2017

Effects Of Maternal And Child Depressive Symptoms And Child'S Perceived Stress On Glycemic Control As Mediated By Cortisol In Prepubertal Children With Type 1 Diabetes

Sara Laubinger Davis
University of Alabama at Birmingham

EFFECTS OF MATERNAL AND CHILD DEPRESSIVE SYMPTOMS AND CHILD'S PERCEIVED STRESS ON GLYCEMIC CONTROL AS MEDIATED BY CORTISOL IN PREPUBERTAL CHILDREN WITH TYPE 1 DIABETES

by

SARA DAVIS

MARTI RICE, CHAIR
ANNE-MARIE KAULFERS
JOHN LOCHMAN
SHANNON MORRISON
ERICA PRYOR

A DISSERTATION

Submitted to the graduate faculty of The University of Alabama at Birmingham,
in partial fulfillment of the requirements for the degree of
Doctor of Philosophy

BIRMINGHAM, ALABAMA

2017

EFFECTS OF MATERNAL AND CHILD DEPRESSIVE SYMPTOMS AND CHILD'S PERCEIVED STRESS ON GLYCEMIC CONTROL AS MEDIATED BY CORTISOL IN PREPUBERTAL CHILDREN WITH TYPE 1 DIABETES

SARA DAVIS

NURSING

ABSTRACT

Introduction: Type 1 diabetes (T1D) is one of the most common diseases of childhood affecting over 167,000 children under the age of 20. Despite adequate insulin regimens and concurrent treatments, many children still have trouble achieving glycemic control as evidenced by elevated HbA1c levels. Previous research indicates that parent-child interactions and parental involvement in diabetic care influence glycemic control. However, these relationships may be impaired in mothers with depressive symptoms or in children who have high levels of depressive symptoms or perceived stress. Moreover, cortisol, a stress hormone, may mediate the proposed relationships. Therefore, the purpose of this study was to generate hypotheses on the relationships between maternal depressive symptoms, child depressive symptoms, child's perceived stress, cortisol, and glycemic control in prepubertal school-aged children diagnosed with T1D.

Methods: Recruitment occurred at a pediatric endocrinology clinic in the Southeast US using convenience sampling. Data collection occurred on the day of the child's routine endocrinology visit and included surveys completed by the mother and child, 2 salivary samples from the child collected 3 hours apart, and review of the medical record to obtain HbA1c, height, and weight.

Results: Thirty children and their mothers were enrolled in the study. Ages of children ranged from 6.9 to 12.2 years. Most children were female (70%), Caucasian

(76.7%), and socioeconomically diverse. HbA1c values ranged from 6.1% to 12.2%. Eighteen children showed normal declines in cortisol from morning to afternoon samples while twelve children had increases in cortisol. Using relevancy thresholds for effect sizes, several relationships between variables of interest may be clinically meaningful.

Conclusions: Results from the pilot study have shown recruitment, participation, and data collection in this specific population is feasible in school age children. As a pilot study, conclusions about the relationships between variables of interest cannot be made at this time. However, examination of effect sizes between variables of interest supports the need for future research in a larger, more representative sample, including the continued assessment cortisol may have as a mediator between maternal depressive symptoms, child depressive symptoms, child's perceived stress, and glycemic control.

Keywords: depressive symptoms, perceived stress, diabetes, glycemic control, cortisol, school-aged children

DEDICATION

I am forever grateful to by husband, Tyler, and my children, Nicholas and Evelyn. Because of your continued love and encouragement, this journey has been possible.

ACKNOWLEDGMENTS

I would like to thank my fellow LECHN peers who continue to be wonderful mentors and fuel my desire to excel as a nurse researcher. A special thanks to Dr. Marti Rice who has been a constant source of support and inspiration as I pursued this degree. Also, special thanks to my committee members for their countless hours providing feedback and answering questions along the way.

This dissertation study would not have been possible without the help of the wonderful staff and health care providers at the pediatric endocrinology clinic who always greeted me with a smile and supported me through screening, recruitment, and data collection. Many thanks for introducing me to such wonderful patients and families.

The completed coursework and dissertation study were supported from the Leadership Education in Child-health Nursing (LECHN) – Maternal Child Health Bureau (grant number T80MC09653, PI: A. Turner-Henson); and, Sigma Theta Tau Zeta Gamma Chapter – Mobile, AL. The contents of this dissertation are solely the responsibility of the author and do not necessarily represent the official views of the above-mentioned funding sources.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1

INTRODUCTION

Type 1 diabetes is an endocrine disorder in which the body fails to produce insulin (Centers for Disease Control and Prevention [CDC], 2015a). It is characterized by destruction of beta cells in the pancreas, severely diminished or absent insulin production, and elevated blood glucose levels (CDC, 2015a). Without the means to prevent or cure type 1 diabetes, treatment includes managing symptoms of type 1 diabetes by following a strict insulin regimen as well as dietary and lifestyle changes (CDC, 2015a). Although the exact cause of type 1 diabetes is unclear, there is belief that this disorder is autoimmune in origin (Piganelli, 2014). Type 1 diabetes, sometimes referred to as juvenile diabetes, is usually first seen in children and adolescents, with the average age of onset and diagnosis being 8.1 years old (CDC, 2015a, Pettitt et al., 2014).

Approximately 167,000 children under the age of 20 have type 1 diabetes, with non-Hispanic white children aged 10 to 19 years being the most likely to be diagnosed (American Diabetes Association [ADA], 2015c). Each year it is estimated an additional 18,000 children are newly diagnosed with type 1 diabetes (CDC, 2015a). In 2012, type 1 and type 2 diabetes accounted for $245 billion in direct and indirect medical expenditures and diabetes was the seventh leading cause of death in the United States (ADA, 2013). Short-term complications from diabetes include weight loss, fatigue, and diabetic ketoacidosis, while chronically uncontrolled diabetes results in cardiovascular disease,

nephropathy, and neuropathy (CDC, 2015a). Intensive insulin therapy to reduce blood glucose levels and maintain them within normal limits in patients with type 1 diabetes has been shown to decrease risk of and/or slow progression of diabetes-related retinopathy, neuropathy, nephropathy, and cardiovascular disease (Diabetes Control and Complications Trial [DCCT] Research Group, 1993; DCCT/Epidemiology of Diabetes Interventions and Complications [EDIC] Study Research Group, 2005). Moreover, patients with type 1 diabetes who use intensive insulin therapy and maintain blood glucose levels within normal limits have a lower overall risk of mortality associated with complications from diabetes such as cardiovascular disease or albuminuria (Orchard et al., 2015). Due to the devastating comorbidities associated with uncontrolled diabetes, as well as costs associated with medical expenditures, a goal of diabetes management is to maintain blood glucose levels within normal limits and prevent diabetes-associated complications. Maintenance of blood glucose levels within normal limits is known as glycemic control.

Glycemic control is a measurement of variability in blood glucose levels over a certain period of time. This variability may be related to the variation in blood glucose measurements within the same day (within-day variability) or between days within a specified time point (between-day variability) (Rodbard, 2009). A common measure of glycemic control is glycosylated hemoglobin (HbA1c). HbA1c measures blood glucose variability over the span of three months, with a threshold of 7.5% or greater signifying poor glycemic control in children of all ages (ADA, 2015b).

Despite adequate insulin regimen and concurrent medical treatments, many children still have difficulty achieving glycemic control as evidenced by chronically high

blood glucose levels and elevated HbA1c levels (ADA, 2015b). Recent literature has shown that psychological conditions, including depression and stress, alter neuroregulation of hormones and may induce physiological changes (Gold, 2015; McEwen & Tucker, 2011). This may be especially true for individuals already diagnosed with endocrine disorders like diabetes. Because of the prevalence of diabetes in children, as well as potential complications from uncontrolled diabetes, it is important to understand factors that influence glycemic control. Therefore, the study of potential factors that may inhibit a child from achieving glycemic control is warranted. Based on current research, these factors include maternal depressive symptoms, child depressive symptoms, and child's perceived stress.

Influences on Glycemic Control

Maternal Depressive Symptoms

Glycemic control in children with type 1 diabetes is improved when parents believe in the ability of their children to self-manage their diabetes (Butler et al., 2009). While school-aged children and early adolescents undergo transitions to master skills and promote independence, success in these fields is dependent upon parental support (Davies, 2011). Parental support, through helping the child learn diabetes management and promoting self-care, results in higher self-efficacy in the child and leads to better glycemic control (Butler et al., 2009). Regardless of disease status, parental support may be impaired in mothers who demonstrate high levels of depressive symptoms (Heneghan et al., 2000). The lack of parental support may lead to an impaired mother-child relationship.

The mother-child relationship is profoundly impacted by the expression of maternal depressive symptoms. Maternal depressive symptoms include guilt, negativity, worthlessness, pessimism, and resentment evidenced by behavioral symptoms of depressed mood, social withdrawal, anger, irritability, and crying (Blankfeld & Holahan, 1996; Essex et al., 2011). Maternal depressive symptoms specific to motherhood may be seen with deficits in sensitivity, attunement, and communication towards offspring (Essex et al., 2011). Further, maternal depressive symptoms can result in negative, intrusive parent-child interactions lacking in support, unrealistic expectations of child development, and impaired childrearing (Heneghan et al., 2000).

Mothers' experiences of depressive symptoms may interfere with their ability to care for their diabetic children, which may negatively impact glycemic control (Butwicka, Zalepa, Fendler, Szadkoska, & Mlynarski, 2013). Further, it has been noted that high maternal depressive symptoms correlate with poor disease management and altered metabolic control in children with type 1 diabetes (Rumberg, Lord, Savin, & Jaser, 2017; Wiebe et al., 2011). High maternal depressive symptoms may also impact the child's mental state (Jaser et al., 2008). For example, Jaser and colleagues (2008) found that high levels of depressive symptoms in mothers were associated with high levels of depressive symptoms in school-aged children diagnosed with type 1 diabetes. Moreover, children with greater depressive symptoms exhibit worse glycemic control in comparison to children without depression (Lawrence et al., 2006; McGrady & Hood, 2010).

Child Depressive Symptoms

Associations have been noted between depressive symptoms in children with type 1 diabetes, impaired diabetes management, and poor glycemic control (de Wit et al., 2007; Helgeson, Siminerio, Escobar, & Becker, 2009; Hood et al., 2006; Kongkaew, Jampachaisri, Chaturongkul, & Scholfield, 2013; Korbel, Wiebe, Berg, & Palmer, 2007; McGrady & Hood, 2010). Depressive symptoms in school age children with and without diabetes may be evidenced by sadness, difficulty concentrating, change in grades, loss of energy, acting out or getting in trouble, mood swings, anger and irritability, and suicidal ideation (Anxiety and Depression Association of America, 2016). It is estimated that approximately 15% of children and adolescents diagnosed with type 1 diabetes exhibit depressive symptoms in comparison to 3% of children age 6 to 12 years and 8% of adolescents without diabetes (Anxiety and Depression Association of America, 2016; Hood et al., 2006). It is unclear why children with type 1 diabetes demonstrate higher rates of depression in comparison to their healthy peers; however, it is likely that the additional burdens associated with management of the disease play a significant role (Markowitz, Volkening, Butler, & Laffel, 2015). Regardless, depressive symptoms in children may impair the child's ability to perform self-care related to diabetes management and achieve glycemic control (Hood et al., 2006).

In children, depressive symptoms may negatively impact glycemic control through poor adherence to treatment regimen (Kongkaew, Jampachaisri, Chaturongkul, & Scholfield, 2013). This may be because depressive symptoms, such as difficulty concentrating, loss of energy, or lack of self-esteem, prevent the child from actively participating in the treatment regimen (Markowitz, Volkening, Butler, & Laffel, 2015).

Failure to effectively manage diabetes leads to poor glycemic control, and thus, increases the risk of diabetic ketoacidosis and recurrent hospital admissions (Hood et al., 2006). In adults with type 1 diabetes, depressive symptoms and poor glycemic control are associated with increased incidence of diabetes-associated complications such as stroke, end stage renal disease, and blindness (Ducat, Rubenstein, Philipson, & Anderson, 2015).

Child's Perceived Stress

A child's perceived stress may also be associated with glycemic control (Berlin, Rabideauu, & Hains, 2012; Delamater, Patino-Fernandez, Smith, & Bubb, 2013; Farrell, Hains, Davies, Smith, & Parton, 2004; Worrall-Davies, Holland, Berg, & Goodyer, 1999). Stress is commonly measured as an individual's capacity to handle and resolve challenges (Terzian et al., 2010). Charmandari, Acherman, Carel, Soder, and Chrousos (2012) define stress as "a state of real or perceived threat to homeostasis" (p. 1). Perceived stress is an emotional response in which a person believes that the demands of an external situation are beyond his or her ability to control or cope (Caputo, Gill, Tseh, Jamurtas, & Morgan, 2000; Lazarus, 1990). Children and adolescents may perceive stress from various daily interactions including parental arguments, responsibility of caring for a sibling or parent, neighborhood crime, changing schools, or being a victim of bullying (Terzian et al., 2010). Therefore, child's perceived stress is any stressful event, tangible or intangible, that is relatable to childhood and results in the child feeling threatened, overwhelmed, and/or unable to cope with the demands of the event.

Perceived stress in school age children may result in negative emotional health such as depression, anxiety, and fatigue (Early, Cushway, & Cassidy, 2006; Yarcheski,

Mahon, Yarcheski, & Hanks, 2010). Moreover, children with high levels of perceived stress are more likely to report increased depressive symptoms (Willemen, Koot, Ferdinand, Goossens, & Schuengel, 2008). Physiological changes, such as pain, chronic inflammation, altered metabolic control, and hypertension, have also been associated with perceived stress (Chrousous, 2000; Gold, 2015; Varni et al., 1996**)**. Specifically, children with diabetes and higher levels of stress are more likely to have poorer glycemic control with increased HbA1c levels (Berlin et al., 2012; Worrall-Davies et al., 1999).

Cortisol

One stress hormone, cortisol, is directly related to elevated blood glucose levels in adults and children with diabetes (Marcovecchio & Chiarelli, 2012; Mosbah, Abd-Ellatif, & Sorour, 2011). Cortisol is the primary hormone of the HPA axis---a stress-sensitive neurobiological system that is involved in attention and emotional regulation (McEwen, 1998; McEwen, 2007). While cortisol levels in children without diabetes are associated with maternal depressive symptoms, the relationship between cortisol and depressive symptoms in school age children with type 1 diabetes has not been well studied (Ashman, Dawson, Panagiotides, Yamada, & Wilkinson, 2002; Stewart, Mazurka, Bond, Wynne-Edwards, & Harkness, 2013). Moreover, studies examining the relationship between cortisol and perceived stress in school age children are limited (Chorous & Kino, 2007; Gold, 2015; Maldonado et al., 2008). In addition, no studies have examined cortisol change, determined by the natural rise and fall of cortisol levels throughout the day, as a mediator between maternal depressive symptoms, child depressive symptoms, child's perceived stress and glycemic control in children with type 1 diabetes.

Maternal Depressive Symptoms and Cortisol

Children without diabetes who live with depressed mothers demonstrate abnormal cortisol levels with either elevations or blunting in cortisol rhythm and response noted (Ashman et al., 2002; Lupien, King, Meaney, and McEwen, 2000). Blunted cortisol levels in response to acute stressors were found in children of mothers with chronically elevated depressive symptoms (Fernald, Burke, & Gunnar, 2008; Gump et al., 2009). Relatedly, abnormally high morning cortisol levels (basal cortisol) were seen in children whose mothers exhibited high depressive symptomology (Lupien et al., 2000). In addition, the child's physiological stress response, as evidenced by acute serum cortisol fluctuations, appears greater in children from low socioeconomic families (Fernald et al., 2008; Lupien et al., 2000). These abnormal fluctuations in cortisol appear to be dependent upon the age of the child with younger children more likely to have elevated cortisol levels and older children more likely to experience blunted cortisol levels (Essex et al., 2011). Similar findings related to abnormal cortisol have been found in children with depressive symptoms (Stewart et al., 2013; Suzuki, Belden, Spitznagel, Dietrick, & Luby, 2013).

Child Depressive Symptoms and Cortisol

Though not well studied, there appears to be a relationship between child depressive symptoms and cortisol levels in children. Depressed children and adolescents have shown blunted cortisol in response to stressors (Stewart et al., 2013; Suzuki et al., 2013). However, these studies tend to focus on cortisol reactivity in response to an acute

stressor rather than diurnal pattern of cortisol and chronic stress (Stewart et al., 2013; Suzuki et al., 2013). Regardless, the abnormal levels of cortisol may indicate underlying pathology and damage to the HPA axis in response to chronic stress, evidenced by the inability of the child to mount a stress response or over-reactivity of the stress response (McEwen, 2000; McEwen, 2007). In addition to depressive symptoms, perceived stress experienced by the child may also lead to abnormal changes in cortisol levels.

Child's Perceived Stress and Cortisol

Significant physiological changes are noted in individuals with high levels of perceived stress (Chrousos & Kino, 2007; Gold, 2015). Perceived stress may stem from chronic social conditions such as (but not limited to) poverty, physical illness, parental divorce, and/or loss of a friend (Chrousos & Kino, 2007; Gold, 2015). This perceived stress has the ability to activate pyramidal neurons in the HPA axis through mediation of stress hormones including glucocorticoids and catecholamines (McEwen, 2000; McEwen, 2007) and may result in inflammatory processes and impaired hormonal regulation (Chrousos & Kino, 2007; Gold, 2015). During times of perceived stress, four types of physiologic responses are noted (Gold, 2015). Specifically, metabolic, hormonal, and neurotransmitter responses stimulate the release of cortisol (Gold, 2015). Most researchers measure the relationship between psychological stress and cortisol response using acute social stressors to stimulate emotional stress rather than measuring perceived stress in children (Armbruster, Mueller, Strobel, Lesch, Brocke & Kirschbaum, 2012; Bae et al., 2015). However, these researchers have found associations between emotional

stress and cortisol levels in children both in response to acute social stressors and daily stress perception (Armbruster et al., 2012; Bae et al., 2015; Maldonado et al., 2008).

Cortisol and Glycemic Control

Associations between cortisol and glycemic control may be perpetuated by maternal depressive symptoms, child depressive symptoms, and child's perceived stress. While maternal depressive symptoms, child's perceived stress, and child depressive symptoms negatively impact glycemic control in children with type 1 diabetes, the precise mechanism of how decreased psychological health influences glycemic control is unclear. There is evidence that depression and stress may trigger a physiological stress response in the child through activation of pyramidal neurons in the HPA axis, which then may alter physiological processes and stimulate cortisol release in the body (Gold, 2015; McEwen, 2000; McEwen, 2007). These abnormal changes in cortisol may directly influence glycemic control in children (Forshee et al., 2010; Mosbah et al., 2011, & Trast, 2014). As a stress hormone, cortisol stimulates the liver to cause gluconeogenesis (formation of glucose from non-carbohydrate sources) with a resultant increase in blood glucose (Forshee et al., 2010). The physiological response between abnormally high plasma cortisol levels and increased blood glucose may then lead to poor glycemic control in children with type 1 diabetes (Mosbah et al., 2011). Therefore, cortisol levels in the child with type 1 diabetes may be a proxy measure of the mediating stress response between maternal depressive symptoms, child depressive symptoms, child's perceived stress and glycemic control. In addition to cortisol, there are confounding factors that

influence glycemic control in children. Among these are: puberty, insulin therapy, time-since-diagnosis, ethnicity, and SES.

Confounding Factors

Puberty negatively impacts glycemic control in children diagnosed with type 1 diabetes (Trast, 2014). This relationship is thought to be the result of normal physiologic increases in insulin resistance observed during puberty (Hannon, Janosky, & Arlanian, 2006). Medical regimen, such as type of insulin therapy (i.e., pump versus daily injections), also affects glycemic control in children with type 1 diabetes. Children with type 1 diabetes prescribed continuous subcutaneous insulin infusion, also known as pump therapy, have lower HbA1c levels compared to children receiving multiple daily injections (Fendler, Baranowska, Mianowska, Szadkowska, & Mlyarski, 2011; Paris et al., 2009; Springer et al., 2006). There is also evidence that time-since-diagnosis is a confounding factor on glycemic control in children with type 1 diabetes (Abdul-Rasoul, Habib, & Al-Khouly, 2006; Springer et al., 2006). During the first year after a child's type 1 diabetes diagnosis, glycemic control demonstrates wide variability due to incomplete destruction of pancreatic beta cells and decreased compliance with new medical regimen (Abdul-Rasoul et al., 2006). Lastly, ethnicity and socioeconomic status (SES) are confounding factors on glycemic control in children with type 1 diabetes. Both African American and Hispanic children have worse glycemic control evidenced by higher HbA1c levels and/or higher blood glucose levels than Caucasian children with type 1 diabetes (Auslander, Thompson, Dreitzer, White, & Santiago, 1997; Davis et al., 2001; Delmater et al. 1999; Gallegos-Macias, Macias, Kaufaman, Skipper, and

Kalishman, 2003). Moreover, poor glycemic control is exacerbated in minority children without access to health insurance and from low SES backgrounds (Davis et al., 2001; Delmater et al. 1999; Gallegos-Macias et al., 2003)

Purpose of the Study

Researchers have examined correlations between maternal depressive symptoms, child's perceived stress, child depressive symptoms, child's cortisol levels, and glycemic control independently (Hood et al., 2006; Jaser et al., 2008; Lupien et al., 2000; Markowitz et al., 2015; Stewart et al., 2013; Wiebe et al., 2011; Worrall-Davies et al., 1999), but not concurrently. Additionally, the mechanism of HPA axis dysfunction, evidenced by abnormal changes in cortisol, as a mediator between these psychological factors and glycemic control has not been well studied. Moreover, there is insufficient evidence detailing the influence of maternal depressive symptoms, child depressive symptoms, and child's perceived stress on glycemic control in children younger than 12 years of age diagnosed with type 1 diabetes. Therefore, the purpose of the proposed pilot study was to generate hypotheses on the relationships between maternal depressive symptoms, child depressive symptoms, child's perceived stress, cortisol, and glycemic control in prepubertal school-aged children 7 to 12 years of age diagnosed with type 1 diabetes, as well as to establish effects sizes of influence between variables for a future, fully-powered study.

Conceptual Framework

Associations have been noted between maternal depressive symptoms, child depressive symptoms, child's perceived stress and glycemic control (Hood et al., 2006; Jaser et al., 2008; Wiebe et al., 2011; Worrall-Davies et al., 1999). The pathway between psychological concepts and pathological changes, such as poor glycemic management, may be related to alterations in stress hormones such as cortisol (Marcovecchio & Chiarelli, 2012; McEwen, 1998; McEwen, 2007). While a single theory was unable to guide this study, the combination of two theories, Neuman's Systems Model (Neuman, 1995) and McEwen's Model of Allostasis and Allostatic Load (McEwen, 1998; McEwen, 2007), along with the physiological underpinnings of the HPA axis, may more accurately support the intended research and reflect the proposed conceptual framework.

