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Identifying Disease Characteristics, Parent Experience and Coping Strategies when Predicting Pediatric Illness-Related Stress in Parents of Children with Mitochondrial Disease

Brenda Senger
Gonzaga University, sengerb@gonzaga.edu

IDENTIFYING DISEASE CHARACTERISTICS, PARENT EXPERIENCE AND COPING STRATEGIES WHEN PREDICTING PEDIATRIC ILLNESS-RELATED STRESS IN PARENTS OF CHILDREN WITH MITOCHONDRIAL DISEASE

By

BRENDA ANN SENGER

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To the Faculty of Washington State University:

The members of the Committee appointed to examine the dissertation of BRENDA ANN SENGER find it satisfactory and recommend that it be accepted.

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Ruth C. Bindler, Ph.D., RNC, Chair

_____
Celestina Barbosa-Leiker, Ph.D.

_____
Linda D. Ward, Ph.D., ARNP

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Abstract

By Brenda Ann Senger, Ph.D.
Washington State University
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Chair: Ruth C. Bindler

Mitochondrial disease (mito) is a group of rare, inherited, chronic, life-limiting, incurable neurodegenerative disorders known to affect children early in life, resulting from failure of the mitochondria to turn food into energy. The diagnosis of mito is elusive and complex, with a variety of clinical manifestations, multisystem involvement, and the lack of a reliable biological marker for screening and diagnosis. The unpredictable prognosis and erratic nature of this illness can be overwhelming to parents who bear the daily responsibilities of managing the child's care. Little is known about the experience of parents caring for a child with mito. **Objective:** This research explores the parent experience, disease-related challenges, coping strategies, and pediatric illness-related stress in parents of children with mito. **Methods:** Internet sampling of 231 parents of children with mito included demographic information and three questionnaires: Parent Experience of Childhood Illness (PECI), Coping Inventory for Parents (CHIP) and Pediatric Inventory for Parents (PIP). **Results:** Correlation analysis found significant relationships ($\rho \leq 0.01$, $\rho \leq 0.05$) in illness-related parenting stress associated with parent age,

parent income, parent education, child age, child age at diagnosis, presence of developmental delays, frequency of hospitalizations, number of medical visits, number of organs involved, and number of specialists seen. Regression analysis of 10 models found the following significant ($\rho \leq 0.01$, $\rho \leq 0.05$) predictors of pediatric illness-related stress: frequency of hospitalization over past year, parent income, number of medical visits per year, guilt & worry, emotional resources, unresolved sorrow & anger, long-term uncertainty, and understanding health care. **Conclusions:** The ability to identify disease-related challenges, coping and parent experiences in assessing psychosocial stressors in parents of children with mitochondrial disease is novel and can assist health care professionals to provide disease-sensitive, family-focused care.

Keywords: Mitochondrial Disease, Parents, Stress, Coping, Parent Experience, Childhood Illness

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Dedication

This dissertation is dedicated to the Holy Spirit and to my family: my husband who helped me believe in myself, supported, loved and encouraged me, to my four beautiful children Ryan, Joseph, Teresa, and Sarah who unselfishly gave up countless “mommy” time and who were my biggest cheerleaders, and to future generations of Schaeffers and Sengers who may find their lives challenged by mitochondrial disease.

Chapter One: Introduction

Mitochondrial disease (mito) is a term used to describe a group of rare, inherited, chronic, life-limiting diseases known to occur in childhood, caused by mitochondrial failure that disrupts metabolic function (Haas et al., 2007; Kisler, Whittaker, & McFarland, 2010). Mitochondrial diseases are incurable neurodegenerative diseases caused by defects in the mitochondria of the cell that result in progressive deterioration and weakness (Sexton, Sahhar, Thorburn, & Metcalfe, 2008). The mitochondria are the powerhouses of the cell and they help the body turn food into energy through a series of complex reactions called oxidative phosphorylation, which is needed to sustain life (United Mitochondrial Disease Foundation, 2012a). Primary mitochondrial disease is caused by a genetic mutation either in the nucleus of the cell or in the mitochondria DNA; both mutations alter mitochondrial function and harm the cell. Mitochondrial disorders occur when the mitochondria fail to produce enough energy from food and oxygen, affecting cell and organ performance (Mitoaction, 2009a; United Mitochondrial Disease Foundation, 2012a). The cell dies when the mitochondria stop working, ultimately resulting in organ damage or failure especially in organs with high energy demands such as the brain, heart, skeletal muscle, endocrine, kidney, ears, eyes, intestines, and central nervous system (Haas et al., 2007; Kim et al., 2010).

Mito is complex and multisystem, occurring at various ages with a combination of clinical presentations that make diagnosis difficult (United Mitochondrial Disease Foundation, 2012a). Mito is further complicated by nonspecific signs and symptoms and the lack of a reliable biological marker for screening and diagnosis (Haas et al., 2007). In general, the earlier that symptoms present in life, the more severe the metabolic disorder (Haas et al., 2007). Children with mito present with a variety of clinical manifestations such as muscle

weakness and pain, exercise intolerance, heart failure or rhythm disturbances, movement disorders, dementia, stroke-like events, seizures, gastric reflux, severe vomiting, failure to thrive, constipation, diarrhea, blindness, deafness, droopy eyelids, diabetes, swallowing difficulties, heat and cold intolerance, poor growth, developmental delays, susceptibility to infection, lactic acidosis, and problems with the immune system, heart and kidneys (United Mitochondrial Disease Foundation, 2007, 2012a, 2012b). The complexity of mito's clinical manifestations and multiple organ involvement likely contributes to stress among caregivers of children with mito.

Studies show that parents of children with multiple and severe chronic conditions have more unmet needs than parents of children with single or less severe chronic illnesses (Farmer, Marien, Clark, Sherman, & Selva, 2004). An incurable neurodegenerative disease like mito may have an illness trajectory that is fatal in a short period of time or a trajectory of slow deterioration over several years (Goldman, Hain, & Liben, 2006). Families who have a child with mito likely have unique experiences and challenges associated with the deteriorating and progressive nature of the disease. However, very little is known about the needs and stressors of parents caring for a child with mito (Noorda et al., 2007). Better understanding about parent experiences, coping, and stressors of caring for a child with mito can assist health care professionals in planning effective health interventions for this population. The objective of this study was to explore the parent experience, coping strategies, psychosocial stress, and disease-related challenges and to identify significant predictors of stress in parents of children with mito. Knowledge about pediatric illness-related parenting stress will assist health care professionals in exploring interventions to reduce the impact of these stressors on the family.

Significance

Mito is not a single chronic disease, but rather a spectrum of inherited disorders with a variety of symptoms that result from problems with cellular metabolism (Haas et al., 2007). Although classified as a rare disease by the National Institutes of Health (Office of Rare Disease Research, 2007), high mortality rates and underreporting make the exact prevalence of mito elusive (Haas et al., 2007; Kisler et al., 2010; Saneto & Naviaux, 2010). Evidence suggests a lifetime risk of developing mito anywhere from 1:3000 to 1:5000 before the age of ten years (Haas et al., 2007; Kisler et al., 2010; Mitoaction, 2009a; Saneto & Naviaux, 2010). However, medical experts believe this number is closer to 1:2000 with estimations that mito is reaching childhood cancer proportions (United Mitochondrial Disease Foundation, 2007, 2012a).

Mitochondrial diseases are classified as primary or secondary with over 150 mitochondrial DNA mutations that cause disease (Haas et al., 2007; United Mitochondrial Disease Foundation, 2012b). There are approximately 40 identified diseases; however, all continue to be classified as orphan diseases, meaning they lack pharmaceutical interest or support (United Mitochondrial Disease Foundation, 2012b). Primary mitochondrial diseases typically present early in life and are caused by genetic mutations that damage the electron chain transport of the mitochondria (Haas et al., 2007). Nearly half of children affected by primary mitochondrial disease exhibit symptoms before age five years, and approximately 80% of these children die before the age of twenty years (United Mitochondrial Disease Foundation, 2012b). In secondary mitochondrial diseases, which typically present later in life, the mitochondrial organelle possesses a genetic alteration but does not produce symptoms of disease until triggered by an external environmental stimulus, such as a drug administered

for some other purpose, resulting in mitochondrial dysfunction (Haas et al., 2007; United Mitochondrial Disease Foundation, 2012b).

Medical science has taken a lead role in mitochondrial research by exploring the molecular biology of mito disorders in hopes of finding a cure, biological markers for diagnosis, pharmacological support, and other medical treatments to help slow disease progression (Parikh et al., 2009). Although mitochondrial biology is rapidly becoming one of the fastest-growing areas in genetics, treatment for mito is still in its infancy (Naviaux, 1997; Parikh et al., 2009). Currently long-term management of mitochondrial disease focuses on alleviating symptoms along with the administration of a vitamin compound referred to as a *mitochondrial cocktail* (Kisler et al., 2010; Tarnopolsky, 2008). The broad range of diseases makes it unlikely that a single curative treatment will be found, but like cancer, targeted treatments will likely surface (R. Saneto, personal communication, November 18, 2010). Currently there is no cure or even well-studied, empirically-derived, effective pharmacological or other treatment for mitochondrial disease.

Parent Stress

Many children with mito have a disease trajectory that is unpredictable and tumultuous, sometimes appearing healthy while suffering multiple organ damage (Haas et al., 2007). Some children with mito live fairly normal lives, while others cannot walk, talk, hear, or see (United Mitochondrial Disease Foundation, 2012a). The unpredictable prognosis and erratic nature of this illness can present an overwhelming challenge to parents who bear daily responsibilities of managing the child's care while holding at bay the ubiquitous fear for the child's well-being. In addition to traditional parenting roles, parents of children with chronic illness take on additional responsibilities as medical experts, care coordinators, and advocates

for their children's special needs (Kratz, Uding, Trahms, Villareale, & Kieckhefer, 2009). Many parents of children with mito find themselves teaching undereducated health care professionals about the disease. Multiple stressors should not be underestimated as parents juggle the many practical implications of caring for a medically challenged child and navigating the complexity of the health care system, while possibly grieving the emotional loss of the child they once knew (Kisler et al., 2010).

Parent Experience

Successful management of the child's illness is dependent on the ability of the parent to cope with the affliction, and parental coping is influenced by the ability to resolve uncertainty in the illness (Mishel, 1983). Uncertainty in illness is defined as the inability to determine the meaning of illness-related events (Mishel, 1983). Parent uncertainty leads to worry, ineffective coping, increased psychological stress, and preoccupation with the child's situation as the parent struggles to understand his or her child's health care needs (Mishel, 1983; Santacroce, 2001). Health care management of mito remains ambiguous, leaving both parents and health care team members uncertain about long-term outcomes. The uncertain clinical course of mito produces unique coping needs for parents and children.

Parents of children with mito have unique needs and experiences. Lack of resources and information about this rare disease and the complexities of multi-organ deterioration put parents of children with mito at risk for knowledge deficit. Currently, only 43 mito pediatric clinics exist in the United States to provide specialized care for children with mito and their families (Balcells, 2012; Parikh et al., 2009). The scarcity of mitochondrial metabolism specialists worldwide creates a challenge to adequately address the many needs of children with mito, or to help educate families and health care professionals about mitochondrial

disease. Parents of children with mito experience many gaps in health information, especially during the diagnostic process (Noorda et al., 2007).

Parents of chronically ill children often experience an increase in unmet needs proportionate to the severity and complexity of the child's illness (Farmer et al., 2004). Managing a chronic disorder like mito can place great demands on parents. Parents of children with mito likely need additional support to cope with the many physical, cognitive and psychosocial demands and stressors of this rare and debilitating disease. Although medical science has a growing interest in mitochondrial-related diseases, a review of the literature reveals a gap in understanding the experience, coping and stressors associated with caring for a child with mitochondrial disease (Haas et al., 2007; Kisler et al., 2010; Mitoaction, 2009a).

Statement of the Problem

Little is known about the experiences, coping and psychosocial stressors of parents caring for a child with a mitochondrial illness. Managing a chronic disorder like mito can influence the experience of stress for the child and family (Vermaes, Janssens, Mullaart, Vinck, & Gerris, 2008). Children with mito exhibit an extensive range of symptoms, and each child has a unique disease course requiring specialized care. Understanding factors that contribute to or alleviate stress in parents of children with mito will provide health care professionals with the tools they need to develop interventions that support the needs of the mito family. This research study identifies coping strategies, stressors, and aspects of the parent experience when caring for a child with mito and sets the stage for further research in designing interventions to improve education for parents and health care professionals about the multidimensional effects of mito on the family during the different stages of child development and the various stages of disease progression.

Purpose

The purposes of this exploratory, predictive study were to 1) identify disease-related characteristics, coping, pediatric illness-related stressors, and experiences in parents of children with mitochondrial disease; 2) explore the relationships between disease-related characteristics, coping, experiences with their child's illness and pediatric illness-related stressors in parents of children with mitochondrial disease; and 3) identify factors that are significant predictors of pediatric illness-related stress in parents of children with mitochondrial disease.

Specific Aims

1. Identify family demographic characteristics and disease-related characteristics in mitochondrial disease.
2. Describe the parental experience when caring for a child with mitochondrial disease.
3. Describe coping strategies used by parents of children with a mitochondrial disease.
4. Describe frequency and severity of pediatric illness-related parenting stress in parents of children with a mitochondrial disease.
5. Examine the relationships between pediatric illness-related parenting stress in parents of children with mitochondrial disease and family demographics, disease characteristics, coping strategies, and parent experience of childhood illness.
6. Identify the significant predictors of pediatric illness-related parenting stress in parents of children with mitochondrial disease.

Chapter Two: Review of Literature

Chronic Conditions and Mitochondrial Disease in Children

Medical advances have increased the lifespan and decreased the mortality and morbidity rates in children with chronic conditions, creating a growing population of children with special health care needs (Allen, Vessey, & Schapiro, 2010). The prevalence of chronic illness in children has increased over the past two decades and although the exact number of children who have chronic conditions and the relative severity of these conditions are unknown, it is estimated that more than four million, or approximately 20%-29%, of North American children are living with a chronic health condition (Allen et al., 2010; Branstetter, Domian, Williams, Graff, & Piamjariyakul, 2008; Moola, 2012). The increased prevalence of chronic conditions is largely due to improvements in medical technology, pharmacotherapeutics, pediatric services, accuracy in diagnosing previously unrecognized illness, and health prevention strategies that assist children who once had life-limiting illnesses to grow into adulthood with increased function and improved quality of life (Allen et al., 2010; Grootenhuis & Bronner, 2009; Moola, 2012).

Chronic diseases in children are defined as illnesses that are present longer than three months and will likely persist for greater than six months, limit participation in age-appropriate activities, cause disfigurement, require dependency on medication, necessitate special diets or medical technology for functioning, or require special ongoing treatments at home or in school (Allen et al., 2010; Moola, 2012; Stein, 1992). The Federal Maternal and Child Health Bureau's Division of Services for Children with Special Health Care Needs (DSCSHCN) defines children with special health care needs as those who have or are at risk for a chronic physical, developmental, behavioral, or emotional condition and who also

require health and related services of a type or amount beyond that generally required by children (United States Department of Health and Human Services, n.d.-a).

Chronic illnesses are complex and have the potential to disrupt and limit fullness of life at any age. However, there are some basic differences in the presentation of chronic illness in children compared to adults, along with variations in disease trajectory and outcomes among pediatric populations. Chronic conditions in children are not as stable as chronic illness in adults; children present with periods of acute exacerbations and remissions along with growth and development concerns that impact the course of the chronic illness (Allen et al., 2010). A large number of pediatric chronic illnesses are considered rare genetic diseases and some are a result of prenatal conditions which increase in morbidity as the child ages (Allen et al., 2010). It is estimated that nearly half of children with life-limiting situations who are in need of palliative care have malignant conditions, while the other half include neurodegenerative diseases, congenital anomalies and chromosomal disorders (Goldman et al., 2006). Illness trajectory for these conditions may be abrupt or gradual and is not easy to predict (Goldman et al., 2006).

Illness Trajectory

Chronic illness trajectories in children result in a variety of patterns along with the potential to become life limiting for the child. Unlike adult illness, pediatric illnesses frequently have an unpredictable trajectory ranging from weeks to years, often requiring ongoing parental support (Schneider, Steele, Cadell, & Hemsworth, 2010). For example, the illness trajectory for a potentially curable malignancy in a child may have subsequent recovery and remission periods intermixed with treatment until the child's condition either improves or deteriorates. A child with cystic fibrosis might maintain functioning for a number

of years with disease modifying treatments until advanced stages of acute deterioration result in lung failure. The trajectory for incurable neurodegenerative diseases may occur in a child who is relatively well at diagnosis but then deteriorates either within a short period of time or slowly over many years (Goldman et al., 2006). Patterns of deterioration vary according to the disease and may create a condition that limits the life of the child (Goldman et al., 2006). Life-limiting illnesses are defined as conditions where a cure may be possible but treatment has failed, or where life expectancy is predicted to be shortened due to the progressive and degenerative nature of the disease (Menezes, 2010). There is limited research to show the day-to-day experience of life-limiting chronic illness in childhood (Menezes, 2010).

Corbin and Strauss' (1991) theory of the trajectory of chronic illness is a research-to-practice model that was developed 40 years ago from a series of studies grounded in sociology to examine the care of dying patients. Although specific chronic diseases may be more prevalent in certain cultures, Corbin and Strauss suggest that the staging and course of the disease can be generalized (Cooley, 1999). Earliest versions of this model were built on qualitative studies to explore how patients, family members and health care professionals employed strategies to shape and manage the course of dying (Cooley, 1999). This theory was adapted for nursing when Juliet Corbin, a nurse scientist, collaborated with Strauss and suggested using this model for management of chronic illness (Cooley, 1999; Corbin, 1991). This theory was primarily intended for the evaluation of chronic illness in adults; however, there is potential for adaptation and use in childhood with the understanding that childhood chronic illnesses have more unpredictable outcomes than those in adults (Cooley, 1999).

For parents of children with chronic conditions, moments of realization of the life-limiting forecast often occur during questions of genetic transference, discussions of

prognosis, the child's acute loss of abilities and slow deterioration, at diagnosis, and during the ongoing cycle of crisis and survival, creating periodic anxiety, increased emotional pressure, and uncertainty for the family (Menezes, 2010). Caring for a child with a life-limiting illness can result in overwhelming challenges and stressors (physical, emotional, financial, social, and spiritual) to parent caregivers (Schneider et al., 2010).

Mito is an example of a chronic childhood illness with an unpredictable clinical course and disease trajectory. This is likely to generate feelings of uncertainty for many parents. There are no current studies that describe feelings of uncertainty, chronic sadness/sorrow or associated emotional challenges in parents of children with mito. Knowledge about the experience associated with parenting a child with mitochondrial disease and understanding the relationship between this parent experience and illness-related pediatric stress will afford opportunities to introduce interventions to reduce the negative impact of these factors.

Health Care Needs of Families with Chronic Illness

Children with chronic conditions have a greater frequency of unmet needs than children in general (Allen et al., 2010). Unmet needs include but are not limited to difficulty receiving home health care, getting referrals, obtaining specialty services, locating mental health services, finding a skilled provider, and maintaining continuity of care; many unmet needs also result from the lack of health care insurance coverage (Allen et al., 2010). Parent and family health, ethnicity, culture, socioeconomic status, education, and sources of health care insurance affect the child's ability to access health care services and influence compliance with disease management plans (Allen et al., 2010). Medical care is complex and costly, with many treatments that were once provided in hospitals now being shifted to family members at home and to community providers (Allen et al., 2010).

The diagnosis of a chronic illness in a child marks the end of a previously known world for parents and siblings. For some, a diagnosis brings relief and for others a state of uncertainty with a period of adaptation to a new way of life (Fisher, 2001). In a review of the literature, Fischer (2001) found that parents of children with chronic illness are in need of normalcy, certainty, control over stressors, information, and partnership with health care professionals. Many parents used information to reduce uncertainty, gain control and better partner with health care professional (Fisher, 2001).

Parent Experience of Chronic Illness

Parent functioning has been consistently identified as a predictor of the psychological adjustment in children with chronic illnesses (Bonner et al., 2006). Subjective parent distress is shown to be an important factor in child outcomes in that family factors can exacerbate or mitigate the impact of disease on the chronically ill child (Bonner et al., 2006). Thompson and Gustafson (1996) discuss the impact of maternal adaptation to a child's chronic illness and the important contribution it has to child adjustment. Illness-related uncertainty is a common parent experience when caring for a child with a chronic illness (Bonner et al., 2006). Studies about uncertainty show a relationship between illness uncertainty and psychological distress such as anxiety, depression, cognitive disturbances and feelings of helplessness (Bonner et al., 2006). Emotional resources are helpful to mitigate the effects of uncertainty.

Pediatric Parenting Stress

Pediatric parenting stress refers to the stress experienced by parents of children with chronic illness which is considered separate from general parenting stress and associated caregiver burden (Mitchell et al., 2009; Streisand, Braniecki, Tercyak, & Kazak, 2001). Family health theories suggest that parental health and behaviors likely play a role in child

adaptation to illness (Mitchell et al., 2009); therefore, understanding stress and anxiety associated with being a parent of an ill child and applying appropriate interventions to reduce stress and anxiety will likely improve adaptation to illness by the child.

Pediatric illness is a family affair (Grootenhuis & Bronner, 2009). All families experience stress, and each family has its own unique approach and strategies to manage stressors (Bomar, 2004). Parental stress related to a child's chronic condition is a cross-cultural phenomenon (Allen et al., 2010). Chronic childhood illness is recognized as a stressor for children and their families (Thompson & Gustafson, 1996). The level of stress is related to the individual's appraisal of the degree of threat in a situation along with available resources and individual coping strategies (Thompson & Gustafson, 1996). Coping is the multidimensional process that refers to the ways in which people deal with stress (Gutenberg, 2002). Psychological adjustment to parental stress, when caring for a child with a chronic condition, has been shown to be related to the duration of illness and functional impairment more than the severity of illness (Thompson & Gustafson, 1996).

Children depend on adults for care. Caring for a child with a chronic illness is more stressful than caring for a healthy child, and parents, especially mothers, bear the brunt of the responsibilities associated with this care (Grootenhuis & Bronner, 2009). There is a strong relationship between parental health and child health outcomes, with parent and child psychological reactions being significantly correlated; the higher the parental stress the greater the level psychological distress for the child (Grootenhuis & Bronner, 2009; Moola, 2012). A distressed parent is less emotionally available to his or her child (Santacroce, 2002). Family functioning and support along with disease pathophysiology, prognosis, and severity of illness influence the child's developmental outcomes (Allen et al., 2010). Parents spend much energy

balancing medical care concerns, activities of daily living, financial obligations, and travel for medical appointments, all which have been associated with decreased quality of life for parents, and which sometimes lead to mental health problems in mothers (Grootenhuis & Bronner, 2009). Understanding the experiences of parents can help provide better health outcomes to children with chronic conditions and improve their quality of life (Moola, 2012).

Parents require specialized knowledge, skills, and organization to raise a child with a chronic condition (Ray, 2002). Parents of children with medically complex conditions have extraordinary burdens (Gravelle, 1997). The visible demands associated with caring for a chronically ill child at home include the technical aspects of medical care, sophisticated clinical judgment, and vigilant monitoring of symptoms or problems (Ray, 2002). Children with chronic conditions may experience developmental delays, behavioral problems, and impaired social skills compared to their unaffected peers (Allen et al., 2010; Grootenhuis & Bronner, 2009). The invisible demands of parenting a child with special needs include worry and fear about the unpredictable nature of the illness trajectory, public reaction to the child's disability, and wondering how their child will fit into the world, gain acceptance, achieve tolerance and make friends (Ray, 2002). Developmental lags, stigmatization and uncertainty associated with the illness trajectory are major stressors for children and parents (Allen et al., 2010). Parents can feel overwhelmed and frustrated advocating for their child while navigating the complex health care system, working with social services and working with the educational system to meet the many complex needs of their child, especially when their child is newly diagnosed (Ray, 2002).

Parent Coping

Successful psychological care of a child's illness is influenced by the parent's ability to cope and manage the stressors involved in the child's treatment. (Mishel, 1983). Coping is an active process involving the use of existing family resources and the development of new resources to help strengthen the family unit and relieve or reduce the impact of stressor events (McCubbin & McCubbin, 1987). How well a parent can cope is influenced by the degree of uncertainty in the situation (Mishel, 1983). Uncertainty has been described as a cognitive stressor, a perceptual state of doubt and the inability of a person to ascribe meaning to the illness-related events (Johnson Wright, Afari, & Zautra, 2009; Mu, Wong, Chang, & Kwan, 2001). Mishel introduced The Theory of Uncertainty initially as a way to understand adjustment to acute illness, but over time this theory has been applied to understanding chronic illness where uncertainty evolves (Johnson Wright et al., 2009; Mishel, 1988). Mishel (1988) describes uncertainty as having four distinct characteristics: 1) ambiguity about the illness state; 2) lack of information about the illness, treatment and management; 3) complexity of available information; and 4) unpredictability about the illness course and outcomes (Santacroce, 2002). Higher levels of uncertainty are associated with emotional distress, poor psychosocial adjustment and less functional coping (Santacroce, 2002).

Chronic conditions in children increase the risk of parental psychosocial maladjustment, especially for the mother (Thompson & Gustafson, 1996). Commonalities of childhood chronic conditions that influence psychological adjustment include disease rareness, age at onset, loss of function, impact on mobility, the course of the illness in terms of fatality, predictability of improvement or decline, cognitive functioning, the ability of the child to communicate, and visibility of the illness, or how noticeably different the child

appears (Thompson & Gustafson, 1996). Study results are mixed in understanding if socioeconomic status, family functioning, marital adjustment, and parental social support affect psychosocial adjustment in parents (Thompson & Gustafson, 1996). The literature notes that parents with greater social support (Barakat & Linney, 1992) and good family interactions (Perrin, CC, & JB, 1993) have better adjustments to stress whereas behavior problems in the child, increased care-giving demands and being a single parent increase the risk factors of psychosocial adjustment (Grootenhuis & Bronner, 2009).

