is designed to directly map onto the PPPHM assigned interventions (Kazak et al., 2015). Given the use of the PAT 2.0 measure in previously collected data for this research study, the PPPHM is an important framework to use as a foundation to understand potential interventions. In addition to the PPPHM framework, the multidimensional Biobehavioral Model theoretical framework suggests that perceived stress, coping skills and emotional distress among other factors influence the perceived pain and cancer-related quality of life for pediatric cancer patients (Varni, Burwinke & Katz, 2004; Appendix B). This model hypothesizes that the family environment, perceived social support and coping skills operate as moderating variables of the predictor variable of stress and outcome variable of pain perception. The current research study has adapted the Biobehavioral Model (Appendix C) with family beliefs serving as the moderator for the predictor variable of
caregiver stress and outcome variables of child treatment/procedural anxiety and child pain interference. The adapted model tests the main research question: does the relationship between caregiver stress and pediatric cancer patient treatment/procedural anxiety and pain interference vary by family beliefs?

The research predicts the hypothesis that positive family beliefs held by caregivers will attenuate the relationship between high stress and high treatment/procedural anxiety and pain interference reported by the child and caregiver. The main predictor variable, caregiver stress, gathers information on the stress response of a caregiver to a particular event and is specific to the child’s illness. The outcome variables of child treatment/procedural anxiety, child pain interference and caregiver-proxy reports of child treatment/procedural anxiety and pain interference are important in understanding the level of anxiety and pain interference the child is experiencing in the context of their cancer treatment. The family beliefs variable was operationalized as the caregiver’s internalized perspective and interpretation of the anticipated effects of their child’s cancer diagnosis and treatment on the wellbeing, self-efficacy and functioning of the family (Kazak et al., 2004). In developing the family beliefs subscale, Kazak and colleagues (2004) used question constructs within the family beliefs subscale which evaluated malleable (e.g., My child will be in a lot of pain) and dispositional based beliefs (e.g., Our marriage or family will fall apart). Within the subscale of 9 items, 5 items were dispositional based beliefs, and 4 items were malleable beliefs (Appendix K). Malleable beliefs have been found to develop over time and dispositional beliefs remain stable over time (Daniel et al., 2020; Hudson et al., 2021). Thus, family beliefs are not reactions to an event, and can operate as a moderating variable. The variable relationships
will be analyzed with the covariates of money problems from low to high and family problems from low to high.

**Background and Significance**

**Caregiver Stress and Child Treatment/Procedural Anxiety**

There is significant research that indicates that a caregiver’s psychological state can influence the psychological state of their child. Platt and colleagues (2016) evaluated potential mediators of the association between stressful incidences experienced by the child and child anxiety with 130 child participants ages seven to thirteen. Parenting stress mediated the effect of stressful life incidences on the child’s anxiety level. This study supported the “stress-mediated pathway” theory, which suggests that stress responses are transferred from parent to child regardless of the parent’s prior psychological state. The transfer of stress responses from parent to child was also found by Becker et al. (2010), who conducted a study with 38 anxious mothers and 37 non-anxious mothers each with one child ages six to fourteen years old. The results showed a significant relationship between mother’s anxiety level and their child’s anxiety level. It was also found that this relationship was mediated by the development of the child’s external locus of control, which occurs when a child of anxious parents feels that they do not have control over anxiety-related circumstances. Further, the child’s external locus of control was also found to mediate maternal control behavior and child anxiety. In addition to the relationship between child anxiety and external locus of control, caregiver stress has also been found to be associated with external locus of control in pediatric illness populations. The study of parental external locus of control and its impact on caregiver stress level has also been evaluated. Bennett and colleagues (2013) found that among 37 caregivers of
children with brain tumors, heightened caregiver stress level was significantly associated with increased external locus of control. Additionally, the strongest predictor of caregiver stress level was endorsement of an external locus of control by caregivers. Caregivers in this study often blamed themselves for their child’s illness (Bennett et al., 2013). The relationship between stress, anxiety, and external locus of control between parent and child is particularly relevant to the pediatric cancer population where a lack of control is a common experience and heightened stress may lead to poorer child outcomes.

Prior studies have found that caregiver stress and child anxiety are significantly correlated in pediatric cancer populations. Specifically, Okado et al. (2014) conducted a study of 397 parent-child participants with children ages 8-17 years old; 255 of the participants were parent-child dyads with children on active treatment for cancer (46%) or cancer survivors (54%). The control group for the study was 142 parent-child dyads without cancer. It was found that parent and child symptoms, specifically, anxiety, depression, and post-traumatic stress were significantly associated within the population of children with cancer. In comparison, this correlation was not found in the control group of child-parent dyads. This suggests that the unique experience of childhood cancer further strengthens the relationship between caregiver and child stress responses as well as psychosocial functioning.

**Family Beliefs of Caregiver**

Identification of caregivers’ cancer-related family beliefs about their child’s diagnosis is an important aspect of creating targeted interventions to decrease psychosocial distress (Kazak et al., 2004). Kazak et al. (2004) developed the Family Illness Beliefs Inventory using factor analysis as a valid statistical tool for evaluating
caregiver’s beliefs about how their family will cope with their child’s cancer diagnosis and treatment. It was found that of the five factors of belief (e.g., “treatment-related suffering, death and devastation, caregiver competence, connection and finding meaning”) regarding different aspects of treatment were more malleable than others (Kazak et al., 2004). For example, caregiver beliefs about treatment-related side effects such as nausea and procedural pain were strongly associated with intensity of the patient’s treatment. This finding suggests that a cognitive behavioral therapy intervention-based approach could assist with addressing beliefs from such side effects (e.g., “my child will be in a lot of pain”) which are found to be more malleable. Thus, the identification and understanding of family beliefs is integral to providing targeted psychological support to both parents and children in cancer treatment (Kazak et al., 2004).

Previous research on the family beliefs of caregivers within pediatric cancer populations has shown that caregiver beliefs are associated with stress level reactions to an event (Quine & Pahl, 1991). Rosenberg et al. (2013) conducted a study with 81 children ages two to eighteen years old who were primarily (91%) receiving cancer-directed therapy treatment. The researchers found that caregivers who endorsed the belief that their child’s cancer diagnosis was curable through treatment had lower levels of distress. Caregivers who understood their child’s prognosis as aligned with their primary treatment goals and beliefs also reported lower levels of distress. Caregivers that reported their child to be experiencing anxiety and sadness had increased levels of distress in comparison with caregivers who reported their child was in pain. Interestingly, even if the child’s illness was incurable, parents still reported lower levels of distress if their
understanding aligned with their treatment goals. This suggests that caregiver’s beliefs influence perception of child pain levels as well as the stress reaction to the child’s treatment and prognosis.

In addition to research on the relationship between family beliefs and child treatment goals, caregiver’s belief about their child’s emotion socialization can also impact caregiver stress level in the pediatric cancer population. Faith et al. (2019) conducted a study with 134 caregivers, siblings and pediatric cancer patients (median age twelve) on treatment. The study evaluated the differences in caregiver’s emotion and socialization beliefs for both their child with cancer and their child’s sibling. Additionally, the study examined if caregiver’s beliefs about emotion socialization influenced the relationship between parent and child coping styles for both the child with cancer and their siblings. Caregivers communicate the value and approval or disproval of emotions through emotion socialization, the socialization of a child’s understanding, processing and outward expression of emotion. Therefore, caregivers’ belief of their child’s emotion socialization during times of increased stress such as cancer treatment can have influences on the psychological wellbeing of both caregivers and children. The study results reported that beliefs about emotion socialization operated as a moderator of coping in both caregivers and their child with cancer. Although this study focuses on the emotional aspects of caregiver beliefs towards their child, the results of caregiver beliefs as moderator between caregiver and child psychological coping contributes to insight into understanding of family beliefs in the context of pediatric cancer.

*Caregiver Stress, Pediatric Pain and Caregiver Beliefs*
Past research findings have shown a connection between a parent’s catastrophizing about pain leading to a greater experience of pain in children as well as negative outcomes over time. Pagé et al. (2013) provided an example of this by conducting a longitudinal research study, which found among 83 children ages eight to eighteen years old undergoing surgery that increased parental catastrophizing before their child’s surgery was correlated with higher child pain reports two weeks post-surgery.

The correlation between caregiver distress and pediatric pain has been studied utilizing different conceptual frameworks. The multidimensional Biobehavioral Model of Pediatric Pain hypothesized that many factors influence pediatric pain perception and Health Related Quality of Life outcomes such as perceived stress, coping strategies and emotional distress (Varni, Burwinke & Katz, 2004; Appendix B). Vetter et al. (2013) suggest that pediatric pain is viewed as a multidimensional construct with biological and psychosocial elements. Using the Biobehavioral Model of Pediatric Pain, Vetter et al. (2013) discovered significant correlations between pediatric pain intensity, patient pain coping and the parent’s own level of chronic pain intensity, which further validated the Biobehavioral Model of Pediatric Pain.