The conceptual framework in the current study (see Figure 1.1) uses the principles of Neuman's systems theory to connect maternal depressive and child depressive symptoms with glycemic control. Neuman's systems theory (see Appendix A) is a wholistic [sic] model of homeostasis and balance that is both philosophical and biological in nature (Neuman, 1995). Health is presented as a dynamic and ever-changing continuum between wellness and illness (McEwen & Willis, 2002; Neuman, 1995). When studying the effects of maternal depressive symptoms, child depressive symptoms, and child's perceived stress on glycemic control, and the mediational effects of HPA axis dysfunction evidenced by change in cortisol, maternal depressive symptoms may be classified as an environmental variable that alters a child's homeostasis and causes stress within the child (Neuman, 1995).

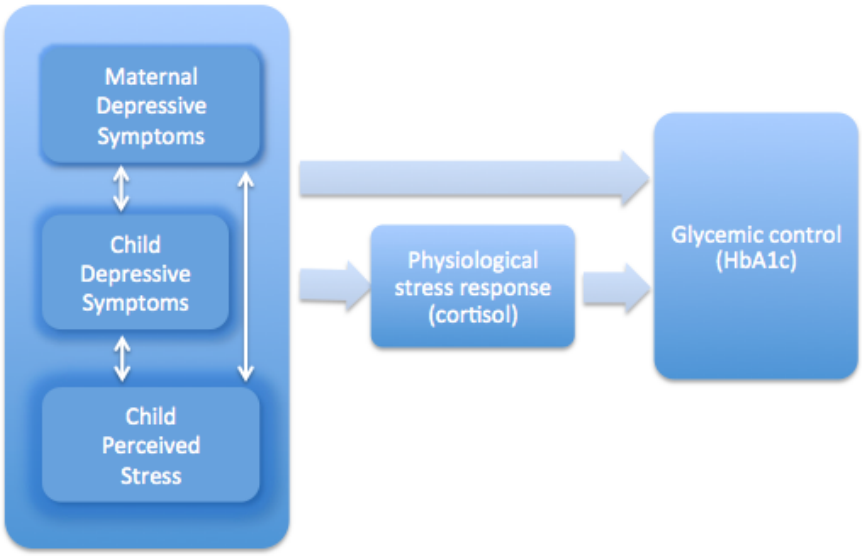


Figure 1.1. Proposed conceptual diagram

Applying Neuman's theory to the current study, the child with diabetes is thought to contain two lines of defense, the flexible and normal line of defense, that protect the child from environmental stressors, such as maternal depressive symptoms (Neuman, 1995). Stressors must first break the flexible line of defense, which act as a buffer system, before they break the normal line of defense (Meleis, 2012). When the flexible line of defense is crossed and the normal line of defense is broken by stressors, the internal homeostatic system of the child is disrupted and the child is thrown into a state of chaos (Neuman, 1995). The child's state of wellness is determined by his or her ability to rebound from the break in the lines of defense and return to a state of homeostasis using internal lines of resistance (Neuman, 1995). The child may then have to rely on the lines of resistance, such as coping mechanisms, to help the child reestablish homeostasis (Freese et al., 1998). If the child is unable to maintain homeostasis and experiences chaos in one domain, then he or she may experience disruptions in another of the five domains:

physiological, psychological, sociocultural, developmental, and spiritual (Freese et al., 1998; McEwen & Willis, 2002; Neuman, 1995). High levels of maternal depressive symptoms may break the normal and flexible lines of defense in the child and the child may experience deficits in the psychological or physiological domains evidenced by depressive and/or stress symptoms in the psychological domain and/or abnormal glycemic control in the physiological domain. Moreover, child depressive symptoms may interfere with the child's coping mechanisms, and inhibit the child's return to homeostasis. The state of dysregulation presented in Neuman's system model may be compared to McEwen's model of allostasis and allostatic load when examining child's perceived stress.

In a predominately physiological model that links the autonomic and adrenocortical systems (see Appendix A), McEwen's model utilizes three main concepts: stress, allostasis, and allostatic load (McEwen, 2000). The term allostasis, introduced by Sterling and Eyer (1988), refers to daily processes during which the body actively responds to changes and maintains homeostasis (McEwen, 2007). Allostatic load is wear and tear caused by chronic stress that leads to pathophysiology within the body and inability of the body to maintain homeostasis (McEwen, 2007). McEwen notes that there are good and bad stressors, both of which activate pyramidal neurons in the HPA axis through mediation of stress hormones including glucocorticoids and catecholamines (McEwen, 2000; McEwen, 2007). To better apply McEwen's model of stress and allostasis and more thorough understanding of the HPA axis is necessary.

The HPA axis is comprised of the hypothalamus, pituitary and adrenal glands (Brasher & Jones, 2010). HPA axis activity is evidenced by levels of its primary

hormone, cortisol (Essex et al., 2011; Koss et al., 2012; McEwen, 2000). Through positive and negative feedback loops, cortisol is regulated in the blood with high levels of cortisol inhibiting ACTH secretion and low levels of cortisol stimulating ACTH secretion (Brasher & Jones, 2010; Chrousos & Kino, 2007). As a homeostatic system, continued stimulation of the hypothalamus from physiological stress leads to continued secretion of cortisol, increased basal levels of cortisol, and disappearance of the normal diurnal pattern of cortisol (Chrousos & Kino, 2007). When the system is unable to terminate the stress response, chronically high levels of cortisol represent HPA dysregulation (McEwen & Tucker, 2011). Relatedly, abnormally low levels of cortisol may represent alterations in the physiologic stress response because the HPA axis is unable to mount any response to a stressor due to burn out from over-activation of the system (McEwen & Tucker, 2011). In children, the normal diurnal rhythm is demonstrated by levels of cortisol that peak in the morning and gradually decline the rest of the day; if the child naps in the early afternoon, there is an anticipated peak in cortisol levels in the early afternoon (Clements, 2013). The absence of normal diurnal patterns in children may be evidenced by abnormal changes in cortisol levels or failure to see a decline in cortisol levels from morning to late morning or early afternoon levels (Aguilera, 2011). Both McEwen's model and a physiological understanding of the HPA axis are used to explain the relationship between child's perceived stress, cortisol, and glycemic control.

In McEwen's model of stress and allostasis, perceived stress leads to allostatic load in the child both through behavioral response moderators and physiological responses (McEwen & Tucker, 2011). If the child experiences chronic perceived stress that is not identified and treated properly, the child may experience loss of circadian

rhythm with abnormal change in cortisol levels. This abnormal response is the child entering a state of allostatic load and HPA axis dysfunction (McEwen, 2000). Prolonged exposure to stress leads to adrenal over-activity, continued activation of stress hormones, and inability of the body to terminate the stress response (McEwen, 2000; McEwen, 2007). Failure to habituate to the same stressor leads to abnormal levels of cortisol, and inappropriate circadian changes in cortisol in children, because the stressor continues to activate the HPA axis despite negative feedback (McEwen & Tucker, 2011). HPA axis dysregulation may then be evidenced by abnormal changes in cortisol levels within the child (McEwen, 2007). If the body is unable to resume allostasis, the body then enters a state of allostatic load during which continued activation of the stress response eventually leads to the atrophy and death of pyramidal neurons in the hippocampus (McEwen, 2000). This may then lead to physiological changes, such as chronically high blood sugar levels, in response to chronically elevated or abnormal cortisol levels (Forshee et al., 2010; Mosbah et al. 2011). Similarly, there is some evidence that low and blunted cortisol levels are associated with lower plasma glucose levels (Sprague & Arbelaez, 2011). While this may increase the risk of hypoglycemia, low cortisol levels do not appear to hinder the patient's ability to self-correct a hypoglycemic crisis (Sprague & Arbelaez, 2011).

In summary, Neuman's systems theory helps to explain how psychological stressors may adversely affect the physiological domain of the child, as evidenced by the inability of the child to maintain glycemic control when confronted with chronic maternal depressive symptoms. Moreover, the child may also experience depressive symptoms in relation to maternal depressive symptoms, thus inhibiting his or her ability to cope and

maintain homeostasis in the presence of the chronic stressor. The physiological response may then be explained by disruption in the HPA axis and allostatic load. Failure to terminate chronic stressors, such as depressive symptoms and perceived stress, results in HPA dysregulation and abnormal changes in cortisol. As a stress hormone, cortisol plays a direct role in blood glucose regulation, and thus may serve as a mediator between chronic stressor and the outcome variable of glycemic control. Using the supporting theoretical frameworks, maternal depressive symptoms, child's perceived stress, and child depressive symptoms may directly impact the HPA axis (Gump et al., 2009; Romeo & McEwen, 2007) and influence glycemic control in diabetic children (Jaser et al., 2008). Since the relationships between these variables, especially ones using cortisol as a mediator, have not been well studied, a pilot study determining effect sizes to generate hypotheses is warranted.

Research Questions

R1. What are the effect sizes of the relationships between maternal depressive symptoms and child's perceived stress, maternal depressive symptoms and child depressive symptoms, and child's perceived stress and child depressive symptoms?

R2. What are the effect sizes of the influence of maternal depressive symptoms, child depressive symptoms, or child's perceived stress on child's glycemic control?

R3. What amount of the total effect of maternal depressive symptoms, child depressive symptoms, and child's perceived stress on glycemic control is accounted for by the mediated effect of cortisol?

R4. What are the effect sizes of the relationships between time-since-diagnosis, treatment modality, ethnicity, and SES and glycemic control?

Significance of the Study

Because of the devastating effects of uncontrolled type 1 diabetes mellitus on health and systemic well-being, an objective of Health People 2020 is improving glycemic control in people diagnosed with diabetes (US Department of Health and Human Services, 2013). Key to improving glycemic control, and thus reducing comorbidities, is an understanding of factors that contribute to poor glycemic control in various patients and age groups. In this study the investigator examined the relationships between child's depressive symptomatology and perceived level of stress and mother's depressive state while assessing associations with child's glycemic control. Additionally, the mediating role of the physiological stress response (dictated by HPA axis function and change in cortisol levels) between maternal depressive symptoms, child depressive symptoms, child's perceived stress, and child's glycemic control in prepubertal children with diabetes 7 to 12 years old was addressed. The use of cortisol as a biomarker in research to objectively measure physiological stress response in children is invaluable to the understanding of HPA axis function and stress response in children. The results of the study may inform researchers of alternative factors affecting glycemic control in type 1 diabetic children. Identification of such factors may lead researchers to formulate social and behavioral interventions that increase glycemic control and promote disease management in children with type 1 diabetes mellitus.

Assumptions

1. Health and well-being of the child are impacted by maternal characteristics.
2. Children are able to self-identify stressful events that occur daily.
3. Depressive symptoms, perceived stress and cortisol levels can be measured in 7 to 12 year old children.
4. Perceived stress affects physical health and well-being.

Summary

The purpose of the research study was to examine factors that may influence glycemic control and determine the effect size of the relationships between the proposed psychological concepts, cortisol, and glycemic control. Maternal depressive symptoms, child's depressive symptoms, and child's perceived stress may influence metabolic control when mediated by cortisol; however, further research is needed to examine effect sizes between variables, especially using cortisol as a mediator, to determine if relationships are clinically meaningful. McEwen's and Neuman's models, as well as the physiological underpinnings of the HPA axis, were used to explain and clarify the interactions between the concepts of maternal depressive symptoms, child's depressive symptoms, child's perceived stress, HPA dysfunction and cortisol levels, and child's glycemic control.

CHAPTER 2

LITERATURE REVIEW

The purpose of this study is to generate hypotheses on the relationships between maternal depressive symptoms, child depressive symptoms, child's perceived stress, cortisol, and glycemic control in prepubertal school-aged children 7 to 12 years of age diagnosed with type 1 diabetes. In the following literature review, research related to associations between maternal depressive symptoms, child depressive symptoms, child's perceived stress and child's glycemic control, as well as the mediating role cortisol may play in the relationships is examined and critiqued. Literature to examine confounding factors on glycemic control, including: puberty, time-since-diagnosis, treatment modality, SES, and ethnicity is also reviewed. Although the literature contains research on the main concepts in a variety of ages and populations, the primary focus of the review is research with children aged 6 to 12 years with type 1 diabetes.

Sources from professional and national organizations dedicated to the study, treatment, and prevention of diabetes, such as the Centers for Disease Control and Prevention and the American Diabetes Association, were screened for relevant literature. Additionally, the following terms were used in various combinations to search PubMed, CINAHL, and PsycINFO: "maternal depressive symptoms AND/OR maternal depression", "mother", "cortisol", "pediatric", "glycemic control", "HbA1c", "child", "school age", "stress", "perceived OR emotional", "type 1 diabetes", "diabetes",

"diabetes mellitus", and "HPA AND/OR hypothalamic pituitary adrenal axis" (see Figure 2.1). Articles were filtered to include human studies written in English. Additionally, literature was excluded if it did not pertain to children age 6 to 12 years with diabetes. If literature could not be found on children ages 6 to 12 years with diabetes, then the review was widened to include all children with diabetes. If literature was still not available, then literature from healthy children age 6 to 12 years was reviewed, followed by literature on children of all ages, and finally literature in the adult population. The following review will address glycemic control and the relationship with maternal depressive symptoms, child depressive symptoms, and child's perceived stress. Then it will highlight cortisol as a mediator and cortisol's relationship with maternal depressive symptoms, child depressive symptoms, and child's perceived stress.

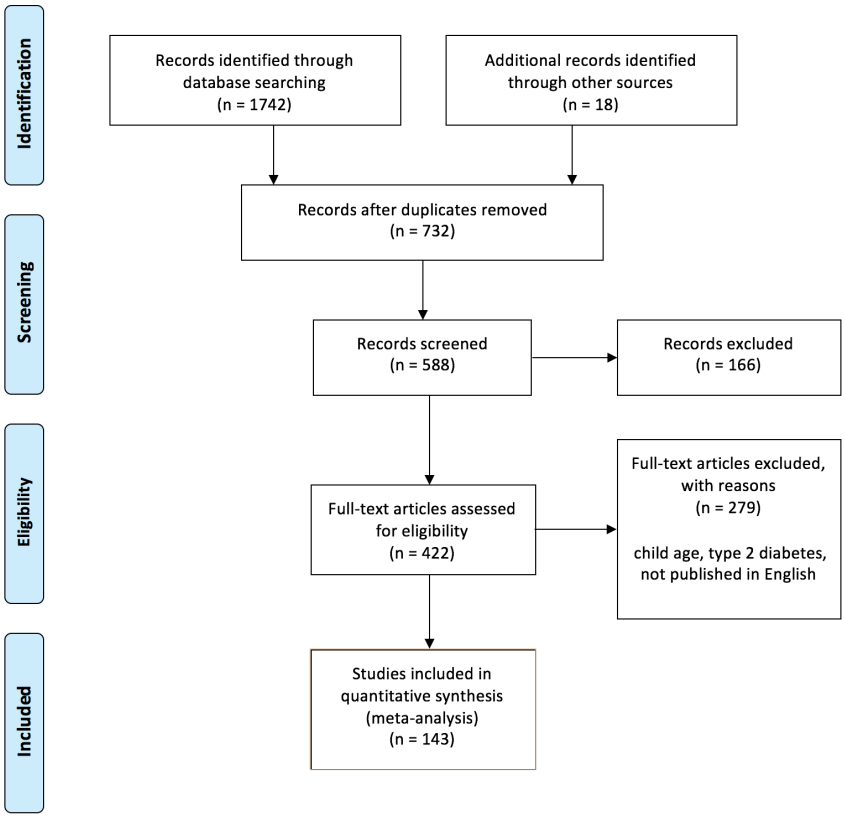


Figure 2.1. PRISMA diagram for literature review

Type 1 Diabetes

Of the 1.25 million people diagnosed with type 1 diabetes in the United States, over 200,000 are children under the age of 20 (ADA, 2015b). Maahs, West, Lawrence, and Mayer-Davis (2010) report that 1 in 300 children in the United States under the age of 18 have a diagnosis of type 1 diabetes and approximately 18,000 children are newly diagnosed with type 1 diabetes annually (ADA, 2015b). Overall, rates of type 1 diabetes in the Unites States are slightly higher in females and highest in non-Hispanic Caucasians compared to other race and ethnicities; however, it appears that among children, both girls and boys are equally affected (Maahs et al., 2010). Incidence of type 1 diabetes

diagnosis peaks between 5 and 14 years of age and declines after puberty (Maahs et al., 2010). Among children diagnosed with diabetes, almost all children under 10 years of age are diagnosed with type 1 diabetes, whereas children ages 10 to 19 years are more likely to be diagnosed with type 2 diabetes (Maahs et al., 2010).

In the United States, both type 1 and type 2 diabetes account for $245 billion in total cost with $176 billion spent on direct medical cost; it is estimated that medical expenses for individuals with diabetes is 2.3 times more than individuals without diabetes (ADA, 2013). Uncontrolled diabetes with chronically elevated blood glucose levels can result in various complications including, but not limited to, nephropathy, neuropathy, stroke, hypertension, and diabetic ketoacidosis (ADA, 2015a). To evaluate whether a patient's treatment plan is effective in controlling diabetes, clinicians monitor glycemic control (Rodbard, 2009).

Glycemic Control

Glycemic control is the variability of blood glucose levels over a defined period of time (Rodbard, 2009). For the purposes of this review, HbA1c will serve as the primary measure of glycemic control and terminology will be used interchangeably. Severity of type 1 diabetes and the prediction of unfavorable health outcomes associated with diabetes is often measured by HbA1c values (ADA, 2015a). While other methods to monitor and diagnose diabetes include Fasting Plasma Glucose and 2-hour Plasma Glucose test, the HbA1c value is often used since it has greater convenience for sample collection and shows less day-to-day variability (ADA, 2015a). HbA1c values of 5.7% to 6.4% indicate pre-diabetes or moderate control of diabetes and values greater than 6.5%

confirm diabetes diagnosis or indicate increased non-compliance of diabetes management (ADPH, 2010). Once diagnosed, target values for glycemic control, when measured by HbA1c values, vary by age. Regardless of confounding factors, the targeted HbA1c value for children age 7 to 12 years with type 1 diabetes is less than 7.5 % (ADA, 2015a).

HbA1c is directly associated with blood glucose levels (Gallagher, Le Roith, & Bloomgarden, 2009). During periods of hyperglycemia, glucose readily passes through the cell membrane and attaches to hemoglobin within the erythrocyte (Gallagher et al., 2009). Glycosylated hemoglobin is the complex formed by a two-step Maillard reaction when glucose attaches to the hemoglobin molecule at the N-terminal valine on the beta chain (Gallagher et al., 2009). The initial bond between the hemoglobin and glucose molecule is nonenzymatic and forms an aldamine (Schiff base) which is reversible (Gallagher et al., 2009). However, the aldamine rearranges to form a ketamine. The ketamine is known as HbA1c and once formed these glucose attachments are maintained for the life of the erythrocyte, approximately 106 to 117 days (Gallagher et al., 2009). As plasma glucose concentrations increase, more glucose molecules are readily available to cross the erythrocyte membrane and attach to hemoglobin. Therefore, HbA1c directly increases as a result of increased plasma glucose (Gallagher et al., 2009).

Influences on Glycemic Control

Maternal Depressive Symptoms and Glycemic Control

The relationship between maternal depressive symptoms and glycemic control is important to understand as researchers theorize high depressive symptomatology in mothers may interfere with their ability to help manage diabetes and lead to worse

glycemic control (Blankfeld & Holahan, 1996; Butwicka, et al., 2013; Cote et al., 2003; Heneghan et al., 2000; Jaser et al., 2010). Maternal depressive symptoms in mothers of children diagnosed with type 1 diabetes has been widely studied in the literature, although findings on the relationship between maternal depressive symptoms and glycemic control in children, measured as HbA1c, are mixed (Kovacs et al. 1990; Wiebe et al., 2011; Cote, 2003). Most often, "maternal depressive symptoms" has been conceptually defined as mothers who exhibit symptoms characteristic of depression, such as low energy and social withdrawal but do not necessarily meet a Diagnostic and Statistical Manual of Mental Disorders (DSM) diagnosis of depression (Clayton, Stewart, Wiebe, McConnel, & Hughes, 2013; Jaser et al., 2008; Wiebe et al., 2011). Other researchers have looked at depressive symptoms in mothers as a component of parental psychological stress which includes anxiety, depression, and posttraumatic stress disorder (Whittemore et al., 2013) or psychosocial adjustment (Jaser & Grey, 2010). Moreover, terminology to describe depressive symptoms in mothers has varied; most researchers have used "maternal depressive symptoms" (Clayton et al., 2013; Wiebe et al., 2012), while others have used variations of parental or maternal psychological/psychosocial distress (Kovacs et al., 1990; Jaser et al., 2008; Whittmore et al., 2012), "maternal depression" (Mackey et al., 2014), and parental "negative affect" (Butler et al., 2009). Perhaps attributable to these variations in conceptualization and terminology, some researchers have found no relationship between maternal depressive symptoms and HbA1c (Kovac et al., 1990), while others have found that HbA1c is directly associated with maternal depressive symptoms (Rumberg et al., 2017; Wiebe et al., 2011), or that

children of mothers with higher depressive symptomatology scores tended to have higher HbA1c levels although not statistically significant (Butwicka et al., 2013).

Though assumptions have been made in literature, the mechanism of how maternal depressive symptoms is related to glycemic control in children is unclear. Mothers of children diagnosed with type 1 diabetes may be more likely to exhibit depressive symptoms over time (Kovacs et al., 1990). Depressive symptomatology may lead mothers to be overly or minimally involved in diabetes treatment of their child (Wiebe et al., 2011) or less-likely to utilize health care services for diabetes care (Cote et al., 2003). Maternal depressive symptoms may also impact glycemic control through reduced adherence to disease management (Mackey et al., 2014). For example, severity of maternal depressive symptoms has been noted to be an independent predictor of hospitalization related to diabetic ketoacidosis or hypoglycemia (Butwicka et al., 2013). Failure of the mother to aid school-age children in diabetes management is believed to be related to expression of depressive symptoms such as social withdrawal, low energy, and hostile parenting (Wiebe et al., 2011) and acts as a potential risk factor for poor glycemic control in the child (Jaser & Grey, 2010). Moreover, the rigorous demand placed on mothers of diabetic children to achieve metabolic control, coupled with negative family functioning and coping strategies, may increase or worsen depressive symptomatology (Jaser et al., 2008; Kovacs et al., 1990). Although maternal depressive symptoms and glycemic control are likely to be associated, variations in findings on the relationship between the two may be attributable to study design, conceptual definitions, sample demographics, or methods used to measure variables (Polit & Beck, 2012). Findings on

the association between maternal depressive symptoms and glycemic control will be discussed further in light of these variables.