Kovacs' et al. (1990) longitudinal study of parental adjustment in families with insulin dependent diabetes mellitus (IDDM) found that parents who initially had trouble adjusting to their child's diabetes experienced greater difficulties adjusting later as the disease progressed (Kovacs et al., 1990). This study also found that the mother's emotional symptoms and maternal depression/anxiety were not always related to the child's medical regime (metabolic control, hospitalizations, or compliance), suggesting that mothers generally found it easier to cope the longer the child had the illness; however, mothers experienced increased emotional distress if the diabetes became difficult to manage (Kovacs et al., 1990). Although the severity of illness, number of hospitalizations and duration of treatments have been shown to impact stress in parents, these factors are not as significant to parent psychosocial adjustment as are emotional support and positive coping (Grootenhuis & Bronner, 2009).

Moola (2012) conducted a qualitative study comparing the similarities and differences in pediatric caregivers' experience and stress when caring for a child with cystic fibrosis (CF) and congenital heart disease (CHD), two diseases with very different illness trajectories. Analysis of the data revealed three main themes. 1) Parental stress was present in both groups as a chronic burden that was always lurking, with parents worried about deterioration,

treatment adherence, and impact of illness on scholastic performance; however, each group narrated this stress in different ways (Moola, 2012). Parents of children with CHD experienced high levels of stress during diagnosis, surgical treatment and immediate recovery but stress dissipated following surgery when the child began to thrive, whereas parents of child with CF experienced the same peak stress at diagnosis and treatments with manifestations of chronic stress that never resolved, with projected worry of inevitable deterioration of their child's health 2) The time consuming nature of treatment and the life-limiting nature of the disease were specific sources of stress for parents of CF only. 3) Both sets of parents dealt with chronic stress by learning to put their child's illness into perspective (Moola, 2012).

Parenting a medically fragile child results in psychosomatic stress, anxiety, and fear about the progressive nature of disease, concerns about normalcy, and the need to keep constant vigilance of complex medical needs of the child (Moola, 2012). Moola's (2012) review of the literature also documented the perspective of fathers as caregivers, showing decline in parent psychosocial and physical health and highlighting positive experiences such as personal growth and appreciation for the things in life that really matter when caring for a child with a chronic illness. Religion and spiritual concerns are also important for family coping especially for those families facing child suffering and the possibility of disability or death (Allen et al., 2010). Although caring for a child with a chronic condition requires additional hours of care per day compared to a healthy child, chronic illness also provides the opportunity for parents to engage in meaningful and transformational experiences with their child and to gain appreciation for what really matters in life (Moola, 2012).

Successful management of the child's illness is dependent on the ability of the parent to cope with the illness (Mishel, 1983). There are no studies describing the coping strategies of parents caring for a child with mito. Assessment of effective and/or ineffective coping strategies, along with understanding the relationship between coping and pediatrics-related parenting stress can assist parents to develop successful coping strategies needed for parenting a child with mito and provide health care professionals with insight about how parents manage a mitochondrial illness.

Goals for Children with Special Health Care Needs

Since the passage of the Social Security Act in 1935 and the birth of Title V, the Federal Government has pledged support to improve maternal and child health nationwide (United States Department of Health and Human Services, n.d.-b). In 1989, the Federal Social Security Act required Title V programs to provide and promote family-centered, community-based and coordinated care for children and their families with special health care needs and to facilitate and develop community-based systems of services (United States Department of Health and Human Services, 2008; Voices, 2005). Title V programs complement Medicaid and the Children's Health Insurance Programs (CHIP) by giving Federal block grant funds to create community infrastructure to support the delivery of quality health care services for women and children (United States Department of Health and Human Services, 2012b). Federal law mandates that every state have a Title V program to assist families and children with disabilities and chronic conditions to make sure that no child or youth with special health care needs goes without required services (Allen et al., 2010).

Title V programs, the Maternal and Child Health Bureau and the Department of Children with Special Health Care Needs (DSCSHCN) and the American Academy of

Pediatrics work to improve the health of the nation's women and children (United States Department of Health and Human Services, n.d.-b). These institutions are working together to advance the nation's Healthy *People's 2020* goals to: 1) to attain high quality, longer lives free of preventable disease, disability, injury, and premature death; 2) achieve health equity, eliminate disparities, and improve the health of all groups; 3) create social and physical environments that promote good health for all; and 4) promote quality of life, healthy development and healthy behaviors across all life stages (United States Department of Health and Human Services, 2010). Targets of progress will be measured using healthy life expectancy, limitation of activity, chronic disease prevalence, physical and mental unhealthy days, assessment of race/ethnicity, gender, socioeconomic status and disability and quality of life (United States Department of Health and Human Services, 2010). The overall goals for healthcare maintenance for children with special needs are to promote normal growth and development to minimize biological disorder, maximize the child's potential, prevent family dysfunction, provide access to a medical home, and increase the number of children who receive family centered, comprehensive and coordinated care (Allen et al., 2010; United States Department of Health and Human Services, 2012a).

Mitochondrial Disease

Much can be learned from prior research that focused on chronic conditions in childhood; however, the wide variety of causation and complexity of parental needs demand that individual diseases be investigated comprehensively. One such category of diseases is comprised of mitochondrial diseases. Little research has been done to identify parent experiences specific to this condition or those that are common to other chronic childhood conditions. Mitochondrial diseases are complex, multifaceted, progressive genetic childhood

illnesses that result from the failure of mitochondria to effectively generate energy from food and oxygen, causing damage to cells and organs (Haas et al., 2007; Kisler et al., 2010; Noorda et al., 2007; Read, 2003). The serious nature of these illnesses is likely an overwhelming challenge for families, especially parents who are the primary caregivers of their child. Parents need support to manage the many physical, cognitive and psychosocial demands and stressors of these rare debilitating diseases.

Mitochondria. Mitochondria are small cellular organelles that serve as the power generators for the cell, converting nutrients and oxygen to adenosine triphosphate (ATP), the chemical that powers cellular metabolism; without mitochondria humans would not survive (Davidson, 2012). Scientists hypothesize that millions of years ago mitochondria were independent living organisms that created a symbiotic relationship with a larger organism, exchanging nutrients provided by the larger organism for energy provided by the mitochondria (Davidson, 2012). Mitochondria are distinctly different from other cell organelles because they have their own DNA and can grow and reproduce independently (Davidson, 2012).

Mitochondrial disease was first recognized in 1962 by a group of investigators at Karolinska University in Stockholm who noticed abnormal mitochondria in the muscle of an adult woman being treated for hypermetabolism (Dimauro, 2011). Since then, mitochondrial morphology and disease recognition have grown in both understanding and complexity. Pediatric cases were identified in the late 1980s (United Mitochondrial Disease Foundation, 2012b). Mitochondrial depletion disorders were first described in 1991 and the first autosomal recessive mutation causing Leigh Syndrome was identified in 1995 (Bourgeron et al., 1995; Naviaux & Nguyen, 2004; Sexton et al., 2008). The clinical diagnosis and genetic inheritance

of Alpers Syndrome, caused by a mitochondrial mutation, was noted in the 1990s with mitochondrial respiratory chain abnormalities in the livers of affected children confirmed in 2001(Naviaux & Nguyen, 2004; Sexton et al., 2008).

Mitochondrial Genetics. Mitochondria are inherited through the maternal lineage. It is suggested that during reproduction, the sperm uses energy from mitochondria that are located in its tail to travel to the egg, but during fertilization the tail falls off, leaving the new organism with only mitochondria from the egg that the mother provided (Davidson, 2012). Although mitochondria are transferred through maternal lineage, genetic mutations causing mitochondrial diseases can occur from either nuclear DNA (nDNA) or mitochondria DNA (mtDNA), which all result in energy deficiency (Boles & Mason, n.d.; Kisler et al., 2010). Mitochondrial DNA (mtDNA) diseases are almost exclusively inherited from the mother, whereas nuclear-related diseases (nDNA) follow Mendelian law of inheritance patterns, most often autosomal recessive, with inheritance from either the mother or the father (Boles & Mason, n.d.; Kisler et al., 2010). Mutations in nDNA account for 70 to 75% of mitochondrial diseases in children, usually occurring during infancy or early childhood with more severe symptoms and higher early mortality than mtDNA mutations; mtDNA mutations are typically less complex and usually present later in life (Balcells & Turco, 2008; Boles & Mason, n.d.; Kisler et al., 2010) . For individuals with known mtDNA mutations, maternal guilt related to the possibility of genetic transference because the mitochondrial disease is passed through maternal inheritance (Read, 2003).

Recognition of Mitochondrial Disease. Mitochondrial diseases are defined as a heterogeneous group of disorders in which ATP production is disrupted due to a deficiency of any mitochondria-located protein involved in energy metabolism (Boles & Mason, n.d.; Haas

et al., 2007; Kisler et al., 2010). Mitochondrial dysfunctions, recognized as the most common neurometabolic childhood disorder, have a complicated clinical diagnosis, lack biological markers and present with non-specific signs and symptoms (Hass et al., 2007). Children with mito typically appear normal at birth and often present clinically with mild developmental delays or subtle neurological symptoms that are not always associated with a disease process (Read & Calnan, 2000). Mitochondrial diseases are usually progressive and typically involve organs with high energy demand; however, any organ or tissue can be affected (Haas et al., 2007; Kisler et al., 2010). As a general rule, the involvement of three or more organ systems without a unifying diagnosis should raise suspicion for mitochondrial disease, as should symptoms that become worse with an acute illness or present in atypical fashion (Haas et al., 2007, p. 1327; Read & Calnan, 2000).

Mitochondrial disease can present with non-specific symptoms at any age and in any organ. The earlier the mitochondrial disease presents in life, the more severe the metabolic disorder (Haas et al., 2007). Symptoms might include muscle weakness, hypotonia, vital sign instability, sensorimotor loss, feeding trouble, behavior problems, sleep disorders daytime fatigue and worsening of symptoms with dehydration, to name a few (Read & Calnan, 2000). Later onset tends to follow a chronic illness pattern that waxes and wanes; however, any physiologic stressor, such as an acute illness, can quickly cause sudden deterioration and disease progression (Haas et al., 2007).

Diagnosis of Mitochondrial Disease. Diagnosis of a child with mito can be very challenging due to the variations of clinical symptoms and lack of a biological marker. Diagnosis is multifaceted and typically consists of medical history, clinical presentation, and tissue biopsy and analysis in specialized laboratories. Preliminary findings may indicate the

need for imaging studies, metabolic screening tests and genetic assays (Haas et al., 2007; Kisler et al., 2010). Diagnostic results may be ambiguous; therefore diagnostic classifications of *definite, probable, possible* or *unlikely* are currently used to categorize the likelihood of mitochondrial diseases (Haas et al., 2007, p. 1331). Mitochondrial diagnostic criteria comprise a combination of clinical symptoms, metabolic and imaging results, skeletal muscle morphology and biochemical investigations of the skeletal muscles (Wolf & Smeitink, 2002). The diagnostic evaluations typically proceed from less invasive clinical evaluation to more invasive imaging, on to metabolic screening tests and genetic assays (Wolf & Smeitink, 2002). Prognosis for mito remains elusive and highly dependent upon the type of disease, degree of involvement of various organs, and severity of clinical symptoms; however, cardiac involvement significantly decreases survival rates (Kisler et al., 2010; United Mitochondrial Disease Foundation, 2012b). Additional genetic testing and counseling may be required with a referral to a mitochondrial specialist, especially if signs and symptoms strongly suggest mito (Haas et al., 2007).

Management of Mitochondrial Disease. Treatment for mito is dependent on the type and severity of mitochondrial involvement. Health care objectives for managing mito range from preventing physiologic stress such as dehydration and avoiding mitochondrial toxins to acute symptom management (Parikh et al., 2009). Acute presentation of pediatric mito may include seizures, encephalopathy, lactic acidosis, and stroke-like events, requiring supportive treatments that include anticonvulsants, fluid resuscitation, sedation, and possible intensive care (Kisler et al., 2010). Underlying infections, fever and vomiting should be aggressively treated with intravenous fluids with high dextrose content (10% to 20%) as these are conditions are considered catabolic stressors (Parikh et al., 2009). Prompt treatment of

infections may defer or prevent acute deterioration that is often associated with a concurrent illness (Kisler et al., 2010).

Most children present with a variety of less acute, nonspecific clinical symptoms such as recurrent vomiting, failure to thrive, hypotonia, developmental delays, and abnormal posturing, which require more long-term management (Kisler et al., 2010). The key to long-term management is understanding the complexity and multi-systemic involvement and that the disease course is unpredictable and progressive (Kisler et al., 2010). Chronic manifestation of mito in children may be associated with 1) musculoskeletal impairments with weakness and spasticity; 2) epilepsy, which is often resistant to multiple anticonvulsants; 3) progressive hearing loss and vision impairments; 4) cardiomyopathy often requiring a pacemaker; 5) nutritional and gastrointestinal complications such as dysphagia, dysmotility, gastro-esophageal reflux, constipation, pseudo-obstruction and delayed gastric emptying, making nutritional maintenance a challenge; and 6) respiratory complications from neurological involvement and skeletal malformation (Kisler et al., 2010).

Long-term management of mito continues to be supportive therapy and management of acute manifestations. The goals for treatment include symptom management, maintaining optimal health, using preventive measures to keep symptoms from worsening during times of physical stress such as infection or dehydration, and avoiding known mitochondrial toxins (Parikh et al., 2009). Scientific support is growing for the use of vitamin supplementation as a means to promote mitochondrial health in the absence of a cure or a definitive way to halt disease progression (Parikh et al., 2009). Antioxidant supplements, also known as the mitochondrial cocktail, act to remove toxic metabolites from the body and promote energy production in the form of ATP while bypassing the metabolic defect (Kisler et al., 2010;

Parikh et al., 2009). The mitochondrial cocktail consists of a specialized mixture of one or more vitamins (E, C, riboflavin, B complexes), coenzyme Q10, L-creatine, L-carnitine, L-arginine and folinic acid, depending on the mitochondrial diagnosis and needs (Parikh et al., 2009). Supplementation is intended to promote enzymatic reactions, reduce excessive free radicals that can damage mitochondrial function and reduce toxic acyl coenzyme A produced during the oxidative phosphorylation process (Parikh et al., 2009).

Other long-term supportive treatment approaches include: 1) healthful nutrition to support mitochondrial function and to prevent secondary dysfunction associated with illness-related cachexia; 2) immunizations to protect against infectious diseases that may be life-threatening for a mito patient; 3) avoidance of mitochondrial toxins known to impair mitochondrial functions such as medications containing valproic acid; 4) ketogenic diet which may optimize mitochondrial function; and 5) co-enzyme Q10, also known as ubiquinone, which is integral in mitochondrial electron transport chain function (Parikh et al., 2009). Treatment varies significantly in effectiveness and individual patient requirements, with no supporting evidence that any of these treatments are effective (Noorda et al., 2007).

On June 8, 2011, Edison Pharmaceuticals announced enrollment criteria for EPI 743, the first drug to be investigated and used for mitochondrial diseases (Mitoaction, 2011). EPI 743 is a small molecule drug that is currently in clinical trials with an orphan drug designation by the FDA to treat only patients who are seriously ill with an inherited mitochondrial respiratory chain disorder (United Mitochondrial Disease Foundation, 2011). Its mode of action is to synchronize energy generation in mitochondria with the need to counter cellular redox stress (Edison, 2011). Eligible patients must be within 90 days of end of life care (United Mitochondrial Disease Foundation, 2011). EPI-743 is an experimental drug and can

only be obtained through clinical trial enrollment, but this is the first step in providing patients clinically diagnosed with mito a possible pharmaceutical option (Mitoaction, 2011; United Mitochondrial Disease Foundation, 2011).

There are limited available treatment options for children with mito and a scarcity of mitochondrial specialists worldwide (Haas et al., 2007). A multidisciplinary approach by health professionals is needed to address the complexity of care required to manage mitochondrial illness. Communication between parents and multiple health care providers is essential (Kisler et al., 2010). Families of children with mito not only travel long distances to obtain metabolic services, but they often see multiple specialists requiring frequent trips between home, school, clinics and hospitals. Mito families need extra service provisions, accurate information, durable medical equipment, home therapy support and education (Kisler et al., 2010). Not only do parents carry the burdens of having a child with a chronic and potentially life-limiting condition, but many also suffer financial strain and grieve the loss of the child they once knew. The child's level of functioning may fluctuate from day to day, with continual care plan adjustments requiring close interactions between parents and health care professionals (Kisler et al., 2010)

Parent Experiences of Mitochondrial Disease

Mitochondrial diseases vary in clinical presentation, impact on organs, rate of progression and age of onset, thereby influencing the family experience of parenting a child with mito (Noorda et al., 2007). Although there is growing interest in the biochemical understanding of mito, there is also a gap in understanding the impact of caregiving, psychosocial stressors and coping experience of parents managing a child with a mitochondrial disease (Noorda et al., 2007). Understanding the experience of caring for a

children with special health care needs in the home is important as parents balance numerous role conflicts and medical challenges (Ratliffe, Harrigan, Haley, Tse, & Olson, 2002).

Noorda et al., (2007) conducted a multi-approach pilot study and survey of parents of children with mito along with a systematic review of mitochondrial literature to identify needs and problems in everyday life of parents and children with mito. Their inquiry revealed gaps in the number of studies completed to understand the needs and problems of children and families living with mitochondrial disease, especially compared to the number of clinical and biochemical studies of mitochondrial disease (Noorda et al., 2007; Read, 2003). In this study, Noorda (2007) conducted two focus group interviews of ten parents who had a child with mito. Parents were invited to talk about their experiences and concerns about their need for information. The results from the focus groups revealed a gap in the giving of information to parents by health care professionals to improve quality of life for families (Noorda et al., 2007). Many parents wanted information about symptoms, prognosis and consequences of their child's illness and felt that the disease stage, coping phase and presence of support influenced their ability to process information (Noorda et al., 2007). The results from these focus groups were used to develop a closed-format questionnaire that was then distributed to 76 parent participants, of which 37 (49%) responded (Noorda et al., 2007). The results of this study concluded that parents had a high need for information particular to symptoms, prognosis, life expectancy, alternatives and conventional medical treatments and genetics, especially during the diagnostic stage (Noorda et al., 2007).

Systematic review of the literature by Noorda et al. (2007) revealed that there were no studies to specifically address the needs and problems of children with mitochondrial disease, and only two studies that identified the needs of mothers of children with mitochondrial

disease. Based on the results from this review and focus groups, the authors recommend further research to explore the needs and problems of parents and children with mitochondrial disease with first steps to address the physical, psychological, social and spiritual needs of parents with children in the different stages of child development and disease process (Noorda et al., 2007). The authors concluded that health care professionals can base health information on identified needs for effective care planning to improve quality of life for parents and children living with mitochondrial disease (Noorda et al., 2007).

Impact on Mothers. Caring for a child with a chronic illness is particularly stressful for the primary caregiver, who in most cases is the mother (Ratliffe et al., 2002). The impact on mothers has been explored in the literature, particularly because of the relationship between maternal inheritance and mitochondrial disease. Read (2003) documented the adverse effects on mothers of children with mito comparing socioeconomic and psychoaffective strain and use of health services in mothers of children affected with phenylketonuria (PKU) and mitochondrial disease, both biochemical genetic disorders. Using telephone interviews, data were obtained from 29 mothers of children with PKU and 29 mothers of children with mito. Information was collected about the family demographics, out-of pocket expenses, number of work days missed, the number and types of health services used and assistive devices required by the child (Read, 2003). Mothers were asked to state the degree to which their lives were affected by the child's illness and developmental behaviors (Read, 2003). Read used the Parenting Stress Index to describe the socioeconomic and psychoaffective strain on the mother as an illness stressor and noted an increased need for health services required to care for a child with a biochemical genetic disorder (Read, 2003).

Read (2003) also found that children with mitochondrial disease suffered greater strain, required a significantly greater number of health care services, had greater involvement with specialists, and more hospitalizations than children with PKU. The study indicated that children with mito experienced impairments in activities of daily living, communication, socialization and motor skills, and that mothers of children with mito had significantly more stress, strain and worry, with increased financial burden compared to those mothers of children with PKU. Read recommends the need for ongoing assessment of uncertainty in illness, and exploring physical and psychosocial needs during the delivery of health information to families with mitochondrial disease.

Varvogli and Waisbren (1999) examined personality profiles of 42 mothers of children with various mitochondrial disorders by administering the Minnesota Multiphasic Personality Inventory, Second Edition (MMPI-2). Over 50% of the children in the study had special needs such as wheelchair dependence, developmental delays, gastrointestinal tube feedings, and vision problems (Varvogli & Waisbren, 1999). They found that 56% of the mothers had elevated scores in one scale and 42% had elevated scores on three or more scales of the MMPI-2: Hypochondriasis, Hysteria and Paranoia, and Psychopathic Deviate (Varvogli & Waisbren, 1999). Elevated scores were significantly related to the age of the mother: the younger the mother the greater the psychopathology noted, while the age of the child did not impact on the mothers' personality profile scores (Varvogli & Waisbren, 1999). It was suggested that situational stress may be related to these elevated scores of mothers of children with mitochondrial disorders who face a frightening diagnosis and numerous demands associated with caring for these children (Varvogli & Waisbren, 1999). In other studies of children with chronic illness, maternal mental health was directly associated with the

perceived of the impact of the child's disease, raising the question of whether the child's mitochondrial disorder had an impact on the mother's emotional state (Ireys & Silver, 1996; Varvogli & Waisbren, 1999). Future studies are needed to determine the impact of illness on mothers of children with mitochondrial diseases.

Mothers of children with chronic illness are generally more prone to depression, anxiety and stress (Boles et al., 2005). Boles et al. (2005) further suggest that anxiety and stress are increased specifically in mothers of children with a maternally inherited (mtDNA) mitochondrial disorder. In their study, the Beck Depression Inventory, Beck Anxiety Inventory and a non-standardized mental health questionnaire were given to 15 mothers of children with presumed mtDNA disorders and 17 mothers of children with autosomal recessive (nDNA) metabolic disorders. The authors reported statistically higher scores in depression and anxiety of mothers in the mtDNA group than mothers of children in the nDNA group. The study questionnaire also revealed a striking higher incidence of depression among first degree relatives of mothers in the mtDNA group, suggesting a genetic predisposition to mental health conditions are not entirely explained by the burden of caring for a child with chronic illness but perhaps related to the genetic transference of the mitochondrial disease (Boles et al., 2005).

A recent study conducted in Korea investigated caregiver burden and health-related quality of life of 33 mothers of children with mitochondrial disease compared to 33 mothers of children with intractable epilepsy (Kim et al., 2010). The authors administered the Zarit Burden Inventory, Medical Outcomes Short Form 36, short version of the World Health Organization Quality of Life Inventory, Beck Depression Inventory, and Beck Anxiety Inventory to all participants. Their study revealed that mothers of children with mitochondrial

disease have significantly higher caregiver burden and lower quality of life with greater levels of depression and anxiety than parents of children with intractable epilepsy (Kim et al., 2010). Mothers also reported guilt and anxiety associated with maternal inheritance influencing their perception of caregiver burden and ability to handle stress of caring for a child with mitochondrial disease (Kim et al., 2010). The results strongly suggest a link between psychological distress and burden of care, although not causality; the authors recommend finding strategies to assess emotional elements of caregiving to ease anxiety, guilt and caregiver burden in mothers of children with mito (Kim et al., 2010).

Health Related Quality of Life. There is little known about health related quality of life and predictors of parent functioning in children with mitochondrial diseases. Hatzmann et al. (2009) explored health related quality of life (HRQoL) in parents of children with metabolic diseases, including families with mitochondrial disease. Their study aim was to examine medical, socio-demographic and psychosocial determinants of HRQoL in parents of children with metabolic diseases (Hatzmann et al., 2009). The authors conducted a cross-sectional study exploring HRQoL, and social and financial consequences of parents caring for a chronically ill child with metabolic disease in the Netherlands (Hatzmann et al., 2009). HRQoL surveys were administered to 108 parents with children ages 1-19 years in three major classes of inherited metabolic diseases: mitochondrial disorders (n=56), lysosomal storage disorders (n=34), and disorders of amino acid metabolism and transport (n=18) (Hatzmann et al., 2009). The results from this study indicated that psychosocial determinants appeared to be most important in predicting HRQoL over socio-demographic and medical variables, with emotional support and friendship contributing the most as positive predictors of HRQoL. The only medical variables reported to affect HRQoL were progression of illness,

administration of tube feedings, and if the child had social interactions that interfered with activities of daily life (Hatzmann et al., 2009). The authors recommend futures studies to include greater analysis of psychosocial determinants and measurements of coping styles.

Family Experience. Read & Calnan (2000) provided a scientific description of mitochondrial disorders and shared three case studies of children with various mitochondrial dysfunctions as exemplars for recommending nursing care to families with mitochondrial disease. The case studies included a teenager with Kearns-Sayre Syndrome, a five year old with Leigh Syndrome and a young adult with suspected Wolfram Syndrome, all caused by malfunction of the mitochondria. Their findings showed that parents desired information, needed to be control of their child's health care, and were reliant on competent health care providers as a means for coping (Read & Calnan, 2000). Unfortunately the evasive nature of mito still leaves health care providers learning about the effects of this disease. Parents want information about diagnosis, treatment, and genetic transmission (Read & Calnan, 2000). Health care professionals are challenged to learn about the effects of mito and enter into conversations with families about diagnosis, treatment options and disease transmission (Read & Calnan).

Family Support Framework. There is an absence in the literature of a mitochondrial family support framework model with the exception of a study completed by Nishio (1997). Nishio presents a case study of one specific family affected by mitochondrial disease to provide an overview of mitochondrial encephalopathies and to present a protocol to guide nursing practice centered on perceived family needs, nursing interventions, and outcomes of care (Nishio, 1997). The case study family consisted of the mother, a second husband, and three (of five) surviving children who were noted to have a mtDNA mutation (Nishio, 1997).

The mother shared her lived experience and feelings of denial, anger, frustration, sorrow, hope, and acceptance of how this disease affected her family (Nishio, 1997). Nishio (1997) proposed nursing protocols based on Dungan's Model of Dynamic Integration to address the perceived needs of families, nursing interventions, and outcomes of care. Dungan's Model of Dynamic Integration is relevant when assessing family transitions due to illness with the assumptions that life events, like a having an ill child, are part of the total life experience for the family and that timely nursing interventions can assist with balancing these experiences (Nishio, 1997). Dungan's Model was used a framework for Nishio's study to focus on the needs, interventions and outcomes of care for a child with mito. The results from the case study indicate that families have a need for knowledge, assistance with managing stress and strain and coping, locating financial resources, validation of caregiving competency, and coaching to focus on the strengths of the family (Nishio, 1997).