Although findings have shown that caregiver distress and child pain are correlated, differences have been found between child and parental-proxy reports on pain. Birnie et al. (2020) conducted a recent study with 806 children, median age 14.5 years old in which pediatric chronic pain was evaluated through patient’s self-report and caregiver reports of chronic pain functioning using the PROMIS pediatric measure. It was hypothesized that greater agreement between caregiver and patient reports would exist for observable pain in contrast with internal measures such as anxiety and
depression. It was found that both caregiver and child pain were significantly associated across both internal and external measures; however, greater pain catastrophizing was associated with greater differences in reports between caregiver and child. Although caregiver beliefs may have a role in the connection between caregiver stress and child pain levels, findings suggesting significance within pediatric chronic pain populations have been tenuous. Simons et al. (2011) evaluated how caregiver beliefs influence child pain acceptance. The study participants were 195 caregiver-child dyads of children with persistent pain. The children were ages 8-17 years of age. The study found that for children living with chronic pain, factors such as caregiver distress and external responses to pain significantly influenced the child’s pain levels. However, the relationship between child pain and caregiver beliefs about the child’s pain was not found to be significant. The study suggests the need for further research into caregiver beliefs about child’s acceptance of pain.

The previous findings suggest significant correlations between caregiver distress and child pain for both the general pediatric and chronic pain pediatric populations. This supports similar findings among pediatric cancer patients and caregivers. Additionally, heightened stress levels of caregivers within the pediatric cancer population may also strengthen the association between caregiver distress and child pain levels. Uhl et al. (2020) developed a comprehensive review of the role of caregivers in the management of pain for children with pediatric cancer. The management of cancer-related pain is often understood through a biopsychosocial lens with physical and psychological aspects of pain viewed as integral parts of the pain experience. Caregivers have been found to be a vital part of the child’s pain experience during cancer treatment because of their
involvement with pain treatments (Uhl et al., 2020). Further, the correlation between caregivers’ response to pain and the child’s pain severity is commonly found in the pediatric cancer population (Uhl et al., 2020). Given the high level of stress often associated with a caregiver seeing their child in pain, caregivers often become very focused on their child’s pain experiences. This focus on pain level can cause a child to fixate on their own pain, which increases experiences of pain and fear (Uhl et al., 2020). Thus, the association between caregiver distress and over-involvement in the pain experience of the child leads to higher levels of pain reported by the child (Uhl et al., 2020).

**Gaps in Research**

Although there have been important findings in the significant correlation between caregiver and child psychological functioning in the pediatric cancer population, there are still noteworthy gaps in the research regarding the psychological experience of a pediatric cancer diagnosis and treatment for both child and caregiver (Daniel et al., 2014). Family beliefs are especially relevant in pediatric cancer because they may serve as critical influences on psychosocial outcomes for caregivers and children. Few studies, however, have examined these beliefs in families with children undergoing cancer treatment as well as family beliefs moderating the relationship between caregiver stress and procedural/treatment anxiety and pain of the child. Previous studies have investigated other areas of belief in the context of pediatric cancer such as religious beliefs, which was found to be a potential protective factor against psychological distress in caregivers (Nam et al., 2016). McCubbin et al. (2002) utilized the Resiliency Model of Family Stress, Adjustment and Adaption to evaluate family appraisal in the context of resiliency. The
findings indicated that attitudes that centered on positive beliefs led to greater resiliency in the family unit. Additionally, there is a paucity of research regarding the role of family beliefs in the context of pain in pediatric cancer, which may be because of the lack of significant associations found previously between beliefs and child pain conducted in general pediatric and pediatric chronic pain populations. However, it is important to evaluate this role of beliefs in populations undergoing life threatening illness, which may exacerbate the importance of beliefs. The PAT 2.0 measure is widely used to predict psychosocial risk in the pediatric cancer population, however, there is a gap in knowledge for the specific family belief subscale used in the PAT 2.0 measure (Kazak et al., 2018). Further, the relationship of family beliefs to childhood treatment/procedural anxiety and pain interference has yet to be explored in this context.

**Research Aims**

In the current study, the predictor variable is caregiver stress, the outcome variables are child reported treatment/procedural anxiety and pain interference and caregiver-proxy report of child treatment/procedural anxiety and pain interference. The moderating variable is family beliefs. The main hypothesis is that positive family beliefs held by caregivers will attenuate the relationship between high stress and high treatment/procedural anxiety and pain interference reported by child and caregiver-proxy report. The study uses an adapted version of Biobehavioral Model theoretical framework, which demonstrates the influence of perceived stress, coping skills and emotional distress among other factors on perceived pain interference and treatment/procedural anxiety for pediatric cancer patients (Varni, Burwinke & Katz, 2004; Appendix B). The study aims are:
**Aim 1.** To investigate the relationship between caregiver stress level and degree of treatment/procedural anxiety of the child when moderated by family beliefs.

*Hypothesis 1a.* It is hypothesized that positive family beliefs will attenuate the relationship between high caregiver stress and high caregiver-proxy report of the child’s treatment/procedural anxiety level (Appendix D).

*Hypothesis 1b.* It is hypothesized that positive family beliefs will attenuate the relationship between high caregiver stress and high child’s report of treatment/procedural anxiety (Appendix E).

**Aim 2.** To investigate the relationship between caregiver stress and pain interference of child when moderated by family beliefs.

*Hypothesis 2a.* It is hypothesized that positive family beliefs will attenuate the relationship between high caregiver stress and high caregiver-proxy report of the child’s pain interference (Appendix F).

*Hypothesis 2b.* It is hypothesized that positive family beliefs will attenuate the relationship between high caregiver stress and the high child’s report of pain interference (Appendix G).

The covariates of money problems and family problems will also be included in moderation models reflecting additional variables of interest as identified in the Biobehavioral model (Varni, Burwinke & Katz, 2004).

The Psychosocial Assessment Tool Oncology (PAT2.0) measured the variables of caregiver stress level and family beliefs. The Patient-Reported Outcomes Measurement Information System (PROMIS) Pain Interference Scale measured the variables of child pain and caregiver-proxy report of pain interference. The Pediatric Quality of Life
Inventory Cancer Module (PedsQL) measured child treatment/procedural anxiety and caregiver-proxy report of child treatment/procedural anxiety. The covariates of money problems and family problems were measured with the PAT 2.0 measure.

The hypothesis is plausible given the breadth of research on the strong correlation between caregiver stress, child psychological functioning and pain perception. However, as a result of the gap in research for family beliefs as a moderator, the validity of family beliefs as a moderator in this relationship still remains uncertain. Further, the significance of family beliefs, and the impact on the child’s own psychological functioning has not been thoroughly explored. The concept of perceived control by the caregiver and its relationship to stress reduction as well as family beliefs is another important aspect to this research question and hypothesis. If the family belief variable is not a significant moderator, it could be because the question constructs in the family belief subscale include both malleable and dispositional belief-based questions, which may limit the influence of this variable. However, if the hypothesis is supported, the results will lead to better understanding of the signs of high-risk caregivers and their children. Additionally, the findings could provide further nuance to the PPPHM framework (Appendix A) in terms of developing targeted interventions which focus on cultivating a positive set of family beliefs.
Method

Procedure

This study has a correlational research design. The proposed study is a secondary analysis of data collected from May 2017-August 2019 for the study, “Clinical Validity of the PROMIS Pediatric Sleep Short Forms in Children Receiving Treatment for Cancer” by Daniel et al. (2020). Eligible subjects were caregiver-patient pairs, specifically 59 children ages 8-17 and 59 caregivers completed the measures, for children under age eight (5-7), 42 caregivers completed only the caregiver-proxy report for their child. Child participants were undergoing active cancer treatment between 2-12 months after diagnosis at The Children’s Hospital of Philadelphia. It was determined that participants who were receiving palliative care, unable to complete measures in English, had a developmental delay, or were not treated at Children’s Hospital of Philadelphia were ineligible to participate in the study (Daniel et al., 2020). Children between ages 8-17 years old were eligible to complete self-report questionnaires since they were determined to be old enough to adequately understand and respond to the questions (Varni et al., 2007). The PROMIS measure given has been validated for use in self-report for ages 8-17 years and is applicable to all measures used in the study (Varni et al., 2010). Study participants were identified through the tumor registry and clinic roster, and then contacted through email and at clinic appointments at Children’s Hospital of Philadelphia. The caregiver participants provided consent and the child participants provided assent. Participants completed the survey at their clinic appointment or remotely online. Participants completed the questionnaire online through REDCAP (Research Electronic Data Capture), a data collection tool hosted by Children’s Hospital of
Philadelphia, with the exception of two participants who completed paper versions of the
survey due to technological issues. Both caregiver and child participants received gift
cards of $20 for caregiver and $15 for children for their time.