Often, maternal depressive symptoms have not been examined as a predictor of HbA1c; rather, the two variables have been examined as confounding factors or indirectly with another variable, such as adherence, mediating the two (Butler et al., 2009; Butwicka et al., 2013; Clayton et al., 2013; Cote et al., 2003). However, when maternal depression was examined as a predictor of glycemic control, positive associations were noted between maternal depressive symptoms and glycemic control (Rumburg et al., 2017). Conversely, high maternal depressive symptoms may actually predict lower HbA1c values in children, especially in mothers reporting they had more responsibility of diabetes management for their child at baseline (Wiebe et al., 2011). Wiebe and colleagues (2011) note that these findings are likely associated with extremes in maternal depressive symptoms such as controlling and overbearing parenting styles and/or withdrawal, impaired childrearing, and deficits in communication between the mother and the child (Heneghan et al., 2000; Wiebe et al. 2011). Other variations in research findings may be attributable to variability in the study population (Polit & Beck, 2012).

In some studies, HbA1c levels exhibited floor effects with children having low HbA1c levels and limited variability (Butler et al., 2009; Butwicka et al., 2013; Jaser & Grey, 2008). Floor effects may mask significant findings between maternal depressive symptoms and glycemic control (Polit & Beck, 2012). An example of this was seen in a study by Butwicka and colleagues (2013), where all children had relatively good HbA1c levels ranging from 6.8 to 8.2% at the time of enrollment. Populations of children who

had higher HbA1c values (8.8%) and who did not exhibit floor effects related to HbA1c were more likely to have significant associations between maternal depressive symptoms and child glycemic control (Mackey et al., 2014; Rumberg et al., 2017). Additionally, lack of association between maternal depressive symptoms and glycemic control may be related to how glycosylated hemoglobin data were collected. Across studies, methods to collect HbA1c were not consistent (Kovacs et al., 1990), HbA1c levels were not collected at the same time as survey completion (Cote et al., 2003; Kovacs et al., 1990), or HbA1c levels were recorded from self- or physician- report (Cote et al., 2003). These variations may have led some researchers to find associations between maternal depressive symptoms and HbA1c (Wiebe et al., 2011), where others have not (Butwicka et al., 2003; Cote et al., 2003; Kovacs et al., 1990; Jaser et al., 2008).

Patient demographics may also play a role in the associations noted between maternal depressive symptoms and glycemic control. Ages of child participants have ranged from 8 to 18 years with significant associations between maternal depressive symptoms and glycemic control noted in children age 10 to 16 years (Jaser & Grey, 2010; Rumberg et al., 2017; Wiebe et al., 2011). Moreover, Kovacs and colleagues (1990) found that mothers with higher SES had more depressive symptomatology than mothers with lower SES. This may impact other findings as a number of studies have used samples from high SES (Jaser et al., 2008; Jaser & Grey, 2010). Additionally, researchers have included predominantly Caucasian samples (82-83%) (Cote et al., 2003; Jaser et al., 2008; Jaser & Grey, 2010). The limited variability in sample population may mask research findings in other races or ethnicities or decrease generalizability of findings (Polit & Beck, 2012).

Differences in findings between studies may be also be related to other factors such as variations in tools to measure maternal depressive symptoms. While glycemic control has been objectively measured as HbA1c, measures for maternal depressive symptoms have all been dependent on self-report measures for measurement. Moreover, no tool has been used consistently to measure depressive symptoms. Among the tools used to measure depressive symptoms in mothers, the most commonly used was the Center for Epidemiologic Studies Depression Scale (CES-D) (Jaser et al., 2008; Jaser & Grey, 2010; Weibe et al., 2011); however, a variety of tools have been used. For example, Kovacs and colleagues (1990) measured depressive symptoms using the Beck Depression Inventory (BDI) while other researchers used the Patient Health Questionnaire (PHQ-9) (Rumberg et al., 2017); Brief Symptom Inventory (BSI) (Cote et al., 2003), and the Hamilton Depression Rating Scale (HDRS) (Butwicka et al., 2013). All of these scales examine symptoms of depression. The PHQ-9, CES-D and BDI are 9, 20 and 21-item scales, respectively, that are administered by self-report and specifically pertain to depressive symptoms (Jaser et al., 2008; Kovacs et al., 1990, Radloff, 1977; Rumberg et al., 2017). The BSI is also self-administered, although it includes items not only related to depressive symptoms (Cote et al., 2003). The HDRS is administered by a trained clinician and is commonly used to assist in diagnosis of depression (Butwicka et al., 2013). Of these studies, only researchers that used the CES-D or PHQ-9 to measure depressive symptoms found some association with glycemic control in children (Jaser & Grey, 2010; Weibe et al., 2011).

Findings related to associations between maternal depressive symptomatology and glycemic control are mixed (Jaser et al., 2008; Wiebe et al., 2011). Some researchers

(Butwicka et al., 2013; Cote et al., 2003; Jaser & Grey, 2008; Kovacs et al., 1990) have found no associations, or rather "protective" associations (Wiebe et al., 2011) between maternal depressive symptoms and glycemic control. Variations in findings between maternal depressive symptoms and glycemic control may be attributed to a number of factors related to patient demographics or methodological issues such as floor effects (Polit & Beck, 2012). Despite these findings, expression of depressive symptoms in mothers has the potential to influence glycemic control in children with diabetes by altering maternal involvement in diabetic care and management (Butwicka et al., 2013; Cote et al., 2013; Jaser & Grey, 2010).

Child Depressive Symptoms and Glycemic Control

Maternal depressive symptoms and child depressive symptoms may be related (Malcarne, Hamilton, Ingraam, & Taylor, 2000). The association between maternal and child depression has been noted in children with type 1 diabetes, with depressive symptoms in mothers acting as a predictor of depressive symptoms in children (Jaser et al., 2008; Wiebe et al., 2011). Moreover, children with type 1 diabetes are more likely than their peers without diabetes to suffer from depression (Grey, Whittemore, & Tamborlane, 2002; McGrady & Hood, 2010). "Child depressive symptoms" has been poorly defined in various studies. Similarly, terminology for child depressive symptoms has varied with researchers using "depressive symptoms", "depressed mood", and "depression" interchangeably (Korbel et al., 2007; Lawrence et al., 2006; Stewart et al., 2005; Whittmore et al., 2014). Regardless, many researchers have relied on the negative effects depression has on family and functioning in children to describe depressive

symptoms in children (McGrady et al., 2009; McGrady & Hood, 2010; Whittmore et al., 2014). Others have defined "child depressive symptoms" as depressed mood and symptoms characteristic of depression in children (Korbel et al., 2007; Lawrence et al., 2006), as clinical diagnosis of major depressive disorder (Stewart et al., 2005), or as part of more comprehensive psychological alterations, like internalizing symptoms (Naar-King et al., 2006). Similar to maternal depressive symptoms, "child depressive symptoms" may be conceptually defined as symptoms characteristic of depression in children, but not dependent on a DSM diagnosis (Korbel et al., 2007; Lawrence et al., 2006; Whittemore et al., 2013). Perhaps the best definition of "child depressive symptoms" was provided by Kongkaew and colleagues (2013) stating, "such children are often found to have a negative self-perception, low self-esteem and an ineffective coping style" (p. 204). Interestingly, parents may be aware of these depressive symptoms; when examining depressive symptoms in children with diabetes, parent-proxy scores for the Children's Depression Inventory (CDI) were highly correlated with self-report scores by children (Hood et al., 2006). Depressive symptoms in children may also predict poor glycemic control either directly (Grey, Whittemore, & Tamborlane, 2002; Hood et al., 2006; Hood, Rausch, & Dolan, 2011) or indirectly through impaired adherence to treatment (Korbel et al., 2007; McGrady & Hood, 2010; Steward et al., 2009).

The relationship between child depressive symptoms and glycemic control has been well-studied in literature; many researchers report that as depressive symptoms in children increase, glycemic control, indicated by high HbA1c values, decreases (Hood et al., 2006; McGrady & Hood, 2010) and that child depressive symptoms are a predictor of glycemic control (Hood, Rausch, & Dolan, 2011). While most studies examining the

relationship have been cross-sectional, a few have been longitudinal (Helgeson et al., 2009; Kongaew et al., 2013; McGrady & Hood, 2010). It is interesting to note that longitudinal studies report higher effect sizes between child depressive symptoms and glycemic control (Kongaew et al., 2013). Additionally, while some longitudinal studies have found that child depressive symptoms and glycemic control are not correlated concurrently, they predict decreased glycemic control over time (Helgeson, 2009). Conversely, other studies have found that child depressive symptoms were correlated with present HbA1c value, but not future HbA1c values (McGrady & Hood, 2010).

The association between child depressive symptoms and glycemic control may be influenced by variations in study demographics. With the exception of Lawrence and colleagues (2006) who studied children with type 1 and type 2 diabetes and Naar-King and colleagues (2006) who included a mainly African American study population from low SES, most studies have used a predominantly Caucasian study sample from high SES (Jaser & Grey, 2008; McGrady & Hood, 2010). Additionally, research examining child depressive symptoms and glycemic control has included children with more variability in HbA1c values with average HbA1c levels being 8% or higher in many studies (Helgeson et al., 2009; Hood et al., 2006; Naar-King et al., 2006).

While variations in study demographics have been noted, most studies have included equal numbers of male and female participants (Helgeson et al., 2009; Naar-King et al., 2006; Lawrence et al., 2006). It is interesting to consider gender differences since children with high depressive symptomatology were more likely to be female and have higher HbA1c levels than children without elevated depressive symptoms (Hood et al., 2006; Lawrence et al., 2006). However, this is contrary to findings by Naar-King and

colleagues (2006) who found that although males had poorer treatment adherence for diabetes management, there were no significant differences in HbA1c levels between males and females. Moreover, few studies have examined depressive symptoms in children younger than 10 years of age with type 1 diabetes (Jaser & Grey, 2008; Kongaew et al., 2013). This may be attributed to few instruments that have been validated to measure depressive symptoms in children less than 10 years of age. For example, while the CESD is mainly used in adults, it has only been validated in children as young as 12 (Lawrence et al., 2006). Despite this, Lawrence and colleagues (2006) used the instrument in children as young as 10 and found correlations between mild expression of depressive symptoms in both genders and glycemic control.

Contrary to research examining maternal depressive symptoms and glycemic control, measurement of child depressive symptoms has been more consistent. With the exception of Naar-King and colleagues (2006), most studies have used the CDI or the CES-D (de Wit et al., 2007; Hood et al., 2006; Jaser & Grey, 2010; Lawrence et al., 2006; Stewart et al., 2009) to measure depressive symptoms in children. Similar to the 20-item CES-D, the CDI is a 27-item self-report scale used to measure depressive symptoms (McGrady & Hood, 2010). However, the CDI has been validated in children as young as 7 years of age, whereas the CES-D has only been validated in children as young as 12 years (Lawrence et al., 2006). Regardless of whether the CDI or CES-D was used, most researchers have found correlations between depressive symptoms in children and glycemic control (de Wit et al., 2007; Helgeson et al., 2009; Hood et al., 2006; Kongkaew et al., 2013; Korbel et al., 2007; McGrady & Hood, 2010).

Similar to associations between maternal depressive symptoms and glycemic control, some studies have found associations between child depressive symptoms and glycemic control (Di Wit et al., 2007; Hood et al., 2006; McGrady & Hood, 2010; Stewart et al., 2009), where others have not (Helgeson et al., 2009; Korbel et al., 2007). Although findings are mixed, the association between depressive symptoms in children and glycemic control is important to understand as children and adolescents who exhibit high levels of depressive symptoms may be more likely to be withdrawn and therefore less rigorous in monitoring and managing abnormal blood glucose levels leading to poor glycemic control (McGrady & Hood, 2010). Moreover, depressive symptoms in children may be more closely related to intense diabetes management therapy and disease burden (Hood et al., 2006) or self-care behaviors (Helgeson et al., 2009). Additionally, as noted with maternal depressive symptoms, depressive symptoms in children may lead to altered disease management which may not have an instant effect on glycemic control, but may influence glycemic control over time (Helgeson et al., 2009).

Child's Perceived Stress and Glycemic Control

There have been few studies examining child's perceived stress and glycemic control in children with type 1 diabetes. Stress was best defined by Delamater and colleagues (2013) as "an experience (objective and/or subjective) that diminishes the psychological and physical resources of a person" (p. 50); perceived stress may be better conceptualized as stress, as previously noted, that a person is able to identify. However, perceived stress in children with diabetes has been labelled in a variety of ways; some researchers have used the term "perceived diabetes-related stress" (Berlin et al., 2012) or

"diabetes-related stress" (Delamater et al., 2013), whereas others have used "general stress" (Farrell et al., 2004), "chronic stress" (Hilliard et al., 2016), and "adverse life events" (Worrall-Davies, 1999). Regardless, Liakopoulou and colleagues (2001) found that maternal expressed emotion, such as hostility, affects glycemic control in diabetic children in the form of increased HbA1c levels. Hostility may be a sign of impaired parenting from maternal depression (Heneghan et al., 2000) and may increase stress perceived by the child (Terzian et al., 2010). Moreover, children with diabetes experience high levels of stress surrounding disease management (Berlin et al., 2012; Delamater et al., 2013; Worrall-Davies, 1999); this stress may increase as length of diabetes diagnosis increases (Delamater et al., 2013). The stress children face in an attempt to adhere to their diabetes management, as well as lack of support or pressure from parents to help manage the disease (Berlin et al., 2012), make perceived stress from the child an important factor to consider when studying glycemic control. Stress may impact glycemic control because impaired coping mechanisms make it hard for children to adhere to the medical regimen of managing diabetes (Delamater et al., 2013).

Associations between stressful life events, which may increase emotional stress, and glycemic control in children with diabetes have been noted (Worrall-Davies, 1999). Moreover, glycemic control may be more closely related to sources of emotional stress, rather than a total stress score. For example, Berlin and colleagues (2012) reported children with higher levels of perceived family-related stress had significantly higher HbA1c levels. HbA1c levels were also associated with parental sources of stress and stressful events related to diet management (Delamater et al., 2013). Variations in

findings between sources of stress and glycemic control may be related to study variables such as age of the participants or measurement of variables in the study.

As noted in findings between glycemic control and maternal depressive symptoms, methods used to collect HbA1c may masks findings or contribute to variations in finding between common sources of stress, such as peers and family, and associations with glycemic control (Delamater et al., 2013). For example, in a study by Delamater and colleagues (2013) HbA1c was only reported on 65% of the sample. Additionally, tools to measure perceived stress in children have been limited.

Despite multiple studies looking at stressful events and glycemic control in adolescents with diabetes (Berlin et al., 2012; Delamater et al., 2013; Farrell et al., 2004), few studies have examined perceived stress and glycemic control in children younger than 10. The limited amount of literature on perceived stress in children younger than 10 years with type 1 diabetes may be related to few validated instruments that measure the concept of perceived stress in these young children (Delamater et al., 2013). Most studies have used the Diabetes Stress Questionnaire (DSQ) (Berlin et al., 2012; Farrell et al., 2004) or the Diabetes Stress Questionnaire for Youths (DSQ-Y) (Delamater et al., 2013). These tools are 65-item self-report measures used to examine occurrence of stressful events related to diabetes management at the time of survey completion in individuals with type 1 diabetes (Berlin et al., 2012; Delamater et al., 2013). Some researchers have used a second tool, such as the Life Stressors and Social Resources Inventory (LISRES-Y), a 208-item survey that measures frequency of stressors in different components in life, in conjunction with the DSQ (Farrell et al., 2004). However, these tools to measure stress may have more subject burden, have not been validated in children younger than

10 years, and most participants have been young adolescents or older at the time of administration (Delamater et al., 2013). One of the only studies to examine stressful events in children with diabetes as young as 6 years was conducted by Worrall-Davies and colleagues (1999) using the Newcastle Child and Family Life Events Interview Schedule, a semi-structured interview given to parents to assess stressful life events over the past 12 months. Additionally, the occurrence of stressful events related to diabetes may not impact the child as much as perception and frequency of stressful events experienced daily in childhood. This may be better measured in children using a tool such as the Feel Bad Scale (Lewis, Siegel, & Lewis, 1984), a 40-item tool to measure frequency and severity of events over the last 12 months specific to childhood which may be perceived as stressful by the child.

While associations were noted between stress and glycemic control (Berlin et al., 2012; Delamater et al., 2013; Worrall-Davies et al., 1999), many researchers suggest these relationships may be mediated by adherence behavior related to disease management. In particular, adolescents who experience more stressors are less likely to monitor for and correct high blood glucose levels (Farrell et al., 2004). Therefore, it is important to not only study the association between child perceived stress and glycemic control, but also additional factors that may mediate the relationship between the two variables.

Cortisol

Cortisol is a functional measure of stress adaptation in the HPA axis (Hellhammer et al., 2008) and is a commonly used biomarker to measure psychological stress as well

as mental and physical diseases (Hellhammer, Wust, & Kudielka, 2008). Cortisol is an appropriate and strong choice for use as a biomarker in research because it is an accurate representation of HPA axis function and physiological stress response (Chrousos & Kino, 2007; Hellhammer et al., 2008). In people with normal sleep-wake patterns, cortisol follows a diurnal pattern. Three to five hours after sleep begins, there is a peak in ACTH (Brasher & Jones, 2010). This is followed by a peak in cortisol with the highest concentration noticed just before awakening until approximately 45 minutes after waking (Brasher & Jones, 2010; Hellhammer et al., 2008). Levels in cortisol decrease as the day progresses (Brasher & Jones, 2010) although young children also have a peak in cortisol concentration noted upon waking from afternoon naps (Fernald, Burke, & Gunnar, 2008; Hanrahan et al., 2006). Because of daytime naps taken by infants and very young children, cortisol does not follow the normal diurnal pattern seen in adults (significantly higher levels in the morning compared to afternoon levels) until the child is 4 years of age (Wilkinson & Goodyer, 2011). In addition to these diurnal patterns of cortisol, cortisol levels also peak approximately 15 to 30 minutes following a stressful event such as a needle stick (Hanrahan et al., 2006).

Abnormal levels of cortisol, especially elevated levels, represent malfunction of the HPA axis and failure of the body to adequately adapt to physiological stress (McEwen, 2007). These significantly elevated levels of cortisol were best evidenced in children in daycare settings. Geoffroy, Cote, Parent, and Seguin (2006) note, in a review, that children exposed to chronic stress associated with daycares had cortisol levels that rose throughout the day when compared to children who stayed home and had cortisol levels that followed a normal diurnal pattern. The elevations in cortisol throughout the

day were more significant in preschool aged children and children in low-quality daycare settings (Geoffroy et al., 2006).

Non-invasive methods of collecting cortisol, while also being a relatively inexpensive, easy, and non-invasive biomarker to collect (Hanrahan et al., 2006), make it a promising biomarker to measure physiological stress in children and adults (Hanrahan, McCarthy, Kleiber, Lutgendorf, & Tsalikian, 2006). Cortisol is found in a variety of mediums including blood, urine, and saliva (Hellhammer et al., 2008). More recently, Meyer and Novak (2012) investigated a novel approach using cortisol found in hair follicles as a biomarker for HPA activity. While cortisol represents a myriad of endocrine and neurological mechanisms specific to HPA axis function, it may have limitations when it is used as a biomarker in research. There are a multitude of individual factors that uniquely impact cortisol levels (Hanrahan et al., 2006). While salivary and serum levels of cortisol are comparatively accurate correlates, salivary cortisol concentrations tend to be slightly higher than serum levels of cortisol (Hellhammer et al., 2008). Moreover, prepubertal participants have demonstrated hypo-cortisol levels in response to chronic stressors when compared with adult counterparts (Romeo & McEwen, 2006). Despite these limitations, cortisol may still offer a wealth of information about HPA axis especially as a mediator between maternal depressive symptoms, child depressive symptoms, child's perceived stress and glycemic control in children with type 1 diabetes.

Maternal Depressive Symptoms and Cortisol

Research examining the relationships between maternal depressive symptoms and cortisol levels in school age children is limited to children without diabetes. Despite this,

findings on the association between abnormal levels of cortisol in children and maternal depressive symptoms have been mixed (Ashman et al., 2002; Lupien et al., 2000). Mixed findings may be related to methodology, age of the child, and/or how researchers conceptualized and measured cortisol.

Similar to studies on maternal depressive symptoms and glycemic control, "maternal depressive symptoms" has been defined as symptoms characteristic of depression in mothers (Essex et al., 2011; Fernald et al., 2008; Gump et al., 2009) or as clinical history of, or diagnosis of, depression in mothers (Ashman et al., 2002). Other studies have not clearly defined maternal depressive symptoms (Lupien et al., 2000). Moreover, different terms such as "depressive symptoms/symptomatology" (Fernald et al., 2008; Gump et al., 2009), "depressed mothers" (Ashman et al., 2002), "maternal depression" (Essex et al., 2011), and "depressive state" (Lupien et al., 2000) have been used to describe maternal depressive symptoms. This has most-likely lead to various methods used to measure depressive symptoms in mothers. In addition to using the CES-D to measure depressive symptoms (Fernald et al., 2008; Gump et al., 2009), some researchers have used a subscale on the Derogatis Stress Profile (DSP) (Lupien et al, 2000), while other have depended on maternal self-report of history of depression (Ashman et al., 2002). The DSP is a 77-item self-report scale that measures stress and has a subscale which includes measures of anxiety, hostility and depression (Lupien et al., 2000).

Additionally, conceptualization and measurement of cortisol has varied. Some researchers have looked at chronic stress and cortisol change by assessing diurnal patterns and basal levels of cortisol to evaluate cortisol's relationship with maternal

depressive symptoms (Lupien et al., 2000) while other researchers measure cortisol reactivity to acute stressors as a means of identifying associations between cortisol and maternal depressive symptoms (Gump et al., 2009; Fernald et al., 2008). Still other studies have included both acute and chronic measures of stress with cortisol change (Ashman et al., 2002). These differences in methodology may help explain differences in findings between cortisol and maternal depressive symptoms.

In this regard, Lupien and colleagues (2000) collected two samples of cortisol between 8 and 9 am and averaged values to obtain a basal morning cortisol level that was used to assess chronic stress and HPA axis dysfunction. Researchers noted that children had higher levels of salivary cortisol when they lived with mothers exhibiting increased depressive symptomatology (Lupien et al., 2000). Similarly, researchers have collected morning and evening samples of cortisol in children to examine changes in cortisol levels throughout the day (Ashman et al., 2002). This may be a better indicator of diurnal disruption in cortisol and signify chronic stress alterations (McEwen, 2007). However, researchers did not find associations between the change from morning to evening cortisol levels and maternal depressive symptoms (Ashman et al., 2002).