Parent Stress. It is well documented in the literature that families of medically fragile children face multidimensional stresses or tasks (Ratliffe et al., 2002). Parents of children with mito experience uncertainty about long-term outcomes, whether or not their child will survive, and the child's ability to function in the future. Parents of children with biochemical genetic disorders like mito are at high risk for parenting stress (Waisbren, Rones, Reach, Marsden, & Levy, 2004). Waisbren et al., (2004) conducted a study to examine the predictors of parent stress in parents of children with a biochemical genetic disorder identified through clinical presentation or by newborn screening (Waisbren et al., 2004) Parents of 263 children with biochemical genetic disorders, including some known mitochondrial disorders, participated in the study using the Parenting Stress Index-short form (PSI-SF) to measure stress as the dependent variable (Waisbren et al., 2004). This study found that child development related to

the timing, diagnosis and treatment correlated with stress, as did difficulties meeting the child's health care needs and the number of people in the parents' social support network (Waisbren et al., 2004). Early diagnosis of illnesses in children through newborn screening resulted in higher levels of adaptive functioning and fewer hospitalizations with significantly lower levels of parenting stress (Waisbren et al., 2004). Because mito does not have a reliable screening marker, the authors recommend continued research to examine predictive factors in biochemical genetic disorders like mitochondrial disease (Waisbren et al., 2004).

Summary

Review of the literature regarding parents of children with mito revealed studies about the needs and problems of families in the diagnostic stage (Noorda et al., 2007), stress, depression, impact on mothers (Read, 2003), caregiver burden, HRQoL (Hatzmann et al., 2009; Kim et al., 2010) and qualitative studies about the parent experience (Read & Calnan, 2000); however, there are no studies that explore the impact of pediatric illness-related stress associated with caring for a child with mito. Parents of children with mito are likely to experience a variety of illness-related stressors related to caring for a child with a rare, complex and unpredictable chronic illness, and understanding the dynamics of these stressors can help inform the health care community about parent needs, thus optimizing the use of nursing interventions to reduce or eliminate stressors and facilitate coping strategies.

Parents of children with chronic health conditions are at increased risk for emotional distress and family dysfunction because of the demands of caring for a child with special needs (Farmer et al., 2004). Stress associated with uncertainty about the child's health outcomes in addition to the challenges of navigating a complex health care system can decrease the parent's ability to promote the child's health (Farmer et al., 2004). Parents of

children with mitochondrial disease not only experience these challenges but also are met by health care professionals who have a limited understanding of the unique needs associated with this population. Despite the growing number of children being diagnosed with mito, many health care professionals still know very little about the disease process or impact to family. Results of this study will inform health care professional about the needs of parents caring for a child with mito.

Hill's Model of Family Stress

There are many frameworks that explain the dynamics of family stress. Most models have evolved from Reuben Hill's (1949, 1958) ABC-X Model of Family Crisis (Bomar, 2004). Hill, known as "the father of family stress theory," made a significant contribution to understanding family stress with his ABC-X formula (Weber, 2011). The ABC-X formula focuses primarily on pre-crisis variables of the families: Factor A represents the crisis-precipitating event/stressor, Factor B is the family's crisis-meeting resources which interacts with factor C, the definition the family makes of the event, to produce Factor X, the crisis (Weber, 2011). This model was designed to identify resources and coping behaviors that help families make positive adaptations to stressful situations (Lee, 2009). Hill's (1949, 1958) stress theory speculates that acute stressors lead to family crises; however, protective factors such as the family's perception of the event and family resources can buffer the impact of the stressors (Lee, 2009). Hill's ABC-X model (1949, 1958) maintains that families faced with stressors (A) utilize positive and negative family resources (B) and perceptions of how to approach problems (C) to either cope or succumb to the crises (X) (Bomar, 2004; Kahl, Steelman, Koch, Dougan, & Catsambis, 2007; Lee, 2009).

In this model (see Figure 1), Factor A is the precipitating event or stressor. Hill (1958) described the precipitating event or stressor, such as having a child diagnosed with mitochondrial illness, as a situation which the family views as problematic with little or no prior preparation (Weber, 2011). The degree of stress depends on the hardship and appraisal of the stressor determined by the family (Weber, 2011). Factor B is the family's stress-meeting resources, or coping strategies, that determine the adequacy or inadequacy of the family's ability to handle the stressful event and to manage the situation (McCubbin & McCubbin, 1987; Weber, 2011, p. 83). Factor C is the subjective definition of the family stress event and the defining hardships noted by the family (Weber, 2011). In this study it is the expression of the parent's experience of childhood illness. According to Hill, (1958) the event, family resources, and definition of the event interact to lead to crisis (Weber, 2011). Stressors can be actual or perceived threats that disrupt the family equilibrium, and family resources and the meaning the family assigns to the event can impact the ability of the family to cope and determine how the family responds to the stressors (Bomar, 2004).

Many researchers have studied the impact of caring for a child with a chronic condition, finding that socio-economic status, coping style, child behavior, care-giving demands, social support, and age are predictors of parental stress, but there is limited research exploring the experience of parents or predictors of stress in parents who care for a child with mitochondrial disease (Hatzmann et al., 2009). This study will utilize Hill's ABC-X model to explain how parents of children with a mitochondrial disease (Factor A) have at their disposal resources for coping (Factor B) and a unique experience of childhood illness (Factor C) that influence the impact of parental stress (Factor X). The hypothesis for this study is that family demographics and disease-related characteristics associated with a mitochondrial condition

(Factor A, AIM 1), parent resources for coping (Factor B, AIM 3) and parent experience associated with childhood illness (Factor C, AIM 2) will significantly relate to and be predictive of pediatric illness-related parenting stress (Factor X, AIMS 4, 5, and 6).

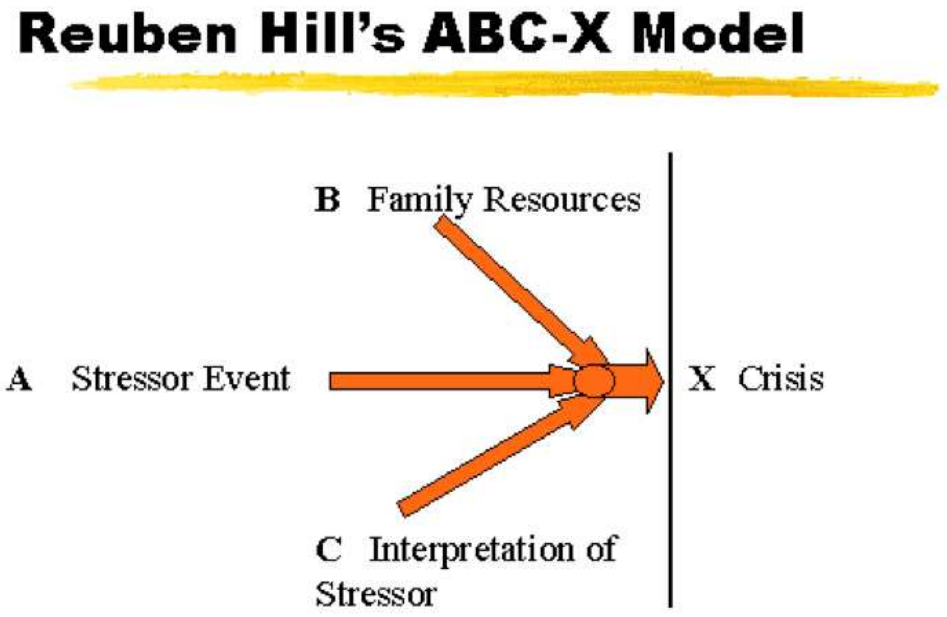

Figure 1: Adaptation of Reuben Hill's ABC-X Model of Family Crisis.
SOURCE: Starbuck, G. (2000). Chapter Fourteen: Crisis and Violence in Families

Chapter Three: Methodology

This chapter describes the methods used to identify and explore the relationships between demographic and disease-related characteristics, experiences of childhood illness, and coping strategies with pediatric illness-related parenting stress in parents of children with mitochondrial disease.

Research Design

This research used an exploratory and predictive cross-sectional study design employing survey collection for data analysis. The main phenomenon of interest for this study was the parent experience and stress when caring for a child with mitochondrial disease. An exploratory design was chosen because there is limited information about parenting a child with mito, specifically in exploration of the relationship among demographics and disease characteristics, parent experience associated with caring for a child with a chronic illness, coping strategies and pediatric illness-related parenting stress.

This research explored the relationships among the study variables. Although there is research documenting the relationship between stress and coping in parents of children with chronic illness, there have been no reported studies that specifically describe the relationship between demographic and disease characteristics, coping strategies, pediatric illness-related parenting stress or the experience of pediatric chronic illness when caring for a child with a mitochondrial disease. Furthermore, this study used a hierarchical linear regression model to examine predictors of parenting stress when parenting a child with mito.

If pediatric illness-related parenting stressors can be predicted in parents of children with mito, then health care professionals can initiate interventions to reduce the impact of these stressors on the family. Demographic and disease characteristics, coping strategies and

specific experiences of caring for a child with a chronic illness are likely to predict the occurrence of parent stress. If stressors can be predicted from knowledge of the disease characteristics, experience and coping of parents care for a child with mito, then perhaps appropriate nursing interventions can help reduce stressful events for these families.

Recruitment and Procedures

This study used nonprobability convenience sampling by recruiting parents of children with mitochondrial disease who met the inclusion criteria during a four-month period of time using Internet resources. Advantages of web-based and email data collection include reduced response time, lower costs than paper and pencil, ease of data entry, flexibility and control over survey format (Granello & Wheaton, 2004). Limitations for web-based and email surveys include potential lack of representativeness of the sample, lower response rates than traditional mail surveys, and measurement errors related to navigation within the survey screen or technical difficulties interrupting survey responses (Granello & Wheaton, 2004). Errors in responses can occur for various reasons, ranging from human error to technical difficulties. Concerns about representativeness of the sample were addressed by targeting webpages that are known to attract individuals in the mito community. One limitation of providing direct access to the surveys without providing a passcode includes the chance that respondents could take the survey twice. Although this is unlikely, it is more likely without a password. A major limitation of this sample method is the potential for bias of self-selection that may create an atypical representation of the target population in regards to age, motivation, activity level or other correlates of health consciousness which may affect the ability to generalize outcomes (Portney & Watkins, 2009, pp. 154-155). This sample was recruited from three Internet webpages and associated social media platforms known to the

mitochondrial community: 1) MitoAction webpage (mitoaction.org) and Facebook page, 2) United Mitochondrial Disease Foundation webpage (UMDF.org) and Facebook page, and 3) Mitochondrial Research Guild of Seattle Children's Hospital webpage (nwmito-research.org) and Facebook page. Internet sampling limits the accessibility of the sample to those individuals who have Internet access and who frequent the webpages being surveyed.

The Internet has become one of the top three resources individuals choose for answers to health questions (Fox & Purcell, 2010). In January 2008, 80% of Americans used the Internet for health information, making the Internet, not the health care provider, the leading source for health information (Elkin, 2008; Fox & Purcell, 2010). According to the PEW Internet & American Life Project, 51% of Americans with chronic disease have looked online for health topics with 34% of health searchers using social media (Elkin, 2008; Fox & Purcell, 2010). Today, patients (and parents) are not only reading and learning about health news, but they are discussing and sharing healthcare experiences online (Sarasohn-Kahn, 2008). The most common media platforms used by consumers are Wikipedia (21%); message boards and online forums from Yahoo and Google Health (15%); social networks such as Facebook (6%); video-sharing sites like YouTube (5%); blogs from sources like WebMD and Healthline (4%); and live chat rooms (4%) (Elkin, 2008). Patients with chronic illness use the Internet to gain knowledge specific to their health condition, to exchange information and ideas, and to receive and provide emotional and practical support for managing their illness. (Fox & Purcell, 2010; Sarasohn-Kahn, 2008).

Parents of children with mito also frequent online resources for information and social support. Two prominent national Internet resources known to the mito community used for

recruitment in this research were: 1) The United Mitochondrial Disease Foundation (UMDF.org) and 2) MitoAction (mitoaction.org).

UMDF was founded in 1996 through a merger of several smaller foundations established by individuals who lost loved ones to mito, and has grown into a nationally recognized nonprofit organization (United Mitochondrial Disease Foundation, 1996). UMDF is represented across the nation with 50 local chapters with groups and ambassador programs to support their mission "to promote research and education for the diagnosis, treatment and cure of mitochondrial disorders and to provide support to affected individuals and families" (United Mitochondrial Disease Foundation, 1996).

MitoAction is a nonprofit organization founded by a patient (also a parent of two children with mito) and her nurse practitioner in 2003 because they wanted to put their ideas into "ACTION" (Balcells, 2009). In November of 2006, Cristy Balcells, RN, MSN, community health nurse and mother of three, including a child with Leigh's disease (a known mitochondrial illness) became the executive director of MitoAction (Mitoaction, 2009b). MitoAction is dedicated to supporting patients with a mitochondrial condition and their caregivers to improve "quality of life for all who are affected by mitochondrial disorders through support, education and advocacy initiatives" (MitoAction, 2009c). MitoAction reports that over 1000 families regularly access their webpage (C. Balcells, personal communication June 15, 2011).

A U.S Northwest Internet resource, the Mitochondrial Research Guild, was also utilized in this research. The Mitochondrial Research Guild is a special interest guild of Seattle Children's Hospital founded by local families to "raise awareness, promote research and improve the quality of medical care" available to children with mito (Mitochondrial

Research Guild, 2011). The author of this dissertation is a member of the Mitochondrial Research Guild.

Social media groups such as Facebook known to the mito community were also used for recruitment purposes. The UMDF Facebook page reports 5,583 members (Facebook, 2012c), and, MitoAction has 3,027 Facebook likes (Facebook, 2012a). The Mitochondrial Research Guild of Seattle Children's Hospital Facebook page reports 200 members (Facebook, 2012b). Although it is impossible to know the exact numbers of parents of children with mito who are members of these web resources or how many individuals are members of all three organizations, recruitment from these organizations provided for a substantial number of parent participants who met the research inclusion criteria and helped obtain the power analysis requirements.

Statistical power tests the function of the significance criterion, variance in the data, sample size and effect size (Portney & Watkins, 2009). The significance criterion (alpha) reduces the chance of Type I error (rejecting the null hypothesis when it is true; for example: parents of children with mito do not have pediatric illness-related stress) by requiring stronger evidence to demonstrate significant differences (Portney & Watkins, 2009). Statistical power is increased when variance within a set of data is reduced. Variance can be reduced and power increased by increasing the size of the sample: the larger the sample the greater the statistical power (Portney & Watkins, 2009). In studies where relationships are of interest, effect will be the degree of correlation or association between variables (for example, the size of the effect in the relationship between disease characteristic, coping, parent experience and pediatric illness-related stress in parents with mito). To determine the appropriate sample size for this study, a priori power analysis was conducted using GPower (Erdfelder, Faul, & Buchner,

1996). A linear multiple regression fixed model, R squared, deviation from zero analysis was conducted with power set at 0.80 and significance of α=.05, expecting a medium effect (f^2 =.15) with 24 independent variables which yielded 172 participants needed for this study (G*Power Version 3.1). Cohen's f^2 effect size, by convention, is used to measure the effect size F-test for multiple correlation regression (small=.02, medium =0.15, large = 0.35) (Erdfelder et al., 1996).

Webpage administrators agreed to advertise the research study and to post information about the study with a URL hyperlink to the set of research surveys on their webpage as well as information explaining the purpose of the study, directions for accessing the surveys, and contact information of the researcher (See Appendix A). Webpage administrators also sent regional announcements to members via emails and listservs. The researcher obtained permission from each Facebook administrator to use the Facebook pages to encourage participation in the study. To launch the survey study, MitoAction interviewed the author on a one-hour podcast/webcast on MitoAction.org about stress and coping for parents of children with mito. After the survey study went live, the researcher monitored response rates weekly and gave reminders to encourage participation. Webmasters placed announcements about the research study in a prominent location on the webpages' home pages, where they remained for four months (118 days). While the surveys were open, the researcher posted reminders on the Facebook pages (See Appendix B). Facebook account administrators also sent occasional reminders to members directing participants to information about the research study, the researcher's direct email and URLs for the set of surveys. The researcher was available via email to provide technical assistance and was able to answer questions and assist in completion of the survey. Respondents clicked on the link, filled out the set of surveys and

clicked on the “submit” button when they were finished. Care was taken to protect confidentiality and anonymity during survey collection by not requiring or collecting email addresses. Respondents were informed of risks and the survey process. When the number of respondents slightly exceeded the calculated power analysis (n=172) for a total of 231 participants, the webmasters removed the announcements from the webpages and Facebook pages, and the researcher closed the surveys.

Inclusion criteria for the sample population consisted of parents with at least one living child (age birth-18 years) who had a “confirmed”, “probable” or “possible” diagnosis of mitochondrial disease. To participate in the study, respondents had to read and understand the English language and have access to the Internet. Two screening questions were asked prior to access to the questionnaires to assure representation of inclusion criteria: 1) Are you a parent (biological or non-biological) of a living child diagnosed with a “confirmed”, or “probable” or “possible” mitochondrial disease? 2) Have you or anyone in your house already completed this survey? Respondents who answered “yes” to question 1 and “no” to question 2 were directed to the research questionnaires. Respondents who answered “no” to question 1 or “yes” to question 2 were not provided with access to the research questionnaires.

The following survey questionnaires were accessible as one survey “set” in the following order: 1) Parent Experience of Childhood Illness (PECI), 2) Coping Health Inventory for Parents (CHIP), 3) Pediatric Inventory for Parents (PIP) 7-day, 4) Pediatric Inventory for Parents (PIP) 30-day, and 5) Mito Demographic and Disease Related Characteristics Questionnaire. The “set” of surveys were calculated to take approximately 15-20 minutes to complete based on a small sample group who took the surveys prior to their being announced on the webpages.

Web instructions directed participants to the survey housed on Qualtrics, a secure service database warehouse that provides website hosting and analysis of research surveys (Qualtrics, 2012a). Qualtrics is a survey creation and management tool that meets rigorous privacy standards imposed on health care records by the Health Insurance Portability and Accountability Act (HIPAA) securing all accounts and guaranteeing data protection (Qualtrics, 2012b). Washington State University subscribes to Qualtrics and grants access to student researchers. *Display logic, skip logic* and *request response* are features that were used to assure that informed consent was obtained, that the majority of the questions in the survey were answered, and that respondents met the inclusion criteria to access the survey. *Request response* reminded the participant to answer all of the questions on the page before moving to the next page on the survey, without forcing the participant to make a response. Participants had unlimited access to complete an open survey if they were interrupted, experienced survey fatigue, or needed to resume the survey for any reason. Incomplete surveys were not recorded in the data collection (Qualtrics, 2009).

Human Subjects Protection

Prior to data collection, Institutional Review Board (IRB) approval was obtained from Washington State University's IRB board along with the permission of webpage administrators to utilize UMDF, MitoAction and The Research Guild of Seattle's webpages and Facebook pages (See Appendix C for IRB and webpage approval). Confidentiality was protected for all participants and their children to ensure privacy through de-identified web-based data collection. Although the data obtained is about living individuals and is collected through interactions with individuals, the data collected did not contain identifiable private information.

Informed consent was collected from each participant by placing an Informed Consent Screening Question at the beginning of the survey and asking the respondent to click “I agree” before they were allowed to access the surveys. The full name and contact information of the researcher was also provided on the webpage along with an explanation of the research project.

This study was also designed to collect demographic characteristics for analysis of impact of pediatric illness-related stress on families. Demographic information was carefully designed so the participants cannot be identified. All research participants had the freedom to withdraw at any time with no adverse consequences. Permission for use of survey questions from the original authors was collected prior to commencing the study (See Appendices D, E, and F).

Measures

Demographic and Disease-Related Questionnaire: This study captured demographic and disease-related information in order to create a comprehensive and accurate description of the research sample and population from which it was drawn (Sifers, Puddy, Warren, & Roberts, 2002). Thompson and Gustafson (1996), in their collection of work exploring adaptation to chronic childhood illness, noted relationships among certain demographic variables and adaptation to chronic illness in both parents and children. Child demographic and disease related dimensions identified as important in categorizing and adapting to chronic conditions included: disease rareness, age of onset, loss of function and impact to mobility, course of illness and progressive decline, ability for the child to communicate, and visibility of the disease to the community (Thompson & Gustafson, 1996). Parental adjustment to chronic illness showed correlations to such variables as degree of social support, parent age,

and financial distress (Thompson & Gustafson, 1996). Common demographic characteristics noted in research include age, gender, and disease classifications; less common variables are ethnicity and social economic status (Sifers et al., 2002).

For this study a demographic survey questionnaire was developed to identify family demographics parent characteristics (gender, marital status, age, biological relationship to the child, marital status, income, level of education, ethnicity, and race), and child characteristics (gender, current age, age of symptoms, age of diagnosis, number of children in household with mito, child with developmental delays), and disease-related information (type of mitochondrial disease, confirmed diagnosis if known, organ involvement, use of specialty services, last hospitalization, number of hospitalizations in past year, and number of office visits in past year). The demographic tool used the federal recommendations for collecting data on race and ethnicity (Federal Register, 1995), the 2012 Health and Human Services Poverty Guidelines for the 48 contiguous states and District of Columbia (United States Health and Human Services, 2012). The tool was reviewed and approved by a pediatric expert, statistician, and mitochondrial consultant. Selection of disease characteristics was informed by review of literature of children with chronic illness and specific needs related to mitochondrial disease as noted in the textbook, *Living Well With Mitochondrial Disease* (Balcells, 2012). Identified variables provided descriptive data about the research population for possible comparisons with other pediatric chronic illnesses and were used to examine correlations and predictive impact of certain variables on pediatric illness-related parenting stress (See Appendix G).

Parent Experience of Child Illness: The PECI was developed within the Division of Pediatric Neuro-Oncology and Pediatric Hematology-Oncology at a medical center in the

Southeast United States to measure parent adjustment associated with illness–related concerns such as emotional resources, chronic sorrow and uncertainty in parents of children with chronic illness (Bonner et al., 2006). A multidisciplinary team generated a preliminary list of items from clinical findings related to parenting a child with chronic illness (Bonner et al., 2006). The PECI consists of 25 items that measure the following constructs: Guilt & Worry, Unresolved Sorrow & Anger, Long-term Uncertainty, and Emotional Resources. This self-reporting measure is written at an approximate 4th grade reading level. This questionnaire is intended to measure thoughts and feelings related to parenting a child who is living with, or who has experienced, a chronic illness (Bonner et al., 2006). Each statement is intended to describe the parent's thoughts and feelings over the past month by rating each item on a five-point Likert-type scale as follows: 0 = "Never", 1 = "Rarely", 2 = "Sometimes", 3 = "Often", and 4 = "Always" (See Appendix H).

The 25-item version of the PECI was subjected to an Exploratory Factor Analysis (EFA) using oblique rotation because of supporting theoretical factors assuming the factors to be intercorrelated (Bonner et al., 2006). Five factors were initially extracted from the PECI and accounted for 60% of the variance; however, due to significant cross loadings only four factors were retained accounting for 56% of the total variance. 1) Guilt & Worry (11 items, questions 3, 6, 7, 10, 13, 14 [reverse coded], 16, 20, 22, 24, and 25) accounted for 35% of variance; 2) Unresolved Sorrow & Anger (8 items, questions 1, 2 [reverse coded], 12, 15, 17, 19, 21, and 25) accounted for 8.54% of variance; 3) Long-term Uncertainty (5 items, questions 1, 4, 8, 9, and 18) accounted for 6.23% of variance; and 4) Emotional Resources (5 items, questions 2 [not reverse coded], 5, 11, 14 [not reverse coded], and 23) accounted for 5.62% of variance. Guilt & Worry consists of parents' concerns about their child's future and

well-being, and personal guilt. Unresolved Sorrow & Anger items relate to feelings of grief and anger over having to experience the chronic illness of a child. Long-term Uncertainty contains items describing sadness about the paths their children's lives might have taken had they not become ill, as well as concerns about what their children's lives might be like in the future, and the fourth factor, Emotional Resources includes feeling of competency and self-efficacy where higher scores reflect fewer perceived emotional resources (Bonner et al., 2006).

Four additional measures were administered to 202 primary caregivers of pediatric patients (ages less than 1 year through 17 years) diagnosed with a brain tumor along with the PECI to validate construct validity of the PECI: 1) Caregiver Strain Questionnaire (CSQ): a 21-item self-reporting measure to assess adults' perception of difficulties associated with their parenting role and having internal consistency between 0.71-0.93; 2) Impact on Family Scale (IFS): a 33-item self-report measure used to determine how family functioning is affected by an illness, with internal consistency reliability reported at 0.88; 3) Brief Symptom Inventory (BSI): a 53-item self-report inventory for adolescents and adults designed to reflect a broad range of psychological symptoms such as depression and anxiety, reporting good test-retest reliability; and 4) Impact of Event Scale (IES) a 15-item questionnaire used to assess the frequency of post traumatic stress disorder symptoms during the previous week, also reporting high internal consistency and test retest reliability (Bonner et al., 2006). To determine construct validity, each subscale of the PECI was compared with scores obtained from the BSI, CGSQ, IES and IFS using Pearson's product moment correlations (Bonner et al., 2006). In this study, Guilt & Worry, Unresolved Sorrow & Anger and Emotional Resources subscales on PECI significantly correlated with scores obtained from the BSI, CGSQ, IES and

IFS. There is no documentation of construct validity with the subscale Long-term Uncertainty. Cronbach's alpha for PECI scores ranged from .72-.89 for each of the four subscales, (Guilt & Worry α = .89, Unresolved Sorrow & Anger α =.86, and Long-term Uncertainty α = .80, Emotional Resources α = .72) (Bonner et al., 2006). No Cronbach's alpha was reported for the overall scale.

PECI subscales were scored independently by adding all the items in the subscale and dividing by the number of items in the subscale. Questions 2 and 14 were reverse coded for subscales Guilt & Worry and Unresolved Sorrow & Anger and questions 1, 2, 14 and 25 were scored on two subscales. There were no total scores indicated for the PECI tool.