In total, 718 children were screened for eligibility and 535 children did not meet
the eligibility requirements due to being outside of the age range or off treatment. 183
children were eligible to participate as well as 121 caregiver-child dyads. Additionally,
62 caregivers only were eligible. Of the eligible caregivers, 79 declined due to the
following reasons: not enough time (4%), no interest (6%), did not want to participate in
research (.5%), child was not well enough (.5%), the child aged out of the study before
consenting (1%), there was a change in the child’s disease status (2.7%) and passive
refusal (27%). After caregiver completion of measures, 43 children declined study due to
under age 8 (19%), caregiver or child declined (1%) and child passive refusal (3.2%).
There were 104 consenting caregivers who agreed to participate in the study. However,
two withdrew after consent and one did not complete the key study variables. In total,
101 caregivers completed the measures and 59 children assented and completed the study
measures (Appendix H; Daniel et al., 2020).

Participants

Within the study sample of 101 caregivers and 59 child participants, 89% of the
caregivers were female and 58% of the children were female. The average age of the
child participants was 10 years old. The race/ethnicity of the child participants were
84.7% White, 11.9% African American, 5.1% Asian, 8.4% multiple races, 5.1% had
more than one race selected and 1.7% were Hispanic. The caregiver participants were
81.18% White, 9.9% African American, 1.9% Asian, 1.96% multiple races and 4.9%
Hispanic (Appendix I; Daniel et al., 2020). The observed power of the sample with medium effect size and alpha set at .05 was .85 (Faul, Erdfelder, Lang, & Buchner, 2007).

**Measures**

The measures for this research study are self-report questionnaires that were given to both caregiver and child. Self-report measures effectively assess psychological states which is necessary for the analysis of the caregiver and child responses. In assessing reporter perceived stress levels, self-report measures are important for understanding the reporter’s appraisal of their own private behavior and perceptions. Additionally, the caregiver and child are able to reflect back on past and present behavior. The self-report questionnaires were accessible to both child and caregiver. Overall, these self-report questionnaires have high validity, internal consistency and test-retest scores.

**The Psychosocial Assessment Tool Oncology (PAT2.0)**

The PAT 2.0 measure was designed to screen for psychosocial risk in the families of children with cancer. The PAT 2.0 is a two-page self-report measure containing seven subscales (Family Structure and Resources, Family Social Support, Family Problems, Parent Stress Reactions, Family Beliefs, Child Problems, Sibling Problems) with 15 item sets including yes/no, categorical responses and Likert-type scales. Subscale are totaled and adjusted by the division of number of high-risk items over total number of items in each subscale (McCarthy et al., 2009). The adjusted subscale scores range from 0 to 1 with total PAT 2.0 score ranging from 0 to 7. Depending on the total PAT 2.0 score, families are categorized into Universal (low risk category), Targeted (elevated risk) and Clinical (highest risk). The internal consistency for the PAT 2.0 measure was high.
and exhibited good test-retest reliability for mothers ($r = .78, p < .001$) and ($r = .87, p < .001$) for fathers. The criterion validity was established by comparing the PAT 2.0 total scores with validation instruments of the Behavioral Assessment Scale for Children-Second Edition Parent Rating Scales (BASC-2) ($\alpha = .80-.94$), Acute Stress Disorder Scale ($\alpha = .96$), Family Environment Scale (FES)-Conflict and Cohesion Scales ($\alpha = .75, \alpha = .78$), State-Trait Anxiety Inventory (STAI-Y) State Scale ($\alpha = .89-.96$) (Pai et al., 2007). For six of the seven sub-scales an alpha coefficient of above .60 was obtained. The sub-scale with the highest internal consistency was family problems ($\alpha = .72$). The sub-scales with the lowest internal consistency were family beliefs ($\alpha = .59$) and structure/resources ($\alpha = .62$). The family beliefs subscale had an internal consistency of ($\alpha = .59$) with four items analyzed due to the theoretical nature. Further, the four items chosen reflected cancer-related beliefs and demonstrated adequate internal consistency with test-retest reliability of $r = .78 (p < .001)$ for mothers, and $r = .87 (p < .001)$ for fathers. The internal consistency reliability for the PAT 2.0 Cancer Module Scales was $\alpha = .72$ for the child and $\alpha = .87$ for the parent (Varni et al., 2002). It was found that the PAT 2.0 is a useful screening tool for pediatric cancer patients and their families (Pai et al., 2007).

**PAT 2.0: Caregiver Stress Subscale.** This predictor variable, caregiver stress was determined to have a moderate internal consistency for this study which was tested using Cronbach’s alpha of .70 and the criterion-related validity was correlated with outcome variables associated with psychosocial risk with mother’s acute stress score of .59. Additionally, the construct validity for acute stress for mothers was .59 and for fathers .46 (Pai et al., 2007). The caregiver stress continuous variable was measured by parent self-report questionnaire within a 5-item subscale with questions referenced in
subscale 1. Participants rated statements based on 4-point Likert scale (value-0-\textit{not at all}, value 1-\textit{sometimes}, value 2-\textit{often}, value 3-\textit{very much}) with higher scores indicating higher levels of caregiver stress and lower scores indicating lower levels of caregiver stress. The composite score was created from an average of responses of participants. The range for this scale is 0 to 15 (Appendix J).

**PAT 2.0: Family Beliefs Subscale.** The family beliefs moderating variable assesses caregiver beliefs, which evaluates another layer of the caregiver’s psychological functioning. This variable was developed with the input of 84 clinical experts in the field of pediatric oncology who rated the level of risk of 18 domains, family beliefs included. It was determined that family beliefs was a significant variable to measure risk factors and ongoing distress levels of caregivers. The items for each domain were developed to correspond with the overall domain of family beliefs. The scales were also based on the theoretical framework, social ecological perspective of child health (Kazak et al., 2002). For this study sample, the internal consistency was tested using Cronbach’s alpha in which subscale score was found to be .57. This score is consistent with the Cronbach’s alpha result of .59 which was found when the measure was initially validated and thus is acceptable for use (Pai et al., 2007). The test-retest score for mothers was .78 and .87 or fathers, both were significant ($p<.001$) (Pai et al., 2007). This variable is on a 9-item subscale (Appendix K). Caregivers rated statements based on a 4-point Likert scale (value 1-\textit{not true for me}, value 2-\textit{a little true for me}, value 3-\textit{mostly true for me}, value 4-\textit{very true for me}). A composite score was created for average family beliefs of participants; some items were recoded in analysis so that higher scores indicated more negative family beliefs. The following questions were recoded: \textquote{My child will be in a lot
of pain”, “Our marriage or family will fall apart”, “this is a disaster”, “People will pull away from us,” and “cancer is a death sentence.” The score range is positive to negative family beliefs: value 1 -very positive to value 4 -very negative), range (10-40) (Appendix K).

**PAT 2.0: Covariate- Money Problems.** The covariate, money problems had the following question: “Is the family having money problems?” The score range was low to high (1-no money problems, 2-some problems, 3-many problems, 4-it’s hard for the family to meet its needs). Previous research by Karlson and colleagues (2013) has found that the PAT measure has found greater financial difficulties to be significantly associated with caregiver stress level. Thus, inclusion of a question as a covariate assessing financial issues within the family was included.

**PAT 2.0: Covariate- Family Problems Subscale.** The covariate family problems was measured on a 10 item subscale (Appendix L). The family problems subscale was measured with no/yes for 10 items. In analysis these items were be dummy coded 0=No and 1=yes. The range after dummy coding was low to high levels of family problems, range (0-10). Internal consistency for this study sample was tested for family problems using Cronbach’s alpha in which subscale score was found to be .57. Family functioning is a key component of the PPPHM which evaluates family psychosocial risk level in pediatric cancer (Kazak et al., 2015). Thus, the covariate of family problems was selected given its overall assessment of family functioning. (Appendix L).