In contrast to studying cortisol levels as they rise and fall during the day, other researchers have examined cortisol in response to acute stressors to measure acute stress response in the child (Gump et al., 2009; Fernald et al., 2008). Cortisol was collected multiple times during a 1 to 2-hour span before, during, and after an acute stressor to measure cortisol reactivity (Ashman et al., 2002; Gump et al., 2009; Fernald et al., 2008). Children age 7 to 9 years with mothers exhibiting increased depressive symptoms had higher levels of baseline cortisol before the acute stressor (Ashman et al., 2002) or an

exaggerated cortisol response to the stressor (Gump et al., 2009). This is different than the blunted cortisol response to an acute stressor noted in young children (2.5 to 5 years old) of mothers with high levels of depression (Fernald et al., 2008). The variability in cortisol response (hypo- or hyperactive reactivity) as well as cortisol change throughout the day may be explained further by age of the child (Essex et al., 2011) or other risk factors such as low SES (Fernald et al., 2008).

Findings on the relationship between maternal depressive symptoms and changes in cortisol may be attributed to better support systems or prevalence of risk factors such as poverty, single-parent households, and lack of parental education (Fernald et al., 2008; Heneghan et al., 2000; Hood et al., 2005). Similar to the findings of Lupien's and colleagues (2000) that high SES was a protective factor for cortisol change, Essex and colleagues (2008) did not find significant changes in cortisol related to depressive symptoms until the child was exposed to other risks factors, such as expressed reoccurring family anger. Further, children's cortisol levels varied with the type of early life exposure and tended to oscillate between hypercortisolism and hypocortisolism as the child aged and entered puberty (Essex et al., 2011, Fernald et al., 2008; Lupien et al., 2000). Specifically, in a longitudinal study, Essex and colleagues (2011) found that children exposed to high levels of maternal depression had lower morning cortisol levels with steeper slopes in cortisol at age 9; however, these levels of morning cortisol in children of depressed mothers tended to increase until age 15 at which time there was blunting in cortisol levels throughout the day. These findings are consistent with McEwen's (2007) findings on HPA axis function, allostasis, and allostatic load as well as Trast's (2014) report on the influence of puberty on growth hormone and cortisol levels.

Associations between cortisol and maternal depressive symptoms may also vary based on demographics of the study population. For one, the relationship between maternal depressive symptoms and cortisol may be masked by SES of the family. Children with high SES in one study had lower cortisol levels overall despite maternal depressive symptoms (Lupien et al., 2000). Additionally, there have been a wide age range of children included in various studies with some as young as 2.5 to 5 years (Fernald et al., 2008) and others as old as 9 to 15 years (Essex et al., 2011). Other studies measured longitudinally from the age of 3 months to 10 years (Gump et al., 2009). Age of the child and SES are important to consider because discrepancies have been noted in cortisol in low SES and high SES children. Further, excessive elevations in basal rates associated with maternal depressive symptoms, may not emerge until the child is between 8 and 10 years (Lupien et al., 2000). Similar findings regarding age were noted by Gump and colleagues (2009) who did not find significant changes in cortisol until the child was 9 years, at which time children of mothers with chronically elevated depressive symptoms had lower baseline levels of cortisol indicating hypocortisolism. Additionally, these children had exaggerated cortisol response to acute laboratory stressors (Gump et al., 2009).

Despite variations in findings, the association between maternal depressive symptoms and change in cortisol is important to understand because associations between maternal depressive symptoms and cortisol levels in children have been found by multiple researchers, especially when combined with other risk factors such as low SES or increased frequency of stressful life events (Ashman et al., 2002; Fernald et al., 2008; Gump et al., 2009; Lupien et al., 2000). However, while some researchers have identified

associations between maternal depressive symptoms and cortisol, others have also observed low levels of cortisol (Gump et al., 2009). In contrast, other researchers have observed higher than normal levels of cortisol (Ashman et al., 2002; Fernald et al., 2008). These variations in cortisol levels may be better explained by child age and pubertal status (Essex et al., 2011) or by other factors yet to be studied.

Child Depressive Symptoms and Cortisol

Similar to research on maternal depressive symptoms and child cortisol levels, there is limited research examining child perceived stress and cortisol levels in children with diabetes. Further, very few studies have examined depressive symptoms and cortisol levels in school age children (Goodyer et al., 1998). Moreover, in research examining child depressive symptoms and cortisol, "child depressive symptoms" has mainly been conceptualized as an internalizing disorder (Bae et al., 2015; Stewart et al., 2013) or as a diagnosis of major depressive disorder (MDD) as classified by DSM criteria (Goodyer et al., 1998; Stewart et al., 2013; Suzuki et al., 2013). The terms "major depressive disorder", "internalizing disorders", and "depression" have been used interchangeably to describe depressive symptoms in children in these studies (Bae et al., 2015; Goodyer et al., 1998; Stewart et al., 2013; Suzuki et al., 2013). Regardless of varying definitions and terminology, depression in children may be characterized by chronically blunted cortisol reactivity and failure to acclimate to stressful events (Suzuki, Belden, Spitznagel, Dietrick, and Luby, 2013).

Of the limited studies examining depressive symptoms and cortisol in school age children, one study used the DHEA:cortisol ratio to examine alterations in physiological

stress within the body (Goodyer et al., 1998). DHEA and cortisol are believed to act as antagonists and change in response to each other; therefore, an altered ratio indicates impaired physiological stress (Goodyer et al., 1998). In this study, researchers found that abnormal DHEA:cortisol ratios (with hypocortisolism) were associated with, and predicted longer duration of, major depressive disorder when cortisol was measured over a 24-hour period (Goodyer et al., 1998). Other researchers have used the BDI-II (Stewart et al., 2013) or the Preschool Age Psychiatric Assessment (Suzuki et al., 2013) to measure depressive symptoms severity in adolescents and preschool children in addition to obtaining a diagnosis of MDD in these children. These tools measure depressive symptom severity; however, BDI-II is a revised, 21-item self-report tool used in children and adolescents (Stewart et al., 2013) whereas the Preschool Age Psychiatric Assessment is a semi-structured interview for young children and their parents performed by a trained clinician to measure psychiatric conditions such as depression. In these studies, multiple samples of cortisol were collected over 1 to 2 hours before, during, and after an acute stressor. In preschool children, cortisol reactivity following the acute stressor was blunted in children with current depression or a history of depression when compared with children without depression (Suzuki et al., 2013). In adolescents, depressive symptoms were not associated with cortisol (Stewart et al., 2013). However, depressed adolescents who exhibited rumination had higher levels of post-stress cortisol and took longer to recover to baseline cortisol levels following the stressful event than their depressed peers without rumination (Stewart et al., 2013).

Although some researchers suggest that depressive symptoms are associated with cortisol (Suzuki et al., 2013), limited research studies, as well as variability in study

design, make it difficult to discern if these relationships between cortisol and depressive symptomatology in school age children are meaningful. Moreover, previous studies have used diagnostic cut-offs for depression rather than measuring depressive symptoms as a continuum (Goodyer et al., 1998; Suzuki et al., 2013). This may be a concern as some children might exhibit depressive symptoms which may interfere with diabetes management, but not be considered depressed (McGrady & Hood, 2010). Despite this, it appears that the relationships between depressive symptoms and cortisol are amplified when the child experiences other confounding factors such as increased stress, lack of support symptoms, or impaired family functioning (Goodyer et al., 1998; Stewart et al., 2013; Suzuki et al., 2013).

Child's Perceived Stress and Cortisol

Cortisol is a main hormone released in response to stress and activation of the HPA axis (Chrousos & Kino 2007; Gold, 2015); however, few studies have examined perceived stress and cortisol levels in school age children. In these studies, stress is commonly defined as a state in which demands exceed the ability to cope (Armbruster et al., 2012; Bae et al., 2015; Maldonado et al., 2008). However, stress perceived or experienced by a child has been conceptualized in various ways. Many researchers used physiological underpinnings of stress to define a stress response in children (Armbruster et al., 2012; Bae et al., 2015). Other researchers have used stressful life events experienced by the child or stress that the child experiences daily to describe stress in the child (Maldonado et al., 2008). Moreover, Maldonado and colleagues (2008) are the only researchers to use the term "stress perception" in their study of stress and cortisol.

Regardless of how stress is defined and termed, very few researchers have attempted to measure stress perception by the child and associations with cortisol (Maldonado et al., 2008). Most researchers have only attempted to create social stressors (Bae et al., 2015) or measure stressful life events (Armbruster et al., 2012) in relation to cortisol. While several studies involving children have incorporated acute stressors to stimulate stress and associations with cortisol (Gump et al., 2009; Fernald et al., 2008; Stewart et al., 2013; Suzuki et al., 2013), there are no studies involving children with diabetes.

While studies have included healthy children of similar ages (8-14 years), they have varied in how they measure stress in the child as well as cortisol. In addition to previously mentioned variations in collection of cortisol, various tools to measure or stimulate emotional stress in children have been used. Both Bae and colleagues (2015) and Armbruster and colleagues (2012) used the Trier Social Stress Test for Children (TSST-C) to stimulate social stress acutely in a laboratory setting; these researchers also measured cortisol reactivity in response to the acute stressor. The TSST-C stimulates stress in the child by requiring the child to speak and perform a task in front of an audience (Armbruster et al., 2012). In addition to the TSST-C, Armbruster and colleagues (2012) also recorded stressful life events experienced by the child. The only researcher to look at chronic changes in cortisol and daily stress perception in the child used the Children Daily Stress Inventory (CDSI), which is a 48-item survey assessing stressors specific to childhood (Maldonado et al., 2008).

Despite differences in how stress and cortisol were measured in children, significant findings have been noted. For example, Maldonado and colleagues (2008) found that children with higher levels of daily perceived stress had lower morning

cortisol levels when cortisol was collected upon waking and 30 minutes later to assess the cortisol awakening response. These blunted morning levels suggests that daily perceived stress impacts cortisol through chronic changes in HPA axis (Maldonado et al., 2008). Moreover, children with internalizing and externalizing disorders or who experienced increased frequency of stressful life events had lower cortisol reactivity in response to the acute social stressor of the TSST-C (Armbruster et al., 2012; Bae et al., 2015).

Overall, there is a lack of literature on child stress perception and cortisol. Moreover, all studies in this review were performed outside the United States in Spain and Germany. This may limit generalizability of findings since tools used to measure stress may not be validated or applicable to children in the United States. Additionally, only Maldonado and colleagues (2008) use the term perception to conceptualize and operationalize stress. Other researchers have used acute social stressors or stressful life events (Armbruster et al., 2012; Bae et al., 2015). It seems there is an assumption that stressful life events and acute social stressors make a child feel stressed. However, this may not be the case since children may respond differently to the same stressors (Garner, 2013). Therefore, it may be beneficial for researchers to not only measure frequency of stressful events, but also include the child's perception of the stressful events.

Cortisol as a Mediator

It is important to understand factors which may alter cortisol levels, such as maternal depressive symptoms (Ashman et al., 2002; Fernald et al., 2008; Gump et al., 2009; Lupien et al., 2000), child depressive symptoms (Goodyer et al., 1998; Suzuki et al., 2013), or child perceived stress (Armbruster et al., 2012; Bae et al., 2015; Maldonado

et al., 2008) because cortisol has a direct effect on plasma glucose levels (Forshee et al., 2010). In cellular tissues throughout the body, cortisol binds with glucocorticoid receptors to activate molecular and systematic changes (Chrousos & Kino, 2007). Cortisol stimulates tissues and organs within the body such as the liver to cause gluconeogenesis (formation of glucose from noncarbohydrate sources) with a resultant increase in blood glucose (Forshee et al., 2010). Cortisol further increases blood glucose by inhibiting cellular uptake and oxidation of glucose by adipose, muscle, and lymphatic tissue thus ensuring adequate glucose stores to help curb the effects of the initial stressor (Brasher & Jones, 2010; Forshee et al., 2010). This excess glucose is reserved for use by the brain during acute stress (Aguilera, 2011; Hellhammer et al., 2008).

In addition to physiological underpinnings of cortisol's effect on plasma glucose, associations between cortisol and glycemic control have been found in children with type 1 diabetes (Marcovecchio & Chiarelli, 2012; Mosbah et al., 2011). Specifically, higher cortisol levels were associated with higher HbA1c levels in children with type 1 diabetes whose pancreatic β-cells were nonfunctioning (Mosbah et al., 2011). Moreover, researchers have proposed that the relationship between stress and elevated blood glucose levels are mediated by stress hormones (Marcovecchio & Chiarelli, 2012). Marcovecchio and Chiarelli (2012) theorize that during stressful situations insulin sensitivity is reduced, glycogen storage in muscle is decreased, hepatic gluconeogenesis is increased, and stress hormones are released that may induce hyperglycemia. Together, these actions may be exaggerated in children with type 1 diabetes and lead to poor glycemic control.

While there are physiologic underpinnings detailing cortisol's effects on blood glucose and HbA1c levels in children with type 1 diabetes, there are conflicting findings

on the role cortisol may have in the relationships between maternal depressive symptoms, child depressive symptoms, child perceived stress and glycemic control. In the studies on these variables, mixed findings on the relationship between maternal depressive symptoms, child depressive symptoms, and child perceived stress with cortisol have been noted (Armbruster et al., 2012; Ashman et al., 2002; Bae et al., 2015; Fernald et al., 2008; Gump et al., 2009; Lupien et al., 2000; Stewart et al., 2013; Suzuki et al., 2013). This may be related to differing conceptual and operational definitions of the proposed concepts (occurrence of stressful life events versus stress perceived by the child), how variables were measured, or sample populations (Polit & Beck, 2012). However, if these psychological symptoms are associated with abnormal cortisol levels, then it may be reasonable to expect changes in glycemic control based on physiological stress mechanisms (Brasher & Jones, 2010; Forshee et al., 2010; Marcovecchio & Chiarelli, 2012; Mosbah et al., 2011). Therefore, more research is needed to understand what role, if any, cortisol may play in the mediation between maternal depressive symptoms, child depressive symptoms, child perceived stress and glycemic control.

Confounding Factors

Glycemic control in children with type 1 diabetes is negatively impacted by puberty (Trast, 2014). During puberty, insulin resistance in children increases (Hannon et al., 2006), thus requiring children to increase insulin dosages to maintain adequate glycemic control (Trast, 2014). Changes in hormones, specifically growth hormone and cortisol, are also thought to contribute to poor glycemic control during puberty; this is especially seen in overnight fasting glucose levels and elevated HbA1c (Trast, 2014).

Children with type 1 diabetes also enter puberty later than children without diabetes with the average age of onset for girls and boys being 11.4 years and 12 years, respectively (Rohrer et al., 2007). During puberty, children with type 1 diabetes are more likely to have poor glycemic control evidenced by elevated levels of HbA1c, need for greater insulin dosages, and more episodes of diabetic ketoacidosis (Trast, 2014). While changes in hormones during puberty are associated with insulin resistance and glycemic control (Hannon et al. 2006; Trast, 2014), other confounding factors, such as insulin regimen, may affect glycemic control.

Insulin therapy for children with type 1 diabetes is primarily managed in two ways: multiple daily injections (MDI) and continuous subcutaneous insulin infusion (CSII) (Malik & Taplin, 2014). Numerous studies have shown that children obtain better glycemic control, measured by HbA1c levels, when they use CSII compared to MDI (Fendler, Baranowska, Mianowska, Szadkowska, & Mlyarski, 2011; Paris et al., 2009; Springer et al., 2006). Further, children on CSII may require less insulin than children using MDI (Shashaj & Sulli, 2009). However, some researchers have found that there is no significant difference in HbA1c levels between children who use MDI vs CSII (Malik & Taplin, 2014; Nahban et al., 2009). Moreover, Batajoo, Messina, & Wilson (2012) have found that there is no difference in long-term efficacy between children who use MDI versus children who use CSII, with no significant differences in glycemic control seen between the groups at 30 months post-transition to pump therapy. Differences in glycemic control between children who use MDI versus CSII to manage diabetes may be attributed to other confounding factors such as time-since-diagnosis (Springer et al., 2006).

There is evidence that time-since-diagnoses contributes to glycemic control in children with type 1 diabetes. Springer and colleagues (2006) found that longer duration of diabetes diagnosis was associated with poor glycemic control and higher HbA1c levels. Moreover, immediately following diagnosis some children experience what is clinically referred to as "the honeymoon phase". The honeymoon phase in patients newly diagnosed with type 1 diabetes affects glycemic control in children within the first year following diagnosis (Abdul-Rasoul et al., 2006). The honeymoon phase, characterized by partial remission of diabetes, is common in children 5 to 12 years old and can last up to one year with approximately 10% of children still found to be in remission 12-months post-diagnosis (Abdul-Rasoul et al., 2006). In addition to time-since-diagnosis, ethnicity and SES may impact glycemic control in children with type 1 diabetes.

African Americans with type 1 diabetes demonstrate poorer glycemic control than Caucasian counterparts (Auslander et al., 1997). However, this relationship may be more closely related to SES. Delamater and colleagues (1999) found that African American were less likely to have insurance than Caucasian and Hispanic youth; this may result in decreased health care, limited help managing diabetes, and poor glycemic control. Moreover, Davis and colleagues (2001) found that only African American ethnicity and lower SES were associated with poor glycemic control in children with type 1 diabetes. Similar findings were reported by Gallegos-Macias and colleagues (2003) who found that Hispanic youth had worse glycemic control than Caucasian youth with type 1 diabetes. These findings were associated with lower SES in Hispanic youths, as well as lower rates of health insurance for Hispanic children (Gallegos-Macias et al., 2003).

Gaps within the Literature

Although there have been multiple studies that have examined maternal depressive symptoms and glycemic control in children, there is a lack of knowledge regarding the mechanism of this relationship. To date, some studies have found associations between these maternal depressive symptoms and glycemic control (Rumberg et al., 2017; Wiebe et al., 2011) while others have not (Jaser et al., 2008; Kovacs, 1990). This relationship may be better explained by examining other variables since combination of maternal depressive symptoms with other risk factors increase the occurrence of negative psychological and health outcomes in children (Essex et al., 2011; Jaser & Grey, 2010; Lupien et al., 2000). Similarly, findings related to associations between child depressive symptoms and glycemic control are mixed. While most researchers note correlations between the two (Di Wit et al., 2007; Hood et al., 2006; McGrady & Hood, 2010; Stewart et al., 2009), others do not (Helgeson et al., 2009; Korbel et al., 2007). Additionally, the majority of studies examining perceived stress and depressive symptoms in children have been conducted in adolescents and children older than 10 years or children without diabetes. While current studies demonstrate strong associations between child's perceived stress and glycemic control, this relationship has not been examined in prepubertal children. Again, this may be attributed to a lack of instrumentation, such as perceived stress measures, validated in children under 10 years of age to operationally measure the proposed concepts, or it may be attributable to alterations in methodology employed by different researchers (Polit & Beck, 2012).

Although associations between maternal depressive symptoms, child depressive symptoms, child's perceived stress and cortisol in children have been noted, no studies

have examined the proposed relationships concurrently in children with type 1 diabetes. The only research examining cortisol is children with type 1 diabetes examines the physiological underpinnings and effects of cortisol on plasma glucose levels (Marcovecchio & Chiarelli, 2012; Mosbah et al., 2011). Studies that have examined cortisol in children without diabetes appear to have focused on child's cortisol levels in relation to alterations in maternal depressive symptoms rather than child depressive symptoms and child's perceived stress (Essex et al., 2011; Lupien et al., 2000). Moreover, most research studies involving cortisol levels in children have examined cortisol reactivity in response to acute physical or psychosocial stressors rather than assessing stress perceived by the child (Ashman et al., 2002; Gump et al., 2009; Fernald et al., 2008; Stewart et al., 2013; Suzuki et al., 2013). While these researchers have found blunted or exaggerated cortisol responses to acutely stressful events, they have also noted elevated or decreased basal levels of cortisol in children exposed to depressive symptoms or perceived stress.

These findings may suggest chronic damage to the HPA axis and cortisol rhythms that are abnormal in children. These abnormalities may be evidenced by atypical changes in cortisol from morning to afternoon samples (Hellhamer et al., 2008; McEwen, 2007). However, no study has examined cortisol change in relationship to maternal depressive symptoms, child depressive symptoms, or child's perceived stress in diabetic children age 7 to 12 years. Considering the impact of elevated and abnormal cortisol levels on plasma glucose (Marcovecchio & Chiarelli, 2012; Mosbah et al., 2011; Sprague & Arbelaez, 2011), these relationships are important to understand given the complexity of obtaining glycemic control in children.

Summary

The content of this chapter provided a review of the literature surrounding concepts and relationships in the research study. Findings have been mixed. While some studies show associations between maternal and child depressive symptoms with glycemic control and cortisol, others do not. Moreover, the associations between depressive symptoms and cortisol are varied, with some studies demonstrating elevated cortisol responses and others revealing blunted cortisol levels. Further, many studies looking at these relationships have focused on very young preschool children or older adolescents. The literature presented in this review has highlighted the gaps in scientific knowledge and supported the need to examine the proposed relationships further.

CHAPTER 3

METHODOLOGY

The purpose of this study was to establish the effect sizes necessary to determine the influence of maternal depressive symptoms, child depressive symptoms, and child's perceived stress on glycemic control in prepubertal school-aged children 7 to 12 years of age with type 1 diabetes mellitus, when mediated by cortisol. Researchers have examined the associations between maternal depressive symptoms, child's perceived stress, child depressive symptoms, child's cortisol levels, and glycemic control independently but not concurrently (Hood et al., 2006; Jaser et al., 2008; Lupien et al., 2000; Markowitz et al., 2015; Stewart et al., 2013; Wiebe et al., 2011; Worrall-Davies et al., 1999). In addition, the mechanism of physiological stress, evidenced by change in cortisol, as a mediator between these psychological factors and glycemic control has not been well studied. Moreover, there is little or inconstant evidence detailing the amount of variance in glycemic control in children age 7 to 12 years diagnosed with type 1 diabetes explained by maternal depressive symptoms, child depressive symptoms, and child's perceived stress. The purpose of this chapter is to outline and support the methodology for the current study including the research design, sample, setting, instrumentation, and data analysis plan.

Pilot Study

Design of the current study was informed by a smaller pilot study implemented by the principal investigator (PI) to examine feasibility of recruitment, instrument administration to children as young as 6 years old, and data collection in the clinic setting. Of the 15 children identified by the clinical endocrinologist based on age and diagnoses of type 1 diabetes, three child-mother dyads were unable to be reached for follow up recruitment and screening (wrong number or no answer), four children did not qualify for the study (diagnosis, age, puberty, and length of diagnosis), and one child qualified but could not participate due to schedule conflicts. One child-mother dyad also qualified for the study, but was excluded because the mother could not attend the scheduled endocrinology appointment with her child to complete consent and self-report questionnaires in the clinic.