Coping Health Inventory for Parents: The Coping Health Inventory for Parents (CHIP) was developed by McCubbin, McCubbin, Nevin, and Cauble in 1979 and introduced in 1981 as a measurement instrument to assess parent coping and perceptions of managing family life when they have a child who is seriously and/or chronically ill (McCubbin & McCubbin, 1987). Construction of the CHIP was guided by various theories from individual psychology of coping theories, social support theories and Hill's Family Stress Theory (McCubbin & McCubbin, 1987). Family health care teams and parents of chronically ill children also contributed to the CHIP's construction (McCubbin & McCubbin, 1987). The CHIP is a parental self-reporting instrument consisting of a checklist with 45 specific behaviors on which parents are asked to record how helpful the behavior is in their particular family situation on a scale of 0-3 (0 = "Not Helpful", 1 = "Minimally Helpful", 2 = "Moderately Helpful", 3 = "Extremely Helpful") (McCubbin & McCubbin, 1987). Subscale scores were calculated by summing the items listed in the specific subscale (scoring the "I do not cope this way" as zero). Parents also had the option to indicate if they do not cope in this

manner because it is not possible (Hobdell et al., 2007). A total score was obtained by summing the number reported by the respondent for each item in the CHIP instrument (See Appendix I).

The CHIP inventory originally contained 80 items but was reduced to 45 items using the factoring with iterations method. The scree test and resulting eigenvalues and Varimax rotation determined the final three subscales: 1) Coping Pattern I: Family Integration, Co-operation and an Optimistic Definition of the Situation. This subscale is composed of 19 behaviors that focus on strengthening family life and relationships and the parent's outlook on life with a chronically ill child; items include questions 1, 3, 6, 8, 11, 13, 16, 18, 21, 23, 26, 28, 31, 36, 38, 41, 43, 44, and 45. 2) Coping Pattern II: Maintaining Social Support, Self Esteem and Psychological Stability. This subscale consists of 18 items, which involve the parents' efforts to develop relationships with others, engage in activities which enhance feelings of individual identity and self worth, plus behaviors to manage psychological tensions and pressures; items include questions 2, 4, 7, 9, 12, 14, 17, 19, 22, 24, 27, 29, 32, 33, 34, 37, 39 and 42. 3) Coping Pattern III: Understanding the Health Care Situation Through Communication with Other Parents and Consultation with the Health Care Team. This subscale contains eight behaviors exploring the parents' relationships with health care professionals and other parents of chronically ill children including developing more knowledge and understanding of the illness, home care treatments and prescribed medical regimens; items include questions 5, 10, 15, 20, 25, 30, 35, 40 (McCubbin & McCubbin, 1987). These three subscales represent different positive coping patterns explaining 71.1% of the variance of the original correlation matrix (McCubbin & McCubbin, 1987). Higher coping scores represent increased use of coping; increased use of coping is interpreted as indicative of

increased stress (Hobdell et al., 2007). Cronbach's alphas originally computed for the items on each coping subscale indicated reliability of 0.79 for the first two subscales and 0.71 for the third subscale (McCubbin & McCubbin, 1987). In a more recent study conducted by Hobdell et al, (2007) regarding coping in children with epilepsy, a Cronbach's alpha of 0.92 was reported for the entire instrument. Construct validity was tested against the subscales from CHIP using discriminant analysis between low conflict and high conflict in families who had a child with cerebral palsy (McCubbin & McCubbin, 1987). In a study of parents (n=185) of children with cystic fibrosis, construct validity assessment of the CHIP in all three coping subscales was significantly associated with the family interpersonal relationships dimension of family life (McCubbin & McCubbin, 1987).

A systematic review of the CHIP was conducted during a four year period from 1981-1984 including 22 studies that incorporated the CHIP into the research design and protocol, with a total of 1,116 persons completing the instrument (McCubbin & McCubbin, 1987). This review found differences in coping patterns between mothers and fathers, correlations between coping and family factors and between coping and child factors, and also explained the relationship between coping and population demographics.(McCubbin & McCubbin, 1987)

Pediatric Inventory for Parents: The Pediatric Inventory for Parents (PIP) (Streisand, Branieki, Tercyak & Kazak, 2001) was developed in response to the need for a parent-related pediatric-specific stress measure to assess stress among parents of children with a critical illness (Streisand et al., 2001). The PIP was intended to measure the origin of the stress and the periods of the illness cycle most highly related to distress to serve as an indicator of treatment and interventions to reduce stress (Streisand et al., 2001).

The PIP was developed at the Children's Hospital of Philadelphia using empirical literature on parenting stress, past research findings, and clinical experience of three pediatric psychologists within the oncology department (Streisand et al., 2001). The final version of the PIP includes 42 items grouped into four domains: 1) Communication (with child and health care team), 9 items (2, 7, 12, 17, 22, 27, 32, 37, and 40); 2) Emotional Distress, 15 items (1, 4, 6, 9, 11, 14, 16, 19, 21, 24, 26, 29, 31, 34, and 36); 3) Medical Care, 8 items (3, 8, 13, 18, 23, 28, 33 and 38); and 4) Role Function 10 items (5, 10, 15, 20, 25, 30, 35, 39, 41, and 42). Parents rate each item using a 5-point Likert-type Scale (1 = "Not at all", 2 = "Rarely", 3 = "Sometimes", 4 = "Often", 5 = "Extremely") in terms of frequency or *How Often* the event occurred over the last week (1 = "Not at all", 2 = "A Little", 3 = "Sometimes", 4 = "Very Much", 5 = "Extremely") and in terms of level of difficulty or *How Difficult* the event was over the past week (Streisand et al., 2001) (See Appendix J). Frequency and difficulty scores are added separately for each of the four domain scales, then these scores are added together to form an overall total frequency score (Total PIP Frequency) and total difficulty score (Total PIP Difficulty) (Streisand et al., 2001). Higher scores indicate greater frequency and difficulty (Streisand et al., 2001, p. 157). Internal consistency was examined by calculating Cronbach's alphas for the total and four domain scales for both the PIP-F (α=0.95) and PIP-D (α=0.96) scales (Streisand et al., 2001). Coefficient alphas for the total scores were strong with reliability estimates for the individual scales all above 0.80 (Streisand et al., 2001). Total PIP Frequency and Total PIP Difficulty scores significantly correlated with the STAI State Anxiety Scale and the Parenting Stress Index Short Form (difficult child, parent child dysfunctional interaction and parent domain) to establish construct validity; parenting stress was present while controlling for demographic variables, general parenting stress and parent

response bias (Streisand et al., 2001). Total PIP Frequency score accounted for 43% of the variance in parental anxiety and Total PIP Difficulty score accounted for 45% of the model's anxiety score variance (Streisand et al., 2001). This suggests that there are components of pediatric illness-related parenting stress, separate from general parenting stress, that are associated with parental anxiety and stress, suggesting that this tool is effective at targeting both parental stress and anxiety (Streisand et al., 2001).

Statistical Analysis

The purposes of this exploratory predictive study were to 1) identify family demographics, disease-related characteristics, coping strategies, parent experiences in caring for a child with a chronic illness and pediatric illness-related parenting stress in parents caring for children with mitochondrial disease; 2) explore the relationships between family demographics, disease-related characteristics, coping strategies, parent experiences in chronic illness, and pediatric illness-related parenting stress in parents caring for children with mitochondrial disease; and 3) identify factors that are significant predictors of pediatric illness-related parenting stress in parents of children with mitochondrial disease. This study had six specific aims; thus analyses are described separately for each aim. All analyses were conducted in SPSSv20.

Missing data were assessed for random occurrence or for patterns. After listwise deletion was applied, only completed cases were analyzed. Survey questions were designed to "request responses" from participants for each question to reduce the number of incomplete cases (with the exception of the PIP, "request responses" was not an available option on Qualtrics for this type of survey format).

Multivariate statistical testing involves three general assumptions: 1) normality, 2) linearity, and 3) homoscedasticity (Mertler & Vannatta, 2005). Each of the individual variables were tested for normal distribution using skewness and kurtosis coefficients to assess the degree of symmetry of the distribution of scores about the mean and the degree of peakedness of the distribution. Scatterplots were used to assess bivariate normality. Residual plots were assessed for nonlinear (curved pattern) or linear (points clustering around the zero line) relationships to test for homoscedasticity. Homoscedasticity is the assumption that the variability in scores for one continuous variable is roughly the same at all values of another continuous variable (Mertler & Vannatta, 2005). Survey answers were assessed to determine if responses were valid or answered incorrectly.

AIM 1: The first study aim was to identify family demographic and disease-related characteristics in mitochondrial disease. Frequency distributions and descriptive statistics were obtained to describe the demographic and disease-related characteristics by assessing the means and standard deviations of continuous variables and recording the percentage of categorical variables described and characterized in the sampled population. The variables used for descriptive purposes were as follows: parent gender, parent marital status, parent biological relationship to the child, parent age, parent level of education, parent ethnicity and race, parent income, child gender, child known/confirmed diagnosis, child age, child age at onset of symptoms, child age at diagnosis, child with developmental delays, number of children with mito in household, number of organs involved, number of specialty services used, number of hospitalizations in past year, last hospitalization, number of office visits in past year, and type of mitochondrial disease.

AIM 2: The second aim of this study was to describe the parental experience when caring for a child with mitochondrial disease. The PECI tool was used as a measurement of parent experience when caring for a child with mito. PECI data were collected and responses scored. Two items on the PECI were reverse-coded, and all items in each subscale were added and then divided by the total number of items in the subscale. Descriptive statistics were used to summarize responses reporting the frequency of responses with mean and standard deviations for each subscale.

AIM 3: The third aim of this study was to describe coping strategies used by parents of children with a mitochondrial disease. The analysis of data for the CHIP was similar to the PECI. Total coping scores and subscale scores were obtained by summing the number chosen by the respondent (disregarding the "I do not cope this way, which is equivalent to 0) (McCubbin, Thompson, & McCubbin, 2001). Descriptive statistics were used to summarize responses, reporting the frequency of responses with mean and standard deviations for both the total scale and each subscale.

AIM 4: The fourth aim of this study was to describe frequency and severity of pediatric illness-related parenting stress in parents of children with a mitochondrial disease. The analysis of data for the PIP was similar to the PECI and the CHIP. The PIP was scored separately for each of the four domains (Communication, Emotional Distress, Medical Care, Role Function) across two scales: Frequency (F) and Difficulty (D). The total score comprised of the sum for each of the four domains yielding Total PIP Frequency and Total PIP Difficulty scores. Descriptive statistics were used to summarize responses reporting the frequency of responses with mean and standard deviations to specific questions for each subscale across both domains (F) and (D).

AIM 5: The fifth aim of this study was to examine the relationships between pediatric illness-related parenting stress in parents of children with mitochondrial disease and family demographics, disease characteristics, coping strategies, and parent experience of childhood illness. This researcher was interested in the relationship between identified independent variables (IV) from the demographic and disease-related characteristics survey, PECI (subscales scores), and CHIP (subscales and total scale scores) with the dependent variable (DV) pediatric illness-related parenting stress subscales and total frequency and difficulty.

Pearson's Product Moment Correlation analysis was used to examine the parametric covariance statistics of the direction and magnitude of relationship of these variables (Portney & Watkins, 2009). Scatter plots were used to visually clarify the strength and shape of the relationship looking for patterns in which the values of Y change in proportion to values of X (Portney & Watkins, 2009). Correlation coefficients were used to describe the strength and direction of relationships between two variables and provide an index that reflected a quantitative measure of the relationship (Portney & Watkins, 2009). Correlation coefficient values range from -1.00 for a perfect negative relationship to 0.00 for no relationship to +1.00 for a perfect positive relationship. The closer the value is to +/- 1.00 the stronger the strength of the association between two variables (Portney & Watkins, 2009). This study examined the direction and magnitude of the relationship (using Pearson's *r*) between the identified independent variables associated with disease characteristics, parent experience, and coping, and the dependent variable of pediatric illness-related parenting stress.

For this study, the mean score for each variable, subscale, and total scale were included for correlational analysis. Nominal variables that were used in the correlational

analysis were coded as follows: parent gender (0 = father, 1 = mother), parent marital status (0 = single/divorced/widowed, 1 = married/partnered), parent biological relationship to the child (0 = biological parent, 1 = step or adoptive parent), child confirmed diagnosis (0 = no, 1 = yes), parent level of education (0 = equal to high school-12th grade or less, 1 = beyond high school), child gender (0 = male, 1 = female), frequency of hospitalizations (0 = none, 1 = under 6 months, 2 = over 6 months), and last hospitalization (0 = none, 1 = under 6 months, 2 = more than 6 months), ethnicity (1 = Hispanic or Latino, 2 = Non Hispanic), race (1 = Caucasian, 2 = Other), number of office visits in past year (0 = under 12, 1 = more than 12), income (0 = under $59,000, 1 = over $60,000), and developmental delays (0 = no, 1 = yes). Independent variables from the PECI included scores from subscales: Guilt &Worry, Unresolved Sorrow & Anger, Long-term Uncertainty and Emotional Resources. Independent variables from the CHIP included scores from each subscale: Coping Pattern I: Family Integration, Coping Pattern II: Maintaining Social Support and Coping Pattern III: Understanding the Health Care Situation, and total CHIP score. The dependent variable (DV) was obtained from the PIP inventory in each of the four domains: Communication, Emotional Distress, Medical Care, and Role Function, across 2 scales: Frequency and Difficulty, and Total PIP Frequency and Total PIP Difficulty scores.

The output resulted in a correlation matrix used to examine the correlation coefficients for all pairs of variables at one time and the degree and direction of correlations between the variables using Pearson's *r* (Portney & Watkins, 2009). Significance ($\rho \leq .05$) was examined to determine how likely it was that an observed correlation value would have occurred by chance (Portney & Watkins, 2009). Only significant ($\rho \leq .05$) demographic variables were entered into

the regression model and all variables from the PECI and CHIP were included. This strategy was chosen due to potential limited sample size.

AIM 6: The sixth aim of this study was to identify the significant predictors of pediatric illness-related parenting stress in parents of children with mitochondrial disease. Results from predictive studies can assist in clinical decisions and interventions (Portney & Watkins, 2009). Due to concerns about sample size and the number of variables entered into the regression model only significant demographic variables were used in the regression model. Demographic variables were selected based on significance of correlations using Pearson's *r*. Nominal variables that were considered for the regression formula were coded as follows: parent gender (0 = father, 1 = mother), parent marital status (0 = single/divorce/widow, 1 = married/partner), parent biological relationship to the child (0 = biological parent, 1 = step or adoptive parent), child confirmed diagnosis (0 = no, 1 = yes), parent level of education (0 = equal to high school-12th grade or less, 1 = beyond high school), child gender (0 = male, 1 = female), frequency of hospitalizations (0 = none, 1 = under 6 months, 2 = over 6 months), and last hospitalization (0 = none, 1 = under 6 months, 2 = more than 6 months), ethnicity (1 = Hispanic or Latino, 2 = Non Hispanic), race (1 = Caucasian, 2 = Other), number of medical visits in past year (0 = under 12, 1 = more than 12), income (0 = under $59,000, 1 = over $60,000), and developmental delays (0 = no, 1 = yes). The following interval data were entered into the regression model: parent age, child age, child age at onset of symptoms, child age at diagnosis, number of children with mito in household with mito, number of organs involved, and number of specialty services used.

Predictive statistics, such as regression, apply correlations to describe the nature of the existing relationship among variables to generate a hypothesis for clinical situations and to

quantify clinical outcomes (Portney & Watkins, 2009). A predictive correlation study tries to predict a behavior or response based on the observed relationship using correlations and regression (Portney & Watkins). The primary purpose of regression analysis is to develop an equation that can be used for predicting values and to explain causal relationships among variables (Mertler & Vanatta, 2005). Multiple regression models, like those used in this study, examine the relationship of multiple predictor variables and the dependent variable (Mertler & Vanatta, 2005). Regression relies on the correlation between the DV and IV in order to make predictions about the DV (Mertler & Vanatta, 2005). Regression coefficients provide information about how much of the DV is explained by the IV and measure the strength of the relationship between the variables (Portney & Watkins, 2009).

Assumptions associated with regression analysis include normality, linearity, and homoscedasticity along with additional assumptions of equality of variance, random normal distribution of scores and equal standard deviations around the regression line, and multicollinearity. When a linear regression model is a good fit, the residual scores will randomly scatter close to zero (Portney & Watkins, 2009). Data points that do not seem to fit with the cluster of scores are known as outliers. Frequency distribution and histograms box plots were used to identify outliers.

In order to make predictions the researcher must know (1) the extent to which points are scattered around the line, (2) the slope of the regression line, and (3) the point at which the line crosses the Y-axis (Mertler & Vanatta, 2005). The extent to which the points are scattered around the line is directly related to the correlation coefficient, or the Pearson *r*, the stronger the relationship the higher the degree of predictability. The distance between the predicted values and the regression line are called residuals. Residuals represent the degree of error in

the regression line and help to establish the accuracy of prediction while considering the variance of the error on either side of the regression line (Portney & Watkins, 2009). The standard error of the estimate (SEE) is the standard deviation of the distribution of errors dispersed around the regression line (Portney & Watkins, 2009).

The algebraic expression of the regression line is y=a+bx+e. The slope determines the amount of change in the DV(y) that accompanies one unit (point, year, degree etc.) change in the IV(x). Knowledge about where the regression line crosses the Y-axis (the value of y when x is zero, also known as the Y-intercept) will provide the constant value for the DV (Mertler & Vanatta, 2005), or the mean of y when x is zero.

The coefficient of determination (R^2) represents the total variance in the y scores that can be explained by the x scores indicating the accuracy of prediction based on x and providing a more meaningful description of the relationship (Portney & Watkins, 2009). Analysis of variance of regression statistically makes inferences about the regression equation to determine the likelihood that relationship between x and y is not likely to be the result of chance (Portney & Watkins, 2009). A non-significant F-test indicates that the observed relationship could have occurred by chance and that the regression line does not provide a reasonable basis for predicting values of y.

In this study, hierarchical multiple regression was used to examine the influence of several predictor independent variables on the dependent variables (frequency and difficulty of pediatric illness-related parenting stress). Hierarchical multiple regression specifies the order in which variables are entered into the regression analysis model based on theoretical knowledge about the influence of the predictor variables (Mertler & Vannatta, 2005). In previous predictive studies of stress in parents of children with chronic illness, several

variables were known to predict stress: such as length of illness, parent age, child age, disease rareness, severity of illness, social support and coping (Grootenhuis & Bronner, 2009; Thompson & Gustafson, 1996).

Variables: This researcher was interested in the predictive influence of the following independent variables: parent gender, parent marital status, parent biological relationship to the child, child confirmed diagnosis, parent age, parent level of education, child age, child gender, child age at onset of symptoms, child age at diagnosis, number of children with mito in household, number of organs involved, number of specialty services used, frequency of hospitalizations, last hospitalization, ethnicity, race, number of office visits in past year, income, developmental delays, guilt & worry, unresolved sorrow & anger, emotional resources and long-term uncertainty, family integration, maintaining social support, understanding the health care situation, and CHIP total score. The dependent variables (DV) were the 4 domains in the PIP inventory (Communication, Emotional Distress, Medical Care, Role Function), across two scales: Frequency (F) and Difficulty (D) and Total PIP Frequency and Total PIP Difficulty scores. This regression analysis analyzed ten regression models:

1. Models 1-4: Predicting Communication, Emotional Distress, Medical Care and Role Function ***Difficulty*** in Pediatric Illness-related Stress
    a. Step one: enter only significant ($\rho<.05$) demographic variables from the correlation matrix to analyze their predictive ability on communication-difficulty, emotional distress-difficulty, medical care-difficulty, and role-stress-difficulty in pediatric illness-related parenting stress.

b. Step two: add all subscales and total scores from the CHIP and PECI to analyze their predictive ability on ***difficulty*** in pediatric illness-related parenting stress.

2. Models 5-8: Predicting Communication, Emotional Distress, Medical Care and Role Function ***Frequency*** in Pediatric Illness-related Stress
    a. Step one: enter only significant ($\rho<.05$) demographic variables from the correlations matrix to analyze their predictive ability on communication-frequency, emotional distress-frequency, medical care-frequency, and role-stress- frequency in pediatric illness-related parenting stress.
    b. Step two: add all subscales and total scores from the CHIP and PECI to analyze their predictive ability on ***frequency*** in pediatric illness-related parenting stress.
3. Models 9-10: Predicting Difficulty and Frequency ***Total Scores*** in Pediatric Illness-related Stress Difficulty and Frequency in Pediatric Illness Related Parenting Stress.
    a. Step one: enter only significant ($p<.05$) demographic variables from the correlations matrix to analyze their predictive ability on ***total*** difficulty and frequency pediatric illness-related parenting stress (PIP-F and PIP-D).
    b. Step two: add subscales and total scores from the CHIP and PECI to analyze their predictive ability on ***total*** frequency and difficulty pediatric illness-related parenting stress (PIP-F and PIP-D).

The overall ANOVA "F" score was used to determine if the relationship in each model likely happens by chance or if the relationship is significant. The standardized coefficients (beta) explain the rate of change in y for one standard deviation increment of x, the outcome

variable increases or decreases by the corresponding standard deviation. The model R square statistic accounted for the percent of variance in each model. The R square change is a measure of additional explained variation moving from step one (inclusion of significant demographic information) to step two (inclusion of the CHIP and PECI information) in each regression model. This regression analysis provided information about the predictive relationship between the significant IVs and the frequency and difficulty of pediatric illness-related parenting stress to determine if the psychosocial factors (CHIP and PECI) relate to parenting stress above and beyond the basic demographic information.

Chapter Four: Results

This chapter describes the results from data that identified disease characteristics, parent experiences of childhood illness, coping strategies and pediatric illness-related parenting stress in parents of children with mitochondrial disease. The purposes of this study were to 1) identify family demographics, disease-related characteristics, coping strategies, parent experiences in caring for a child with a chronic illness and pediatric illness-related parenting stress in parents of children with mitochondrial disease; 2) explore the relationships between family demographics, disease-related characteristics, coping strategies, parent experiences in caring for a child with a chronic illness and pediatric illness-related parenting stress; and 3) identify factors that were significant predictors of pediatric illness-related parenting stress. All analyses were conducted using SPSS v20.

Recruitment and Procedures

Completion numbers for each section of the survey included: PECI n=364, CHIP, n = 322, PIP 7-day n = 263, PIP 30-day n=224, and demographics n=231. Because the child with mitochondrial disease often has periods of illness and wellness, participants were asked to take the PIP questionnaire twice in the same survey set, the first time reflecting on the past seven days and then immediately repeating the PIP questionnaire reflecting on the past 30 days during their child's illness.

Statistical Analysis

Missing Data: Missing data were carefully analyzed because of the high dropout rate (36%) from those who started the survey (n = 362) to those who completed the last question (n = 231). This large portion of the missing data is considered a failure in response rate (Portney & Watkins, 2009) since respondents failed to comply with the answering all survey

questions. The large amount of data was not completed because of possible survey fatigue. This data was not considered missing data for the purpose of this research study. The survey "set" administered to the parents contained 5 separate survey instruments in the following order: 1) PECI, 2) CHIP, 3) PIP 7-day, 4) PIP 30-day 5) demographics. The PIP 30-day was a replica of the PIP 7-day except for asking the parents to reflect over the past 30 days rather than the past 7 days when answering the questions. This was conducted to assess the level of stress noted over time since mito symptoms have periods of exacerbation. It was noted that during the PIP 30-day survey many parents stopped taking the survey possibly due to survey fatigue. The PIP 30-day was not used in this research due to the high drop out rate. Missing at random data (n= 96) was considered from the remaining surveys. Listwise deletion of missing variables was used during regression analysis. Due to the variability in the number of participants answering the different questionnaires, the researcher reports sample size for each study variable independent of the total number of responses to the survey "set" as an account of study participation.

Assumptions: All continuous variables were assessed for normality, linearity, homoscedasticity and multicollinearity. Histograms of each continuous variable roughly approximate a bell-shaped curve with skewness and kurtosis values less than 3 and 5, respectively, demonstrating normal distribution of variables. Linearity findings through scatterplots showed that variables related in a linear manner around the slope. Bivariate correlations indicate independence of variables ruling out multicollinearity among the predictor variables. Regression analysis is robust even if one or more assumptions are not completely met (Portney & Watkins, 2009)

Outliers were noted in three independent variables using Q-Q plots. 1) PECI-Long-term Uncertainty noted one outlier, but histogram and skewness (-.486)/kurtosis (-.152) values were consistent with normality so this outlier was retained. 2) Child Age at Onset of Symptoms noted 16 outliers with slight skewness to the left noted in the histogram. Q-Q plots showed slight curvilinear shape, but skewness (2.315) and kurtosis (4.536) values were consistent with normality. In this analysis, children beyond the age of six years were considered outliers; however, they were not eliminated from this study since 1) this finding (children showing mito symptoms early in life) is consistent with the literature, 2) many of the outliers were older children, and 3) this study aimed to explore the ages of all children birth to 18 years. The age of the child is believed to have a role of stress in the family and is thought to be a significant predictor of family stress, so this variable was retained. 3) The CHIP-Coping Pattern I: Family Integration identified two outliers whose coping scores were below 10, indicating that these individuals have less need of coping. Skewness (-.335) and kurtosis (-.240) indicated normal distribution, therefore all coping outliers were retained, since this study is primarily exploratory in nature and attempts to assess a broad range of coping strategies. Data for the parent age variable noted two parents had answered that their ages were 3 and 9; these data were removed from the data set assuming that these were erroneous reports.

AIM 1: The first purpose of the study was to identify family demographic and disease-related characteristics in mitochondrial disease. Parent and child demographic and disease-related characteristics were examined using frequency distributions and descriptive statistics (see Table 1 and Table 2). The majority of participants from the sample were Caucasian (97%); biological mothers (89%), with a mean age of 42 years (*SD* = 8.3); married or partnered (81%) with four or more years of a college education (66%); and had an annual

income above $60,000 USD (63%). The majority of the families had one child with mito living at home (80%) and the average age for the child with mito was 9.85 years (*SD* = 5.24). The majority of the children had a known mitochondrial disease (64%) (see Table 3) and started to have symptoms of mito on average between the child's second and third year of life (*M* = 2.24, *SD* = 3.89), receiving a confirmed diagnosis of mito around the age of six years (*M* = 6.16, *SD* = 5.01). Children in the entire data set had an average of at least six organs affected by mito (*M* = 6.02, *SD* = 2.55) and see on average seven different specialists (*M* = 7.49, *SD* = 3.26) with at least 12 or more office visits per year (60%). Parents reported that many of the children had developmental delays (71%) and many had been hospitalized within the past year (61%).