*The Patient-Reported Outcomes Measurement Information System (PROMIS) Pain Interference Scale*
The PROMIS Pain Interference Scale measure was designed to assess general pediatric pain across a wide variety of disorders. The outcome variable, child pain interference was operationalized using the Pediatric Pain Interference Scale and given to children ages 8-17 years old. The PROMIS Pediatric Pain Interference Scale was completed by both caregiver and patient. An aspect of self-report was understanding the degree the child was experiencing pain. Items were rated on a scale of never (0) to always (5) with higher scores indicating high level of pain interference. An Item Response Theory (IRT) analysis was conducted for the PROMIS pediatric item bank to create the Pediatric Pain Interference Scale. 3,048 respondents completed items for pediatric pain. Raw scores were converted into T-scores using the IRT derived scoring through (www.healthmeasures.net). The pain interference item pool had a T-score mean of 50 and standard deviation of 10 (Varni et al., 2010). This measure was found to have strong reliability (Cronbach’s alpha=.90-.95) for caregiver and patient reports and clinical validity for use in pediatric oncology (Hinds et al., 2019).

The question items for the pain interference scale for child report are referenced in Appendix M. The child rated statements based on 5-point Likert scale (value 1-never, value 2-almost never, value 3-sometimes, value 4-often, value 5-almost always.) Higher scores indicated increased levels of child pain interference and lower scores indicated lower levels of pain interference. A composite score was created for the sum of responses of participants. The range of the subscale was (5-40). The outcome variable, caregiver-proxy pain inference report was operationalized in the caregiver report with questions referenced in Appendix N. The caregiver rated statements based on 5-point Likert scale (value 1-never, value 2-almost never, value 3-sometimes, value 4-often, value 5-almost
always.) Higher scores indicated increased levels of child pain and lower scores indicated lower levels of pain. For the study sample, internal consistency was tested for caregiver-proxy report of child pain using Cronbach’s alpha in which subscale score was found to be .94. This was determined to be consistent with the validation study Cronbach’s alpha score. Additionally, for the study sample, the internal consistency was tested for child report of pain inference using Cronbach’s alpha in which subscale score was found to be .93. This was also determined to be consistent with the validation study’s Cronbach’s alpha score (Hinds et al., 2019). A composite score was created for the sum of responses of participants. The range of the subscale was 8 to 40 (Appendix D; Appendix E).

**Pediatric Quality of Life Inventory (PedsQL)**

The Pediatric Quality of Life Inventory—Cancer Module (PedsQL) was designed to measure the health-related quality of life for children ages 2-18 years old. Additionally, the PedsQL was developed for both parent and child self-report. This instrument has been shown to be reliable and valid for assessing quality of life in the pediatric cancer population. The internal consistency reliability for the Cancer Module Scales was $\alpha=.72$ for the child and $\alpha=.87$ for parents (Varni et al., 2002). The PedsQL cancer module was created with eight scales: pain and hurt (2 items), nausea (5 items), procedural anxiety (3 items), treatment anxiety (3 items), worry (5 items), cognitive problems (5 items), perceived physical appearance (3 items) and communication (3 items). The format has Likert response scale with lower scores indicating fewer symptoms. The instruments used for construct validation were the Children’s Depression Inventory, State-Trait Anxiety Inventory for Children, Self-Perception Profile for Children and Adolescents and the Child Behavior Checklist (Varni, Seid & Rode, 1999) as well as the Pediatric Cancer
Quality of Life Inventory (Varni et al., 2002). This measure has high levels of internal consistency and reliability for child self-report of procedural anxiety (α=.82) and treatment anxiety (α=.79). The internal consistency and reliability for caregiver-proxy report was procedural anxiety (α=.93) and treatment anxiety (α=.91). The reliability for caregiver-proxy reports subscales were (α=.80 to .90) (Varni et al., 2002).

The dependent outcome variable, procedural and treatment anxiety was a continuous variable on a 6-item subscale. This treatment/procedural anxiety variable was given to both child and caregiver. The child ages 8-17 subscale is referenced in Appendix O. The child participants rated statements based on 5-point Likert scale (value 1-never, value 2-almost never, value 3-sometimes, value 4-often, value 5-almost always). Higher scores indicated increased levels of child treatment/procedural anxiety and lower scores indicated lower levels of treatment/procedural anxiety. The caregiver-proxy report of child treatment/procedural anxiety questions are referenced in Appendix P. The caregiver rated statements were based on 5-point Likert scale (value 1-never, value 2-almost never, value 3-sometimes, value 4-often, value 5-almost always). Higher scores indicated increased levels of the caregiver’s proxy report of child treatment/procedural anxiety and lower scores indicated lower levels of the caregiver’s proxy report of child treatment/procedural anxiety. A separate composite score was created for the sum of child self-report, and the sum of the caregiver-proxy report responses. For this study sample, internal consistency was tested for caregiver-proxy report of child treatment/procedural anxiety using Cronbach’s alpha in which the subscale score was found to be .88. Internal consistency was tested for child report of treatment/procedural anxiety using Cronbach’s alpha in which the subscale score was found to be .88. These
alpha scores are within the range of the validation study (α=.80 to .90) (Varni et al., 2002). The subscale ranges are 6 to 30 (Appendix O; Appendix P).

**Data Analysis**

In the preliminary data analysis, descriptive statistics were conducted for the demographic variables of race, sex and age as well the for the key study variables of caregiver stress, family beliefs, child pain interference, caregiver-proxy report of child pain interference, child anxiety, caregiver-proxy report of child treatment/procedural anxiety, family problems and money problems. Missing data was treated using PROCESS macro’s default listwise detection of missing data (Hayes, 2017). In preliminary analysis, one caregiver participant did not complete the key study variables. Thus, this participant data was excluded from the study (Appendix H).

Pearson correlations were used to analyze and compare relationships between the study variables of caregiver stress, family beliefs, child pain interference, caregiver-proxy report of child pain interference, child treatment/procedural anxiety, caregiver-proxy report of child treatment/procedural anxiety, family problems and money problems.

A simple moderation analysis was used to analyze the influence of family beliefs on caregiver stress and anxiety and pain interference outcomes with the covariates of family problems and money problems. The data was analyzed using SPSS Version 28 (IBM Corporation, U.S.A) and Hayes’s (2017) PROCESS macro 4.0. Using the PROCESS macro 4.0, the mean was centered for each variable in the moderation model, and the covariates of money problems and family problems were entered into moderation model 1. The Johnson-Neyman technique was used through PROCESS macro 4.0 to reduce the selection of arbitrary values of the moderator used to deduce the conditional
effect of the predictor variable on the outcome variable. The moderation model 1 was used for each moderation analysis (Hayes, 2017).

**Analysis for Aim 1.** To test hypothesis 1a, moderation analysis was conducted using PROCESS macro 4.0 (Hayes, 2017) and SPSS Version 28 (IBM Corporation, U.S.A). Caregiver stress was entered as the predictor variable, family beliefs as the moderation variable, caregiver-proxy report of child treatment/procedural anxiety as the outcome variable with the covariates of money problems and family problems. PROCESS macro 4.0 mean centered the variables to reduce the threat of multicollinearity (Appendix Q).

To test hypothesis 1b, moderation analysis was conducted using PROCESS macro 4.0 (Hayes, 2017) and SPSS Version 28 (IBM Corporation, U.S.A). Caregiver stress was entered as the predictor variable, family beliefs as the moderation variable, child reported treatment/procedural anxiety as the outcome variable with the covariates of money problems and family problems. PROCESS macro 4.0 mean centered the variables to reduce the threat of multicollinearity (Appendix R).

**Analysis for Aim 2.** To test hypothesis 2a, moderation analysis was conducted using PROCESS macro 4.0 (Hayes, 2017) and SPSS Version 28 (IBM Corporation, U.S.A). Caregiver stress was entered as the predictor variable, family beliefs as the moderation variable, caregiver-proxy report of pain interference as the outcome variable with the covariates of money problems and family problems. PROCESS macro 4.0 mean centered the variables to reduce the threat of multicollinearity (Appendix S).

To test hypothesis 2b, moderation analysis was conducted using PROCESS macro 4.0 (Hayes, 2017) and SPSS Version 28 (IBM Corporation, U.S.A). Caregiver stress was
entered as the predictor variable, family beliefs as the moderation variable, child reported pain interference as the outcome variable with the covariates of money problems and family problems. PROCESS macro 4.0 mean centered the variables to reduce the threat of multicollinearity (Appendix T).