Table 3.1

Demographic Data from Small Pilot Study (n=6)

Variable	*N (%)*	*M (SD)*	*Range*
Age (years)		8.46 (2.36)	6.3-12.2
Gender			
Female	4 (66.7)		
Male	2 (33.3)		
Race			
White	5 (83.3)		
Black	1 (16.7)		
Yearly household income			
<$30,000	4 (66.7)		
$31-50,000	1 (16.7)		
$51-70,000	1(16.7)		
Use an insulin pump?			
Yes	4 (66.7)		
No	2 (33.3)		

In the small pilot study (n=6), ages of participants ranged from 6.3 to 12.2 years old (see Table 3.1). The majority of participants were female (66.7%), white (83.3%), used a pump (66.7%), and lived in a household with an annual income less than $30,000 (66.7%). HbA1c values ranged from 8.5% to 10.3%. Four children showed a decline in cortisol from morning to afternoon samples, while two children had increases in cortisol between the morning and afternoon samples (.018 mcg/dL and .402 mcg/dL). Scores for the Center for Epidemiologic Studies Depression Scale- Revised (CESD-R) ranged from 9 to 25, while scores for the Center for Epidemiologic Studies-Depression Scale for Children (CESD-C) and the Feel Bad Scale (FBS) ranged from 6 to 21 and 62 to 126, respectively (see Table 3.2).

Table 3.2

Descriptive Statistics for Study Variables from Small Pilot Study (n=6)

Variable	*M (SD)*	*Range*
HbA1c (%)	9.5 (.703)	8.5-10.3
First Cortisol Sample (μg/dL)	.192 (.086)	.127-.315
Second Cortisol Sample (μg/dL)	.189 (.187)	.052-.547
Cortisol change (μg/dL)	.003 (.211)	(-.402)-.205
Time between samples (minutes)	184.2 (8.6)	175-195
CESD-R Total Score	14.7 (6.5)	9-25
CES-DC Total Score	12.2 (5.7)	6-21
Feel Bad Scale Total Score	93.8 (28.3)	62-126

Data collection in the clinic was successful. All participants arrived at the clinic an hour before their scheduled appointment to complete surveys and provide the first

salivary sample. The first samples were collected between 08:30 and 09:45. After the child's routine endocrine appointment, all participants returned to the clinic to provide the second saliva sample. Second samples were collected between 11:30 and 12:45; time between the first and second sample varied from 2 hours 55 minutes to 3 hours 15 minutes. Most children were able to complete the survey instruments, though children younger than 7 years took longer to complete the CES-DC and Feel Bad Scale and had difficulty understanding some items. Thus, 6 year olds were not included in the larger study. Mothers did not report difficulty completing the demographic data or CESD-R, although some wrote additional information or alternate answers on the demographic data sheet. Due to scheduling conflicts with some mothers as potential participants, alternative methods to include mothers, such as mailing, emailing, or sending surveys home were considered for the larger study. All participants were given a $10 gift card to a local restaurant to have lunch during the break between the first and second salivary cortisol collections. Upon completion of data collection, the mother was given $10 and the child was given a small toy or game that did not exceed $5 in value.

Design

For the current study, the researcher used a correlational, hypothesis-generating design to examine the relationships between the school age diabetic child's perceived stress, child depressive symptoms, maternal depressive symptoms, child's physiological stress (measured by change in cortisol), and glycemic control. As a pilot study, this design was appropriate to determine effect sizes between variables of interest in order to

design and implement a future study that is fully-powered (Polit & Beck, 2012; Tabachnick & Fidell, 2013).

Sample and Setting

Setting

The PI recruited and enrolled participants for the study from a pediatric endocrinology clinic in the southeastern United States. Patients at the clinic had a variety of endocrine-related diagnoses, primarily diabetes. Between May 2015 and May 2016, the clinic saw approximately 414 children age 0 to 18 years with type 1 diabetes; 138 patients were between the ages of 7 to 12 years. Consent, assent, and data collection occurred in the clinic in private, quiet areas. The clinic was selected as the primary site for recruitment and data collection due to its large, accessible population of children diagnosed with type 1 diabetes, representing various socioeconomic status (SES) levels, ethnicities, and levels of glycemic control.

Sample and Population

Convenience sampling was used for recruitment purposes. The target population for the study included boys and girls diagnosed with type 1 diabetes, and their mothers. Inclusion criteria for mothers included that they: (a) were the biological mother of a child with a diagnosis of type-1 diabetes; (b) declared they have primary responsibility for diabetes management; (c) had the ability to read, write, and speak English; and, (d) were older than 18 years of age. Inclusion criteria for children included that they: (a) were boys and girls age 7 to 12 years, (b) had had a diagnosis of type-1 diabetes for at least 1 year;

(c) were currently treated with insulin; (d) were in regular contact with their mother; (e) had the ability to read, write, and speak English; and, (f) were pre-pubertal. Children were excluded from the study if they (a) had been diagnosed with comorbidities or endocrine disorders, such as Cushing's or Addison's disease; (b) had onset of puberty; and/or, (c) had taken steroid-based medications within the last 3 months.

While glycemic control in children younger than 7 years may be affected by the proposed concepts, instruments to measure the variables of interest are limited. In the small pilot study (n=6) completed by the PI to assess feasibility in preparation for the current study, children younger than 7 had difficulty completing some measures. Moreover, diabetic children enter puberty at a later age than non-diabetic children, with diabetic boys' average age at onset of puberty being 12 years and girls' average age of onset at puberty being 11.4 years (Rohrer et al., 2007). Children entering puberty experience variations in glycemic levels and insulin resistance, and children with type 1 diabetes often have poor glycemic control (Hannon et al., 2006; Trast, 2014). Therefore, children younger than seven were excluded from the study and screening was employed to exclude older children in the study who had experienced onset of puberty (see Appendix B). Since the clinic does not routinely collect puberty status on patients, the Rating Scale for Pubertal Development (Carskadon & Acebo, 1993; Petersen, Crockett, Richards, & Boxer, 1988) was used to screen children for inclusion in the study. The screening tool is a validated measure to obtain pubertal status non-invasively using 5 Likert-type items and may be administered by self-report or interview. Scores for items are averaged and scores of 3 or less indicate prepubertal status. Internal consistency for

the tool is satisfactory (α= .67 to .70) and pubertal status reported by parents and children is positively correlated (Carskadon & Acebo, 1993).

Since the PI intended to examine the relationship between maternal environmental factors, such as depressive symptoms on child glycemic control, this study was limited to biological mother-child dyads in regular contact. Additionally, children were excluded from the study if they had been diagnosed with diabetes for less than a year. In the first year following diagnosis with type 1 diabetes, many children experience a honeymoon phase which may alter the amount of insulin required by the child and influence glycemic control (Abdul-Rasoul et al., 2006). Moreover, children with endocrine disorders such as Addison's or Cushing's disease have variations in cortisol which pathologically affect blood glucose levels (Huether & McCance, 2012). Similarly, children taking steroid-based medicines, such as inhalers for asthma, may have alterations in blood glucose levels and higher HbA1c values (Black et al, 2011). Therefore, children who had taken steroid-based medicines in the last 3 months were also excluded from the study.

Sample Size and Power Analysis

Using Tabachnick and Fidell's (2013) formula, it was estimated a minimum sample size of 108 dyads would be needed to employ a fully powered study. However, the purpose of the current pilot study was to explore clinically meaningful relationships between proposed variables, ascertained through examination of effect sizes. Therefore, the PI recruited 25 dyads using convenience sampling in addition to 6 dyads previously enrolled in the small pilot study for feasibility. Effects sizes and attrition rates found in the current study may be used in future power analyses to determine minimal sample

sizes required for fully-powered studies examining the variables of interest (Polit & Beck, 2012; Suresh & Chandrashekara, 2012).

Protection of Subjects

Approval from two Institutional Review Boards (IRBs), at the home institution of the investigator and the site of data collection, were obtained prior to initiation of recruitment or data collection (see Appendix E). The study is classified as no greater than minimal risk to the subject since non-invasive techniques, such as surveys and salivary collection, were employed to collect data outside of the routine clinic appointment for children. Prior to data collection, consent was obtained from mothers and assent obtained from children participating in the study.

Potential risks associated with data collection in the child included mild anxiety or embarrassment associated with spitting into a cup during salivary collection. Both the mother and child faced potential risks of mild emotional discomfort during survey completion due to the sensitive nature of questions asked regarding depressive symptomatology or stressful experiences. To minimize these potential risks, mothers and children completed data collection separately and all data were collected in a quiet, private area of the clinic in which only the researcher and participant were present. Confidentiality was maintained; if a participant indicated suicidality during data collection or experienced extreme emotional distress (crying, notably upset, or anxious) not relieved by the data collector, he or she would be referred to primary physician at the endocrinology clinic. No participants expressed extreme emotional distress or suicidality during data collection. Mothers and children were also reminded throughout the study

that they were able to withdrawal or stop data collection at any point without repercussion.

All participants were assigned a random identification number. Data collected on paper were stored in a locked cabinet accessible only to the PI. Electronic data were stored on an encrypted USB drive also accessible only to the PI. Personal identification data, used for recruitment and screening purposes, were stored separately in the locked office of the primary clinician at the pediatric endocrinology clinic. All researchers involved in data collection had previous experience assessing and collecting data from children in various health care settings and completed training from the National Institute of Health on protecting human research participants.

Data Collection Instruments

Demographic Data

Demographic data were collected from mothers using a survey developed by the PI and refined based on findings from the small pilot study with 6 participants (see Appendix C). Data collected included child age, school grade, health history for both the child and mother including report of fever in child in the last 72 hours, self-reported race, sex, current treatment regimen for diabetes, duration of diabetes diagnosis, annual household income, type of health insurance, and level of education. Height and weight that were collected by the clinic on the day of data collection were obtained from the medical record and used as demographic data.

Center for Epidemiologic Studies Depression Scale-Revised

Depressive symptoms in mothers were measured using the CESD-R (Eaton, Muntaner, Smith, Tien, & Ybarra, 2004). This tool is a revision of the Center for Epidemiologic Studies Depression Scale created by Radloff in 1977 and is intended to measure symptoms of a major depressive episode using a classification scheme consistent with DSM-IV diagnostic content and process (Van Dam & Earleywine, 2011). The revised scale includes new diagnostic symptoms of depression identified in the DSM-IV such as psychomotor agitation, suicidal ideation, and anhedonia while maintaining sensitivity and improving specificity of the tool (Eaton, et al., 2004; Van Dam & Earleywine, 2011). Additionally, the revision was necessary to remove eight items from the CES-D that are no longer related to the definition of major depression (Eaton et al., 2004).

The CESD-R is a 20-item self-report scale (see Appendix C). CESD-R responses for each item range from 0 to 4 on an ordinal scale of frequency. Although responses to items range from 0 to 4, the top two responses (3 and 4) may be assigned a value of 3 to make scores comparable to the original CES-D (CESD-R, 2008). Therefore, total scores range from 0 to 60 with higher scores indicative of increased depressive symptomatology and scores less than 16 signifying no clinical significance. For statistical purposes, total scores are treated as interval data and analyzed accordingly.

Administration. The CESD-R is in the public domain and easily accessible. It is free and permission does not need to be obtained to use the measurement (CESD-R, 2013). The tool can be administered via computer, telephone, or paper (CESD-R, 2013; Eaton et al., 2004). While this tool can aid in diagnosis of depression, it is not a

diagnostic tool and can be self-administered by the general population (Eaton et al., 2004). There is no special training required by data collectors or raters (CEDS-R, 2013). However, raters and participants should be aware of an unsolicited break in confidentiality if survey participants communicate an imminent desire or precise plan to commit suicide (Eaton et al., 2004).

Psychometric properties. Eaton et al (2004) performed initial testing for the scale on 27 individuals of the general population and 14 psychiatric in-patients. Reliability tests revealed Cronbach's α of 0.96 (Eaton et al., 2004). Surveys administered to 1,055 participants indicated good internal consistency (α= 0.93) and established content validity using exploratory factor analysis (Eaton et al., 2004; Waltz, Strickland, & Lenz, 2010). Further analyses by Eaton et al. (2004) using similar methods indicated good reliability and validity of the CESD-R when the scale was administered in a web-enabled version, translated and administered in Spanish, and administered to parents and vulnerable populations (low-income women with high risk of depressive symptoms). Further, Olagunju et al. (2013) used the scale to identify depressive symptoms in 200 cancer patients in Nigeria; they found the scale had high reliability (Cronbach's α=0.86), while specificity and sensitivity were 68.7% and 96.4%, respectively.

Van Dam and Earleywine (2011) confirmed the results by Eaton et al. (2004). Van Dam and Earleywine (2011) validated the tool using two sample groups. Sample one consisted of 6,971 adults recruited from a list-serv who were primarily male (80.7%) and Caucasian (89.4%). Sample two consisted of 245 undergraduate psychology students who identified primarily as Caucasian (72.8%). In sample one, there was good reliability and high internal consistency (Cronbach's α= 0.923). Additionally, exploratory factor

analysis was performed by randomly dividing the first sample by half and performing parallel analysis to reveal eigenvalues larger than one (Van Dam & Earleywine, 2011) suggesting confirmation of construct validity (Waltz et al., 2011). Correlation between the CEDS-R and the State-Trait Inventory for Cognitive and Somatic Anxiety Scale was 0.737 ($p<0.01$) (Van Dam & Earleywine, 2010).

Center for Epidemiologic Studies-Depression Scale for Children

Depressive symptoms in children were measured using the CES-DC. To develop the CES-DC, researchers modified items from the CES-D to make them comprehendible for children (Faulstich, Carey, Ruggiero, Enyart, & Gresham, 1986; Fendrich, Weissman, & Warner, 1990). The scale is validated for children age 7 to 17 years (Faulstich et al., 1986).

The scale contains 20 items, with 4-items being positive phrased and reversed scored to aid in validity (see Appendix C) (Weissman, Orvaschel, & Padian, 1980). Each item is based on a Likert-type scale, with scores ranging from 0-3. Items 4, 8, 12, and 16 are reversed scored. Lower scores indicate lower depressive symptomatology and higher scores indicate high depressive symptomatology. Scores for each item are added to obtain a total score; total scores for the survey can range from 0-60. Fifteen is used as the cutoff mark for high depressive symptomatology in children (Weissman et al., 1980). For data purposes, scores are treated as interval data and analyzed appropriately.

Administration. The CES-DC is in the public domain, is free to use, and does not require special permissions to administer. While this tool is indicative of depressive symptoms in children, it is not to be used as a diagnostic tool. Therefore, there is no

training required for individuals administering the tool. The tool is administered via paper and pencil and takes 10 minutes or less to complete. In the current study, the PI read all items and choices to the child while the child followed along with his or her copy of the tool to account for differences in reading levels of children enrolled in the study.

Psychometric properties. Initial validation by Faulstich et al. (1986) was based on administration to 148 children and adolescents in the United States who were primarily Caucasian (57%) and male (78%). Internal consistency of the CES-DC measured by reliability coefficients was $\alpha = .84$, while test-retest reliability over 2 weeks was .51 (Faulstich et al., 1986). Fendrich et al. (1990) also found good internal reliability ($\alpha = .89$) for adolescents, though reliability was lower in children who were 6 years old ($\alpha = .78$). More recently, the CES-DC has been adapted and validated in children outside of the United States. Betancourt et al. (2012) validated the CES-DC in children in Rwanda and have found good internal reliability ($\alpha = .86$) and test-retest reliability ($r = .85$) while Barkmann, Erhart, and Schulte-Markwort (2008) validated the tool in German children and found good internal reliability for children age 11 and older ($\alpha = .83$). The CES-DC has been found to correlate with other depressive measures for children such as the Child Depression Inventory, $r = 0.61$ (Faulstich et al., 1986). However, the tool shows stronger psychometric properties in adolescents than in children (Barkmann et al., 2008; Faulstich et al., 1986; Fendrich et al., 1990). Limitations in validation of the CES-DC may be attributed to the fact that behavioral signs of depression are not as clearly understood in children.

Feel Bad Scale

Perceived stress in children was measured using the FBS (Lewis, Seigel, & Lewis, 1984). The scale is designed and validated to measure stress in children ages 8 to 12 years (Lewis et al., 1984). In the small pilot study to test feasibility of administering the Feel Bad Scale to children as young as 6 years, the PI found that 6 year olds had trouble understanding items in the scale and took longer to complete the instrument. However, participants who were 7 years and older were able to complete the scale with minimal help from the PI. Therefore, the scale was used in the larger study to measure perceived stress only in children 7 years and older. Potential differences in scores between 7 year olds and older children in the larger study were examined during data analysis.

The FBS is a 40-item measure that is divided into 2 sections (see Appendix C). The first section focuses on how stressful situations make (or would make the child feel) if they happened to the child. The second part assesses how often the stressful event has happened to the child in the past year (Lewis, Siegel, & Lewis, 1984). Each section has 20 items, with 17 normative and 3 non-normative stressors (Lewis et al., 1984; Ryan-Wenger, Wilson, & Broussard, 2012). These stressful items were developed from incidents children reported as being stressful or which made them feel nervous, bad, or worried (Lewis et al., 1984; Ryan-Wenger et al., 2012.). These items are presented on a self-report, Likert-type scale and assess both frequency (1-"Never" to 5-"Always") and severity (1-"Not bad" to 5-"Terrible") of stressful events. A total Feel Bad score is obtained by multiplying the frequency by severity of each item and summing the

products (Lewis et al., 1984). Scores may range from 20 to 500 (Lewis et al., 1984). For data analysis, scores are considered interval data and analyzed as such.

Administration. While the FBS is in the public domain and is free to use, permission was sought from the tool developers by the PI for use in the current research study (see Appendix D). The tool is not diagnostic of stress, and should only be used an indicator of stressful events. The scale is meant to be self-administered with pencil and paper. However, to account for differences in reading levels of children, the PI read all items and item choices aloud to the child participant while the child read his or her copy of the instrument.

Psychometric properties. Reliability coefficients of the FBS ranges from .82 to .85 in studies ranging from 1,026 to 2,480 children of all races and ethnicities (Jenkins, Rew, & Sternglanz, 2005; Lewis et al., 1984). These findings were further supported by Adams and Weaver (1986) who reported internal consistency of the scale as .82 when used to study perceived stress in children with chronic disease (n=35). Strong construct validity as determined by factor analysis with results indicating a three-factor model with eigenvalues greater than one; factors include anxiety about conflicts with adults, moving from one place to another, and self-image and peer relationships (Lewis et al., 1984).

Salivary Cortisol

Cortisol was collected and measured through salivary samples. Although salivary cortisol concentrations tend to be higher than serum levels of cortisol (Hellhammer et al., 2008), using high sensitivity enzyme immunoassay the serum-saliva correlation is .91 (Salimetrics, 2014). Normal values for salivary cortisol for children age 8-11 years range

from 0.084-0.839 μg/dL when collected within an hour of waking up and 0-0.215 μg/dL when collected in the evening (Salimetrics, 2014). Since normal cortisol levels are highest in the morning, approximately 45 minutes after waking, and fall throughout the day with the sharpest decline between 08:00 and 15:00 (Brasher & Jones, 2010; Hellhammer et al., 2008), two samples of cortisol were collected from each participant to assess the change in cortisol. To control for diurnal variations in cortisol levels, the PI standardized times for specimen collection by collecting samples from all participants around the same time point each day and allowing enough time to see the change in cortisol levels from morning to afternoon (Hanrahan et al., 2006). This was accomplished by collecting the first sample between 07:00 to 10:30 and collecting the second sample a minimum of 3 hours later between 11:30 and 14:00.

Following collection, samples were stored in the -20° C freezer at the clinic until the end of the data collection day when they were transported on ice and stored in a -80° C freezer. For analysis, batched samples were placed on dry ice and shipped via overnight delivery to Salimetrics, LLC where they were analyzed using high sensitivity enzyme immunoassay with sensitivity <0.007 ug/dL and range 0.012 to 3 μg/dL (Salimetrics, 2014). Duplicate cortisol assays were run for all samples. The mean value obtained between the duplicate tests represent the cortisol level for the salivary sample.

Since abnormal changes in cortisol represent malfunction of the HPA axis and failure of the body to adapt to physiological stress (McEwen, 2007), the change is the level of cortisol from first collection to second collection was used for analysis. This change was classified as “normal” represented by a decrease in cortisol level in the second sample, “blunted” represented as no change (or change less than 0.01μg/dL) in

cortisol level between the first and second sample, and "abnormal" represented by an increase in cortisol level from first to second sample.

HbA1c

Glycemic control is the measurement of blood glucose variability over a certain period of time (Rodbard, 2009). There are numerous ways to measure glycemic control including mean glucose values, Index of Glycemic Control (IGC), Glycemic Risk Assessment Diabetes Equation (GRADE), and High Blood Glucose Index (HGI) (Rodbard, 2009). A commonly used clinical measurement for glycemic control is HbA1c (ADA, 2012). HbA1c measures blood glucose variability over the span of three months, with a threshold of 7.5% or greater indicating poor glycemic control in children age 6-12 years with type 1 diabetes (ADA, 2015). Because HbA1c measures the average variation of glycemic control over the last three months, the researcher ensured that questionnaires and HbA1c levels were collected on the same day to ensure correlation of data. Additionally, although the American Diabetes Association (2012) recommends the National Glycohemoglobin Standardization Program (NGSP) certified method that is standardized to the Diabetes Control and Complications Trial (DCCT) assay to measure HbA1c levels, not all laboratories use this method. Therefore, the PI verified laboratory techniques and ensured the same methodology was used in the clinic setting with all children in measuring levels of HbA1c to enhance validity in data collection and results.

To help relieve participant burden and control costs of the study, HbA1c values collected on the day of data collection were obtained from the child's medical record. HbA1c values are normally collected in the clinic on all children with type 1 diabetes

during their routine endocrinology appointment. To verify that the HbA1c values reflect the time period of depression and stress inventories, the researcher ensured that HbA1c values recorded in the medical record and used for data analyses were collected on the same day as questionnaire completion. HbA1c samples and analysis were collected by the clinic nurse. Using a capillary blood sample obtained by finger prick, a small sample of blood (1.5mcL) was collected from the child and analyzed using an Alere Afinion AS100 Analyzer in the clinic. Values reported by the Afinion AS100 may range from 4-15% HbA1c in intervals of 0.1%. Sensitivity and specificity for the Alere Afinion AS100 Analyzer are 86% and 92% respectively. The nurse collecting the HbA1c level recorded the value in the patient's medical record. Since all specimens for all participants were processed on the same quality-controlled device using the same technique by the same nurse, the researcher may be fairly certain that HbA1c scores are standardized between participants.