Table 1

Demographic and Disease Characteristics

Characteristics	n	(%)
Parents		
Fathers	11	(5)
Mothers	219	(95)
Parent Relationship		
Adoptive/Step	14	(6)
Biological	217	(94)
Marital Status		
Single/divorced/widowed	45	(19)
Married/partnered	185	(81)
Parent Education Completed		
≤High school to grade 12	30	(13)
≥College	199	(87)
Child Gender		
Male	112	(49)
Female	119	(51)
Ethnicity		
Not Hispanic/Latino	219	(96)
Hispanic/Latino	10	(4)
Race		
White	219	(97)
Multi-race	5	(2)
Asian	1	(.4)
Income		

< $59,999	81 (37)
>$60,000	141 (63)
Hospitalizations over the Past Year	
None	91 (39)
Currently-6 months	117 (51)
More than 6 months	23 (10)
Last Hospitalization	
Never	41 (18)
1-6 months	78 (34)
More than 7 months	111 (48)
Number Medical Visits per Year	
0-12	91 (40)
More than 12	140 (60)
Child with Developmental Delays	
Yes	162 (71)
No	65 (29)
Mitochondrial Diagnosis	
Known	146 (64)
Unknown	81 (36)
Number of Children in Household	
One	177 (80)
Two	37 (17)
≥Three	8 (3)

Table 2

Demographic and Disease Characteristics Mean and SD

Characteristics	n	*M*	*SD*
Parent age in years	227	42.34	8.30
Child age in years	220	9.85	5.24
Child age at:			
Symptoms	225	2.24	3.89
Diagnosis	215	6.16	5.01
Organs involved	227	6.02	2.55
Specialty services used	231	7.49	3.26

Table 3

Types of Mitochondrial Disease

Type	n (%)
Aplers Disease	1 (0.4)
Carnitine Deficiency	3 (1.3)
Co-enzyme Q10 Deficiency	5 (2.2)
Complex I, II, III, IV, V Deficiency	66 (29.0)

Fatty Acid Oxidation Disorders (FAOD)	2 (0.9)
Kearns-Sayre Syndrome (KSS)	2 (0.9)
Leigh's Disease	13 (5.7)
Leber's Hereditary Optic Neuropathy (LHON)	1 (0.4)
Mitochondrial Encephalomyopathy Lactic Acidosis and Stroke like Episodes (MELAS)	10 (4.4)
Myoclonic Epilepsy and Ragged-Red Fiber Disease (MERRF)	1 (0.4)
Mitochondrial Cytopathy	3 (1.3)
Mitochondrial DNA Depletion	3 (1.3)
Myoneurogastrointestinal Disorder and Encephalopathy (MINGIE)	1 (0.4)
Pearson Syndrome	2 (0.9)
Pyruvate Deficiency	6 (2.6)
Respiratory Chain Deficiency	2 (0.9)
Very Long Chain Aycl-CoA Dehydrogenase Deficiency (VLCAD)	2 (0.9)
Other	23 (10.0)
Unknown name of child's mitochondrial disease	81 (35.0)

AIM 2: The second aim of this study was to describe the parental experience when caring for a child with mitochondrial disease. As noted in Chapter 3, the PECI was used to collect data on the experience of childhood illness in parents of children with mito. This questionnaire is concerned with perceptions related to parenting a child who is living with or who has experienced a chronic illness to determine how well the survey statements described the participants' thoughts and feelings over the past month (Bonner et al., 2006). The PECI is a 25-item tool; the higher the score on the PECI, the more Guilt & Worry, Sorrow & Anger, Long-term Uncertainty and perceived Emotional Resources of the parent. In this study, the mean scores ranged from 2.09-2.56. This suggests respondents have medium to high feelings of Guilt & Worry, Sorrow & Anger, Long-term Uncertainty, and perceived Emotional Resources with reported ratings noted on the survey between "sometimes" and "often." Mean scores for the PECI subscales are listed in Table 4.

Table 4

Parent Experience of Childhood Illness (PECI)

Subscale	n	Mean	SD	Range
Guilt & Worry	358	2.30	.650	.27-3.73
Unresolved Sorrow & Anger	364	2.09	.730	.38-4.00
Long-term Uncertainty	365	2.56	.690	.20-4.00
Emotional Resources	364	2.36	.615	.60-4.00

Note: PECI scores are a calculation of the mean of the category scored

AIM 3: The third aim of this study was to describe coping strategies used by parents of children with a mitochondrial disease. The Coping Health Inventory for Parents (CHIP) was used to collect data on the experience of childhood illness in parents of children with mito. This inventory was developed to assess parents' appraisal of their coping responses to the management of family life when they have a child member who is seriously and/or chronically ill (McCubbin & McCubbin, 1987). The CHIP consists of three subscales: 1) Coping Pattern I: Family Integration, 2) Coping Pattern II: Social Support, and 3) Coping Pattern III: Understanding Health Care. Coping behaviors are developed in response to stressful situations and therefore high coping scores (CHIP) reflect participant's experience of increased stress, thus utilizing more coping behaviors (Hobdell et al., 2007). Coping scores also indicate the use of coping behaviors to help reduce the stressful event. Mean scores for the total CHIP and subscales are listed in Table 5.

Table 5

Coping Health Inventory for Parents (CHIP)

Scale	n	Mean	SD	Range
Family Integration	318	34.28	10.49	6-57
Social Support	321	25.20	10.04	1-54
Understanding Health Care	323	15.02	4.78	1-24
Total Score	318	74.48	21.94	16-135

Note: CHIP Subscale scores were calculated by summing the items listed in the specific subscale score and reporting the mean of the total score.

AIM 4: The fourth aim of this study was to describe the *Frequency* and *Difficulty* of pediatric illness-related parenting stress in parents of children with a mitochondrial disease. The Pediatric Inventory for Parents (PIP) lists difficult events which parents of children who have (or have had) a serious illness sometimes face (Streisand et al., 2001). Higher scores on the PIP reflect increased parent stress. Each domain, 1) Communication, 2) Medical Care 3) Emotional Distress, and 4) Role Function, is scored separately across the two scales (Frequency and Difficulty). The total score for the PIP is comprised of the sum from each of the four domains, yielding Total PIP Frequency and Total PIP Difficulty scores ranging from 42-210. Mean scores for each of the domains the total scores are listed in Table 6.

Table 6

Pediatric Inventory for Parents (PIP)

Scale	n	Mean	SD	Range
Total Scores				
Frequency	212	123	31.6	47-202
Difficulty	181	119	34.9	42-209
Communication				
Frequency	258	24	6.7	10-41
Difficulty	233	23	8.0	9-45
Emotional Distress				
Frequency	256	49	11.7	18-73
Difficulty	240	49	13.2	15-74
Medical Care				
Frequency	252	23	7.8	8-40
Difficulty	239	20	7.6	8-40
Role Function				
Frequency	246	27	8.1	11-50
Difficulty	231	27	9.2	10-50

Note: PECI Subscale scores were calculated by reporting the mean of the total score.

AIM 5: The fifth aim of this study was to examine the relationships between pediatric illness-related parenting stress (PIP) in parents of children with mitochondrial disease and family demographics, disease characteristics, coping strategies (CHIP), and parent experience of childhood illness (PECI). Bivariate correlations were examined between the PIP total scale and subscales in both frequency and difficulty and demographic and disease-related characteristics. Pearson's correlations were used to identify the significant relationships for the continuous variables and point biserial correlations identified significant dichotomous variables. Positive significant relationships ($\rho \leq 0.01$, $\rho \leq 0.05$) were noted among hospitalizations in the past year, number of specialists seen, number of organs involved, developmental delays and number of office visits. Negative significant relationships ($\rho \leq 0.01$, $\rho \leq 0.05$) included parent age, child age, income, and child age at diagnosis. (see Table 7).

Table 7

Correlations of Demographic and Disease-Related Variables with PIP

Measure	TOTAL F	TOTAL D	COM F	COM D	ED F	ED D	MC F	MC D	RF F	RF D
Hospital Past Year	.435**	.360**	.396**	.240**	.330**	.285**	.407**	.327**	.298**	.318**
Parent Age	-.288**	-.215**	-.175*		-.195**	-.199**	-.330**	-.270**	-.244**	-.268**
Child Age	-.242**	-.254**		-.148*	-.157*	-.200**	-.297**	-.215**	-.213**	-.270**
Income	-.162*	-.191*		-.208**	-.166*	-.205**	-.143*	-.224**	-.230**	-.236**
Specialty	.309**	.187*	.227**		.152*		.348**	.153*	.271**	.257**
Organs	.216**	.177*	.136*		.194**	.143*	.149*		.231**	.245**
Office Visits	.303**	.210**	.233**		.210**		.298**	.102*	.201**	.210**
Developmental Delays							.209**		.198**	.168*
Age at Diagnosis							-.209**			-.178*
Parent Education					-.144*					

Note. *Correlation is significant at 0.05 level (2-tailed). **Correlation is significant at 0.01 level (2 tailed). TOTAL F = Total Frequency, TOTAL D = Total Difficulty, COM F = Communication Frequency, COM D = Communication Difficulty, ED F = Emotional Distress Frequency, ED D = Emotional Distress Difficulty, MC F = Medical Care Frequency, MC D = Medical Care Difficulty, RF F = Role Function Frequency, RF D = Role Function Difficulty.

PECI and CHIP correlations with the PIP identified significant relationships between all PECI subscales and PIP scales across both Frequency and Difficulty domains, with moderate to high correlations noted throughout. PECI Guilt & Worry, Unresolved Sorrow & Anger and Long-term Uncertainty showed positive relationships with PIP, suggesting that parents experience stress-associated Guilt & Worry, Unresolved Sorrow & Anger and Long-term Uncertainty. The PECI-Emotional Resources and CHIP-Family Integration, CHIP-Social Support and CHIP-Total Scores were inversely related to parenting stress (with the exception of CHIP Family Integration and Chip Health Care and Medical Care (F)) indicating that perceived Emotional Resources, Family Integration and Social Support were negatively associated with illness-related parenting stress (see Table 8).

Table 8

Correlations of CHIP and PECI with PIP

Measure	TOTAL F	TOTAL D	COM F	COM D	ED F	ED D	MC F	MC D	RF F	RF D
PECI Guilt & Worry	.635**	.691**	.536**	.619**	.693**	.711**	.424**	.553**	.499**	.570**
PECI Sorrow & Anger	.551**	.607**	.439**	.540**	.580**	.588**	.319**	.459**	.503**	.566**
PECI Long-term Uncertainty	.489**	.534**	.413**	.484**	.549**	.533**	.289**	.398**	.413**	.450**
PECI Emotional Resources	-.292**	-.367**	-.234**	-.411**	-.379**	-.410**	-.029**	-.214**	-.260**	-.276**
CHIP Family Integration		-.175*		-.203**		-.179*	126*			
CHIP Social Support		-.177*		-.193**		-.175**				
CHIP Health							.149*			

Care										
CHIP Total		-.163*		-.207**		-.171**				

Note: *Correlation is significant at 0.05 level (2-tailed). **Correlation is significant at 0.01 level (2-tailed). TOTAL F = Total Frequency, TOTAL D = Total Difficulty, COM F = Communication Frequency, COM D = Communication Difficulty, ED F = Emotional Distress Frequency, ED D = Emotional Distress Difficulty, MC F = Medical Care Frequency, MC D = Medical Care Difficulty, RF F = Role Function Frequency, RF D = Role Function Difficulty.

The CHIP subscales had both positive and inverse relationships with the PIP. CHIP Coping Pattern I: Family Integration, Coping Pattern II: Social Support and Total Scores were inversely related to Total PIP Difficulty, PIP-Communication (D) and PIP-Emotional Distress (D). Coping Pattern I: Family Integration and Coping Pattern III: Understanding Health Care were positively related to PIP-Medical Care (F) suggesting increased illness-related stress that is associated with Understanding Health Care and Family Integration in terms of frequency in receiving medical care (see Table 8).

AIM 6: The sixth aim of this study was to identify the significant predictors of pediatric illness-related parenting stress in parents of children with mitochondrial disease. Hierarchical multiple regression was used to examine the influence of significant demographic characteristics, disease-related characteristics, parent experience of chronic illness (PECI) and coping patterns (CHIP) on parenting stress (PIP). Regression examining the relationship between significant predictor variables and difficulty of stress resulted in 10 models:

Model 1: Difficulty in Communication (n=178): Step 1: The overall model was significant $F(3, 174) = 6.19$ $\rho \leq .001$. Hospitalizations over Past Year, Child Age, and Income were significant variables included in this regression model based on the correlation matrix (see Table 7). Hospitalizations over Past Year ($b = .153$, $\rho = .040$) positively predicted Difficulty in Communication, and Income ($b = -.200$, $\rho = .007$) negatively predicted Difficulty

in Communication. Child Age did not predict Difficulty in Communication. This model accounted for 10% of the variance of Difficulty in Communication. Step 2: The overall model was significant $F(10, 167) = 14.60$ $\rho \leq .001$ along with change in $R^2 = .37$ ($\rho \leq .001$). Adding PECI subscales, CHIP subscales and total CHIP scores into the regression model showed PECI-Guilt & Worry ($b = .381$, $\rho \leq .001$) positively predicted Difficulty in Communication and PECI-Emotional Resources ($b = -.192$, $\rho = .013$) negatively predicted Difficulty in Communication. Non-significant variables in the overall model included Hospitalizations over Past Year, Child Age, Income, PECI - Sorrow & Anger, PECI - Long-term Uncertainty, CHIP - Coping Pattern I: Family Integration, CHIP – Coping Pattern II: Social Support, CHIP: Coping Pattern III: Understanding Health Care and Total CHIP. This model accounted for 47% of the variance in predicting Difficulty in Communication.

Model 2: Difficulty in Emotional Distress (n=179): Step 1: The overall model was significant $F(5, 173) = 5.95$, $\rho \leq .001$. Hospitalizations over Past Year, Child Age, Income, Parent Age and Number of Organs were significant variables included in this regression model based on the correlation matrix (see 7). Hospitalizations over Past Year ($b = .220$, $\rho =. 003$) showed a positive significant relationship with Difficulty in Emotional Distress. Child Age, Parent Age, Income, and Number of Organs did not predict Difficulty in Emotional Distress. This model accounted for 15% of the variance of Difficulty in Emotional Distress. Step 2: The overall model was significant $F(12, 166) = 21.05$ $\rho \leq .001$along with change in $R^2 = .46$ ($\rho \leq .001$). Adding PECI subscales, CHIP subscales and total CHIP scores into the regression model showed Hospitalizations over the past year ($b = .139$, $\rho = .011$) and PECI - Guilt & Worry ($b = .470$, $\rho \leq .001$) positively predicted Difficulty in Emotional Distress, and PECI - Emotional Resources ($b = -.137$, $\rho = .044$) negatively predicted

Emotional Distress. Non-significant variables in the overall model included Child Age, Parent Age, Income, Number of Organs, PECI - Sorrow & Anger, PECI - Long-term Uncertainty, CHIP - Coping Pattern I: Family Integration, CHIP - Coping Pattern II: Social Support, CHIP - Coping Pattern III: Understanding Health Care and Total CHIP. This model accounted for 60% of the variance in predicting Difficulty in Emotional Distress.

Model 3: Difficulty in Medical Care (*n*=181): Step 1: The overall model was significant $F(6, 174) = 7.98$, $\rho \leq .001$. Hospitalizations over Past Year, Child Age, Parent Age, Income, Specialty Services, and Medical Visits were significant variables included in this regression model based on the correlation matrix (see Table 7). Hospitalizations over Past Year ($b = .246$, $\rho = .002$) positively predicted Difficulty in Medical Care, and Income ($b = -.190$, $\rho = .007$) negatively predicted Difficulty in Medical Care. Child Age, Parent Age, and Specialty Services did not predict Difficulty in Medical Care. This model accounted for 22% of the variance of Difficulty in Medical Care. Step 2: The overall model was significant $F(13, 167) = 9.63$ $\rho \leq .001$ along with change in $R^2 = .21$, $\rho \leq .001$. Adding PECI subscales, CHIP subscales and total CHIP scores into the regression model showed Hospitalizations over the Past Year ($b = .173$, $\rho = .014$) and PECI - Guilt & Worry ($b = .328$, $\rho \leq .001$) positively predicted Difficulty in Medical Care. Income ($b = -.151$, $\rho = .019$) negatively predicted Difficulty in Medical Care. Non-significant variables in the overall model included Child Age, Parent Age, Specialty Services, Medical Visits, PECI - Sorrow & Anger, PECI - Long-term Uncertainty, CHIP - Coping Pattern I: Family Integration, CHIP – Coping Pattern II: Social Support, CHIP: Coping Pattern III: Understanding Health Care and Total CHIP. This model accounted for 43% of the variance in predicting Difficulty in Medical Care.

Model 4: Difficulty in Role Function (*n*=167): Step 1: The overall model was significant $F(9, 157) = 5.87$, $\rho \leq .001$. Hospitalizations over Past Year, Child Age, Parent Age, Income, Specialty Services, Medical Visits, Number of Organs, Developmental Delays, and Child Age at Diagnosis were significant variables included in this regression model based on the correlation matrix (see Table 7). Hospitalizations over Past Year ($b = .177$, $\rho =. 035$) and Number of Organs ($b = .193$, $\rho =.018$) positively predicted Difficulty in Role Function, and Child Age ($b =-.304$, $\rho =.011$) negatively predicted Difficulty in Role Function. Income, Parent Age, Specialty Services, Medical Visits, Developmental Delays and Age at Diagnosis did not predict the dependent variable. This model accounted for 25% of the variance of Difficulty in Role Function. Step 2: The overall model was significant $F(16, 150) = 10.59$ $\rho \leq .001$ along with change in $R^2 = .28$, $\rho \leq .001$. Adding PECI subscales, CHIP subscales and total CHIP scores into the regression model showed Income ($b = -.138$, $\rho = .030$) negatively predicted Difficulty in Role Function, and PECI - Sorrow & Anger ($b = .342$, $\rho \leq .001$) and CHIP- Coping Pattern III: Understanding Health Care ($b = .152$, $\rho = .049$) positively predicted Difficulty in Role Function. Non-significant variables in the overall model included Hospitalizations over Past Year, Child Age, Parent Age, Specialty Services, Medical Visits, Number of Organs, Developmental Delays, Age at Diagnosis, PECI - Guilt & Worry, PECI - Long-term Uncertainty, CHIP - Coping Pattern I: Family Integration, CHIP - Coping Pattern II: Social Support, and Total CHIP. This model accounted for 53% of the variance in predicting Difficulty in Role Function

Model 5: Total PIP Difficulty (*n* =135): Step 1: The overall model was significant $F(7, 127) = 5.28$, $\rho \leq .001$. Hospitalizations over Past Year, Child Age, Parent Age, Income, Specialty Services, Medical Visits and Number of Organs were significant variables included

in this regression model based on the correlation matrix (see Table 7). Hospitalizations over Past Year (b = .238, ρ = .011) positively predicted Total PIP Difficulty, and Child Age (b = -.257 ρ = .022) negatively predicted Total PIP Difficulty. Income, Parent Age, Specialty Services, Medical Visits and Number of Organs Involved did not predict the dependent variable. This model accounted for 23% of the variance of Total PIP Difficulty. Step 2: The overall model was significant $F(14, 120) = 14.34$, $\rho \leq .001$ along with change in $R^2 = .40$ ($\rho \leq .001$). Adding PECI subscales, CHIP subscales and total CHIP scores into the regression model showed Hospitalizations over Past Year (b = .159, ρ = .026), Medical Visits, (b = .133, ρ = .036), PECI - Guilt & Worry (b = .374, $\rho \leq .001$), and PECI - Sorrow & Anger (b =.203 ρ = .034) positively predicted Total PIP Difficulty. Non-significant variables in the overall model included Child Age, Income, Parent Age, Specialty Services, Number of Organs, PECI - Long-term Uncertainty, PECI - Emotional Resources, CHIP - Coping Pattern I: Family Integration, CHIP - Coping Pattern II: Social Support, CHIP - Coping Pattern III: Understanding Health Care and Total CHIP. This model accounted for 63% of the variance in predicting Total PIP Difficulty.

Hierarchical regression examining the relationship between significant predictor variables and *frequency* of stress resulted in the following five models.

Model 6: Frequency in Communication (n =205): Step 1: The overall model was significant $F(5, 199) = 9.20$, $\rho \leq .001$. Hospitalizations over Past Year, Parent Age, Specialty Services, Number of Organs and Medical Visits were significant variables included in this regression model based on the correlation matrix (see Table 7). Hospitalizations over Past Year (b = .296, $\rho \leq .001$) positively predicted Frequency in Communication, and Parent Age (b = -.137, ρ = .048) negatively predicted Frequency in Communication. Use of Specialty

Services, Number of Organs involved and Medical Visits did not predict the dependent variable. This model accounted for 19% of the variance of Frequency in Communication. Step 2: The overall model was significant $F(12, 192) = 11.23$, $\rho \leq .001$along with change in $R^2 = .23$ ($\rho \leq .001$). Adding PECI subscales, CHIP subscales and total CHIP scores into the regression model showed Hospitalizations over Past Year ($b = .191$, $\rho = .005$) and PECI - Guilt & Worry ($b = .348$, $\rho \leq .001$) positively predicted Frequency in Communication. Non-significant variables in the overall model included Parent Age, Specialty Services, Number of Organs, Medical Visits, PECI - Sorrow & Anger, PECI - Long-term Uncertainty, PECI - Emotional Resources, CHIP - Coping Pattern I: Family Integration, CHIP – Coping Pattern II: Social Support, CHIP - Coping Pattern III: Understanding Health Care, and Total CHIP. This model accounted for 41% of the variance in the model in predicting Frequency in Communication

Model 7: Frequency in Emotional Distress (n=192): Step 1: The overall model was significant $F(8, 183) = 5.60$, $\rho \leq .001$. Hospitalizations over Past Year, Parent Age, Child Age, Specialty Services, Number of Organs, Medical Visits, Income and Education of Parent were significant variables included in this regression model based on the correlation matrix (see Table 7). Hospitalizations over Past Year ($b = .249$, $\rho = .001$) positively predicted Frequency in Emotional Distress. Parent Age, Child Age, Specialty Services, Number of Organs, Income, and Medical Visits did not predict Frequency in Emotional Distress. This model accounted for 20% of the variance of Frequency in Emotional Distress. Step 2: The overall model was significant $F(15, 176) = 18.50$, $\rho \leq .001$along with change in $R^2 = .42$ ($\rho \leq .001$). Adding PECI subscales, CHIP subscales and total CHIP scores into the regression model showed Hospitalizations over Past Year ($b = .167$, $\rho = .004$), Medical Visits ($b = .115$,

ρ =032), PECI - Guilt &Worry (b =.419 , $\rho \leq .001$), PECI - Long-term Uncertainty (b =.148, ρ =.040), and CHIP - Understanding Health Care (b = .142, ρ =.038) positively predicted Frequency in Emotional Distress. Non-significant variables in the overall model included Parent Age, Specialty Services, Number of Organs, Income, Education of Parent, PECI - Sorrow & Anger, PECI - Emotional Resources, CHIP - Coping Pattern I: Family Integration, CHIP – Coping Pattern II: Social Support, and Total CHIP. This model accounted for 61% of the variance in the model in predicting Frequency in Emotional Distress.

Model 8: Frequency in Medical Care (n=185): Step 1: The overall model was significant $F(9, 175) = 10.95$, $\rho \leq .001$. Hospitalizations over Past Year, Parent Age, Child Age, Specialty Services, Number of Organs, Medical Visits, Income, Developmental Delays, and Age at Diagnosis were significant variables included in this regression model based on the correlation matrix (see Table 7). Hospitalizations over Past Year (b = .252, ρ = .001) and Medical Visits (b = .163 ρ = .017) positively predicted Frequency in Medical Care. Parent age (b = -.178, ρ = .038) and Child Age (b = -.211, ρ = .043) negatively predicted Frequency in Medical Care. The use of Specialty Services, Number of Organs, Income, Developmental Delays, and Age at Diagnosis did not predict Frequency in Medical Care. This model accounted for 36% of the variance of Frequency in Medical Care. Step 2: The overall model was significant $F(16, 168) = 8.94$, $\rho \leq .001$ along with change in R^2 = .10 ($\rho \leq .001$). Adding PECI subscales, CHIP subscales and total CHIP scores into the regression model showed Hospitalizations over Past Year (b = .163, ρ =.025), Medical Visits (b = .160, p = 013), and PECI - Guilt & Worry (b =.230 , ρ =.011) positively predicted Frequency in Medical Care. Non-significant variables in the overall model included Parent Age, Specialty Services, Number of Organs, Child Age, Income, Developmental Delays, Age at Diagnosis, PECI -

Sorrow & Anger, PECI - Emotional Resources, CHIP - Coping Pattern I: Family Integration, CHIP - Coping Pattern II: Social Support, CHIP - Coping Pattern III: Understanding Health Care, and Total CHIP. This model accounted for 46% of the variance in predicting Frequency in Medical Care.

Model 9: Frequency in Role Function (n=179): Step 1: The overall model was significant $F(8, 170) = 5.79$, $\rho \leq .001$. Hospitalizations over Past Year, Parent Age, Child Age, Specialty Services, Number of Organs, Medical Visits, Income, and Developmental Delays were significant variables included in this regression model based on the correlation matrix (see Table 7). Income ($b = -.170$, $\rho = .021$) negatively predicted Frequency in Role Function. Hospitalizations over Past Year, Parent Age, Child Age, Specialty Services, Number of Organs, Medical Visits, and Developmental Delays did not predict Frequency in Role Function. This model accounted for 21% of the variance of Frequency in Role Function. Step 2: The overall model was significant $F(15, 163) = 8.24$, $\rho \leq .001$along with change in $R^2 = .22$ ($\rho \leq .001$). Adding PECI subscales, CHIP subscales and total CHIP scores into the regression model revealed Income ($b = -.151$, $\rho = .024$) negatively predicted Frequency in Role Function. PECI - Sorrow & Anger ($b = .273$, $\rho =009$) and CHIP - Understanding Health Care ($b = .198$, $\rho = .016$) positively predicted Frequency in Role Function. Non-significant variables in the overall model included Hospitalizations over Past Year, Parent Age, Child Age, Specialty Services, Number of Organs, Medical Visits, Developmental Delays, PECI - Guilt & Worry, PECI - Emotional Resources, PECI - Long-term Uncertainty, CHIP - Coping Pattern I: Family Integration, CHIP – Coping Pattern II: Social Support, and Total CHIP. This model accounted for 43% of the variance in the model in predicting Frequency in Role Function.