**Human Subjects**

The previous study, “Clinical Validity of the PROMIS Pediatric Sleep Short Forms in Children Receiving Treatment for Cancer” by Daniel et al. (2020) from which the data was collected did use human subjects. The subjects were considered part of a vulnerable population because they were both children and had been diagnosed with pediatric cancer. The research was submitted and approved by the IRB through Rutgers University and at Children’s Hospital of Philadelphia. All caregivers in the study provided informed consent and all children provided assent. The subjects in the study were recruited through clinical appointments and only during outpatient clinic appointments (Daniel et al., 2020). All subjects were given informed consent and completed the measures through REDCAP, which is a secure web application for managing online surveys. REDCAP is also HIPAA compliant. All data from the measures are stored in the Children’s Hospital of Philadelphia’s server. Participant responses are anonymized and access to the data is password protected. Given that these data have been previously collected and will only be used for correlational analysis, there was minimal risk to participants in the study.
Results

Sample Description

There were 101 caregivers that provided self-report and caregiver proxy-reports. 59 caregiver-child dyads completed the measures. Participants ages 8-17 years old completed the child self-report measures (Appendix I).

Correlations Among Study Variables

Correlations between all study variables are described in (Appendix V). A significant positive correlation was found between family beliefs and caregiver stress \( r(101)=.371, p=.001 \). Caregiver stress level was also found to be significantly correlated with caregiver-proxy report of child pain interference \( (r(101)=.211, p=.034) \) and family problems \( (r(101)=.337, p=.001) \), such that as caregiver stress increased so did caregiver-proxy report of child pain interference as well as caregiver report of family problems. Family beliefs were found to be significantly correlated with caregiver-proxy report of child pain interference \( (r(101)=.229, p=.02) \) and family problems \( (r(101)=.268, p=.007) \), indicating that negative family beliefs were associated with caregiver-proxy report of higher child pain interference and caregiver report of increased family problems. Caregiver-proxy report of child pain interference was also significantly associated with child report of pain interference \( (r(59)=.578, p=.001) \), caregiver-proxy report of child treatment/procedural anxiety \( (r(101)=.467, p=.001) \), child report of treatment/procedural anxiety \( (r(59)=.460, p=.001) \), indicating that as child-proxy report of child pain interference increases, child report of pain interference, caregiver-proxy report of treatment/procedural anxiety and child report of treatment/procedural anxiety also increase. Caregiver-proxy report of treatment/procedural anxiety also were significantly
associated \((r(59)=.775, p=.001)\) such that as caregiver-proxy report of treatment/procedural anxiety increased, child report of treatment/procedural anxiety also increased.

**Moderation Analysis**

**Aim 1: Moderation effect of family beliefs on Caregiver Stress and Child Anxiety**

**Hypothesis 1a.** An analysis using Hierarchical Multiple Regression conducted with PROCESS macro 4.0 was used to test the hypothesis that the relationship between caregiver stress and caregiver-proxy report of child treatment/procedural anxiety would be moderated by family beliefs including the covariates of family problems and money problems (Appendix W). Family beliefs did not moderate the relationship between caregiver stress and caregiver-proxy report of child treatment/procedural anxiety, thus the interaction, \(b=.666, t(95)=.034, p=.972\) was not significant. The overall model was not significant, however, it did account for 6% of the variance in child anxiety, \(F(5, 95)=1.38, p=.237, R^2=.0678\) (Appendix X).

**Hypothesis 1b.** An analysis using Hierarchical Multiple Regression conducted with PROCESS macro 4.0 was used to test the hypothesis that caregiver stress and child report of treatment/procedural anxiety would be moderated by family beliefs including the covariates of family problems and money problems (Appendix Y). Family beliefs did not moderate the relationship between caregiver stress and child report of treatment/procedural anxiety \(F(5, 53)=.1055, p=.990, R^2=.0099\). The interaction, \(b=-8.55, t(53)=-.298, p=.766\) was also not significant (Appendix Z).

**Aim 2: Moderation effect of family beliefs on Caregiver Stress and Child Pain**
**Hypothesis 2a.** An analysis using Hierarchical Multiple Regression conducted with PROCESS macro 4.0 was used to test the hypothesis that caregiver stress and caregiver-proxy report of child pain interference would be moderated by family beliefs including the covariates of family problems and money problems (Appendix U). Family beliefs did not moderate the relationship between caregiver stress level and caregiver-proxy report of child pain interference. However, the overall model was significant and explained 11% of variance in child pain interference $F(5, 95)=2.47, p=.037, R^2=.1153$. The relationship between family beliefs and caregiver-proxy report of child pain interference, $b=6.58, t(95)=1.97, p=.051$ was marginally significant. The interaction, $b=11.22, t(95)=1.32, p=.188$ was also not significant. (Appendix AA).

**Hypothesis 2b.** An analysis using Hierarchical Multiple Regression conducted with PROCESS macro 4.0 was used to test the hypothesis that caregiver stress and child report of pain interference would be moderated by family beliefs including the covariates of family problems and money problems (Appendix BB). Family beliefs did not moderate the relationships between caregiver stress level and child report of pain interference $F(5, 53)=.567, p=.724, R^2=.050$. The interaction, $b=2.85, t(53)=.230, p=.818$ was not significant. (Appendix CC).
Discussion

The experience of a cancer diagnosis and treatment can cause significant stress in both children with cancer and their families. Negative stress responses in the cancer population have been found to lead to increased family dysfunction and declines in psychological wellbeing (Gurtovenko et al., 2021; Neugebauer & Mastergeorge, 2021). Prior research on caregiver and child interactions has found that caregiver’s psychological functioning and emotional responses can directly influence the psychological and emotional state of their child (Platt et al., 2016; Jobe-Sheilds et al., 2009). Further, prior studies have shown that caregiver beliefs about their family’s functioning in response to a cancer diagnosis are associated with the caregiver’s reported stress levels (Quine & Pahl, 1991; Fotiadou et al., 2008). Intervention-based approaches aiming to increase psychological wellbeing of caregivers and their children undergoing cancer treatment have been found to be successful when targeting specific stressors in the pediatric cancer population (Li et al., 2011; Lapid et al., 2015). To better understand the relationship between caregiver stress levels, family beliefs related to cancer diagnosis and psychological as well as physical outcomes, this study aimed to evaluate the influence of family beliefs on the relationship between caregiver stress and caregiver’s perception of their child’s pain interference and anxiety levels as well as the child’s report of anxiety and pain interference. Correlations between these variables were also analyzed. Family beliefs were found to not be significant as a moderator between caregiver stress level and caregiver-proxy report of child pain interference, caregiver-proxy report of child treatment/procedural anxiety, child report of pain interference and child report of treatment/procedural anxiety with the covariates of money problems and family
problems. Significant correlations were found between caregiver stress and family beliefs as well as caregiver stress and caregiver-proxy report of child pain interference. Family beliefs was also found to be significantly correlated with caregiver report of child pain interference. Caregiver-proxy report of child pain interference was significantly associated with child report of pain interference and treatment/procedural anxiety in both child and caregiver-proxy reports.

**Sample Comparisons**

Caregiver stress levels in the current sample (M=1.6, SD=.49) were higher in this study in comparison with other pediatric cancer samples (M=.61, SD=.91) (Pai et al., 2007). However, average reports of family beliefs for this study sample (M=1.6, SD=.33) were found to be consistent with caregivers in other pediatric cancer samples (M=1.33, SD=1.24) (Pai et al., 2007). Similarly, caregiver-proxy report of child pain interference (M=51.8, SD=10.66) and child pain interference (M=53, SD=11.65) were comparable to other pediatric cancer samples (M=52.54, SD=9.33; M=52.96, SD=9.24) (Cheng et al., 2022; Varni et al., 2010). However, in contrast with control samples of healthy children, the average pediatric cancer pain interference reported was slightly higher (M=50, SD=10) (Varni et al., 2010). For caregiver proxy-report and child report of treatment/procedural anxiety level, the scores typically from (0-100) for high to low anxiety have been reversed for this study to maintain the direction of the other variable scales, with higher scores indicating higher anxiety. Similar levels of caregiver-proxy report of treatment/procedural anxiety were found in this study sample (M=35, SD=23.95) in comparison with caregiver-proxy reports from other pediatric cancer samples (M=34.11, SD=30.24). However, the child treatment/procedural anxiety reports
(M=34.8, SD=26.34) were higher in this study in comparison with other pediatric cancer samples (M=24.78, SD=27.72) (Varni et al., 2002). Healthy control samples for both caregiver-proxy report and child report of treatment/procedural anxiety had lower levels of treatment/procedural anxiety in comparison with this study sample (M=17.36, SD=17.54; M=19.14, SD=19.64) (Varni et al., 2002). The findings show that this study sample reported similar psychosocial and physical experiences to that of other pediatric cancer populations, however, had higher levels of poor psychosocial and physical functioning in comparison with healthy control groups. The higher average level of caregiver stress and child treatment/procedural anxiety in this sample compared with other pediatric cancer samples could be influenced by time of child diagnosis, sociodemographic factors such as geographic location and income level as well as differing recruitment strategies.