Procedure and Methods

Recruitment consisted of flyers, informational letters, referrals from the pediatric endocrinologist office, and telephone calls. Potential participants were identified based on age and diagnosis by the pediatric endocrinologist at the clinic. The PI contacted potential participants to explain the purpose of the study, confirm interest of mother and children participating in the study, and screen for inclusion and exclusion criteria of both the mother and child (see Appendix B). Once interest was established and screening criteria was met, the PI scheduled data collection for the day of the child's next routine clinic visit. Prior to data collection an informational letter explaining the study as well as a copy

of consent and assent was mailed to participants. A phone call reminding participants of participation in the study was made the day before data collection. Participants were reminded to arrive approximately an hour before their scheduled appointment to begin data collection.

Upon arrival to the clinic, mother-child dyads were escorted to a quiet, private area where consent and assent were obtained together. Consent and assent were reviewed with the mother and child, respectively, and signatures were obtained on the consent and assent. The mother was given a packet of surveys (demographic data and CESD-R) to be completed independently. The data collector explained survey completion to the mother and then directed the mother to a separate, quiet area of the clinic to complete her surveys and to allow for privacy of the child during collection of the first salivary sample.

If the biological mother was unable to attend the clinic appointment with the child, consent for the child's participation was obtained by the guardian escorting the patient to the clinic. The PI sent home or mailed (based on the mother's preference) consent and surveys, as well as a self-address and stamped envelopment, for the mother to complete at home. The PI made follow up phone calls to the mother to ensure the mother received the consent and surveys and allow the mother to ask questions or voice concerns regarding the surveys or consent. After completing the surveys, the mother mailed her responses in a sealed envelope to the PI. Upon receipt of the completed surveys, the PI mailed the $10 incentive to the mother for her participation in the study.

To collect the first salivary sample, the child was instructed to rinse his or her mouth with water by taking a sip of water from a cup, swishing it around his or her mouth, and either swallowing the water or spitting the water back into the cup. The child

then was handed a small bag containing a straw, a rubber band, a tissue, and a small, plastic vial pre-labeled with his or her unique study code number. The child was instructed to remove the straw and the vial from the bag and place the straw in the vial. Depending what was easiest for the child, the child chose to use the straw or spit directly in the vial. Once the child was ready, the researcher instructed the child to place drool into the straw/cup. Lay terminology, "spit into the straw/cup", was be used to help the child understand what he or she is supposed to do. If the child struggled to produce saliva, guided imagery was used to assist the child to think about his or her favorite food and/or the child was asked to chew on the rubber band included in the bag. Saliva was collected over 3 minutes. If the child had trouble producing saliva, an additional 2 minutes were provided to allow the child to collect a minimum of 0.5 mL; allowance of additional time was then noted for data analysis purposes. Once time ended, the data collector instructed the child to remove the straw from the vial (if used) and hand the vial to the data collector. The data collector ensured an adequate sample was obtained and then placed an appropriately colored top on the vial indicating 1st or 2nd salivary collection. Saliva was placed in the -20 °C freezer at the clinic immediately following collection until the end of the data collection day. Straws and other contaminated items were disposed of properly.

Following completion of collection of the first salivary sample, the data collector administered surveys (CES-DC and Feel Bad Scale) to the child. The child was given his or her own copy of the surveys to read as the data collector read the item stems and options aloud to the child. The child marked his or her choice on his or her copy of the

survey. A cover sheet was provided for the child if he or she wished to ensure all answers remain private.

After survey completion, both the child and the mother proceeded to the child's routine clinic appointment. During the endocrinology appointment, the data collector reviewed the CESD-R to ensure the mother did not indicate suicidal ideation or self-harm indicated by any score greater than zero on the items "I wished I were dead" and "I wanted to hurt myself". Following the routine endocrinology appointment, the child and mother were given a small break and a $10 gift card to a local restaurant to have lunch. During this time, height, weight, and the results of the HbA1c analysis were obtained from the medical record.

When a minimum of 3 hours since the first salivary collection time (representative of a morning and afternoon sample) had passed, a second salivary sample was collected from the child using the same collection technique as the first salivary sample. At the end of data collection, both the child and mother were thanked for their time and given incentives for participation in the study. All mothers were given $10.00 in cash and all children were given an age-appropriate small toy, book, or game not exceeding a total of $5.00. Following data collection, cortisol samples were transported on ice and be placed in a -80° freezer where they were banked until completion of data collection from all participants.

A change to protocol was made when it was noted that many individuals were unable to participate in the study because of time constraints or inability to come to the clinic in the morning for data collection. Therefore, protocol for collecting the first sample of saliva was revised to give participants the option of collecting the first sample

of saliva at home if they were unable to attend a morning appointment or were unable to remain near the clinic for three hours. For these participants, the consent, assent, supplies and an informational sheet on how to collect the sample of saliva at home were mailed prior to the day of the scheduled endocrinology appointment. The PI contacted participants via phone to ensure they received materials and address questions or concerns of collecting data at home. Participants were instructed to collect saliva from the child between 07:30 and 08:00 and note the time it was collected. Saliva was collected at home by the parent or guardian using the same technique as saliva that was collected in the clinic. Participants stored the collected saliva in the refrigerator or on ice until it was brought to the clinic later the same day for the child's endocrine appointment and continuation of data collection. Upon arrival at clinic, the salivary sample was stored as previously described. The child then proceeded to provide a second sample of saliva and surveys were completed as previously described.

Data Management

Participant identifiers were coded and stored in a locked cabinet accessible only to the PI. Surveys were reviewed prior to the end of data collection to ensure items were not left blank unintentionally. Completed paper surveys, labeled with unique study code number, were stored in a locked cabinet accessible only to the PI. Paper surveys were transcribed electronically by the PI using double entry verification and saved on an encrypted USB drive. In the event of missing data, cells were left blank during transcription. The electronic database was password protected and accessible only to the PI. Salivary specimens were labeled only with unique study code numbers and shipped to

Salimetrics, LLC for cortisol assay. Salimetrics, LLC provided an electronic copy of cortisol values labeled only with unique study code numbers which were stored using the above mentioned methods. Thirty days after completion of cortisol assay, salivary samples were destroyed by Salimetrics, LLC.

Data Analysis

All data were analyzed using IBM SPSS Version 23. Descriptive statistics and frequencies were examined for demographic and study variables. Interval level variables were assessed for outliers, normal distributions, and linearity (Polit & Beck, 2012; Shadish, Cook, & Campbell, 2002; Tabachnick & Fidell, 2013). Missing data were treated as missing at random and list-wise deletion was used to control for missing data (Shadish, Cook, & Campbell, 2002). While multiple regression models with glycemic control as the outcome variable and cortisol as a mediating variable are ideal to test the relationships in a fully-powered study, this study was not fully powered due to small sample size. Therefore, the purpose of data analysis in the current pilot study was to generate hypotheses instead of testing hypotheses. This was accomplished by determining effect sizes between variables which can be used to design a fully powered study for hypothesis testing. Effect sizes are the strength of association (magnitude) between variables (Tabachnick & Fidell, 2013). Effect sizes were based on Cohen's definition of small, medium, and large effects for association statistics (Tabachnick & Fidell, 2013; Cohen, 1988). For interpretation purposes, a small-medium effect size magnitude was used as the relevancy threshold to determine if relationships are clinically meaningful.

R1. What are the effect sizes of the relationships between maternal depressive symptoms and child's perceived stress, maternal depressive symptoms and child depressive symptoms, and child's perceived stress and child depressive symptoms?

Items on the CESD-R, CESD-C, and Feel Bad Scale were entered as categorical data based on the Likert scale ratings for each measure. The numerical values of items were summed for each survey and total scores were analyzed as interval data. Effect size was determined by Pearson's *r* value when analyzed by bivariate correlation (Polit & Beck, 2012; Tabachnick & Fidell, 2013). Effect sizes for bivariate correlation were based on definitions proposed by Cohen as small (r= .1), medium (r= .3), and large (r= .5) (Cohen, 1988). Effect size was considered meaningful if it reached the relevancy threshold of a small-medium effect indicated by r= .2 or higher.

R2. What are the effect sizes of the influence of maternal depressive symptoms, child depressive symptoms, or child's perceived stress on child's glycemic control?

Determination of effect size was based on a simple linear regression model. Three individual models were built with glycemic control, represented as HbA1c value, as the dependent variable in every model and a single independent variable (maternal depressive symptoms OR child depressive symptoms OR child's perceived stress). Because both the independent and dependent variables were ratio levels of measurement and continuous data, the squared correlation (R^2) was determined to be the effect size since it measures the strength of the association between the variables in a regression model (Tabachnick & Fidell, 2013). Effect sizes for R^2 values were based on definitions proposed by Cohen as small (R^2= .02), medium (R^2= .15), and large (R^2= .35) (Cohen,

1988). Effect size was considered clinically meaningful if it reached the relevancy threshold of a small-medium effect indicated by R^2= .09 or higher.

R3. What amount of the total effect of maternal depressive symptoms, child depressive symptoms, and child's perceived stress on glycemic control is accounted for by the mediated effect of cortisol?

In multiple regression models, such as the mediational model, effect size is considered to be the magnitude of the association between independent variables on the dependent variable when both variables are continuous (Tabachnick & Fidell, 2013). This is indicated by the R^2 and adjusted R^2 values which examine the proportion of variability in the outcome that is attributable to the total model and specific predictors added to the model (Tabachnick & Fidell, 2013).

Cortisol levels were entered as ratio level data (to the nearest thousandth). Since duplicate cortisol assays were run for both first and second samples, the results from the duplicate testing were summed and averaged to find values representing cortisol levels for each individual. Bivariate correlational analysis was used to assess associations between the first cortisol sample and the second cortisol sample and the following variables: maternal depressive symptoms, child depressive symptoms, child's perceived stress, and glycemic control. The cortisol levels of the second salivary sample value was subtracted from the cortisol level of the first salivary sample to obtain a "change" in cortisol from first to second sample. This change in cortisol is what was used as the mediating variable for data analysis.

Mediational analysis was based on the Baron and Kenney (1986) method. The goal of mediational analysis is to examine and establish the effect of maternal depressive

symptoms on cortisol, the effect of maternal depressive symptoms on glycemic control, and the effect of cortisol on glycemic control. First, the researcher must determine that the causal variable is associated with the outcome variable and correlated with the proposed mediator. Next, the researcher must determine that the proposed mediator affects the outcome variable. The final step to is to build a general linear model to examine the effect of the causal variable on the outcome variable when controlling for the proposed mediator. If cortisol acts as a mediator in the relationship between maternal depressive symptoms and glycemic control, then the total effect of maternal depressive symptoms on glycemic control should be greatly reduced (near zero) when controlling for cortisol in the general linear model (Baron & Kenny, 1986). These steps to examine the total effect of mediation by cortisol were repeated with child depressive symptoms and child's perceived stress.

R4. What are the effect sizes of the relationships between time-since-diagnosis, treatment modality, ethnicity, and SES and glycemic control?

Treatment modality was entered as a dichotomous variable (pump vs. multiple daily injections). Effect size for the relationship between treatment modality as a dichotomous variable and glycemic control as ratio data was obtained by correlational analysis. As the correlation coefficient, the point-biserial value was considered to be the effect size of the relationship between treatment modality and glycemic control (Hinkle et al., 2003; Tabachnick & Fidell, 2013).

Time-since-diagnosis (in months) and glycemic control, measured as HbA1c value, were entered and analyzed as ratio data. Effect sizes for the relationship between time-since-diagnosis and glycemic control were determined by Pearson's *r* value when

analyzed by bivariate correlation (Polit & Beck, 2012; Tabachnick & Fidell, 2013). Effect sizes for association statistics were classified according to Cohen (1988) as small (r= .1), medium (r= .3), and large (r= .5). Effect size was considered clinically meaningful if it reached the relevancy threshold of a small-medium effect indicated by r= .2 or higher.

SES was entered categorically as low income (<$30,000/year), medium income ($30,001/year to $70,000/year), and high income (>$70,001/year). Effect size for the relationship between SES and glycemic control was obtained with ANOVA and eta squared was used as the estimate for effect size (Hinkle et al., 2003). Eta squared is the measure of variance in the dependent variable that is attributed to by an independent variable when the independent variable is dichotomous or categorical (Tabachnick & Fidell, 2013). Because SPSS only reports partial eta squared, eta squared was calculated using the formula $\eta^2 = SS_{between} / SS_{total}$ (Levine & Hullett, 2002). Using Cohen's values for effect size (η^2) with ANOVA, it was determined that .01 is small, .06 is medium, and .14 is large (Cohen, 1988). Effect size was considered clinically meaningful if it reached the relevancy threshold of a small-medium effect indicated by η^2=.035 or higher.

Ethnicity/race was categorized as White, Black, Hispanic, Asian, and biracial/other and analyzed as dichotomous data since only two races were reported. As a dichotomous variable, effect size for the relationship between ethnicity and glycemic control obtained by correlational analysis and the point-biserial value was considered to be the effect size of the relationship between ethnicity and glycemic control (Hinkle et al., 2003; Tabachnick & Fidell, 2013).

Summary

This chapter focused on the methodology of the current study. The study used a correlational, hypothesis-generating design. Support was provided for the research design, target sample, setting, protocol, instrumentation, and data analysis plan. Data collection occurred in a clinic setting using self-report surveys and physiologic data. Data analysis focused on correlational analyses and establishment of effect sizes appropriate for the level of measurement of the variable under consideration.

CHAPTER 4

FINDINGS

The purpose of this study was to generate hypotheses, indicated by effect sizes, on the relationships between maternal depressive symptoms, child depressive symptoms, and child's perceived stress on glycemic control in prepubertal school-aged children 7 to 12 years of age with type 1 diabetes mellitus when mediated by cortisol. Given the small sample size, the primary aim of data analysis was to examine effect sizes between variables to generate hypotheses for future, fully powered studies. Effect sizes for confounding factors (time-since-diagnosis, treatment modality, ethnicity, and socioeconomic status [SES]) were also examined. The focus of this chapter is to describe sample demographics as well as report findings on study variables and research questions.

Sample and Setting

Using convenience sampling, a final sample of 30 children with type 1 diabetes and their mothers was recruited from a pediatric endocrinology clinic in the southeastern United States and enrolled in data collection. Data collection occurred over the course of 14 months from December 2015 to March 2017. Of 121 potential participants identified for inclusion in the study based on age and diabetes diagnosis, 84 were able to be reached for follow up recruitment and screening and 69 expressed interest in participating. Of

these, 40 met inclusion criteria for the study. Onset of puberty and lack of maternal involvement were the most common reasons for exclusion as a participant. After mothers and children expressed interest in participating and met screening criteria, informational letters were mailed and appointments were made for data collection coinciding with the child's next routine endocrinology clinic appointment. Because of issues with scheduling or inability to be reached to schedule a time for data collection, only 30 of 40 eligible mothers and their children were consented and enrolled in the study. The participation rate was 35.7% (30/84) among potential participants and 75% (30/40) among eligible participants.

Demographic Data

Demographic data collected included child age, school grade, gender; health history for both the child and mother including self-reported race, current treatment regimen for diabetes, duration of diabetes diagnosis, and child height and weight; annual household income, type of health insurance, and maternal level of education. Interval demographic data were examined graphically for outliers. Ages of participants ranged from 6.9 years to 12.2 years (see Table 4.1) and most children were in 2nd (20%), 3rd (23.3%), and 4th (26.7%) grades. The majority of participants were female (70%), white (76.7%), and used an insulin pump (73.7%). Average length of diabetes diagnosis was 3.48 years, although 10 children were diagnosed less than 20 months but more than 12 months. Seven different mothers reported child diagnoses in addition to type 1 diabetes; two mothers reported their child had a history of asthma with no recent complications, three mothers reported learning delays/disabilities in their child, and two mothers

reported their child had ADD/ADHD. The demographic data sheet also included a question about whether the child had experienced a fever in the last 72 hours (to account for potential variations in salivary cortisol); no fevers were reported.

Table 4.1

Child Demographic Data (n=30)

Variable	*N (%)*	*M (SD)*	*Range*
Age (years)		9.1 (1.39)	6.9-12.2
Time-since-diagnosis (months)		41.7 (27.3)	12-97
BMI		17.2 (1.88)	12-22.54
Gender			
Female	21 (70)		
Male	9 (30)		
Race			
White	23 (76.7)		
Black	7 (23.3)		
Use an insulin pump?			
Yes	22 (73.3)		
No	8 (26.7)		
Child diagnoses			
Asthma	2 (6.7)		
Learning delay/disability	3 (10)		
ADD/ADHD	2 (6.7)		

Family and maternal demographics were also examined (see Table 4.2). Income showed a broad range, with 33.3% of families making less than $30,000/year, 40% of families making $31-70,000/year, and 26.7% of families making more than $71,000/year. Additionally, most families had private pay insurance (56.7%), although 5 mothers did not report this information. Twelve mothers (40%) had a college degree or higher. Two mothers reported a history of depression, while six mothers reported miscellaneous medical diagnoses (anxiety, asthma, hypertension, sickle cell trait, type 2 diabetes). The

majority of mothers reported abstaining from cigarette use (86.7%), and 40% of mothers reported alcohol use.

Table 4.2

Family and Maternal Demographic Data (n=30)

Variable	*N (%)*
Yearly household income	
<$30,000	10 (33.3)
$31-50,000	5 (16.7)
$51-70,000	7 (23.3)
$71-100,000	6 (20.0)
>$100,000	2 (6.7)
Insurance status	
None/Self Pay	1 (3.3)
Private	17 (56.7)
Medicare/Medicaid	7 (23.3)
Missing	5 (16.7)
Mother's education	
High school graduate	18 (60)
College graduate	10 (33.3)
Beyond college	2 (6.7)
Mother's relationship status	
Married	20 (66.7)
Divorced	4 (13.3)
Unmarried	1 (3.3)
Single	5 (16.7)
Mother's use of cigarettes?	
Yes	4 (13.3)
No	26 (86.7)
Mother's use of alcohol?	
Yes	12 (40)
No	18 (60)
Maternal diagnoses	
Depression	2 (6.7)
Learning delay/disability	2 (6.7)
Other	5 (16.7)

Study Variables

The main variables included in the study were maternal depressive symptoms, child depressive symptoms, child's perceived stress, glycemic control and cortisol change. These variables were measured with the Center for Epidemiologic Studies Depression Scale-Revised (CESD-R), the Center for Epidemiologic Studies-Depression Scale for Children (CES-DC), the Feel Bad Scale (FBS), HbA1c, and the difference between two samples of salivary cortisol, respectively. Additionally, time between salivary collections was examined. Descriptive statistics for study variables are reported in Table 4.3.

Table 4.3

Descriptive Statistics for Study Variables (n=30)

Variable	*M (SD)*	*Range*
CESD-R Total Score	9.83 (8.0)	0-29
CES-DC Total Score	11.1 (8.0)	0-30
Feel Bad Scale Total Score	115.1 (46.1)	45-202
First Cortisol Sample (μg/dL)	.212 (.156)	.046-.616
Second Cortisol Sample (μg/dL)	.156 (.114)	.052-.547
Cortisol change (μg/dL)	.056 (.2)	(-.402)-.56
Time between samples (minutes)	206.3 (61.5)	130-375
HbA1c (%)	8.75 (1.2)	6.1-12.2

Center for Epidemiologic Studies Depression Scale-Revised

The CESD-R was used to measure depressive symptoms in mothers. A total score for the measure was obtained by summing items. Scores ranged from 0-29 with a mean of

9.8 (±8.0). Eight mothers scored at or above the cutoff of 16 for clinically significant depressive symptoms, however, none indicated suicide ideation or intent to harm themselves or others which would require referral to a healthcare provider per protocol. The measure showed good internal consistency with Cronbach's α= .87. No outliers were noted upon visual examination of the data.

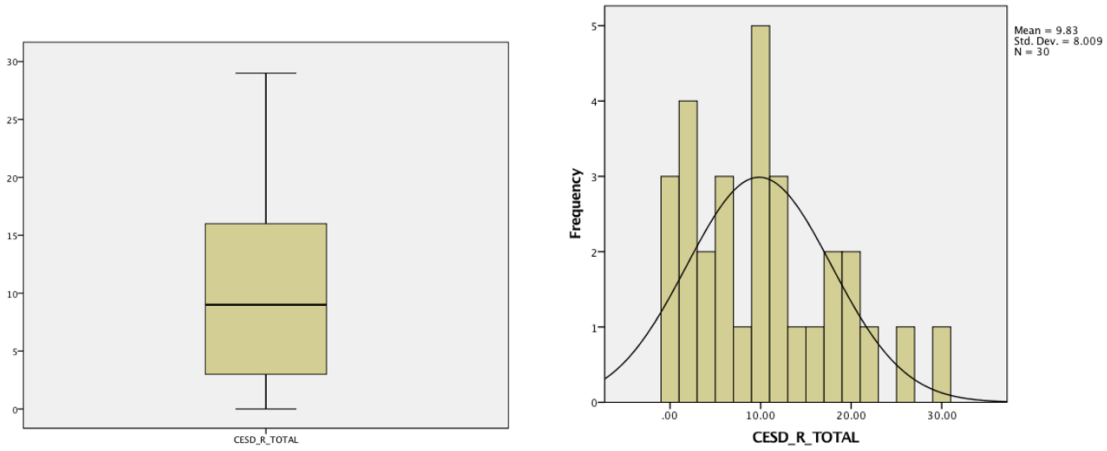


Figure 4.1. Box-plot and histogram for CESD-R scores (n=30).

Center for Epidemiologic Studies-Depression Scale for Children

Depressive symptoms in children were measured using the CES-DC. Four items on the scale were reverse scored to account for positive phrasing and items were then summed to find a total score. Scores ranged from 0-30 with a mean score of 11.1 (±8.0). Nine children scored at or above the cutoff of 15 for clinically significant depressive symptoms, however, none met the protocol for referral to a healthcare provider. Internal consistency of the measure in this population was fair (α=.793). Using visual inspection, no outliers were noted for the CES-DC.

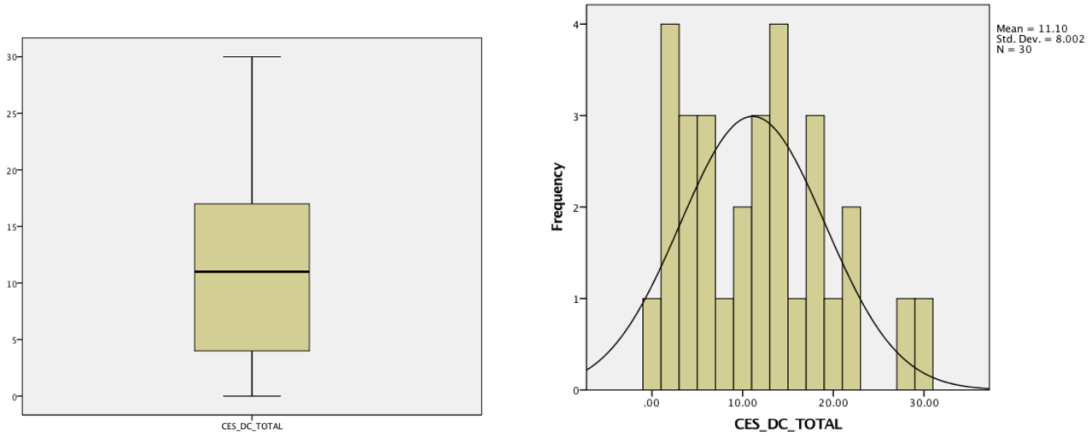


Figure 4.2. Box-plot and histogram for CES-DC scores (n=30).