Model 10: Total PIP Frequency (*n*=155): Step 1: The overall model was significant $F(7, 147) = 8.58$, $\rho \leq .001$. Hospitalizations over Past Year, Child Age, Parent Age, Income, Specialty Services, Medical Visits, and Number of Organs involved were significant variables included in this regression model based on the correlation matrix (see Table 7). Hospitalizations over Past Year ($b = .256$, $\rho = .003$) and Medical Visits ($b = .162$, $\rho = .041$) positively predicted Total PIP Frequency. Income, Parent Age, Child Age, Specialty Services, and Number of Organs did not predict the Total PIP Frequency. This model accounted for 29% of the variance of Total PIP Frequency. Step 2: The overall model was significant $F(14, 140) = 14.93$, $\rho \leq .001$along with change in $R^2 = .31$ ($\rho \leq .001$). Adding PECI subscales, CHIP subscales and total CHIP scores into the regression model showed Hospitalizations over Past Year, ($b = .196$, $\rho = .005$), Medical Visits, ($b = .132$, $\rho = .033$), PECI - Guilt & Worry ($b = .283$, $\rho = .001$), and Unresolved Sorrow & Anger ($b = .282$, $\rho = .024$) positively predicted total PIP Frequency. Non-significant variables in the overall model included Child Age, Income, Parent Age, Specialty Services, Number of Organs, PECI - Long-term Uncertainty, PECI - Emotional resources, CHIP - Coping Pattern I: Family Integration, CHIP – Coping Pattern II: CHIP – Coping Pattern III, Social Support, and Total CHIP. This model accounted for 60% of the variance in the model in predicting Total PIP Frequency (see Table 9).

Table 9

Hierarchical Multiple Regression Analysis Predicting Pediatric Illness-Related Stress in Parents of Children with Mitochondrial Disease

		Hospital In Past Year	Income	Medical Visits	PECI Guilt & Worry	PECI Emotional Resources	PECI Sorrow & Anger	PECI Long Term Uncertainty	CHIP Understanding Health Care
Overall Model	*R2 Change*	*b*	*b*	*b*	*b*	*b*	*b*	*b*	*b*
Communication									
Frequency	.23**	.191 *			.348**				
Difficulty	.37**				.381**	-.192 *			
Emotional Distress									

Frequency	.42**	.167*		.115*	.419**			.148*	.142*
Difficulty	.46**	.139*			.470**	-.137*			
Medical Care									
Frequency	.10**	.163*		.160*	.230*				
Difficulty	.21**	.173*	-.151*		.328**				
Role Function									
Frequency	.22**		-.151*				.273*		.198*
Difficulty	.28**		-138*				.342**		.152*
Total Difficulty	.40**	.159*		.133*	.374**		.203*		
Total Frequency	.31**	.196*		.132*	.283**		.232*		

Note: Significance: $\rho < .05$*, $\rho < .01$ **

Chapter Five: Discussion

The overarching goal of this study was to examine parent experience, coping behaviors and stress when caring for a child with mitochondrial disease. This chapter discusses research findings, methodology and interpretation of the results concerning pediatric illness-related parenting stress according to the study purposes. Study strengths, limitations, and next steps for further research are also discussed. Relevant results for each research aim are discussed to provide an interpretation of findings. Similarities related to parent stress literature are examined to assess the similarities associated with the parent experience, coping and illness-related parenting stress when caring for a child with mitochondrial disease.

AIM 1: The first aim of this study was to identify family demographic and disease-related characteristics of parents of children with mitochondrial disease. As reported in Chapter Four, mothers of children with mito (95%) were the primary respondents for this study. This finding is similar to previous research in child chronic illness where mothers were frequently identified as primary caregivers of children in time of illness (Ratliffe et al. 2002). Fathers (5%) also responded to this survey; however, due to the lower participation of fathers, their responses were not compared with responses of mothers, but further research about the experience of fathers, as primary caregivers should be considered in future research. Many of the respondents (94%) identified themselves as biological parents of the child with mito. This inheritance data was collected to identify any association or relationship between maternal or paternal inheritance of mitochondrial disease and illness-related stress, due to the heredity nature of mito (mtDNA exclusively inherited from the mother and recessive inheritance of nDNA) (Kim et al., 2010; Kisler et al., 2010). This biological-relationship variable did not result in significant findings, implying that genetic transference was not associated with or a

predicator of stress.

The majority of respondents were Caucasian, highly educated, and of higher socioeconomic status, suggesting that perhaps this population had better access to health care information and computer technology leading them to the study's Internet surveys. There is limited research about ethnicity or race in children with mito or other chronic illness to indicate that these findings were consistent with other population demographics. Although seventeen mitochondrial diseases were represented in this study (see Table 3), these results underrepresent the growing number and variety of mitochondrial disorders currently recognized (Haas et al., 2007).

Child gender was equally represented between males and females. Findings indicate that children started having symptoms of mito at around the age of two years and received a diagnosis around the age of six years. Although symptoms of mito can occur at any age (United Mitochondrial Diseases Foundation, 2012a), many children have symptoms before the age of five years (United Mitochondrial Disease Foundation, 2012b). The lapse in time between onset of symptoms and diagnosis could possibly be related to the scarcity of mitochondrial disease specialists available to make an accurate and timely diagnosis and to the non-specificity of many wide-ranging symptoms (Noorda et al., 2007). Having a child with a medical condition without a medical diagnosis could be very stressful. This 4-year gap between symptom onset and diagnosis warrants additional research into the impact of the degree of stress experienced by parents during this time as they wait for a diagnosis.

This study offers new insights about mito-specific disease-related characteristics. Factors such as the number of organ involvement, the number of specialists seen, frequency of medical visits and numbers of hospitalizations over the past year indirectly indicate the

severity of illness associated with mitochondrial disease. Children in this study had an average of six organs affected by mito, visited an average of seven specialists, had more than 12 medical visits a year, and half of the children in this study were hospitalized within the past year. These challenges likely increase the demands of illness, caregiver burden, and illness-related parenting stress.

Comparable demographic data were collected in similar research studies using the PIP to assess parenting stress in children with irritable bowel syndrome, cancer, diabetes, obesity, sickle cell disease, and bladder exstrophy (Guilfoyle, Denson, Baldassano & Hommel, 2011). In those studies, the majority of respondents were mothers, mostly in their early forties, living in a two-parent home and making an income above $50,000 annually. Child age ranged from as young as 6 years to almost 13 years and child gender was equally represented. Those demographic data are similar to the findings of this study, suggesting possible similarities between mito and other childhood chronic diseases (see Table 10).

Table 10

Comparison of Socio-demographic Characteristics of Parenting Stress

Characteristic	Mito	IBD	Cancer	DM	Obesity	SCD	BE
Child							
Age: mean (SD)	9.85 (5.24)	15.4 (1.4)	12.5 (5.2)	12.9 (2.0)	12.7 (2.7)	14.5 (1.4)	6.0 (2.9)
Female %	51	44	50	48	56	45	35
Parent/caregiver Age: mean (SD)	42.3 (8.3)	45.7 (5.6)	41.1 (6.4)	42.3 (6.3)	--	--	36.7
Female	95	89	83	86	94	73	90
Ethnicity (non-Hispanic, white)	96	--	86	79	--	--	--
Marital status/two parent	81	89	85	84	37	44	75
Income <50,000 Mito <59,000	37	10	27	45	--	100	45

Note. Mito = Mitochondrial Disease (n = 231), IBD = Inflammatory Bowel Disease (n = 62) (Guilfoyle et.al, 2012), Cancer (n = 126) (Streisand et al. 2001), Diabetes (n = 134) (Streisand et al. 2005), Obesity (n = 72) (Ohleyer et al. 2007), SCD = Sickle Cell Disease (n = 70) (Logan et al. 2002), BE = Bladder Exstrophy (n = 20) (Mednick et al. 2009).

AIM 2: The second aim of this study was to describe the parental experience when caring for a child with mitochondrial disease. This was conducted using the results calculated from the PECI instrument. Compared with other illness-specific measure for parents, the PECI focuses specifically on subjective distress and perceived emotional resources while providing data about parent adjustment (Bonner et al., 2006). According to Bonner, parents who score high on the Guilt & Worry subscale acutely feel a burden of responsibility that transcends the typical caregiver role. Parents see their child as fragile, have concerns about the child's future, and exhibit acute anxiety about being able to manage problems associated with their child's illness. Higher scores on Long-term Uncertainty relate to fears and worries about prognosis and treatment decisions while higher scores in Unresolved Sorrow & Anger reflect chronic grief and a sense of ongoing loss of the healthy child parents once knew, along with the "normal" course of life taken away by the illness (Bonner et al., 2006). In contrast, higher scores in Emotional Resources reflect parents' perceptions of positive inner resources, such as self-efficacy and confidence in their ability to manage their children's chronic illnesses.

Overall this study's findings suggest moderate to high levels of increased difficulty in parent adjustment associated with mito illness-related concerns (See Table 4) with PECI scores ranging from 2.0-2.56. Although statistical comparison to other studies was not conducted, previous research exploring the experience of parenting a child with chronic illness using the PECI tool indicated that parents of children with brain tumors, cancer and food allergies have lower scores in factors associated with Guilt & Worry, Sorrow & Anger,

and Long-term Uncertainty than parents of children with mito (Bonner et al., 2006; Bonner, Hardy, Willard, & Hutchinson, 2007; Williams, Parra, & Elkin, 2009). Parents of children with brain tumors, cancer and food allergies also scored higher in Emotional Resources than parents of children with mito (Bonner et al., 2006; Bonner et al., 2007; Williams et al., 2009) (see Table 11).

Table 11

Comparison of Parent Experience of Childhood Illness (PECI)

Subscale	Mitochondrial Disease	Brain Tumor	Mother's Pediatric Cancer	Father's Pediatric Cancer	Food Allergies
Guilt & Worry					
Mean	2.30	1.72	1.86	1.80	1.82
SD	(.650)	(.773)	(.66)	(.66)	(.72)
Unresolved Sorrow & Anger					
Mean	2.09	1.51	1.59	1.58	1.52
SD	(.730)	(.820)	(.58)	(.81)	(.72)
Long-term Uncertainty					
Mean	2.56	1.97	2.00	2.00	1.10
SD	(.690)	(.867)	(.73)	(.72)	(.66)
Emotional Resources					
Mean	2.36	2.70	2.72	2.58	2.89
SD	(.615)	(.658)	(.53)	(.62)	(.56)

Note. Mitochondrial Disease (n=358), Brain Tumor (n=149) (Bonner et al, 2006), Pediatric Cancer (n=23 for mothers and fathers) (Bonner, 2007), Food Allergies (n=282) (Williams, Parra, Elkin, 2009). PECI range scores (0-4).

Although mild to moderate levels of parental guilt and worry or feelings of uncertainty are expected in parents of children with chronic illness, excess distress in these areas can have negative consequences on the parent's and child's psychological well-being (Williams et al., 2009). High levels of guilt or worry and uncertainty may impact adaptive coping strategies and produce acute anxiety and worries; such anxiety has been associated with parent

posttraumatic stress resulting in child adjustment problems (Bonner et al., 2006; Bonner et al., 2007; Williams et al., 2009). This study reports significant findings ($\rho < .001$, $\rho < 0.05$) of Guilt & Worry in 8 of 10 regression models as predictors of illness-related parenting stress.

The results of the present study suggest that parents of a child with mito feel a burden of responsibility that exceeds the typical caregiver role, see their child as fragile, and have concerns about the child's future, resulting in parent stress and anxiety. Acute anxiety is consistent with parenting a medically fragile child (Moola, 2012), and previous studies by Kim et al (2010) reported guilt and anxiety associated with caring for a child with a mitochondrial disease. This study's results support previous findings that parents of children with mito experience guilt, worry, sorrow, anger and uncertainty associated with their child's illness. Unresolved sorrow and anger can lead to less adaptive parent functioning and in turn may impact child adjustment to illness (Thompson & Gustafson, 1996).

AIM 3: The third aim of this study was to describe coping strategies used by parents of children with a mitochondrial disease. Coping behaviors are specific actions taken by individuals or families that serve to reduce demands and challenges of stressful situations (McCubbin et al., 2001). Positive coping strategies are key for successful adaptation to stress (Garro, 2004). The Coping Health Inventory for Parents (CHIP) was designed to assess the parent's appraisal of coping behaviors currently used to manage family life when caring for a seriously ill or chronically ill child (McCubbin et al., 2001). Coping behaviors are developed in response to stressful situations. Elevated CHIP scores are interpreted as participants experiencing increased levels of stress; therefore higher coping scores suggest higher stress, with parents demonstrating utilization of coping behaviors to reduce stress (Hobdell et al., 2007; McCubbin et al., 2001). Coping behaviors are often used to mediate between stressful

situations and their outcomes (Garro, 2004). However, this study did not focus on underlying stress that prompted the use of coping behaviors, but rather was interested in exploring the association and predictive relationship of coping behaviors and parenting stress outcomes. Therefore, coping behavior scores are not only an indicator of parental stress but also indicate if that stress persisted and was associated with utilization of specific coping behaviors.

CHIP scores from this study were very similar to the data obtained from parents of children with epilepsy, tube feedings, cardiac disease, and diabetes (Garro, 2004, Hobdell et al, 2007; McCubbin & McCubbin, 2001) (see Table 12). Although total CHIP scores were not reported for all studies, reported subscale scores were similar to scores for parents of children with mito. While variation in CHIP scores between the present study and past studies of children with other diseases was not statistically analyzed, the comparisons do suggest that parents of children with mito may utilize fewer coping behaviors than parents of children with other chronic illness. It is interesting to point out that many children with mito have neurological, cardiac, metabolic, and gastrointestinal deficits with concurrent diagnoses of epilepsy, cardiac disease, diabetes and/or enteral tube feedings. These study comparisons raise questions about the differences in the sampled population, numbers of therapeutic challenges, interventions, and disease trajectories. These findings mark a need for future research in matched group comparisons to further investigate this phenomenon. Decreased reporting of coping behaviors could reflect lack of ability, time, or opportunity for parents of children with mito. Continued research is needed to evaluate the use of coping behaviors in parents of children with mito related to specific disease information and demographic characteristics to determine the coping mechanisms in relationship to these variables.

Table 12

Comparison of Coping Health Inventory for Parents (CHIP)

Scale	Mitochondrial Disease	Epilepsy	Feeding Tubes	Cardiac Illness	Diabetes
Family Integration					
Mean	34.28	37.4	42.31	41.85	44.40
SD	(10.49)	(9.70)	(7.97)	(6.99)	(6.29)
Social Support					
Mean	25.20	34.96	25.43	31.29	32,74
SD	(10.04)	(9.95)	(8.84)	(7.78)	(7.01)
Understanding Health Care					
Mean	15.02	19.9	17.43	14.66	17.80
SD	(4.78)	(5.80)	(3.99)	(4.66)	(4.07)
Total Score		--	--		
Mean	74.48			88.09	94.97
SD	(21.94)			(15.45)	(14.38)

Note. Mitochondrial Disease (n = 318), Epilepsy (n = 67) (Hobdell et al, 2007), Tube Feedings (n = 35) (Garro, 2004), Cardiac Illness (n = 107) (McCubbin & McCubbin, 2001), Diabetes (n = 72) (McCubbin & McCubbin, 2001)

AIM 4 The fourth aim of this study was to describe frequency and severity of pediatric illness-related parenting stress in parents of children with a mitochondrial disease. The PIP instrument is based on a transactional model of stress and coping including a list of medically related situations and thoughts considered to be stressful to parents of children with a childhood illness (Streisand et al., 2001). Higher scores indicate greater frequency and difficulty in these areas (Streisand et al., 2001). By examining responses on the PIP the health care provider or nurse can learn more about which situations are particularly stressful for parents of children with mito.

Data from this study provide preliminary evidence that parents of children with mito experience increased levels of stress both in Frequency and Difficulty when managing their

child's illness. Compared to parents of children with irritable bowel disease (Guilfoyle, Denson, Baldassano, & Hommel, 2012) and cancer (Streisand et al., 2001), parents of children with mito show higher PIP scores in most domains both in Frequency and Difficulty (although statistical comparison was not conducted) (see Table 13). Total PIP scores for both frequency and difficulty of parents of children with mito were also higher compared to parents of children with diabetes (Streisand, Swift, Wichmark, Rusan, & Holmes, 2005), obesity (Ohleyer et al., 2007), sickle cell disease (Logan, Radcliffe, & Smith-Whitley, 2002), and bladder exstrophy (Mednick, Gargollo, Oliva, Grant, & Borer, 2009) (see Table 13). Data suggest that parents of children with mito experience increased levels of stress associated with caring for their ill child, at or even above parents of children with other chronic conditions.

Table 13

Comparison of Pediatric Inventory for Parents (PIP) Scores Across Chronic Conditions

	Mito	IBD	Cancer	Diabetes	Obesity	SCD	BE
Total							
Frequency	123	84.4	94.0	89.3	98.0	105.4	89.8
Difficulty	119	78.8	112.4	78.1	91.9	91.1	90.5
Communication							
Frequency	24	17.8	18.0				
Difficulty	23	14.3	19.8				
Medical care							
Frequency	23	15.9	16.1				
Difficulty	20	12.4	19.3				
Role function							
Frequency	27	18.2	20.6				
Difficulty	27	17.3	29.9				
Emotional Distress							
Frequency	49	33.0	39.2				
Difficulty	49	34.8	48.4				

Note. Mito = Mitochondrial Disease (n=231), IBD = Inflammatory Bowel Disease (n = 62) (Guilfoyle et.al, 2012), Cancer (n = 126) (Streisand et al. 2001), Diabetes (n = 134) (Streisand et al. 2005), Obesity (n = 72) (Ohleyer et al. 2007); SCD = Sickle Cell disease (n = 70) (Logan et al. 2002), BE = Bladder Exstrophy (n = 20) (Mednick et al. 2009). PIP-frequency

and PIP -difficulty scores range: 42 - 210. PIP subscales scores were not available for all samples.

AIM 5 The fifth aim of this study was to examine the relationships between pediatric illness-related parenting stress in parents of children with mitochondrial disease and family demographics, disease characteristics, coping strategies, and parent experience of childhood illness. This is the first known study to examine the correlations between the CHIP, PECI and PIP. Correlation analysis identified ten (of twenty) demographic/disease-related variables with significant ($\rho < 0.05$ - $\rho < 0.01$) relationships with stress: number of hospitalizations in the past year, parent age, child age, income, number of specialty services used, number of organs involved, number of office visits in past year, developmental delays, age at diagnosis, and parent education. Variables that were not significant included: child age at symptom emergence, number of children in the household, confirmed child diagnosis of mito, length since last hospitalization, race, ethnicity, child gender, marital status, parent gender, and biological relationship to the child (see Table 7).

Parent age, child age, child age at diagnosis, parent education and income correlations were inversely related to various PIP scores (see Table 7). This finding suggests that being an older parent, having higher education, having older children, or having a child diagnosed at an older age, along with a higher household income is associated with less Frequency and Difficulty in illness-related parenting stress. The more hospitalizations, frequent use of specialty services, more organ involvement, having a child with developmental delays, and number of office visits were significantly positively related to various PIP outcomes in terms of Frequency and Difficulty, suggesting an association with increased illness-related parenting stress (see Table 7).

Unique to this study were the correlations between the PECI and CHIP with the PIP. Findings indicated that parents who experience Guilt & Worry, Unresolved Sorrow & Anger and Long-term Uncertainty have more associated stress across all domains in both Frequency and Difficulty. Parents who perceive themselves to have more Emotional Resources reported less stress. These findings are not surprising. In previous studies, Guilt & Worry about the child's future and health deterioration have been related to stress and concern in parents (Moola, 2012; Ray, 2002; Read, 2003). Anger & Sorrow have also been associated with emotional distress in parents (Nishio, 1997). Prognosis of mito is uncertain and for many parents, this uncertainty may lead to worry, ineffective coping and psychological stress (Mishel, 1983; Santacroce, 2001).

Results from this study indicate that parents who utilized Coping Pattern I: Family Integration and Coping Pattern II: Social Support report less stress in terms of Total PIP Difficulty, PIP-Communication (D) and PIP - Emotional Distress (D). In contrast, parents who utilized Coping Pattern II: Understanding Health Care demonstrated more stress in terms of PIP- Medical Care (F). These findings suggest that family-focused coping behaviors and social support may be helpful to reduce stress for parents, which is consistent with previous findings that parents with greater social support and good family integration have better adjustments to stress (Ball, Bindler, & Cowen, 2014; Barakat & Linney, 1992; Perrin et al., 1993). A surprising finding is that parents who cope by increasing their understanding of mito seem to experience greater stress in terms of managing medical care frequency. Perhaps this is due to the uncertain outcomes specifically associated with mito, or the lack of literature about mito, or the ambiguous nature of the long-term outcomes of mito that increase the stress response in parents seeking medical understanding (Mishel, 1983). Further research is needed

in this area to better understand why the use of this coping behavior is associated with stress in parents of children with mito.

AIM 6 The sixth aim of this study was to identify the significant predictors of pediatric illness-related parenting stress in parents of children with mitochondrial disease. This is the first study to examine the predictive relationship between specific demographic and disease-related characteristics, a parent coping instrument (CHIP), and a parent experience of chronic illness (PECI) measure with an illness-related measure of parenting stress (PIP) to assess the difficulty of stressful events in parents of children with mitochondrial disease. Results provide initial support for the relationship between pediatric illness-related parenting stress and specific demographic characteristics and parent experiences of illness and coping. Specific variables noted as predictors of stress in this sample included: Hospitalizations over the Past Year (7/10 models), Parent Income (2/10 models), Medical Visits (4/10 models), Guilt & Worry (8/10 models), Unresolved Sorrow & Anger (3/10 models), Long-term Uncertainty (1/10 models), Emotional Resources (2/10 models) and Understanding of Health Care (4/10 models). Parent experience of guilt and worry along with the number of hospitalizations over the past year were most often predictive of parenting stress with the exception of two domains (See Table 9).

Parents who reported feelings of Guilt & Worry conveyed stress across all domains in both frequency and difficulty with the exception of Role Function (F & D). Parents who expressed Unresolved Sorrow & Anger behaviors demonstrated stress in Role Function (F & D) and Total PIPD. These findings suggest that parents of children with mito experience feelings of Guilt & Worry, and Sorrow & Anger. These feelings are associated with illness-related parenting stress. Future research is needed to discover possible causes of Guilt &

Worry and Sorrow & Anger in these families, and how these behaviors more closely relate to parenting stress. This information can provide valuable guidance to health care providers in support of parents to reduce the impact of stress when caring for a child with mito.

As expected, increased number of hospitalizations, frequency of medical visits and lower income were significant indicators of stress in terms of Total PIP Frequency and Total PIP Difficulty , Emotional Distress (F & D), Medical Care (F & D) and Role Function (F & D). Hospitalizations and medical visits, especially when unplanned or accompanied by medical procedures or that are unplanned represent stressful events for children and families (Ball et al., 2014). Hospitalizations may cause additional financial strain for parents especially if one or both parents are absent from work, or if additional expenses are accrued related to travel, hotels, daycare for siblings, and etc. (Ball, et al., 2014). The financial impact of caring for a child with a chronic illness is challenging even with good health insurance coverage, but inadequate finances coupled with unexpected medical expenses place many families in a higher stressed state (Ball et al., 2014). The socioeconomic report in the present study affirms that parents with reduced finances show significantly increased stress. A multidisciplinary approach is needed to assess the burden of hospitalization, the impact of medical visits and reduced income to provide access to community recourses for these families (Ball et al., 2014). Further research is needed to explore the stress associated with hospitalizations, medical visits, and income. This study suggests that supportive care is needed for parents of children with mito during times of hospitalizations and medical visits to help reduce the impact of stress caused by these events. Families who perceive greater emotional resources also reported less stress. Engaging in healthy coping strategies and developing a strong social

infrastructure can help reduce the burden associated with caring for a chronically ill child and decrease parental stress (Ball et al., 2014).

Contrary to expectations that uncertainty of mito would be related to distress, PECI-Long-term Uncertainty only predicted one domain: Emotional Distress (F), and was not predictive in any other PIP subscales or domains. It appears that there is either less uncertainty than initially thought associated with mito or that parents have been able to minimize the distress associated with the uncertainty of their child's diagnosis. Perhaps this is related to the fact that parents are actively seeking medical understanding about mito as indicated by the scores associated with understanding health care coping behavior.

As mentioned earlier, Coping Pattern II: Understanding Health Care indicated a predictive association with stress in terms of Emotional Distress (F), Role Function (F & D) and Total PIP Frequency. More research is needed in this area to determine if parents who are seeking more medical information are finding information, getting accurate information, and understand the medical regimen, outcomes, and prognosis related to mitochondrial disease. It appears that families who are seeking understanding in health care related to mito experience higher distress than parents not seeking health information, which seems counterintuitive when health care interventions often include patient education as a means to help decrease stress in families.

Theoretical framework

The combination of Hill's ABC-X Model of Family Crisis (Bomar, 2004) and the findings from this study help to explain the unique experiences associated with parenting a child with a mitochondrial disease. Mitochondrial disease (Factor A), along with significant family demographics and disease-related characteristics, were explored as precipitating events

or stressors to the family. Ten factors were strongly associated with pediatric parenting stress and three factors (number of hospitalizations, number of medical visits and income) were identified as significant predictors of stress (Factor X). Exploration of the family relationship with resources or coping strategies (Factor B) identified significant relationships between family integration, social support and understanding health care as coping behaviors associated with pediatric parenting stress. Surprisingly, parental attempt to understand health care predicted increased stress for the parent (Factor X). The subjective definition of the event (mitochondrial illness) (Factor C) explored the association between Guilt & Worry, Sorrow & Anger, Long-term Uncertainty, Emotional Resources, and Pediatric Related Parenting Stress, and identified that each factor plays a specific role in predicting parent stress (Factor X). Hill's model of family stress (1958) demonstrates the relationship between stressors and resources (A & B), stressors and perception (A & C), and resources and perception (B & C) that influence the crisis (X) (see Figure 1). This study, because of its exploratory nature, focused on the basic relationships between precipitating stressors and stress (A & X), resources and stress (B & X), and perception and stress (C & X). Understanding the basic relationship between these factors provides valuable information about the stress, predictors of stress, and coping of families with mito. Further research is needed to explore the interactions between mito and coping resources, mito and perception of the illness, coping and perception of the illness and the impact of stress on the entire family.