**Family Beliefs as a Moderator**

The results found that family beliefs did not operate as moderator between caregiver stress levels and child report of treatment/procedural anxiety and pain interference with the covariates of family problems and money problems. However, the overall model of family beliefs moderating the relationship between caregiver stress levels and caregiver-proxy report of child pain interference explained 11% of the variance in caregiver-proxy report of child pain interference. Additionally, although family beliefs did not moderate the relationship between caregiver stress levels and caregiver-proxy report of child treatment/procedural anxiety, it did account for 6% of the variance in caregiver-proxy report of child treatment/procedural anxiety levels. These findings suggest that caregiver stress levels, family beliefs and caregiver-proxy reports of
child treatment/procedural anxiety and pain interference are interrelated. These findings also support previous research on the significant relationship between caregiver stress and caregiver’s perception of their child’s physical and emotional state (Kazak et al., 2004; Fotiadou et al., 2008; Given et al., 1993).

The development and psychometrics of the family beliefs subscale may have contributed to the null moderation findings. In developing the family beliefs subscale, Kazak and colleagues (2004) used differing types of question constructs within the family beliefs subscale which assessed both malleable (e.g., My child will be in a lot of pain) and dispositional based beliefs (e.g., Our marriage or family will fall apart). In preliminary data analysis for this study, the Cronbach’s alpha was analyzed for the separate question constructs of malleable (4 items) and dispositional belief-based questions (5 items) as differentiated by Kazak and colleagues (2004). However, the separate constructs had very low Cronbach’s alpha scores for malleable beliefs (.36) and dispositional beliefs (.44). The family beliefs subscale with combined dispositional and malleable belief question constructs had the highest Cronbach alpha score of (.57). Prior research on beliefs have found that malleable beliefs may develop over time while dispositional beliefs are more stable over time (Daniel et al., 2020; Hudson et al., 2021). Research by Gurtovenko and colleagues (2021) found that caregivers of pediatric cancer patients had month-to-month changes in stress levels. Further, an integrative model of pediatric medical stress developed by Kazak and colleagues (2006) suggests that many factors contribute to the development of trauma in children and families experiencing pediatric cancer. Specifically, factors prior to cancer diagnosis such as decreased psychosocial functioning, high anxiety and stress levels contribute to the development of heightened caregiver
stress during treatment as well as the development of post-traumatic stress symptoms. However, adjustment and coping skills were found to be stable across treatment (Kazak et al., 2006). These findings suggest that the beliefs measured in the family beliefs subscale may not be as responsive as caregiver stress levels and may build upon the caregiver’s perception of the child’s emotional and physical state over time. This building of stress levels may have impacted the influence of the subscale on the relationship between caregiver stress and child treatment/procedural anxiety and pain interference (Kazak et al., 2004). Additionally, previous research has found that caregivers may shield their child from knowing their internally held beliefs about their cancer diagnosis (Penner et al., 2016), which could also contribute to the null moderation findings for child report of anxiety and pain interference.

**Correlations**

Significant positive associations were found between caregiver stress levels and family beliefs about the cancer diagnosis, which reinforces previous findings that the relationship between the caregiver’s belief about a cancer diagnosis and stress both impact caregiver’s psychological wellbeing (Fotiadou et al., 2008; Gurtovenko et al., 2021; Given et al., 1993). Caregiver proxy-reports of treatment/procedural anxiety and pain interference were significantly associated. Additionally, caregiver-proxy report of treatment/procedural anxiety was significantly associated with the child report of treatment/procedural anxiety and caregiver proxy-report of pain interference was significantly associated with the child report of pain interference. These findings are consistent with previous research on the relationship between caregiver-proxy and child reports (Smith et al., 2007). However, caregiver stress was not significantly associated
with the child report of pain interference and treatment/procedural anxiety levels but was associated with caregiver-proxy report of child pain interference and family problems. Family beliefs were also found to not be significantly associated with child report of treatment/procedural anxiety and pain interference.

Null findings regarding the association between caregiver stress and child report of anxiety and pain interference suggest that caregivers could change their behavior towards their child by being overly cautious of their own emotion regulation in order to not cause further distress to their child (Penner et al., 2016). Previous research on coping styles for caregivers of pediatric cancer patients has found that problem-focused coping and cognitive reframing were more effective in decreasing caregiver stress level than emotion-focused coping (Texieria et al., 2018; Martin et al., 2012). However, it has also been found that caregivers of pediatric cancer patients employ emotion-focused coping strategies which aim to control emotional reactions more often than problem-focused coping strategies which aim to actively alleviate the severity of the problem (Sharma et al., 2018). Thus, caregivers may be using emotion-based coping strategies with the purpose of preventing their child from experiencing their own emotional reaction. However, emotion-focused coping has not been found to effectively solve issues and can cause greater distress for the caregiver (Texieria et al., 2018). This emotion-based coping method may also contribute to the null findings between caregiver stress, family beliefs and child report of treatment/procedural anxiety and pain interference.

Another possible explanation for this finding could be that children undergoing treatment may be in various states of cognitive clarity due to medication, pain and lack of sleep (Daniel et al., 2016; Hutchinson et al., 2017). This change in child cognitive
functioning may lead to less awareness of their caregiver’s stress levels. These findings indicate that children may be more protected from their caregiver’s stress than previously found. However, caregivers may be using coping strategies that increase their own internal distress leading to poor psychosocial functioning.

Significant positive associations were found between both child report of treatment/procedural anxiety and caregiver-proxy reports of treatment/procedural anxiety and pain interference. Child reports of treatment/procedural anxiety and pain interference were found to be significantly correlated. This finding shows that although child reports are not significantly associated with caregiver stress and beliefs, they are still consistently reporting similar anxiety and pain levels as their parents. Additionally, the significant associations support previous findings that caregivers are strongly connected to their child’s emotional and physical state (Okado et al., 2014).

The finding that caregiver proxy-report of pain interference is significantly correlated with all study variables except the covariates indicates that caregiver interpretation of their child’s pain interference could be a strong predictor for more general levels of caregiver and family functioning. Previous research evaluating the use of the PAT in predicting symptom burden, has found that the PAT significantly predicted symptom burden and other psychosocial functioning of caregivers and their children with cancer (Russell et al., 2022).

**Study Limitations**

A limitation of the study is the use of a self-report questionnaire, which presents issues such as dependence on reading and verbal skills. The study is also based on cross-sectional data, which captures a moment in time and may exclude the nuances of the
experience of cancer. Additionally, the option to take the self-report questionnaire online increases the susceptibility to responses not given by the selected participant, technology problems and other distractions to the participant. Further, recruitment while waiting for an appointment may bias the results of who may consent to this study. Specifically, the study may be biased towards families experiencing less stress given that those experiencing lower levels of stress may be more likely to consent to filling out the study questionnaires. The study powered to detect the sample with medium effect size with alpha set at .05 was found to be .85 (Faul, Erdfelder, Lang, & Buchner, 2007). However, the study was not powered for the interactions. Other factors may have also contributed to the study results such as limits in the eligibility of the sample participants to first year cancer diagnosis. This eligibility limitation may not account for changes in participants’ emotional states over longer periods of time. For example, caregiver stress could change over time as well as the child’s experience of treatment and procedural anxiety. Thus, the results of the correlational data collected is less generalizable to pediatric cancer patients and families past the first year of diagnosis. Further, limited diversity of participants for both gender and race impede the generalizability of the findings.

The null relationship found between caregiver stress level and the covariate of money problems may have been a limitation of the money problems question. The covariate of money problems was a one item question and thus may not have been a robust enough to assess the relationship of caregiver stress on financial problems. However, previous research by Karlson and colleagues (2013) has found that the PAT measure of caregiver stress was significantly associated with greater financial difficulties. This difference in findings is most likely attributed to the use of the seven item PAT
family structure and resource subscale used to measure financial difficulties in contrast with the one item question specifically targeting financial stress, money problems, used in this study (Karlson et al., 2013). The PAT family structure and resource subscale was not used in this study due to the wide scope of questions that were not specific to financial issues (Pai et al., 2008).

The use of the family beliefs subscale developed specifically for the pediatric cancer population was an additional limitation of the study (Kazak et al., 2004; Appendix K). Although the family beliefs subscale tried to capture the range of both malleable and dispositional beliefs that caregivers may experience, this range may have limited the influence of these beliefs on caregiver’s perceptions of their child’s wellbeing. The family beliefs subscale, tested from the original measure had a relatively low alpha of .57 providing further evidence of the issue with creating a subscale with this range of beliefs (Kazak et al., 2004). Further, previous studies evaluating caregiver perceptions of a child cancer patients’ diagnosis have focused on caregiver optimism level as a predictor of caregiver stress level and coping strategies (Fotiadou et al., 2008; Given et al., 1993). Evaluation of optimism may be a stronger perception-based measure than family beliefs based on previous findings (Fayed et al., 2011; Fotiadou et al., 2008).