Feel Bad Scale (FBS)

The FBS was used to examine child's perceived stress. The scale contains two subscales - one measuring severity of stress and one measuring frequency of stress. A total score was obtained by summing the products found by multiplying corresponding items on each subscale. Scores ranged from 45 to 202, with a mean score of 115.1 (±46.1). Internal consistency of the survey was analyzed by finding Cronbach's α for each subscale and then the total measure. Cronbach's α varied for the severity subscale and the frequency subscales (α=.847 and .771, respectively), but was good overall (α=.861). Visual examination demonstrated no outliers for the FBS.

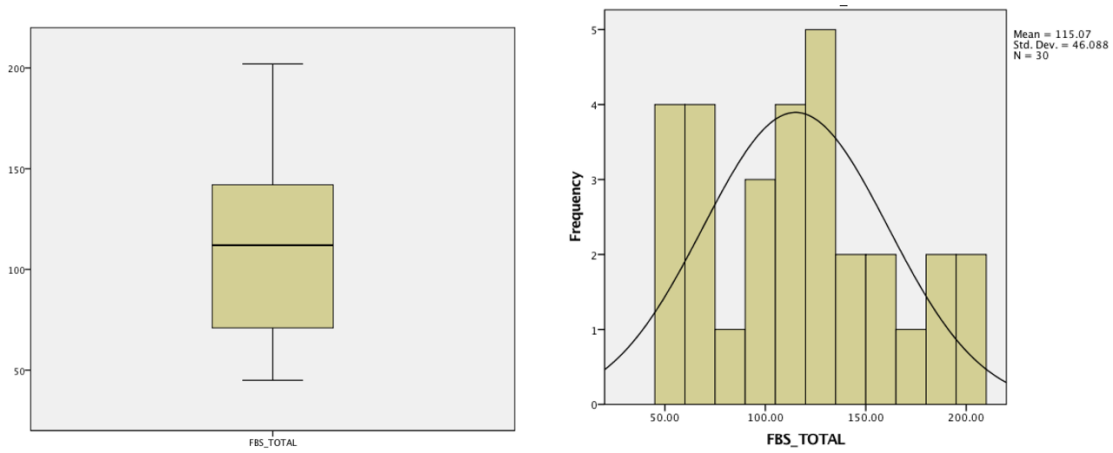


Figure 4.3. Box-plot and histogram for FBS scores (n=30).

Salivary Cortisol

Salivary cortisol was collected two times on the day of data collection. The first collection of salivary cortisol occurred between 06:45 to 10:05 and the second collection occurred between 10:10 to 14:05 with a mean of 206.3 (±61.5) minutes between collection times. Times between salivary collections showed six extreme cases, with times between salivary collections being longer than 266 minutes.

The first salivary cortisol levels ranged from .046 to .616 μg/dL with a mean value of .212 μg/dL (±.156). Because of schedule conflicts, some parents were unable to stay in the clinic for three hours to allow the child to provide both samples of saliva in the clinic. Therefore, the protocol was revised to allow parents to collect saliva from their child at home before arriving for their child's appointment.

For children who collected the first sample of saliva in the clinic, the first cortisol levels ranged from .046 to .467 μg/dL with a mean of .158 μg/dL (±.105). For children who collected the first sample of saliva at home, the first cortisol levels from .093 to .616

μg/dL with a mean of .322 μg/dL (±.188). Additionally, children who collected in the clinic provided the first sample of saliva between 8:00 and 10:05 am with the average time of data collection being 9:05 am (±0:41). Time of collection for children who collected at home was between 6:45 and 8:45 am with 7:20 am (±0:43) being the average time of saliva collection. Cortisol levels in the first sample of saliva from children who collected at home were significantly higher compared to children who collected the first salivary sample in clinic (t= -2.572, p<.05) (See Figure 4.4). This difference is likely due to collections of saliva occurring closer to the time of awakening (Miller et al., 2016). The second salivary cortisol levels ranged from .052 to .547 μg/dL with a mean value of .156 μg/dL (±.114). Visual inspection of the second salivary cortisol showed one outlier (.547). The next highest cortisol value for the second salivary sample was .415 μg/dL.

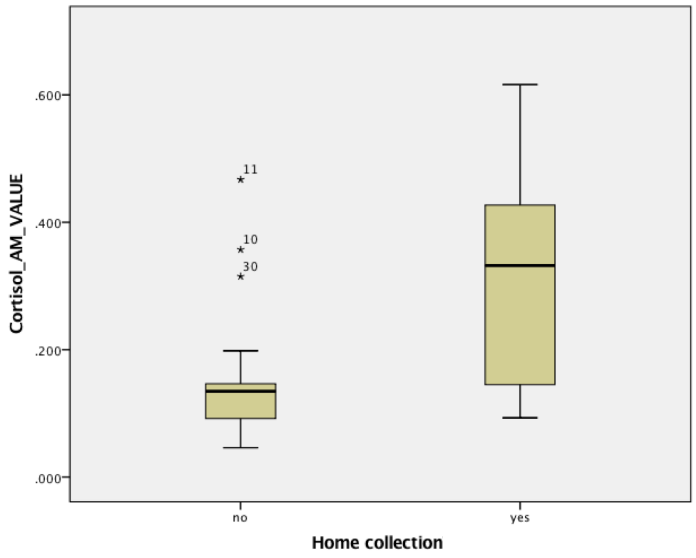


Figure 4.4. Box-plot for first salivary cortisol levels for samples collected in the clinic (n=20) versus at home (n=10).

To obtain a cortisol change value, the second salivary cortisol value was subtracted from the first. Cortisol change varied from -.402 to .56 μg/dL. Negative values represent an increase in cortisol from first to second sample, while positive values represent a decrease in cortisol from first to second sample. Eighteen children had a decrease in cortisol from the first to second sample, while 12 children had an increase in cortisol from the first to second sample. While no children showed "blunted" cortisol change (defined as a change less than 0.01 μg/dL from first to second sample), 4 children did exhibit changes of 0.02 μg/dL or less between the first and second sample. Significant correlations were noted for cortisol change with the first salivary samples (r=.822, p<.05) and second salivary samples (r=.628, p<.05).

An independent samples t-test showed significant differences in cortisol change between children who collected the first salivary sample at home versus in the clinic (t=-3.948, df=28, p<.01). In addition, direction of cortisol change (increases versus decreases) for children who collected the first sample of saliva at home (n=10) and children who provided both samples of saliva in clinic (n=20) were analyzed using a chi-square test (see Table 4.4.) Children who collected the first sample of saliva in clinic were more likely to show unexpected cortisol change values compared to children who collected the first salivary sample at home.

Table 4.4

Differences in Cortisol Change Between Home versus Clinic Collection

	Pearson's χ^2	df	Sig.	Phi	Approx. Sig.
Cortisol Change	5.635	1	.018	.433	.018

Glycemic control

HbA1c was used as a measure of glycemic control in children. HbA1c values ranged from 6.1-12.2%. Mean value for HbA1c was 8.75 (±1.2). Overall, HbA1c displayed no outliers upon visual inspection. Skewness and kurtosis for HbA1c values were .386 and 1.277, respectively. A Shapiro-Wilk test indicated normal distribution (p=.278).

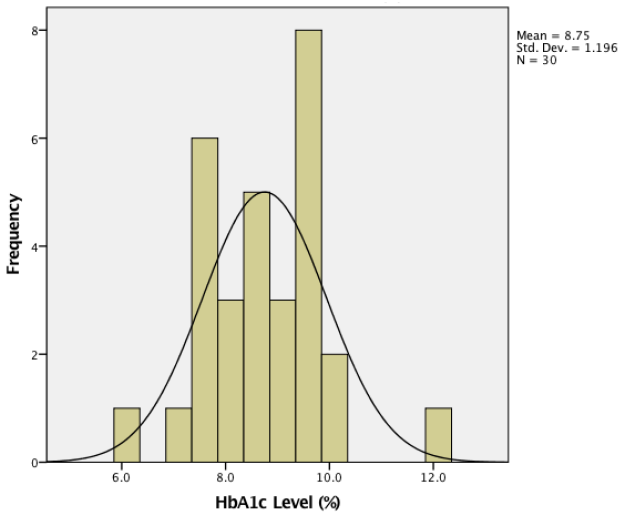


Figure 4.5. Distribution of HbA1c values.

T-tests were used to examine differences in HbA1c by gender, race, and treatment modality. Average HbA1c levels were higher for females (8.85 ± 1.28) than males (8.51 ± 1.02). Additionally, HbA1c levels were higher for blacks (9.07 ± 1.58) than whites (8.66 ± 1.08). However, these differences were not statistically significant (see Table 4.5). Significant differences in HbA1c were noted in treatment modality; children who used a pump had higher HbA1c levels (9.04 ± 1.11) versus children who used multiple daily injections (MDI) (7.95 ± 1.1). In addition to examining variations in glycemic

control by demographic characteristics, an independent samples t-test showed there were no significant differences in HbA1c between children who had declines in cortisol versus children who had increases in cortisol from the first to second sample (*t*=.773, df= 28, p=.446).

Table 4.5

Comparisons of HbA1c and Demographic Data

Variable		t	df	Sig.
Gender	Equal variances assumed	-.710	28	.484
Race	Equal variances assumed	-.807	28	.426
Pump	Equal variances assumed	-2.38	28	.024

Analysis of Research Questions

R1. What are the effect sizes of the relationships between maternal depressive symptoms and child's perceived stress, maternal depressive symptoms and child depressive symptoms, and child's perceived stress and child depressive symptoms?

Pearson's *r* was used to determine effect sizes between maternal depressive symptoms and child's perceived stress, maternal depressive symptoms and child depressive symptoms, and child's perceived stress and child depressive symptoms. Using Pearson's *r* and Cohen's definition for effect size, the relationship between maternal depressive symptoms and child perceived stress was small (*r*=.099; CI [-0.27, 0.443]), the relationship between maternal depressive symptoms and child depressive symptoms was small (*r*=-.091; CI [-0.436, 0.278]), and the relationship between child's perceived stress and child depressive symptoms was small-medium (*r*=.271; CI [-0.098, 0.575]) (see

Table 4.6). Only the relationship between child's perceived stress and child depressive symptoms met the relevancy threshold of 0.2 or greater. Given the wide CI's for these values, interpretation of effect sizes must be made cautiously.

Table 4.6

Correlations Between Maternal Depressive Symptoms, Child Depressive Symptoms, Child's Perceived Stress, Salivary Cortisol Levels, and HbA1c (n=30)

	Pearson's *r* [95% CI]						
	CESD-R	CES-DC	FBS	1st cortisol	2nd cortisol	Cortisol change	HbA1c
CESD-R	1						
CES-DC	-.091 [-0.436, 0.278]	1					
FBS	.099 [-0.27, 0.443]	.271 [-0.098, 0.575]	1				
1st cortisol	.117 [-0.253, 0.457]	-.177 [-0.505, 0.195]	.04 [-0.324, 0.394]	1			
2nd cortisol	.131 [-0.24, 0.469]	.176 [-0.196, 0.504]	.107 [-0.263, 0.449]	-.073 [-0.422, 0.295]	1		
Cortisol change	.017 [-0.345, 0.374]	-.239 [-0.551, 0.132]	-.030 [-0.386, 0.333]	.822* [0.656, 0.912]	-.628* [-0.805, -0.347]	1	
HbA1c	.211 [-0.161, 0.53]	-.184 [-0.51, 0.188]	-.348 [-0.629, 0.014]	.186 [-0.186, 0.511]	-.155 [-0.488, 0.217]	.234 [-0.137, 0.548]	1

*p<.05

R2. What are the effect sizes of the influence of maternal depressive symptoms, child depressive symptoms, or child's perceived stress on child's glycemic control?

Using simple linear regression models, three individual models were built with HbA1c value as the dependent variable and maternal depressive symptoms OR child depressive symptoms OR child's perceived stress as an independent variable (see Table 4.7). Using R^2 values and Cohen's (1988) definitions for effect sizes, maternal depressive symptoms and glycemic control showed a small effect size (R^2=.044), child depressive symptoms and glycemic control showed a small effect size (R^2=.034), and child's perceived stress and glycemic control showed a small-medium effect size (R^2=.121). Since effect sizes were considered meaningful if they reached the relevancy threshold of a small-medium effect (R^2=.09 or higher), the relationship between glycemic control and child's perceived stress may be considered clinically meaningful.

Table 4.7

Regression Models and Effect Sizes for Predictor Variables with HbA1c

Variable	R	R^2	β	Sig.	Effect size
CESD-R	.211	.044	.211	.264	small
CES-DC	.181	.034	-.184	.331	small
FBS	.348	.121	-.348	.060	small-medium

R3. What amount of the total effect of maternal depressive symptoms, child depressive symptoms, and child's perceived stress on glycemic control is accounted for by the mediated effect of cortisol?

Due to the small sample size, this research question could not be evaluated fully. Instead, using the methods described by Baron and Kenny (1986), component steps for evaluation of mediation were examined for effect sizes. The first step in their process is to examine associations between the proposed predictor and the outcome variable.

Bivariate analysis demonstrated a small-to-medium effect size between maternal depressive symptoms and glycemic control (r=.211; CI [-0.161, 0.53]) and a medium effect size between child's perceived stress and glycemic control (r=-.348; CI [-0.629, 0.014]) (see Table 4.6). However, using regression analysis, the relationships between maternal depressive symptoms and child depressive symptoms with glycemic control had small effect sizes as indicated by R^2 values, while the relationship between child's perceived stress and glycemic control had a small-to-medium effect size (R^2=.121) (see Table 4.7).

After examining the relationships between predictor variables and glycemic control, the relationship between cortisol change (the proposed mediator) and glycemic control was examined. Bivariate analysis revealed a small-to-medium effect size between cortisol change and glycemic control (r=.234; CI [-0.137, 0.548]) (see Table 4.6). Despite this, regression analysis of this relationship showed a small effect size (R^2=.055).

The next step in Baron and Kenny's (1986) process is to examine the relationship between the predictors and the mediator variable, cortisol change. Bivariate correlational analysis was used to assess associations between cortisol change and the following predictor variables: maternal depressive symptoms, child depressive symptoms, and child's perceived stress (see Table 4.6). Only the relationship between child depressive symptoms and cortisol change (r=.239; CI [-0.551, 0.132]) met the relevancy threshold of 0.2 for a small-medium effect size that may be considered clinically meaningful. However, this relationship had a small effect size (R^2=.057) when examined with regression analysis (see Table 4.9).

Table 4.8

Maternal Depressive Symptoms as a Predictor of Glycemic Control and Cortisol Change

Model 1		DV= HbA1c			
Predictor	R	R^2	β	Sig.	Effect size
	.211	.044		.264	small
CESD-R			.211	.264	
Model 2		DV= Cortisol change			
Predictor	R	R^2	β	Sig.	Effect size
	.017	.000		.929	small
CESD-R			.017	.929	

Table 4.9

Child Depressive Symptoms as a Predictor of Glycemic Control and Cortisol Change

Model 1		DV= HbA1c			
Predictor	R	R^2	β	Sig.	Effect size
	.181	.034		.331	small
CES-DC			-.184	.331	
Model 2		DV= Cortisol change			
Predictor	R	R^2	β	Sig.	Effect size
	.239	.057		.204	small
CES-DC			-.239	.204	

Table 4.10

Child's Perceived Stress as a Predictor of Glycemic Control and Cortisol Change

Model 1		DV= HbA1c			
Predictor	R	R^2	β	Sig.	Effect size
	.348	.121		.060	small-medium
FBS			-.348	.060	
Model 2		DV= Cortisol change			
Predictor	R	R^2	β	Sig.	Effect size
	.030	.001		.876	very small
FBS			-.030	.876	

R4. What are the effect sizes of the relationships between time-since-diagnosis, treatment modality, ethnicity, and SES and glycemic control?

The point-biserial (r_{pb}) was obtained through correlational analysis and considered to be the effect size of the relationship between treatment modality and glycemic control. The relationship between use of an insulin pump and glycemic control showed a medium-large effect size that was statistically significant r_{pb}=.410 ($p<.05$). Since the effect size for the relationship between treatment modality (use of an insulin pump) and glycemic control was higher than the relevancy threshold of .2 for correlational analysis, it may be considered clinically meaningful.

Since there were only two categorical responses for ethnicity/race, the effect size of the relationship between ethnicity/race and glycemic control was also analyzed through a point-biserial correlation. Using Cohen's definitions for effect size, the effect size of the relationship between ethnicity/race and glycemic control was determined to be small (r_{pb}=.151) and may not be clinically meaningful.

Similarly, the effect size for the relationship between time-since-diagnosis (in months) and glycemic control, measured as HbA1c value, was also determined using correlational analysis. Using Cohen's definition of effect sizes for Pearson's *r*, the effect size of relationship between time-since-diagnosis and glycemic control was small (*r*=.058) and may not be clinically meaningful.

Additionally, ANOVA was used to estimate the effect sizes between SES and glycemic control. SES was categorized as low income (<$30,000/year), medium income ($30,001/year to $70,000/year), and high income (>$70,001/year). Using Cohen's

definition of effect sizes and eta squared values, the effect size between SES and glycemic control was small-medium (η^2=.039). Because .039 is higher than the relevancy threshold of .035, the relationship between SES and glycemic control may be considered clinically meaningful.

Summary

This chapter reported findings of data analysis for the study. The primary purpose of data analysis for this correlational, hypothesis-generating study was to describe the study population and to examine effect sizes of relationships between study variables. Due to a limited sample (n=30) of this pilot study, findings reported in this chapter must be interpreted cautiously. However, potentially clinically meaningful relationships, determined by statistically appropriately relevancy thresholds for type of statistical analysis, were noted between several variables such as the relationships between child depressive symptoms and child's perceived stress, and child's perceived stress and glycemic control.

CHAPTER 5

DISCUSSION

The purpose of this correlational, hypothesis-generating study was to generate hypotheses, indicated by effect sizes, on the relationships between maternal depressive symptoms, child depressive symptoms, and child's perceived stress on glycemic control in prepubertal school-aged children 7 to 12 years of age with type 1 diabetes. Additionally, the researcher sought to examine the effects of cortisol as a potential mediator between maternal depressive symptoms, child depressive symptoms, child's perceived stress, and glycemic control. However, given the small sample size, meditational analysis was deferred in the current study. In this chapter, study findings including sample, variables of interest, and effect sizes between study variables are discussed. Lastly, study limitations and implications for clinical, policy, and research are addressed.

Sample

The sample for this study consisted of prepubertal school-age children. Most children were in 2nd, 3rd, and 4th grades. Previous research addressing children with type 1 diabetes has focused on a slightly older population or included a wide range of children up to 18 years old (Butler et al., 2009; Butwicka et al., 2013; Helgeson et al., 2009; Jaser & Grey, 2010; McGrady & hood, 2010; Wiebe et al., 2011). By focusing on younger

children, the researcher was able to minimize the chance that increases in HbA1c were associated with onset of puberty (Trast, 2014). Additionally, these younger children are likely at a developmental stage where they are still highly dependent upon parental support, but have increased autonomy and are beginning the transition to self-care (Davies, 2011). Therefore, these children may be affected by both parent and peer stressors (Davies, 2011). By focusing on this specific age group, the current study was able to examine both maternal and child characteristics that may impact child well-being, especially in relation to disease management for children with type 1 diabetes.

The majority of child participants were female and white. A number of studies that focused on children with type 1 diabetes also enrolled notably more female participants (Jaser & Grey, 2008; McGrady & Hood, 2010), although other studies had equal number of male and female participants (Heleson et al., 2009; Mackey et al., 2014). Regardless, the higher number of females in the current study is not representative of the target population. Previous reports of prevalence of type 1 diabetes in children have found slightly higher rates in females, though numbers are almost equitable (Maahs et al., 2010; Pettitt et al., 2014). The higher numbers of female children in the current study is unexplained by patient demographics since there were equal numbers of male and female patients ages 7 to 12 with type 1 diabetes seen in the clinic where data collection occurred. While female children with type 1 diabetes may be more likely to enroll in research studies, this finding has not been reported in literature. Most likely, the higher number of female children enrolled in the current study is attributable to recruitment strategies with more mothers of female children able to be contacted for screening and enrollment.

Despite the discrepancies in gender between study and target population, ethnicity was somewhat representative of the target population, although the study did not include Hispanic, Asian/Pacific Islander, or Native American youth. White children are more likely to be diagnosed with type 1 diabetes; incidence in non-Hispanic white youth is 2.55/1,000 versus 1.62/1,000 for black youth, 1.29/1,000 for Hispanic youth, 0.6/1,000 for Asian/Pacific Islander youth, and 0.35/1,000 for Native American youth (Dabelea et al., 2014).

Although BMI is not routinely examined in children with type 1 diabetes, BMI percentiles for age and sex in this sample ranged from the 5th to 85th percentile indicating 90% of the study population had normal or healthy weight (CDC, 2015b). While BMIs and rates of overweight/obesity were lower than nationally reported rates for children ages 6 to 11 years (CDC, 2015b), they are characteristic of children with type 1 diabetes. Weight loss is characteristic of children newly diagnosed with type 1 diabetes (Gregg et al., 2015). A study by Gregg and colleagues (2012) found that although BMIs in children increase the first year following diagnosis with type 1 diabetes, the majority (94%) of children remained in normal or healthy weight categories (BMI percentile <85%). This weight gain, however, is likely from regain of weight lost prior to diagnosis (Gregg et al., 2015). While increased BMI is more commonly associated with onset of type 2 diabetes, researchers have recently found that increased BMI may contribute to the accelerator hypothesis (increased rate of beta cell stress and destruction) and lead to earlier age of onset of type 1 diabetes in children of all ethnicities (Channanath et al., 2017).

Other important child demographic data to consider include length of diagnosis and treatment status. Treatment modality and length of diagnosis were consistent with

previously reported rates in children ages 8 to 12 with type 1 diabetes (Jaser et al., 2008; Jaser & Grey, 2010). Average length of diabetes diagnosis varied in the sample from 12 to 97 months with 3.48 years being the average length of diagnosis. More importantly, only 10 children were diagnosed with type 1 diabetes less than 20 months. This decreased the chance that the child was still experiencing the "honeymoon" phase following recent diagnosis (<12 months) when beta cells are still partially functioning and the child experiences better glycemic control (Abdul-Rasoul et al., 2006). Moreover, the majority of children in the current study were treated with an insulin pump. The number of children using an insulin pump as their primary treatment modality may be attributed to the sample in the study; insulin pump therapy is used more frequently in white, female children from higher SES and with parents who are more educated (Maahs et al., 2010).