Limitations

Psychosocial Internet survey collection poses unique challenges and limitations. One limitation unique to this research is the use of a web-based program, which posed limitations to sampling. Although Internet-based survey methodology allowed access to a large number

of eligible participants in a relatively short time frame, the non-random nature of the sampling from a homogeneous group of parents with one specific illness limited access solely to the population using the Internet. Only parents of children with mito who spoke English and had computer access to the surveys could participate in this study. While capturing one portion of a sample, other members may have been excluded, potentially making the sample less representative of the total mito population and also limiting the ability to generalize the findings to other populations of children with other chronic illness

Self-selection bias is a limitation in an Internet-based study and again causes difficulty with generalization. Survey collection provides subjective information and does not guarantee that the participants accurately answered all of the questions, clearly understood all of the directions or provided truthful answers. Objective information from medical records is more reliable in identifying disease-related and demographic information about parents of children with a confirmed diagnosis. It also cannot be assumed that all participants accurately represented themselves or their experiences on the surveys. Although participants were asked to not take the survey a second time (one survey per family was requested) there is no guarantee that they did not participate more than once. Although computers were identified by IP address, the participants could have used a different computer and retaken the survey. This, however, seems unlikely. Although the study was open to mothers and fathers, the majority of the respondents were mothers limiting data about the impact of stress about fathers.

Midway through the survey, participants were asked to repeat the PIP inventory reflecting on the past 30 days (not the past 7 days as previously asked) with hopes to gain better understanding of the long-term stressors associated with mito; however, the repeated inventory caused a significant dropout of participants, possibly as a result of survey fatigue.

The entire survey "set" was estimated to take respondents about 15-20 minutes to complete; however, data from the survey shows the survey took from 20-30 minutes. Another potential limitation of this study is personal bias of the researcher. The researcher is also a mother of a child with a mitochondrial disease and a participant in support groups associated with mitoAction, UMDF, and the Research Guild of Seattle. Awareness of researcher bias throughout the study was acknowledged and challenged by committee members to prevent unintended influence on the findings.

Application to Nursing Education and Practice

The ability to identify disease and family characteristics and psychosocial stressors of parenting a child with mitochondrial disease can assist health care professionals to provide disease-sensitive, family-focused care. Identification of specific needs and the influence of stressful events in the lives of parents can be valuable to health care professionals in developing interventions and educational programs to help reduce stress and better meet these needs. Although demographic characteristics cannot always be changed, knowledge about the relationship of child health characteristics, such as age of illness, income, and stressors can allow for health interventions to ease the burden of care during these identified phases of childhood development and disease onset. Health care professionals can grow in their understanding of mitochondrial disease to better serve the needs of parents. Parents can benefit from the holistic approach of health care professionals who have a better understanding of the psychosocial needs of the family. Partnering with families to provide a family-centered approach can help minimize fears, reduce anxiety and support families through stressful experiences (Ball et al., 2014).

Findings from this study support previous literature examining the psychosocial

impact of caring for a child with a chronic life threatening illness. This study provides data about parent experiences, resources, distress, coping, and adjustment that may have both research and clinical impact. The findings suggest that parents perceive themselves as having significant emotional distress with few emotional resources to deal their children's condition. These families may be at risk for maladjustment and caregiver fatigue which may impair their ability to effectively manage their child's mito illness. Using results from this study, health care professionals can target specific concerns or worries identified from this study related to reports from the PECI, CHIP, and PIP to help identify stressful situations and implement programs to reduce stress. One example includes addressing stress associated with communication in open discussion about mito with the child, other family members, or the health care team, making communication with the parent a priority intervention during clinical visits (Streisand et al., 2001).

There are several clinical and research implications from this study. Specifically, knowledge that parents report increased stress during medical visits and hospitalization when seeking understanding of mitochondrial disease is valuable information for the health care professional. Parents of children with mito report feeling guilt, worry, sorrow, and anger that need to be addressed by members of the health care profession. More research is needed to better understand the cause of these emotions, but this research is valuable in indicating that this emotional distress exists. This study implies that emotional resources and effective coping behaviors are valuable in minimizing distress, suggesting that support groups could serve as a valuable asset to families especially during times of hospitalizations and medical visits. It is interesting to note that mito families across the globe already recognize the need for community support and are forming support groups with annual mito picnics, online social

networks, and kid camps. More research is also needed to investigate the impact of these social support groups on family stress for this population.

Implications for Future Research

The association between pediatric illness-related parenting stress and hospitalizations, medical visits, income, parent experience of chronic illness and understanding health care appears significant and warrants additional research. Future exploration might include repeated and comparative studies with other childhood chronic illnesses and further exploration of the differences within the mito population such as parent gender, mito diagnosis, ages of children and other identified factors. Although stress and coping is often associated with quality of life (QOL), this study did not explore specific QOL concerns. Additional research is needed to determine the degree of impairment stressors have on QOL perhaps using a QOL assessment measure. Continued research is needed to further examine coping behaviors in the mito community and the use of coping strategies for mediating/protective factors.

Further investigation is needed to better understand the parent experience of caring for a child with mito. A clinical-based study rather than an Internet-based study could help overcome some of the limitations noted in this study and provides additional information about the parent experience, coping, and stress. Research is also needed to measure effectiveness of support groups and other interventions. Mito shares many characteristics and stresses with other chronic diseases, but also has unique differences. Further research comparing the similarities and differences between mito and other chronic illness can illuminate these challenges and provide additional insight about the needs of families with chronic illness.

Summary

This study reported several factors that are significant predictors to parenting stress, confirming the stated hypothesis that family demographics and disease-related characteristics associated with a mitochondrial condition, parent resources for coping, and parent experience associated with childhood illness are significantly related to and predict pediatric illness-related parenting stress. There is an urgent need to understand the parental challenges associated with caring for a child with mitochondrial disease to ease the stress impact to families. Information gained from understanding the relationship between demographic characteristics, parent experience, coping and stress must be disseminated to health care providers such as pediatricians, specialists, and nurses who work closely with families in disease and symptom management. This information can be the basis for health education programs and interventions that can make a significant impact on family health to ease the stress impact on the family.

References

Allen, P., Vessey, J., & Schapiro, N. (2010). *Primary care of the child with a chronic condition* (5th ed.). St. Louis, Missouri: Mosby.

Balcells, C. (2009). mitoACTION. *Letter from the executive director*. Retrieved from http://www.mitoaction.org/letter

Balcells, C. (2012). *Living well with mitochondrial disease: a handbook for patients, parents and families.* . Bethesda, MD: Woodbine House.

Balcells, C., & Turco, J. (2008). mitoACTION. *Genetic inheritance in mitochondrial disease: Fact vs fiction*. Retrieved from http://www.mitoaction.org/blog/genetic-inheritance-mitochondrial-disease-fact-vs-fiction

Ball, J., Bindler, R., & Cowen, K. (2014). *Child health nursing: partnering with children and families* (3rd ed.). New Jersey; Upper Saddle River

Barakat, L., & Linney, J. (1992). Children with physical handicaps and their mothers; the interrelation of social support, maternal adjustment and child adjustment. *Journal of Pediatric Psychology 17*(6), 725-739.

Boles, R., Burnett, B., Gleditsch, K., Wong, S., Guedalia, A., Kaariainen, A., . . . Brumm, V. (2005). A high predisposition to depression and anxiety in mothers and other matrilineal relatives of children with presumed maternally inherited mitochondrial disorders. *American Journal of Medical Genetics, 137B*(1), 20-24. doi: 10.1002/ajmg.b.30199

Boles, R., & Mason, T. (n.d.). United Mitochondrial Disease Foundation. *Inheritance and Genetics*. Retrieved from http://www.umdf.org/site/c.otJVJ7MMIqE/b.5692899/

Bomar, P. (2004). *Promoting health in families: applying family research and theory to nursing practice*. Philadelphia, PA: Saunders.

Bonner, M. J., Hardy, K. K., Guill, A. B., McLaughlin, C., Schweitzer, H., & Carter, K. (2006). Development and validation of the parent experience of child illness. *Journal of Pediatric Psychology, 31*(3), 310-321. doi: 10.1093/jpepsy/jsj034

Bonner, M. J., Hardy, K. K., Willard, V., W, & Hutchinson, K. C. (2007). Brief Report: Pscyhosocial Functioning of Fathers as Primary Caregivers of Pediatric Oncology Patients. *Journal of Pediatric Pscyhology, 32*(7), 851-856. doi: 10.1093

Bourgeron, T., Rustin, P., Chretien, D., Birch-Machin, M., Bourgeois, M., Viegas-Pequignot, E., . . . Rotig, A. (1995). Mutation of a nuclear succinate dehydrogenase gene

results in mitochondrial respiratory chain deficiency. *Nature Genetics, 11*(2), 144-149. doi: 10.1038/ng1095-144

Branstetter, J. E., Domian, E. W., Williams, P. D., Graff, J. C., & Piamjariyakul, U. (2008). Communication themes in families of children with chronic conditions. *Issues in Comprehensive Pediatric Nursing, 31*(4), 171-184. doi: 10.1080/01460860802475184

Cooley, M. E. (1999). Analysis and evaluation of the Trajectory Theory of Chronic Illness Management. *Scholarly Inquiry For Nursing Practice, 13*(2), 75-95.

Corbin, J. (1991). A nursing model for chonic illess managment based upon the trajectory framework. *Scholarly Inquiry for Nursing Practice: An International Journal 5*(3), 155-174.

Davidson, M. (2012). Molecular Expressions: Cell Biology and Microscopy Structure and Function of Cells and Viruses. *Mitochondria*. Retrieved from http://micro.magnet.fsu.edu/cells/mitochondria/mitochondria.html

Dimauro, S. (2011). A history of mitochondrial diseases. *Journal of Inherit Metabolic Disease, 34*(2), 261-276. doi: 10.1007/s10545-010-9082-x

Edison. (2011). PR Newswire. *Edison Pharmaceuticals, inc. to provide expanded access to EPI-743 for mitochondrial disease.* Retrieved from http://investing.businessweek.com/research/stocks/private/snapshot.asp?privcapId=21842899

Elkin, N. (2008). iCrossing. *How america searches: health and wellness*. Retrieved from http://www.icrossing.com/.../how-america-searches-health-and-wellness.pdf

Erdfelder, E., Faul, F., & Buchner, A. (1996). GPOWER: A general power anlaysis porgram. *Behavior Research Methods, Instruments & Computers 28*, 1-11.

Facebook. (2012a). Mitoaction. Retrieved from http://www.facebook.com/mitoaction

Facebook. (2012b). Mitochondrial Research Guild of Seattle Children's Hosptial. Retrieved from http://www.facebook.com/groups/60457421484/members/

Facebook. (2012c). United Mitochondrial Disease Foundation. Retrieved from http://www.facebook.com/groups/umdfgroup/

Farmer, J., Marien, W., Clark, M., Sherman, A., & Selva, T. (2004). Primary care supports for children with chronic health conditions: identifying and predicting unmet family needs. *Journal of Pediatric Psychology, 29*(5), 355-367.

Federal Register. (1995). Office of Managment and Budget. *Standards for the classificaion of federal data on race and ethnicity*. Retrieved from http://www.whitehouse.gov/omb/fedreg_race-ethnicity

Fisher, H. R. (2001). The needs of parents with chronically sick children: a literature review. *Journal of Advanced Nursing, 36*(4), 600-607.

Fox, S., & Purcell, K. (2010). Pew Internet: Pew Internet & American Life Project. *Chronic Disease and the Internet*. Retrieved from http://pewinternet.org/Reports/2010/Chronic-Disease.aspx

Garro, A. (2004). Coping patterns in mothers/caregivers of children with chronic feeding problems. *Journal of Pediatric Health Care, 18*(3), 138-144. doi: 10.1016/j.pedhc.2003.08.001

Goldman, A., Hain, R., & Liben, S. (2006). *Oxford textbook of palliative care for children*. New York: NY; Oxford University Press.

Granello, D., & Wheaton, J. (2004). Online data collection: strategies for research. *Journal of Counseling and Development, 82*(4), 387-394.

Gravelle, A. M. (1997). Caring for a child with a progressive illness during the complex chronic phase: parents' experience of facing adversity. *Journal of Advanced Nursing, 25*(4), 738-745.

Grootenhuis, M. A., & Bronner, M. B. (2009). Paediatric illness! Family matters. *Acta Paediatrica, 98*(6), 940-941.

Guilfoyle, S. M., Denson, L. A., Baldassano, R. N., & Hommel, K. A. (2012). Paediatric parenting stress in inflammatory bowel disease: application of the Pediatric Inventory for Parents. *Child Care Health and Development, 38*(2), 273-279. doi: 10.1111/j.1365-2214.2010.01200.x

Gutenberg, J. (2002). Stress and coping theories. Retrieved from userpage.fu-berlin.de/~schuez/folien/Krohne_Stress.pd

Haas, R. H., Parikh, S., Falk, M. J., Saneto, R. P., Wolf, N. I., Darin, N., & Cohen, B. H. (2007). Mitochondrial disease: a practical approach for primary care physicians. *Pediatrics, 120*(6), 1326-1333. doi: 10.1542/peds.2007-0391

Hatzmann, J., Valstar, M. J., Bosch, A. M., Wijburg, F. A., Heymans, H. S., & Grootenhuis, M. A. (2009). Predicting health-related quality of life of parents of children with inherited metabolic diseases. *Acta Paediatrica, 98*(7), 1205-1210. doi: 10.1111/j.1651-2227.2009.01269.x

Hobdell, E. F., Grant, M. L., Valencia, I., Mare, J., Kothare, S. V., Legido, A., & Khurana, D. S. (2007). Chronic sorrow and coping in families of children with epilepsy. *Journal of Neuroscience Nursing, 39*(2), 76-82.

Ireys, H. T., & Silver, E. J. (1996). Perception of the impact of a child's chronic illness: does it predict maternal mental health? *Journal of Developmental and Behavioral Pediatrics, 17*(2), 77-83.

Johnson Wright, L., Afari, N., & Zautra, A. (2009). The illness uncertainty concept: a review. *Current Pain and Headache Reports, 13*(2), 133-138.

Kahl, S., Steelman, L., Koch, P., Dougan, W., & Catsambis, S. (2007). Revisiting Reuben Hill's theory of familial response to stressors: The mediating role of mental outlook for offspring divorce. *Family and Consumer Sciences Research Journal, 36*(1), 5-21. doi: 10:1177/1077727z07303494

Kim, K. R., Lee, E., Namkoong, K., Lee, Y. M., Lee, J. S., & Kim, H. D. (2010). Caregiver's burden and quality of life in mitochondrial disease. *Pediatric Neurology, 42*(4), 271-276. doi: 10.1016/j.pediatrneurol.2009.11.012

Kisler, J. E., Whittaker, R. G., & McFarland, R. (2010). Mitochondrial diseases in childhood: a clinical approach to investigation and management. *Developmental Medicine and Child Neurology, 52*(5), 422-433. doi: 10.1111/j.1469-8749.2009.03605.x

Kovacs, M., Lyengar, S., Goldston, D., Obrosky, D., Stewart, J., & Marsh, J. (1990). Pscyhologicial functioning among mothers of chldren with insulin-dependent diabetes mellitus: A longitudinal study. *Journal of Consulting and Clinical Psychology, 58*(2), 159-165.

Kratz, L., Uding, N., Trahms, C., Villareale, N., & Kieckhefer, G. (2009). Managing childhood chronic illness: Parent perspectives and implications for parent-provider relationships. *Families, Systems & Health 27*(4), 303-313.

Lee, M. (2009). A path analysis on elder abuse by famiy caregivers: Applying the ABCX Model. *Journal of Family Violence, 24*, 1-9. doi: 10.1007/s10896-008-9192-5

Logan, D. E., Radcliffe, J., & Smith-Whitley, K. (2002). Parent factors and adolescent sickle cell disease: associations with patterns of health service use. *Journal of Pediatric Psychology, 27*(5), 475-484.

McCubbin, H., & McCubbin, A. (1987). *Family assessment inventories for research and practice*. Madison, WI: University of Wisconsin

McCubbin, H., Thompson, A., & McCubbin, M. (2001). *Family measures: stress, coping and resiliency. inventories for research and practice*. Honolulu, Hawaii: Kamehameha Schools.

Mednick, L., Gargollo, P., Oliva, M., Grant, R., & Borer, J. (2009). Stress and coping of parents of young children diagnosed with bladder exstrophy. *Journal of Urology, 181*(3), 1312-1316. doi: 10.1016/j.juro.2008.10.051

Menezes, A. (2010). Moments of realization: life-limiting illness in childhood--perspectives of children, young people and families. *International Journal of Palliative Nursing, 16*(1), 41-47.

Mertler, C., & Vannatta, R. (2005). *Advanced and multivariate statistical methods* (3 ed.). Glendale, CA: Pyrczak Publishing.

Mishel, M. H. (1983). Parents' perception of uncertainty concerning their hospitalized child. *Nursing Research, 32*(6), 324-330.

Mishel, M. H. (1988). Uncertainty in Illness. *IMAGE: Journal of Nursing Scholarship, 20*(4), 225-232.

Mitchell, S., Hilliard, M., Mednick, L., Henderson, C., Cogen, F., & Streisand, R. (2009). Stress among fathers of young children with type 1 diabetes. *Families, Systems & Health 27*(4), 314-324. doi: 10:1037/a0018191

Mitoaction. (2009a). About mitochondrial disease, Mito-FAQ. Retrieved from http://www.mitoaction.org/mito-faq - whatis

Mitoaction. (2009b). Board of directors. Retrieved from http://www.mitoaction.org/board-of-directors

MitoAction. (2009c). Our Mission. Retrieved from http://www.mitoaction.org/about-us

Mitoaction. (2011). EPI-743 investigator team to report on edison mitochondrial drug. Retrieved from http://www.mitoaction.org/epi743

Mitochondrial Research Guild. (2011). Mitochondrial Research Guild, Give Kids the Energy to Dream. *The Guild*. Retrieved from http://www.nwmito-research.org/guild.jsp

Moola, F. J. (2012). "This is the Best Fatal Illness That You Can Have": Contrasting and Comparing the Experiences of Parenting Youth With Cystic Fibrosis and Congenital Heart Disease. *Qualitative Health Research, 22*(2), 212-225. doi: 10.1177/1049732311421486

Mu, P. F., Wong, T. T., Chang, K. P., & Kwan, S. Y. (2001). Predictors of maternal depression for families having a child with epilepsy. *The Journal of Nursing Research 9*(4), 116-126.

Naviaux, R. K. (1997). The Spectrum of Mitochondrial Disease. *Exceptional Parent*, 3-10.

Naviaux, R. K., & Nguyen, K. V. (2004). POLG mutations associated with Alpers' syndrome and mitochondrial DNA depletion. *Annals of Neurology, 55*(5), 706-712. doi: 10.1002/ana.20079

Nishio, K. T. (1997). A family affected by mitochondrial encephalomyopathy: a nursing protocol. *Clinical Nurse Specialist 11*(5), 195-201.

Noorda, G., Hermans-Peters, M., Smeitink, J., Van Achterberg, T., Kemps, H., Goverde, W., & Schoonhoven, L. (2007). Mitochondrial disease: needs and problems of children, their parents and family. A systematic review and pilot study into the need for information of parents during the diagnostic phase. *Journal of Inherited Metabolic Disease, 30*, 333-340. doi: 10.1007/s10545-007-0426-0

Office of Rare Disease Research. (2007). Rare Diseases Information. *Rare diseases and related terms*. Retrieved from http://rarediseases.info.nih.gov/Resources/Rare_Diseases_Information.aspx

Ohleyer, V., Freddo, M., Bagner, D. M., Simons, L. E., Geffken, G. R., Silverstein, J. H., & Storch, E. A. (2007). Disease-related stress in parents of children who are overweight: relations with parental anxiety and childhood psychosocial functioning. *Journal of Child Health Care, 11*(2), 132-142. doi: 10.1177/1367493507076065

Parikh, S., Saneto, R., Falk, M. J., Anselm, I., Cohen, B. H., Haas, R., & Medicine Society, T. M. (2009). A modern approach to the treatment of mitochondrial disease. *Current Treatment Options in Neurology, 11*(6), 414-430.

Perrin, E., CC, A., & JB, W. (1993). in the eyes of the beholder: family and maternal influences on perceptions of adjustment of children with chronic illness *Journal of Developmental Behavioral Pediatrics, 14*(2), 95-105.

Portney, L., & Watkins, M. (2009). *Foundations of clinical research applications to practice* (3 ed.). Upper Saddle River, New Jersey: Pearson Prentice Hall.

Qualtrics. (2012a). Acceptable Use Statement. Retrieved from http://www.qualtrics.com/acceptable-use-statement

Qualtrics. (2012b). Security Statement. Retrieved from http://www.qualtrics.com/security-statement

Ratliffe, C. E., Harrigan, R. C., Haley, J., Tse, A., & Olson, T. (2002). Stress in families with medically fragile children. [Review]. *Issues In Comprehensive Pediatric Nursing, 25*(3), 167-188. doi: 10.1080/01460860290042558

Ray, L. D. (2002). Parenting and Childhood Chronicity: making visible the invisible work. *Journal of Pediatric Nursing, 17*(6), 424-438. doi: 10.1053/jpdn.2002.127172

Read, C. Y. (2003). The demands of biochemical genetic disorders: a survey of mothers of children with mitochondrial disease or phenylketonuria. *Journal of Pediatric Nursing, 18*(3), 181-186. doi: 10.1053/jpdn.2003.36

Read, C. Y., & Calnan, R. J. (2000). Mitochondrial disease: beyond etiology unknown. *Journal of Pediatric Nursing, 15*(4), 232-241. doi: 10.1053/jpdn.2000.8042

Saneto, & Naviaux, R. (2010). Polymerase gamma disease through the ages. *Developmental Disabilities Research Reviews, 16*(2), 163-174. doi: 10.1002/ddrr.105

Santacroce, S. (2001). Measuring parental uncertainty during the diagnosis phase of serious illness in a child. *Journal of Pediatric Nursing, 16*(1), 3-12. doi: 10.1053/jpdn.2001.20547

Santacroce, S. (2002). Uncertainty, anxiety, and symptoms of posttraumatic stress in parents of children recently diagnosed with cancer. *Journal of Pediatric Oncology Nursing, 19*(3), 104-111.

Sarasohn-Kahn. (2008). California Healthcare Foundation. *The wisdom of patients: health care meets online social media*. Retrieved from http://www.chcf.org/publications/2008/04/the-wisdom-of-patients-health-care-meets-online-social-media

Schneider, M., Steele, R., Cadell, S., & Hemsworth, D. (2010). Differences on psychosocial outcomes between male and female caregivers of children with life-limiting illnesses. *Journal of Pediatric Nursing, 26*(3), 186-199.

Sexton, A. C., Sahhar, M., Thorburn, D. R., & Metcalfe, S. A. (2008). Impact of a genetic diagnosis of a mitochondrial disorder 5-17 years after the death of an affected child. *Journal of Genetic Counseling, 17*(3), 261-273. doi: 10.1007/s10897-007-9145-9

Sifers, S. K., Puddy, R. W., Warren, J. S., & Roberts, M. C. (2002). Reporting of demographics, methodology, and ethical procedures in journals in pediatric and child psychology. *Journal of Pediatric Psychology, 27*(1), 19-25.

Starbuks, G., (2000) Chapter Fourteen, Crisis and Violence in Families. [PowerPoint} Mesa State College

Stein, R. E. (1992). Chronic physical disorders. *American Academy of Pediatrics, 13*(6), 224-230.

Streisand, R., Braniecki, S., Tercyak, K., & Kazak, A. (2001). Childhood illness-related parenting stress: the pediatric inventory for parents. *Journal of Pediatric Psychology, 26*(3), 155-162.

Streisand, R., Swift, E., Wichmark, T., Rusan, C., & Holmes, C. (2005). Pediatric parenting stress among parents of children with type 1 diabetes: The role of self-efficacy, responsibility and fear. *Journal Of Pediatric Psychology, 30*(6), 513-521. doi: 10.1093/jpepsy/jsi076

Tarnopolsky, M. A. (2008). The mitochondrial cocktail: rationale for combined nutraceutical therapy in mitochondrial cytopathies. *Advanced Drug Delivery Reviews, 60*(13-14), 1561-1567. doi: 10.1016/j.addr.2008.05.001

Thompson, R., & Gustafson, K. (1996). *Adaptation to chronic childhood illness*. Washington, DC: American Psychological Association

United Mitochondrial Disease Foundation. (1996). Mission. Retrieved from http://www.umdf.org/site/pp.aspx?c=8qKOJ0MvF7LUG&b=7934713

United Mitochondrial Disease Foundation. (2007). Frequently Asked Questions. Retrieved from http://www.umdf.org/site/c.otJVJ7MMIqE/b.5692895/k.B04C/FAQs.htm

United Mitochondrial Disease Foundation. (2011). EPI 743 information and resources, Retrieved from http://www.umdf.org/site/c.8qKOJ0MvF7LUG/b.8050141/k.C20F/EPI_743.htm

United Mitochondrial Disease Foundation. (2012a). About mitochondrial disease *Pamphlet*. Pittsburg, PA: United Mitochondrial Disease Foundation.