Future Directions

Future research directions should further evaluate caregiver stress levels and their impact on the development of caregiver beliefs about cancer diagnosis. The development of targeted interventions aimed at evaluating caregiver stress may lead to positive increases in psychological wellbeing of caregivers and promote improved family functioning during cancer treatment. Additionally, further development of the family
beliefs subscale is needed to address malleable and disposition beliefs and their impact of psychosocial outcomes for caregivers and their children. Improvement of malleable and dispositional beliefs constructs as well as more targeted caregiver stress reaction-based questions may lead to better understanding of beliefs that respond well to therapeutic-based interventions. Further, the inclusion of optimism measures in assessing caregiver stress level and coping strategies in the pediatric cancer population may lead to better targeting of at-risk families. Continued research is needed to understand the role that family beliefs about a cancer diagnosis can have on both caregiver stress levels and the child’s own psychosocial functioning. Additionally, clinically-based interventions, which use cognitive behavioral therapy-based approaches that aim to cognitively restructure malleable beliefs, may be effective in treating caregiver stress levels (Kazak et al., 2004). Future research should aim to develop family beliefs measures with stronger emphasis on assessing caregiver optimism level to improve psychosocial support services for caregivers and their children during pediatric cancer diagnosis and treatment.
Appendix A

Figure. *Pediatric Psychosocial Preventative Health Model (Kazak et al., 2015)*
Appendix B

Figure. Multidimensional Biobehavioral Model of Pediatric Pain (Varni et. al., 2004)
Appendix C

Figure. Adapted Biobehavioral Model
Appendix D

Figure. Conceptual Moderation Model: Aim 1a Model
Appendix E

Figure. *Conceptual Moderation Model: Aim 1b Model*
Appendix F

Figure. Conceptual Moderation Model: Aim 2a Model
Appendix G

Figure. Conceptual Moderation Model: Aim 2b Model
Appendix H

Figure. Participant Eligibility Flow Chart

Children assessed for eligibility (n=718)
- Excluded (n=535)
  - Non-cancer directed treatment (n=280)
  - Non English speaker (n=69)
  - Off treatment (n=62)
  - 12m since Dx (n=62)
  - Not treated at CHOP (n=86)
  - Other (n=13)

Eligible Patients (n=183)
- Eligible Dyads (n=121)
- Eligible Caregivers only (n=62)

Caregiver Declined (n=22)
- Not enough time (n=8)
- Not interested (n=12)
- Does not participate in research (n=1)
- Child not well enough (n=1)
Child aged out of study (n=2)
Change in child’s disease status (n=5)
Passive Refusal (n=10)

Consented Caregivers (n=104)
- Caregiver withdrew after consent (n=2)

Consented Caregivers (n=102)

Patients under 8 (n=53)
Caregiver or Patient declined for patient (n=2)
Patient passive refusal (n=6)

Patients completed measures (n=59)
- Caregiver did not complete key study variables (n=1)

Patients completed study measures (n=59)

Completed caregivers only (n=42)
Completed dyads (n=39)
Appendix I

Table. Study Sample Demographics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Full Sample (n=101)</th>
<th>Complete dyads (n=59)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td><strong>Patient Demographics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age ((M=10.11\text{ years}, SD=4.03, \text{ range 5-17}))</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-7</td>
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<td>58</td>
<td>57.4</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>75</td>
<td>74.25</td>
</tr>
<tr>
<td>African American</td>
<td>11</td>
<td>10.89</td>
</tr>
<tr>
<td>Asian</td>
<td>2</td>
<td>1.9</td>
</tr>
<tr>
<td>Middle Eastern</td>
<td>1</td>
<td>.99</td>
</tr>
<tr>
<td>Multiple Races</td>
<td>8</td>
<td>7.9</td>
</tr>
<tr>
<td>Only Hispanic Ethnicity Endorsed</td>
<td>1</td>
<td>.98</td>
</tr>
<tr>
<td>Other Race</td>
<td>4</td>
<td>3.9</td>
</tr>
<tr>
<td>Ethnicity: Hispanic, Spanish or Latino</td>
<td>7</td>
<td>6.93</td>
</tr>
<tr>
<td><strong>Caregiver demographics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex (female)</td>
<td>89</td>
<td>88.1</td>
</tr>
<tr>
<td>Race</td>
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<td></td>
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<tr>
<td>White</td>
<td>82</td>
<td>81.18</td>
</tr>
<tr>
<td>African American</td>
<td>10</td>
<td>9.9</td>
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<tr>
<td>Asian</td>
<td>2</td>
<td>1.98</td>
</tr>
<tr>
<td>Multiple Races</td>
<td>2</td>
<td>1.96</td>
</tr>
<tr>
<td>Ethnicity: Hispanic, Spanish or Latino</td>
<td>5</td>
<td>4.95</td>
</tr>
</tbody>
</table>
Appendix J

Subscale. *Caregiver Stress Subscale* (Pai et al., 2007):

At any time during the child’s illness have you…(circle one number for each question)

Possible Responses are:

<table>
<thead>
<tr>
<th>Not at all</th>
<th>Sometimes</th>
<th>Often</th>
<th>Very Much</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

a. Had unwanted memories or upsetting dreams about the child being sick?

b. Stayed away from people, places, or things that remind you that the child is sick?

c. Been on the lookout for signs that the illness is getting worse or happening all over again?

d. Felt more jumpy, easily angered, or more likely to act without thinking as a result of illness?

e. Lost interest in being with family and friends, or doing regular activities as a result of the illness?
Appendix K

Subscale. *Family Beliefs Subscale* (Pai et al., 2007):

As a caregiver for the child, how much do you believe…(check one box for each statement)

Possible Responses are:

Not true for me  A little true for me  Mostly true for me  Very true for me

a. The doctors and nurses will know how to help
b. My child will be in a lot of pain
c. Our family will be closer because of this
d. Our marriage or family will fall apart
e. This is a disaster
f. People will pull away from us
g. We’re going to beat this
h. Cancer is a death sentence
i. Everything happens for a reason
Appendix L

Subscale. *Family Problems Subscale* (Pai et al., 2007):

About the adults caring for the child…

Possible Responses are:

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>a.</td>
<td>Has anyone had a lot of worry, fear or anxiety at times?</td>
</tr>
<tr>
<td>b.</td>
<td>Have drugs or alcohol caused problems for anyone in the family?</td>
</tr>
<tr>
<td>c.</td>
<td>Has anyone been sad or depressed at times?</td>
</tr>
<tr>
<td>d.</td>
<td>Does anyone have problems paying attention, staying focused, or concentrating for longer periods of time?</td>
</tr>
<tr>
<td>e.</td>
<td>Have there been relationship problems, fights, or talk about breaking up/divorce?</td>
</tr>
<tr>
<td>f.</td>
<td>Has anyone been in trouble with the law or in jail-now or before?</td>
</tr>
<tr>
<td>g.</td>
<td>Has anyone been told that he or she drinks too much alcohol?</td>
</tr>
<tr>
<td>h.</td>
<td>Has there been legal problems with child custody or fights about who should raise your child?</td>
</tr>
<tr>
<td>i.</td>
<td>Has someone talked about or tried to kill or harm themselves or others?</td>
</tr>
<tr>
<td>j.</td>
<td>Did anyone see a crime or has anyone been a victim of crime, abuse or domestic violence?</td>
</tr>
</tbody>
</table>
Appendix M

Subscale. *Child Pain Subscale* (Varni et al., 2010):

Please select the answer that best reflects your pain experiences in the past 7 days…

Possible Responses are:

<table>
<thead>
<tr>
<th>Never</th>
<th>Almost Never</th>
<th>Sometimes</th>
<th>Often</th>
<th>Almost Always</th>
</tr>
</thead>
</table>

a. In the past 7 days…I had trouble sleeping when I had pain

b. I felt angry when I had pain

c. I had trouble doing schoolwork when I had pain

d. It was hard for me to pay attention when I had pain

e. It was hard for me to run when I had pain

f. It was hard for me to walk one block when I had pain

g. It was hard to have fun when I had pain

h. It was hard to stay standing when I had pain
Appendix N

Subscale. Caregiver-Proxy Report Child Pain Subscale (Varni et al., 2010):

Please select the answer that best reflects your child’s pain experiences in the past 7 days…

Possible Responses are:

Never  Almost Never  Sometimes  Often  Almost Always

a. In the past 7 days…My child had trouble sleeping when he/she had pain
b. My child felt angry when he/she had pain
c. My child had trouble doing schoolwork when he/she had pain
d. It was hard for my child to pay attention when he/she had pain
e. It was hard for my child to run when he/she had pain
f. It was hard for my child to walk one block when he/she had pain
g. It was hard for my child to have fun when he/she had pain
h. It was hard for my child to stay standing when he/she had pain
Appendix O

Subscale. *Child Treatment/Procedural Anxiety Subscale* (Varni et al., 2002):

In the past month how much of a problem has this been for you…

Possible Responses are:

<table>
<thead>
<tr>
<th>Never</th>
<th>Almost Never</th>
<th>Sometimes</th>
<th>Often</th>
<th>Almost Always</th>
</tr>
</thead>
</table>

a. Needle sticks (i.e. injections, blood tests, IV’s) hurt me

b. I get scared when I have blood tests

c. I get scared about having needle sticks (i.e. injections, blood tests, IV’s)

d. I get scared when I am waiting to see the doctor

e. I get scared when I have to go to the doctor

f. I get scared when I have to go to the hospital
Appendix P

Subscale. Caregiver-Proxy Report for Child Treatment/Procedural Anxiety Subscale

(Varni et al., 2002):

In the past month, how much of a problem has your child/teen had with…

Possible Responses are:

<table>
<thead>
<tr>
<th>Never</th>
<th>Almost Never</th>
<th>Sometimes</th>
<th>Often</th>
<th>Almost Always</th>
</tr>
</thead>
</table>

a. Needle sticks (i.e. injections, blood tests, IV’s) causing him/her pain
b. Getting anxious about having blood drawn
c. Getting anxious about having needle sticks (i.e. injections, blood tests, IV’s)
d. Getting anxious when waiting to see the doctor
e. Getting anxious about going to the doctor
f. Getting anxious about going to the hospital
Appendix R
Appendix S
Appendix T
Appendix U
### Appendix V

**Table. Descriptive Statistics and Correlations**

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>M</th>
<th>SD</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Caregiver Stress</td>
<td>101</td>
<td>1.68</td>
<td>0.49</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2. Family Beliefs</td>
<td>101</td>
<td>1.61</td>
<td>0.33</td>
<td>.371**</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3. Caregiver Report of Child Pain</td>
<td>101</td>
<td>51.89</td>
<td>10.66</td>
<td>.211*</td>
<td>.229*</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4. Child Pain Report</td>
<td>59</td>
<td>53.76</td>
<td>11.65</td>
<td>.151</td>
<td>.196</td>
<td>.578**</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>5. Caregiver Report of Child Anxiety</td>
<td>101</td>
<td>35.02</td>
<td>23.95</td>
<td>.154</td>
<td>.169</td>
<td>.467**</td>
<td>.233</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6. Child Anxiety Report</td>
<td>59</td>
<td>34.81</td>
<td>26.34</td>
<td>.056</td>
<td>.006</td>
<td>.460**</td>
<td>.269*</td>
<td>.775**</td>
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<td>-</td>
<td>-</td>
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<tr>
<td>7. Money Problems</td>
<td>101</td>
<td>1.50</td>
<td>0.62</td>
<td>.130</td>
<td>.096</td>
<td>.123</td>
<td>.012</td>
<td>.095</td>
<td>.059</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>8. Family Problems</td>
<td>101</td>
<td>1.72</td>
<td>0.13</td>
<td>.337**</td>
<td>.268**</td>
<td>-0.020</td>
<td>.021</td>
<td>-0.062</td>
<td>.080</td>
<td>.214*</td>
<td>1</td>
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</table>

**Correlation is significant at .01**

*Correlation is significant at .05
Appendix W
Appendix X

Table: Regression Analysis: Caregiver-Proxy Report of Child Treatment/Procedural Anxiety

<table>
<thead>
<tr>
<th>Coeff.</th>
<th>se</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1a.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$F(5, 95)=1.38, \ p=.237,$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$R^2=.0678,$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$MSE=562.916$</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Coeff.</th>
<th>se</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>$\beta_0$</td>
<td>64.475</td>
<td>22.152</td>
</tr>
<tr>
<td>Caregiver Stress ($X$)</td>
<td>$\beta_1$</td>
<td>6.929</td>
<td>5.399</td>
</tr>
<tr>
<td>Family Beliefs ($W$)</td>
<td>$\beta_2$</td>
<td>10.854</td>
<td>7.696</td>
</tr>
<tr>
<td>$X \times W$</td>
<td>$\beta_3$</td>
<td>.666</td>
<td>19.533</td>
</tr>
<tr>
<td>Family Problems</td>
<td></td>
<td>-30.004</td>
<td>18.936</td>
</tr>
<tr>
<td>Money Problems</td>
<td></td>
<td>3.780</td>
<td>3.887</td>
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Notes. *$p<.05$. **$p<.01$. 
Appendix Y
Appendix Z

Table. Regression Analysis: Child Report of Treatment/Procedural Anxiety

<table>
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<th>Coeff</th>
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<th>t</th>
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</thead>
<tbody>
<tr>
<td>Model 1b.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$F(5, 53)=.1055, p=.990,$</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>$R^2=.0099, MSE=752.311$</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Constant</td>
<td>$i_7$</td>
<td>19.287</td>
<td>34.818</td>
<td>.553</td>
</tr>
<tr>
<td>Caregiver Stress ($X$)</td>
<td>$b_1$</td>
<td>1.468</td>
<td>9.585</td>
<td>.153</td>
</tr>
<tr>
<td>Family Beliefs ($W$)</td>
<td>$b_2$</td>
<td>-1.814</td>
<td>10.396</td>
<td>-.174</td>
</tr>
<tr>
<td>$X \times W$</td>
<td>$b_3$</td>
<td>-8.552</td>
<td>28.653</td>
<td>-.298</td>
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<tr>
<td>Family Problems</td>
<td></td>
<td>12.180</td>
<td>30.533</td>
<td>.398</td>
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<td>Money Problems</td>
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<td>1.179</td>
<td>5.810</td>
<td>.202</td>
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Notes. *p<.05. **p<.01.
Appendix AA

Table. Regression Analysis: Caregiver-Proxy Report of Child Pain Interference

<table>
<thead>
<tr>
<th></th>
<th>Coeff</th>
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</thead>
<tbody>
<tr>
<td>Model 2a.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( F(5, 95)=2.47, p=.037^* )</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( R^2=.115, MSE=105.952 )</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( b_0 )</td>
<td>62.077</td>
<td>9.610</td>
<td>6.459</td>
<td>.000</td>
</tr>
<tr>
<td>( b_1 )</td>
<td>3.823</td>
<td>2.342</td>
<td>1.632</td>
<td>.105</td>
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<tr>
<td>( b_2 )</td>
<td>6.580</td>
<td>3.339</td>
<td>1.970</td>
<td>.051</td>
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<tr>
<td>( b_3 )</td>
<td>11.225</td>
<td>8.474</td>
<td>1.324</td>
<td>.188</td>
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<tr>
<td>Family Problems</td>
<td>-11.853</td>
<td>8.215</td>
<td>-1.442</td>
<td>.152</td>
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<td>Money Problems</td>
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<td>1.195</td>
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</table>

Notes. *p<.05. **p<.01.
Appendix BB
Appendix CC

Table. *Regression Analysis: Child Report of Pain Interference*

<table>
<thead>
<tr>
<th></th>
<th>Coef</th>
<th>se</th>
<th>t</th>
<th>p</th>
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</thead>
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<tr>
<td><strong>Model 2b</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$F(5, 53) = .567, p = .724.$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$R^2 = .050, MSE = 141.128$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constant</td>
<td>59.891</td>
<td>15.080</td>
<td>3.971</td>
<td>.000</td>
</tr>
<tr>
<td>Caregiver Stress ($X$)</td>
<td>3.263</td>
<td>4.152</td>
<td>.786</td>
<td>.435</td>
</tr>
<tr>
<td>Family Beliefs ($W$)</td>
<td>5.281</td>
<td>4.502</td>
<td>1.173</td>
<td>.246</td>
</tr>
<tr>
<td>$X \times W$</td>
<td>2.856</td>
<td>12.410</td>
<td>.230</td>
<td>.818</td>
</tr>
<tr>
<td>Family Problems</td>
<td>-4.680</td>
<td>13.224</td>
<td>-.354</td>
<td>.724</td>
</tr>
<tr>
<td>Money Problems</td>
<td>-536</td>
<td>2.516</td>
<td>-.215</td>
<td>.831</td>
</tr>
</tbody>
</table>

*Notes. *$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*$*$^*
References