United Mitochondrial Disease Foundation. (2012b). Mitochondrial disease: general background and overview of NIH efforts. Retrieved from http://www.umdf.org/site/pp.aspx?cx=013792666489486436398%3Au2bg8bixwdy&cof=FORID%3A11&q=nih+efforts&sa=Go&siteurl=www.umdf.org%2Fsite%2Fc.otJVJ7MMIqE%2Fb.5694445%2Fk.C86D%2FAdvocate.htm&c=otJVJ7MMIqE&b=5539825

United States Department of Health and Human Services. (2008). The National Survey of Children with Special Health Care Needs Chartbook 2005-2006. *Core outcomes: key measures of performance*. Retrieved from http://mchb.hrsa.gov/cshcn05/MCO/intro.htm

United States Department of Health and Human Services. (2010). Healthy People 2020. *Brochure*. Retrieved from http://www.healthypeople.gov

United States Department of Health and Human Services. (2012a). Healthy People 2020. *Topics & objectives index-healthy people*. Retrieved from http://www.healthypeople.gov/2020/topicsobjectives2020/default.aspx

United States Department of Health and Human Services. (2012b). Maternal and Child Health. *Partnerships with state medicaid and children's health insurance program (CHIP)*. Retrieved from http://mchb.hrsa.gov/programs/collaboration/index.html

United States Department of Health and Human Services. (n.d.-a). Maternal and Child Health Bureau, . *Division of servies for children with special heath needs (DSCSHN) fact sheet*. Retrieved from mchb.hrsa.gov/about/factsheets/dschcnfacts.PDF

United States Department of Health and Human Services. (n.d.-b). Maternal and Child Health Bureau, Understanding Title V of the Social Security Act. *Brochure*. Retrieved from http://www.amchp.org/AboutTitleV/Documents/UnderstandingTitleV.pdf

United States Health and Human Services. (2012). ASPE.hhh.gov. *2012 HHH Poverty Guidelines*. Retrieved from http://aspe.hhs.gov/poverty/12poverty.shtml

Varvogli, L., & Waisbren, S. E. (1999). Personality profiles of mothers of children with mitochondrial disorders. *Journal of Inherited Metabolic Disease, 22*(5), 615-622.

Vermaes, I. P., Janssens, J. M., Mullaart, R. A., Vinck, A., & Gerris, J. R. (2008). Parents' personality and parenting stress in families of children with spina bifida. *Child: Care, Health and Development, 34*(5), 665-674. doi: 10.1111/j.1365-2214.2008.00868.x

Voices, F. (2005). *Title V: the state program for children and youth with speical health care needs*. Retrieved from http://www.familyvoices.org

Waisbren, S., Rones, M., Reach, C., Marsden, D., & Levy, H. (2004). Brief report: predictors of parenting stress among parents of children with biochemical genetic disorders. *Journal of Pediatric Psychology, 29*(7), 565-570.

Weber, J. (2011). *Individual and family stress and crises*. Thousand Oaks, CA: SAGE.

Williams, N., Parra, G., & Elkin, D. (2009). Subjective distress and emotional resourced in parents of children with food allery. *Children's Health Care, 38*, 213-227. doi: 10.1080/02739610903038792

Wolf, N. I., & Smeitink, J. A. (2002). Mitochondrial disorders: a proposal for consensus diagnostic criteria in infants and children. *Neurology, 59*(9), 1402-1405.

Appendix A: Webpage Announcement:

Invitation to Participate in Mitochondrial Study

Attention: Parents of Children with Mitochondrial Disease,

You are invited to participate in a "set" of surveys to identify the needs of parents caring for a child with a mitochondrial disease. I am a registered nurse completing my doctoral degree in nursing and a mother of a child with a mitochondrial disease (mito). The information gathered from this survey will be used as part of my doctoral dissertation and to educate health care providers about the unique needs associated with caring for a child with mito. All responses are confidential and submitted anonymously, and information will be analyzed as a whole group.

Please click on the URL link (here) to access a set of surveys specific to the needs of parents caring for a child with a mitochondrial disease (only one parent per household should complete the surveys). When taking the surveys, you will be asked to answer questions about parent stress, coping, and the experience of caring for a child with a medical illness. There will also be a few questions about your child's unique mitochondrial disease and household demographics. The set of surveys will take approximately 15-20 minutes to complete.

For additional questions about the survey or about my dissertation project, or for technical assistance please contact me, Brenda Senger, at sengerb@gmail.com.

Thank you in advance for participating in this important study!

Appendix B: Follow - Up Invitation

Attention Parents of Children with Mitochondrial Disease

About one month ago, you were invited to participate in a survey to identify the needs of parents caring for a child with mitochondrial disease (mito). In order to complete this research I need 200 participants. To date, I am short of this goal and in need of your help. Data from this survey will be used to educate health care providers about the needs of parents caring for a child with mito. Your assistance is greatly needed to validate this research study. If you have already responded to this survey, *thank you* for your participation. ***If you have not responded, will you please take time to participate?***

Your experience as a parent of a child with mito is important to share with the health care community. As a mother of a child with mito, I understand how precious time is and know how much time I spend educating health care providers about my child's condition. Please take a few minutes of your time to help me get the word out to the health care community about the needs associated with caring for a child with mito. All responses are confidential and submitted anonymously, and information will be analyzed as a whole group.

Please click on the URL link (here) to access a set of surveys specific to the needs of parents caring for a child with a mitochondrial disease (only one parent per household should complete the surveys). When taking the surveys, you will be asked to answer questions about parent stress, coping, and the experience of caring for a child with a medical illness. There will also be a few questions about your child's unique mitochondrial disease and household demographics. The set of surveys will take approximately 15-20 minutes to complete.
For additional questions about the surveys or about my dissertation project, or for technical assistance please contact me, Brenda Senger, at sengerb@gmail.com

Appendix C: IRB Exemption

IRB Determination of Exemption

MEMORANDUM

TO: Ruth Bindler and Brenda Senger,

FROM: Patrick Conner, Office of Research Assurances (3005)

DATE: 12/12/2012

SUBJECT: Certification of Exemption, IRB Number 12883

Based on the Exemption Determination Application submitted for the study titled "Identifying Disease Characteristics, Parent Experience and Coping Strategies when Predicting Pediatric Illness-Related Stress in Parents of Children with Mitochondrial Disease," and assigned IRB # 12883, the WSU Office of Research Assurances has determined that the study satisfies the criteria for Exempt Research at 45 CFR 46.101(b)(2).

This study may be conducted according to the protocol described in the Application without further review by the IRB.

It is important to note that certification of exemption is NOT approval by the IRB. You may not include the statement that the WSU IRB has reviewed and approved the study for human subject participation. Remove all statements of IRB Approval and IRB contact information from study materials that will be disseminated to participants.

This certification is valid only for the study protocol as it was submitted to the ORA. Studies certified as Exempt are not subject to continuing review (this Certification does not expire). If any changes are made to the study protocol, you must submit the changes to the ORA for determination that the study remains Exempt before implementing the changes (The Request for Amendment form is available online at

http://www.irb.wsu.edu/documents/forms/rtf/Amendment_Request.rtf).

Exempt certification does NOT relieve the investigator from the responsibility of providing continuing attention to protection of human subjects participating in the study and adherence to ethical standards for research involving human participants.

In accordance with WSU Business Policies and Procedures Manual (BPPM), this Certification of Exemption, a copy of the Exemption Determination Application identified by this certification and all materials related to data collection, analysis or reporting must be retained by the Principal Investigator for THREE (3) years following completion of the project (BPPM 90.01). This retention schedule does not apply to audio or visual recordings of participants, which are to be erased, deleted or otherwise destroyed once all transcripts of the recordings are completed and verified.

You may view the current status or download copies of the Certified Application by going to https://myresearch.wsu.edu/IRB.aspx?HumanActivityID=36998

Washington State University is covered under Human Subjects Assurance Number FWA00002946 which is on file with the Office for Human Research Protections (OHRP).

Review Type: New

Review Category: Exempt

Date Received: 11/29/2012

Exemption Category: 45 CFR 46.101 (b)(2)

OGRD No.: N/A

Funding Agency: N/A

You have received this notification as you are referenced on a document within the MyResearch.wsu.edu system. You can change how you receive notifications by visiting

https://MyResearch.wsu.edu/MyPreferences.aspx

Please Note: This notification will not show other recipients as their notification preferences require separate delivery.

Appendix D: Permission for CHIP

Permission to Use Coping Health Inventory for Parents (CHIP)

From: hamilton mccubbin <hamiltonmccubbin@earthlink.net>□**Date:** May 15, 2012 5:31:01 PM PDT□**To:** <sengerb@gonzaga.edu>□**Cc:** "McCubbin, Laurie Dawn" <mccubbin@wsu.edu>, "Sievers, Jason Allen" <jasievers@wsu.edu>□**Subject: Chip information**

Dear Brenda Senger:□□To answer all of your questions - Yes to the measure, yes to directions, yes to reproduction and yes reliability and validity and a lot more. Let us know if we can help you.□□□

Hamilton I. McCubbin PhD□Professor □Myron B Thompson School of Social Work□University of Hawaii at Manoa□Honolulu, HI 96822□email: him@hawaii.edu Cell: 808-286-1724□□

Appendix E: Permission for PECI

Permission to Use Parent Experience of Childhood Illness (PECI)

From: Melanie Bonner, Ph.D. **Sent:** Tuesday, May 01, 2012 8:38 AM **To:** Senger, Brenda A **Cc:** Taryn Allen **Subject:** RE: PECI scale

Dear Brenda,

Happy for you to use the PECI. It is fine to reproduce in electronic format. My graduate student, Taryn Allen will send you a copy of the PECI and scoring information.

Best wishes and keep us posted on your results.

Best,

Melanie J. Bonner, PhD

Professor

Department of Psychiatry and Behavioral Sciences

919-681-0024

bonne002@mc.duke.edu

Appendix F: Permission for PIP

Permission to Use Pediatric Inventory for Parents (PIP)

Dear Colleague,

Thank you for your interest in the Pediatric Inventory for Parents. Included in this e-mail are the measure and scoring instructions. I grant you permission to use the measure in your work. Please keep me informed of any results as your work progresses, and feel free to contact me with any further questions.

In addition to the measure you will also find scoring instructions attached. Further, below are references from investigations that have included the PIP, in addition to the initial article from 2001*.

Best wishes on your research,

Randi Streisand, PhD, CDE

Diabetes Team Director of Psychology Research and Service

Children's National Medical Center

Associate Professor of Psychiatry and Pediatrics,

The George Washington University

(202) 884-2730

rstreis@cnmc.org

Appendix G: Demographic Survey

Mitochondrial Demographic Survey

Screening Questions:

1. Are you a parent (biological or non-biological) of a living child diagnosed with a "confirmed", "probable" or "possible" mitochondrial disease?
    a. Yes (continue survey)
    b. No (discontinue survey with a thank you note)

2. Have you or anyone in your house already completed this survey
    a. Yes (discontinue survey with a thank you note)
    b. No (continue survey)

3. Do you give your consent for taking this survey
    a. Yes, I consent (continue survey)
    b. No, I do not (discontinue survey with a thank you note)

Directions: Please answer the following demographic information about your household and about your child's mitochondrial disease.

A: This section includes information about your child(ren) with mitochondrial disease.

1. How many children younger than 18 years of age, living in your household have a "confirmed", "probable" or "possible" diagnosis of mitochondrial disease?
    a. One
    b. Two
    c. Three
    d. Four
    e. Five
    f. Six or more

If you have more than one child with a mitochondrial disease, please answer the following questions for the child who is the oldest.

2. What is the gender of the child with a mitochondrial disease?
    a. Male
    a. Female

2. What is the current age of the child with a mitochondrial disease?
    a. Drop down menu with options
        i. Under one year – 18 years

3. How old was your child when he or she began showing symptoms of a mitochondrial disease?
    a. Drop down menu with options

        i. Under one year -18 years
4. How old was your child when he or she was diagnosed with mitochondrial disease?
    a. Drop down menu with options
        i. Under one year – 18 years

5. Does your child have developmental delays?
    a. Yes
    b. No

6. If answered, "yes" to question 5, which areas of developmental delay are most affected? (check all that apply)
    a. Physical
    b. Intellectual/Cognitive
    c. Emotional
    d. Social
    e.
7. What type of mitochondrial disease best describes your child's illness?
    a. I do not know the name of my child's mitochondrial disease
    b. Alpers Disease (Progressive Infantile Poliodystrophy)
    c. Carnitine Deficiency
    d. Co-enzyme Q10 Deficiency
    e. Complex I, II, III, IV or V Deficiency
    f. CPEO (Chronic Progressive External Ophthalmoplegia Syndrome)
    g. DAD (Diabetes and Deafness)
    h. FAOD (Fatty Acid Oxidation Disorders)
    i. KSS (Kearns-Sayre Syndrome)
    j. Leigh's Disease or Syndrome
    k. LHON (Leber's Hereditary Optic Neuropathy)
    l. MELAS (Mitochondrial Encephalomyopathy, Lactic Acidosis and Strokelike Episodes)
    m. MEMSA (Myoclonic Epilepsy Myopathy Sensory Ataxia)
    n. MERRF (Myoclonic Epilepsy and Ragged-Red Fiber Disease)
    o. MIRAS (Mitochondrial Recessive Ataxia Syndrome)
    p. Mitochondrial Cytopathy
    q. Mitochondrial DNA Depletion
    r. MNGIE (Myoneurogastrointestinal Disorder and Encephalopathy)
    s. NARP (Neuropathy, Ataxia and Retinitis Pigmentosa)
    t. Pearson syndrome (Sideroblastic Anemia, Bone Marrow and Pancreatic Dysfunction)
    u. POLG Mutation (mtDNA mutation, but without characteristic clinical features)
    v. Pyruvate Deficiency
    w. Respiratory Chain Deficiency
    x. SCAD (Short Acyl-CoA Dehydrogenase Deficiency)
    y. VLCAD (Very Long Chain Aycl-CoA Dehydrogenase Deficiency)
    z. Other

8. For your child, please check ALL organ and systems that have been affected by your child's mitochondrial diagnosis (at this time).
    a. Brain/Neurological System (seizures, ataxia, MRI abnormalities)
    b. Gastrointestinal System (constipation, poor digestion, inability to eat by mouth or gain weight, slow motility)
    c. Hearing (loss of hearing)
    d. Heart and Cardiovascular System (abnormal heart rate, blood pressures, dizziness, poor circulation, pacemaker)
    e. Immunological System (susceptible to infection, chronic sickness)
    f. Liver (problems with liver, liver failure, abnormal liver enzymes)
    g. Mood and Depression Behaviors
    h. Muscle (weakness or pain)
    i. Digestive Organ Problems (pancreatic insufficiency, spleen enlargement, short gut syndrome)
    j. Renal (kidney issues, kidney failure)
    k. Respiratory System (difficulty breathing, shortness of breath)
    l. Skin (rashes, dermatologic issues)
    m. Vision (loss of eyesight, eye fatigue)
    n. Other problems not listed here

9. Please indicate the different types of specialists that you interact with regularly to support your child's health care needs
    a. Cardiologist
    b. Gastrointestinal
    c. Head Ears Eye Nose and Throat
    d. Home Health Care
    e. Hospice
    f. Neurologist
    g. Psychologist
    h. Occupational Therapy
    i. Pediatrician
    j. Physical Therapy
    k. Social Work Services
    l. Speech Therapy
    m. Other

10. Please estimate the number of medical (office) visits your child with mito has had over the past year
    a. 0
    b. 1-2
    c. 3-4
    d. 5-6
    e. 7-8
    f. 9-10
    g. 11-12

h. More than 12

11. Please indicate the number of hospitalizations your child with mito has had over the past year?
    a. 0
    b. 1-2
    c. 3-4
    d. 5-6
    e. 7-8
    f. 9-10
    g. 11-12
    h. More than 12

12. How long ago was the last hospitalization of your child with mito?
    a. My child has never been hospitalized for mitochondrial disease
    b. My child is currently in the hospital
    c. Past week
    d. Past month
    e. Past 3 months
    f. Past 6 months
    g. 1 year or longer

B: This section is information about the parent completing the survey.

13. What is your age in years?
    a. _____years

14. What is your relationship to the child with the mitochondrial disease?
    a. Adoptive father
    b. Adoptive mother
    c. Biological Father
    d. Biological Mother
    e. Step father
    f. Step mother
    g. Other

15. What is your current marital status?
    a. Single
    b. Married
    c. Living with another
    d. Divorced/separated
    e. Widowed
    f. Other

16. What is the highest level of education that you completed?
    a. Never attended school

b. Grades 1-6
c. Grades 7-12
d. 2 years college
e. 4 years college
f. Advanced Degree

17. Which of the following would you say is your ethnicity?
    a. Hispanic or Latino
    b. Not Hispanic or Latino

18. Which one of the following would say is your race?
    a. American Indian or Alaskan Native
    b. Asian
    c. Black or African American
    d. Native Hawaiian or Other Pacific Islander
    e. White

19. How many people in your immediate family are living in your household? (Include yourself, spouse/partner and children)
    a. _____

20. What is your annual household income per year in U.S. Dollars?
    a. Less than $19,999
    b. $20,000 - $39,999
    c. $40,000 - $59,999
    d. $60,000 - $79,999
    e. $80, 000 -$99,999
    f. $100,000- $119,999
    g. $120,000- $139,999
    h. $140,000- $199,999
    i. Greater than $200,000

Appendix H: PECI Scale

Parent Experience of Childhood Illness Scale (PECI)-Short Form ©

This questionnaire is concerned with thoughts and feeling related to parenting a child who is living with, or has experienced a chronic illness. Read each statement and then try to determine how well it describes your thoughts and feelings ***over the past month****.*

	NEVER	**RARELY**	**SOME-TIMES**	**OFTEN**	**ALWAYS**
1. It is painful for me to think about what my child might have been like had s/he never gotten sick.	0	1	2	3	4
2. I am at peace with the circumstanced of my life.	0	1	2	3	4
3. I feel guilty because my child became ill while I remain healthy.	0	1	2	3	4
4. I worry about my child's future.	0	1	2	3	4
5. I feel ready to face challenges related to my child's well being in the future.	0	1	2	3	4
6. I worry that I may be responsible for my child's illness in some way.	0	1	2	3	4
7. I worry that at any minute, things might take a turn for the worse.	0	1	2	3	4
8. I worry about whether my child will be able to live independently as an adult.	0	1	2	3	4
9. I have regrets about decisions I have made concerning my child's illness.	0	1	2	3	4
10. I think about whether or not my child will die.	0	1	2	3	4
11. I am aware of the specific ways I react to sadness and loss.	0	1	2	3	4
12. I experience angry feelings when I think about my child's illness.	0	1	2	3	4
13. I am afraid of this diagnosis occurring in another member of my immediate family.	0	1	2	3	4

14. I trust myself to mange the future, whatever happens	0	1	2	3	4
15. I find it hard to socialize with people who don't understand what being a parent to my child means.	0	1	2	3	4
16. When my child is playing actively, I find myself worried that s/he will get hurt.	0	1	2	3	4
17. I believe I will never be as completely happy or satisfied with my life as I was before my child became ill.	0	1	2	3	4
18. My hopes and dreams for my child's future are uncertain.	0	1	2	3	4
19. I am jealous of parents who have healthy children.	0	1	2	3	4
20. I worry that my child's illness will worsen/return.	0	1	2	3	4
21 Seeing healthy children doing everyday activities makes me feel sad.	0	1	2	3	4
22. I worry about something bad happening to my child when s/he is out of my care.	0	1	2	3	4
23. I can get help and support when I need it.	0	1	2	3	4
24. I wake up during the night and check on my child.	0	1	2	3	4
25. When I am not with my child, I find myself thinking about whether or not s/he is ok.	0	1	2	3	4

Appendix I: CHIP Scale

Coping Health Inventory for Parents (CHIP) Survey

To complete this inventory you are asked to read the list of "Coping Behaviors" below, one at a time. For each coping behavior you used. Please record how helpful it was to your and/or your family. For each coping behavior you did not use please record your "reason" by checking either "Chose not to use" it or "Not Possible".

	Extremely Helpful	**Moderately Helpful**	**Minimally Helpful**	**Not helpful**	**I do not cope this way because**	
Coping Behaviors					**Chose Not to**	**Not possible**
1. Talking over personal feelings and concerns with spouse.	3	2	1	0		
2. Engaging in relationships and friendships, which help me to feel important and appreciated.	3	2	1	0		
3. Trusting my spouse (or former spouse) to help support me and my child(ren).	3	2	1	0		
4. Sleeping	3	2	1	0		
5. Talking with the medical staff (nurses, social worker, etc.) when we visit the medical center.	3	2	1	0		
6. Believing that my child(ren) will get better.	3	2	1	0		
7. Working, outside employment.	3	2	1	0		
8. Showing that I am strong.	3	2	1	0		
9. Purchasing gifts for myself and/or other family members.	3	2	1	0		
10. Talking with other individuals/parents in my same situation.	3	2	1	0		
11. Taking good care of all the medical equipment at home.	3	2	1	0		
12. Eating	3	2	1	0		
13. Getting other members of the family to help me with chores and tasks at home.	3	2	1	0		
14. Getting away by myself.	3	2	1	0		
15. Talking with the doctor about my concerns about my child(ren) with the medical	3	2	1	0		

condition.						
16. Believing that the medical center/hospital has my family's best interest in mind.	3	2	1	0		
17. Building close relationships with people.	3	2	1	0		
18. Believing in God.	3	2	1	0		
19. Develop myself as a person.	3	2	1	0		
20. Talking with other parents in the same type of situation and learning about their experiences.	3	2	1	0		
21. Doing things together as a family (involving all members of the family).	3	2	1	0		
22. Investing time and energy in my job.	3	2	1	0		
23. Believing that my child is getting the best medical care possible.	3	2	1	0		
24. Entertaining friends in our home.	3	2	1	0		
25. Reading about how other persons in my situation handle things.	3	2	1	0		
26. Doing things with family relatives.	3	2	1	0		
27. Becoming more self reliant and independent.	3	2	1	0		
28. Telling myself that I have many things I should be thankful for.	3	2	1	0		
29. Concentrating on hobbies (art, music, jogging, etc.).	3	2	1	0		
30. Explaining family situations to friends and neighbors so they will understand us.	3	2	1	0		
31. Encouraging child(ren) with medical conditions to be more independent.	3	2	1	0		
32. Keeping myself in shape and well groomed.	3	2	1	0		
33. Involvement in social activities (parties, etc.) with friends.	3	2	1	0		
34. Going out with my spouse on a regular basis.	3	2	1	0		
35. Being sure prescribed medical treatments for child(ren) are carried out at home on a daily basis.	3	2	1	0		
36. Building a closer relationship with my spouse.	3	2	1	0		

37. Allowing myself to get angry.	3	2	1	0		
38. Investing myself in my child(ren).	3	2	1	0		
39. Talking to someone (not professional counselor/doctor) about how I feel.	3	2	1	0		
40. Reading more about the medical problem, which concerns me.	3	2	1	0		
41. Trying to maintain family stability.	3	2	1	0		
42. Being able to get away from the home care tasks and responsibilities for some relief.	3	2	1	0		
43. Having my child and the medical condition seen at the clinic/hospital on a regular basis.	3	2	1	0		
44. Believing that things will always work out.	3	2	1	0		
45. Doing things with my child(ren).	3	2	1	0		

Appendix J: PIP Scale

Pediatric Inventory for Parents (PIP)

Below is a list of difficult events which parents of children who have (or have had) a serious illness sometimes face. Please read each event carefully, and circle HOW OFTEN the event has occurred for you in the past 7 days and in the past 30 days, using the 5-point scale below. Afterwards, please rate how DIFFICULT it was/or generally is for you, also using the 5 point scale. Please complete both columns for each item.

EVENT	HOW OFTEN? 1=Never, 2=Rarely, 3=Sometimes, 4=Often, 5=Very often					HOW DIFFICULT? 1=Not at all, 2=A little, 3=Somewhat, 4=Very much, 5=Extremely					HOW OFTEN? 1=Never, 2=Rarely, 3=Sometimes, 4=Often, 5=Very often					HOW DIFFICULT? 1=Not at all, 2=A little, 3=Somewhat, 4=Very much, 5=Extremely				
1. Difficulty sleeping	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
2. Arguing with family member(s)	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
3. Bringing my child to the clinic or hospital	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
4. Learning upsetting news	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
5. Being unable to go to work/job	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
6. Seeing my child's mood change quickly	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
7. Speaking with doctor	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
8. Watching my child have trouble eating	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
9. Waiting for my child's test results	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
10. Having money/financial troubles	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
11. Trying not to think about my family's difficulties	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
12. Feeling confused about medical information	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
13. Being with my child during medical procedures	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
14. Knowing my child is hurting or in pain	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
15. Trying to attend to the needs of other family members	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
16. Seeing my child sad or	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5

EVENT	HOW OFTEN? 1=Never, 2=Rarely, 3=Sometimes, 4=Often, 5=Very often	HOW DIFFICULT? 1=Not at all, 2=A little, 3=Somewhat, 4=Very much, 5=Extremely	HOW OFTEN? 1=Never, 2=Rarely, 3=Sometimes, 4=Often, 5=Very often	HOW DIFFICULT? 1=Not at all, 2=A little, 3=Somewhat, 4=Very much, 5=Extremely
scared.....				
17. Talking with the nurse	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
18. Making decisions about medical care or medicines.....	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
19. Thinking about my child being isolated from others.....	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
20. Being far away from family and/or friends.....	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
21. Feeling numb inside.....	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
22. Disagreeing with a member of the health care team	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
23. Helping my child with his/her hygiene needs.....	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
24. Worrying about the long term impact of the illness.....	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
25. Having little time to take care of my own needs	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
26. Feeling helpless over my child's condition	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
27. Feeling misunderstood by family/friends as to the severity of my child's illness ...	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
28. Handling changes in my child's daily medical routines ..	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
29. Feeling uncertain about the future.....	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
30. Being in the hospital over weekends/holidays.....	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
31. Thinking about other children who have been seriously ill	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
32. Speaking with my child about his/her illness	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
33. Helping my child with medical procedures (e.g.	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5

EVENT	HOW OFTEN? 1=Never, 2=Rarely, 3=Sometimes, 4=Often, 5=Very often	HOW DIFFICULT? 1=Not at all, 2=A little, 3=Somewhat, 4=Very much, 5=Extremely	HOW OFTEN? 1=Never, 2=Rarely, 3=Sometimes, 4=Often, 5=Very often	HOW DIFFICULT? 1=Not at all, 2=A little, 3=Somewhat, 4=Very much, 5=Extremely
giving shots, swallowing medicine, changing dressing)...				
34. Having my heart beat fast, sweating, or feeling tingly.....	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
35. Feeling uncertain about disciplining my child	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
36. Feeling scared that my child could get very sick or die	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
37. Speaking with family members about my child's illness.....	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
38. Watching my child during medical visits/procedures.....	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
39. Missing important events in the lives of other family members	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
40. Worrying about how friends and relatives interact with my child.....	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
41. Noticing a change in my relationship with my partner	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
42. Spending a great deal of time in unfamiliar settings	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5