Maternal characteristics are also important to note as they include socioeconomic status (SES) and maternal education. More than half of mothers were high school graduates and SES was widely distributed with over half of mothers reporting an annual household income of $50,000 or more while 56% of families were private pay insurance. This wide range of SES is in contrast to similar studies that have examined maternal and child characteristics in relation to glycemic control in children with type 1 diabetes (Jaser & Grey, 2010; Jaser et al., 2008; Kovacs et al., 1990; Naar-King et al., 2006). For example, many studies have included samples with higher maternal education and family SES (Jaser & Grey, 2010; Jaser et al., 2008; Kovacs et al., 1990) or participants from predominantly low SES (Naar-King et al., 2006). SES, indicated in this study by household income and insurance status, is important to consider as some researchers have found discrepancies in maternal depressive symptoms and child cortisol levels in mothers

and children from high and low SES families (Kovacs et al., 1990; Lupien et al., 2000). Specifically, mothers from low SES have higher depressive symptomatology while children from low SES are more likely to show blunted or abnormal cortisol patterns (Kovacs et al., 1990; Lupien et al., 2000). Additionally, lower SES has been associated with poor glycemic control and increased depressive symptomatology in children with type 1 diabetes (Hassan et al., 2006).

Marital status was also examined; thirty-three percent of mothers reported being divorced, unmarried, or single at the time of survey completion. This is comparable to reports that 40% of children in Alabama live in a single-parent household (National KIDS COUNT, 2017). The slightly higher marital status in the current study may be reflective of SES and race. Data suggest marital quality and marriage dissolution are associated with race and SES, with Caucasians from higher SES having higher marital quality and lower rates of marital dissolution (Bulanda & Brown, 2007). Two mothers reported a history of depression, although only one of these mothers met the cutoff of 16 for clinically significant depressive symptomatology. Few mothers reported smoking cigarettes or drinking alcohol; both of which have been noted as coping mechanisms in individuals suffering from depression, but do not necessarily indicate a person is depressed (Crocq, 2003).

Study Variables

Maternal Depressive Symptoms

Using Center for Epidemiological Studies Depression Scale-Revised (CESD-R) to measure maternal depressive symptoms, 27% of mothers were at or above the cutoff

value of 16 for clinical significance of depressive symptomatology (CESD-R, 2008). Additionally, two mothers indicated that they had a history of depression, but only one of these mothers was above the cutoff for depressive symptomatology. This may be attributed to the fact that the mother who had a history of depression but scored below the cutoff may have been receiving treatment for depression, which was not assessed since the demographic data sheet did not ask about current diagnoses for mother or medications/treatments currently used by mothers.

While the CESD-R has not been previously used in mothers of children with type 1 diabetes, the instrument showed good internal reliability and the rate of mothers above the cutoff for clinical significance is reflective of other reports that used similar tools to measure depressive symptoms in mothers of children with type 1 diabetes. For example, using the Patient Health Questionnaire (PHQ-9), Rumberg and colleagues (2017) found that 25% of mothers scored above the clinical cutoff for moderate depressive symptomatology while Jaser and Grey (2010) found that 23% of mothers scored above the clinical cutoff for depressive symptoms using the CESD. These rates of depression are higher than noted in mothers from the general population (Ertel, Rich-Edwards, & Koenen, 2011). Ertel and colleagues (2011) noted that approximately 10.2% of mothers in the United States suffer from depression, but this rate is increased in mothers facing adversities such as divorce, low SES, or lack of education. Likely, mothers of children with diabetes may have more depressive symptomatology related to the stress of caring for a child with diabetes.

Child Depressive Symptoms

In the current study, 30% of children scored 15 or above on the Center for Epidemiological Studies- Depression Scale for Children (CES-DC), which is commonly used as the cutoff indicating high depressive symptomatology in children (Weissman et al., 1980). Although the CES-DC has not been widely used in children with type 1 diabetes, these scores are higher than previous reports of depressive symptoms in children with type 1 diabetes. Using the CDI, McGrady and Hood (2010) found that 15.2% of children age 10 to 18 years scored above the clinical cutoff for high depressive symptomatology while Jaser and colleagues (2008) noted 6.5% of children age 10 to 16 years scored above the clinical cutoff. These rates of depressive symptoms are notably higher than 3% reported for children ages 6 to 11 years old in the general population (Anxiety and Depression Association of America, 2016) although children with chronic illnesses have notably higher depressive symptoms (Pinquart & Shen, 2010). Higher scores of depressive symptomatology in children with diabetes are likely associated with stress and anxiety associated with disease management (McGrady & Hood, 2010). Increased child depressive symptomatology noted in the current study may be attributed to stress associated with transition of diabetes care from parents to children as this age group typically becomes more self-sufficient (Davies, 2011). Moreover, research suggests that having a chronic health condition, such as type 1 diabetes, increases the rate of being bullied by peers, and thus, may increase depressive symptomatology in children (Storch et al., 2004; Van Cleave & Davis, 2006). However, it must be considered that scores on the CES-DC may be artificially inflated, or potentially lower than actual scores,

by the inclusion of younger children in the current study since the scale has shown lower reliability in younger children (Fendrich et al., 1990).

In the current study, internal reliability of the CES-DC, measured by Cronbach's alpha, was acceptable although lower than previously reported in other populations of children without diabetes (Barkmann et al., 2008; Betancourt et al., 2012). This may be attributed to the CES-DC being administered to a younger age group. Fendrich and colleagues (1990) noted lower reliability when the tool was administered to children as young as 6 years (α=.78) compared to when the CES-DC was used in adolescents (α=.89). Moreover, Barkmann and colleagues (2008) found lower internal reliability in children younger than 11 years. Therefore, while internal reliability was acceptable in the current study, conclusions about child depressive symptoms should be made with caution and may require further validation to measure depressive symptomatology in younger children.

Child's Perceived Stress

Using the Feel Bad Scale (FBS), perceived stress scores in children were relatively low. Out of a possible score of 500, child's perceived stress ranged from 45-202 with a mean score of 115.1 (±46.1). These scores were similar to findings by Lewis and colleagues (1984) who assessed perceived stress in healthy children. Additionally, internal consistency of the measure was similar to that found by Rew, Horner, and Fouladi (2010) who administered the FBS to healthy children in grades 4 through 6 (.85, .89 and .84, respectively). While actual FBS scores were not reported, Rew and

colleagues (2010) did find that frequency of stress was negatively associated with health behaviors, while total stress was positively associated with health behaviors.

Although the Feel Bad Scale appears to be a good measure of stress in children ages 7 to 12 years and shows adequate internal reliability in the current study, it may not include all stressors that children face today. This may help explain why stress scores were lower in the current population. Potential stressors not included in survey that may affect children today are technological centered items such as cell phones and social media websites (kidshealth.org, 2014). Additionally, the FBS did not include items related to diabetes management, which has been noted as stressful to cope with daily in older children with type 1 diabetes (Delamater et al., 2013).

Cortisol

Salivary cortisol levels were examined by obtaining two collections of saliva 3 hours apart and subtracting the second cortisol level from the first to find cortisol change. Negative values indicated a rise in cortisol from the first to second collection while positive values indicated a fall in cortisol from the first to second sample. In the current study, cortisol change was classified as normal (positive cortisol change value), abnormal (negative cortisol change value), or blunted (<0.01 μg/dL cortisol change value). Sixty percent of children had normal cortisol change while 40% of children exhibited abnormal cortisol change. Of these children, 4 children exhibited changes of .02 μg/dL or less, though they did not meet the criteria of 0.01μg/dL to be considered blunted.

Cortisol change was used to compare cortisol values with normal diurnal changes in cortisol from morning to afternoon levels. The large number of children who exhibited

increases in cortisol from the first to second collection was surprising. Following the normal cortisol rhythm, cortisol levels are expected to rise upon waking and then fall steeply between 1 to 3.5 hours after waking and gradually continue to fall until 11 hours after waking (Miller et al., 2016). It was expected that cortisol levels would display a decrease from first salivary sample to second salivary since the first samples were collected between 06:45 and 10:05 and the last time of cortisol collection was 14:05. Moreover, an average of 206 minutes (3 hours) between salivary collection times should allow adequate time between cortisol collections to note a change in value (Törnhage, 2009).

The higher cortisol level in the second sample may be explained by several factors. First, the failure to see a decline from morning to later in the day may indicate alterations and dysfunction of the of HPA axis (Törnhage, 2009) and signify chronic physiologic stress. Chronic physiologic stress may manifest as permanent alterations in cortisol levels, such as blunted or abnormal diurnal rhythm, and result in physiologic changes such as cardiovascular disease or elevated blood glucose (Brasher & Jones, 2010; Chrousos & Kino, 2007; Forshee et al., 2010). However, in the current study, children with increases in cortisol from the first to second sample did not have significant differences in glycemic control compared with children who showed normal decreases in cortisol from the first to second salivary sample. This may be the result of small sample size.

The other explanation for increases in secondary cortisol levels from the first may be that the child experienced an acutely stressful event between the first and second cortisol collection. Cortisol has been shown to increase an hour following a stressful

event such as a needle stick in healthy children (Hanrahan et al., 2006). Although a needle stick may not act as a stressful event that increases cortisol in children with type 1 diabetes, these children may have received bad news or faced social stressors between the first and second saliva collection that activated the acute cortisol response and increased cortisol levels in the second sample (Armbruster et al., 2012; Bae et al., 2015). While recent changes in the household or stressful events over the last 3 months were included on the demographic data sheet to help explain anomalies in cortisol levels (both first and second samples), stressful events occurring during the child's routine appointment that may have caused acute cortisol reactivity and resulted in a higher cortisol level in the second salivary sample were not assessed the day of data collection.

Additionally, cortisol differences noted in the first saliva sample between children who collected in the clinic versus children who collected at home may be explained by variations in diurnal rhythm. Cortisol peaks upon waking and shows a sharp decline 1 to 3.5 hours after waking (Miller et al., 2016). While data were not collected about wake-time for participants in the current study, cortisol collected at home was collected 1.5 hours earlier, on average, and was higher (.322 μg/dL) than cortisol collected in the clinic (.158 μg/dL). Moreover, significant differences were noted in cortisol change values between children who collected the first salivary sample at home versus in the clinic, with children who collected at home more likely to show a normal cortisol change than children who collected the first salivary sample in clinic. This is somewhat expected, since the first salivary cortisol level is a component of cortisol change. Children who collected at home most likely collected closer to hour of waking than children who

collected in the clinic which may help explain why greater differences between first and second cortisol levels were noted in children who collected at home.

Glycemic Control

HbA1c was used as a measure of glycemic control. HbA1c ranged from 6.1 to 12.2% with an average of 8.75%. Only 5 children (17%) met the clinical threshold for adequate glycemic control in children with type 1 diabetes of 7.5% or less. Moreover, 8 participants (27%) had HbA1c levels greater than 9.5%. These HbA1c values are slightly higher than national averages. HbA1c levels for children with type 1 diabetes in the United States average 8.2%, and approximately 17% of children with type 1 diabetes in the United States have an HbA1c level greater than 9.5% indicating very poor glycemic control (Maahs et al., 2010). Higher HbA1c levels are attributed to several factors such as treatment modality, SES, and ethnicity (Davis et al., 2001; Maahs et al., 2010). While treatment modality (percentage of children using pump therapy) and ethnicity were characteristic of children with type 1 diabetes nationally, this study included a number of children from lower SES families which may contribute to higher HbA1c values seen in the study population. Significant differences in glycemic control between children from low and high SES were not noted in the current study, however, children with lower SES tended to have higher HbA1c values than children with higher SES. Additionally, higher levels of HbA1c in the current study population may be because the smaller sample size is not representative of the target population.

In the current study, there were no significant differences in HbA1c values between males and females. This is consistent with findings by Korbel and colleagues

(2007) who noted no gender differences in glycemic control in children with type 1 diabetes. Additionally, HbA1c was slightly higher in black children in the current study but significant differences in glycemic control were not noted based on ethnicity. Auslander and colleagues (1997) also noted higher HbA1c values in African American children. This subtle variation may be attributed to a culmination of factors that impact HbA1c value in children in addition to ethnicity such as SES and insurance status (Davis et al., 2001). For example, in the current study African American children had lower SES, indicated by yearly household income and Medicaid/Medicare insurance status, although these findings, likely due to sample size, were not significant.

HbA1c values were also examined for variations based on treatment modality (insulin pump therapy versus multiple daily injections). Higher HbA1c values are noted in children using insulin pumps in the current study. This starkly contrasts with reports that children on insulin pumps have lower HbA1c levels (Maahs et al., 2010). Although this finding was unexpected, there are various reasons why children in the current study being treated with pump therapy may have had higher HbA1c values. While patient outcomes, such as incidence of retinopathy, have been improved in patients who use pump therapy, fear of pump-associated incidents in children, such as hypoglycemia, is common and may lead to parents or providers avoiding tight glycemic control for children on pump therapy (Haugstvedt, Wentzel-Larsen, Aarflot, Rokne, & Graue, 2015; Ross et al., 2016). Moreover, it may require six or more months to detect improved glycemic control following initiation of pump therapy (Brorsson, Viklund, Örtqvist, & Lindholm Olinder, 2015). Interestingly, although glycemic control eventually improves after pump therapy initiation, risk for ketoacidosis is increased in children on pump

therapy (Brorsson et al., 2015). Regardless of various reasons why HbA1c is higher in the current population for children on pump therapy, more data, such as time since pump initiation and parental perspectives on pump therapy, and data from a larger study sample are needed to better understand variations in HbA1c between children on pump therapy versus children using multiple daily injections.

Relationships Noted among Research Questions

Analysis of the first research questions revealed a potentially meaningful relationship between child depressive symptoms and child's perceived stress (r=.271). This is not unexpected since studies have shown that depression in children is significantly correlated with stress and stressful events in childhood (Moksnes, Moljord, Espnes, & Byrne, 2010).

In contrast, there was a lack of a clinically meaningful relationship, indicated by effect size, between maternal depressive symptoms and child depressive symptoms. This was surprising since multiple studies have reported significant correlations between the two (Malcarne et al., 2000; Jaser et al., 2008; Wiebe et al., 2011). This may be attributed to instrumentation used in the current study since the CESD-R and CES-DC have not been widely used in children with type 1 diabetes or their mothers before, or may be the result of small sample size that is not entirely representative of the target population.

Although 27% of mothers and 30% of children met clinical cutoffs indicating high depressive symptomatology, effect sizes of the influence of maternal depressive symptoms and child depressive symptoms on glycemic control were small. This is in contrast to previous studies that found that maternal depressive symptoms and child

depressive symptoms were independent predictors of glycemic control in children and adolescents with type 1 diabetes with small-to-medium (R^2=.23) and medium-to-large (R^2=.135) effect sizes, respectively (Hood, Rausch, & Dolan, 2011; Rumberg et al., 2017).

Moreover, only correlational analysis between maternal depressive symptoms and HbA1c showed a small-to-medium effect size that may be clinically meaningful. This is smaller than a previously reported medium effect size (*r*=.35) for the relationship between maternal depressive symptoms and HbA1c (Rumberg et al., 2017), but similar to other reports of small effect sizes (*r*=.1 to .2) (Jaser et al., 2008; Jaser & Grey, 2010). Additionally, the effect size noted using correlational analysis between child depressive symptoms and glycemic control was also smaller than previously reported (*r*=.26) (McGrady & Hood, 2010), although other researchers have similarly found small effect sizes (*r*=.02 to .09) (Wiebe et al., 2011). Again, the smaller than expected effect size may be due to the sample size.

The lack of meaningful effect sizes, and overall lower effect sizes, between maternal depressive symptoms and child depressive symptoms with glycemic control in the current study may be attributable to sample characteristics such as age of the child. Previous research reporting potentially meaningful effect sizes between maternal/child depressive symptoms and glycemic control has used an older population, primarily 13 to 18 years of age (Hood et al., 2011; McGrady & Hood, 2010). Other researchers studying slightly younger children with type 1 diabetes (ages 8 to 15) have been more likely to find small effect sizes (Jaser et al., 2008; Wiebe et al., 2011). These younger children may not be as aware of maternal depressive symptoms; thus, the effects of maternal

depressive symptoms on glycemic control may not be as meaningful. Similarly, maladaptive coping strategies in response to depressive symptoms in the child may not have emerged yet in younger children. Therefore, while these children reported higher depressive scores, they may still be effectively coping with depressive symptomatology and meaningful effects may not be noted in glycemic control yet.

A potentially meaningful relationship was noted between child's perceived stress and glycemic control. This relationship met the relevancy threshold for clinical significance (R^2=.121) with a small-to-medium effect size. Associations between increased stress and stressful life events with poor glycemic control have been noted previously (Worrall-Davies et al.,1999; Berlin et al., 2012). This relationship was expected and is similar to positive associations between stress in children with diabetes and glycemic control noted by Berlin and colleagues, who found a significant correlation with a small-to-medium effect size between the two variables (r=.282, $p<0.01$). Associations between stress and glycemic control have been attributed to maladaptive coping, which leads to decreased treatment adherence and limited self-efficacy in disease management and, thus, results in poor glycemic control (Delamater, de Wit, McDarby, Malik, & Acerini, 2014).

The goal of the third research question was to examine the total effect that cortisol may have as a mediator between selected independent variables and glycemic control. Since the sample size was small, meditational analysis could not be completed. However, components of the meditational analysis process revealed some effect sizes that may indicate clinical meaningfulness. For example, although correlational analysis did not reveal statistically significant relationships, analyses did indicate that multiple

relationships met the relevancy threshold, and thus, may be of clinical importance.

The first step in the modeling process for mediation analysis (Baron & Kenny, 1986) highlighted meaningful effect sizes between maternal depressive symptoms and glycemic control, as well as child's perceived stress and glycemic control. The effect size between maternal depressive symptoms and glycemic control was anticipated as researchers have reported maternal depressive symptoms as a predictor of glycemic control in children (Rumberg et al., 2017).

Interestingly, there was a negative association noted between child's perceived stress and glycemic control; as child's perceived stress increased, HbA1c decreased, and thus, demonstrated better glycemic control. The direction of this relationship was not expected. Overwhelmingly, researchers associate increased stress with poor glycemic control (Hilliard et al., 2016). However, the relationship between stress and glycemic control may be related to various physiological, psychological and health behaviors factors (Hilliard et al., 2016). One such example would be that stress leads to maladaptive coping mechanisms and decreased self-efficacy, which in turn results in poor glycemic control (Delamater et al., 2014). However, the current study did not assess coping mechanisms or child self-involvement in diabetes management. While children may have had higher levels of stress, effective coping mechanisms may have limited the impact that stress had on glycemic control. Even if the child had higher levels of perceived stress, if he or she was not the main provider of care, the effects of stress on glycemic control may have been mitigated. Additionally, these findings may also be an artifact of small sample size.

The second step in the modeling process indicated a potentially meaningful relationship between cortisol change and glycemic control. This finding was anticipated since cortisol is known to have a direct physiological effect on blood sugar, and ultimately, glycemic control (Chrousos & Kino, 2007; Forshee et al., 2010).

The third step in the process of mediation analysis is to examine the relationship between the predictor and mediator variable. Only the relationship between child depressive symptoms and cortisol change had an effect size that may be clinically meaningful. This was an interesting finding, since the relationship between child depressive symptoms and cortisol in school-age children with type 1 diabetes has not been studied previously. However, there is reason to believe that cortisol is related to depression in children (Stewart et al., 2013; Suzuki et al., 2013). Despite these findings, care must be taken when interpreting these effect sizes found with bivariate correlations due to the sample size and wide CI's. Smaller effect sizes (noted by *r* value) may be an artifact of the small sample.

Conclusions about the role cortisol may play as a mediator between maternal depressive symptoms, child depressive symptoms, child's perceived stress and glycemic control cannot be made at this time due to the inability to test hypotheses given the small sample size. However, given the effect sizes, it may be important to consider the effect of cortisol since evidence suggests cortisol is associated with maternal depressive symptoms, child depressive symptoms, and child's perceived stress (Ashman et al., 2002; Maldonado et al., 2008; Suzuki et al., 2013). Findings in the current study indicated there may be meaningful relationships between the predictor variables, glycemic control, and cortisol change; however, conclusions about mediation cannot be made at this time.

In the fourth research question the effect sizes of confounding variables on glycemic control were examined. The relationship between SES and glycemic control showed a small-to-medium effect size. This is similar to findings by Hassan, Loar, Anderson, and Heptulla (2006), that SES is a predictor of glycemic control (R^2=.09, p<.0005). Rewers and colleagues (2014) note that management of diabetes can be expensive, especially equipment and supplies to monitor blood glucose levels. Decreased frequency in monitoring blood glucose levels is significantly associated with worsened glycemic control (Rewers et al., 2014). Therefore, decreased frequency of blood glucose monitoring, related to inability to purchase monitoring supplies, may help explain why individuals from lower SES have poorer glycemic control.

Similarly, a significant medium-to-large effect size was noted between treatment modality (pump therapy versus multiple daily injections) and glycemic control. This was expected as multiple researchers have found similar associations between treatment modality and glycemic control with children using pump therapy having lower HbA1c levels than children using multiple daily injections (Fendler, Baranowska, Mianowska, Szadkowska, & Mlyarski, 2011; Paris et al., 2009; Springer et al., 2006). However, children in the current study using pump therapy had higher HbA1c levels than children using MDI. As previously discussed, higher HbA1c levels in children on pump therapy may be attributed to failure to maintain tight glycemic control in children on pump therapy for fear of pump-associated events, such as hypoglycemia. This unexpected finding in glycemic control between children using pump therapy versus multiple daily injections may contribute to the medium-to-large effect size between treatment modality and glycemic control noted in the current study.

While SES and treatment modality had meaningful effect sizes, the relationships between ethnicity and time-since-diagnosis with glycemic control had small effect sizes that did not meet relevancy thresholds. Still, ethnicity/race is likely associated with glycemic control (Gallegos-Macias et al., 2003). This is especially true for black children. In a study of 55 school-age children (58% white, 16% black, 26% Hispanic), black ethnicity was a meaningful predictor of HbA1c, especially when it was associated with SES (Davis et al., 2001). Similarly, Willi and colleagues (2015) note that even when controlling for SES, significant differences in glycemic control were observed between black children, and white and Hispanic children. However, similar differences in glycemic control were not observed between white and Hispanic children. This was mostly attributed to disparities in treatment methods used in various ethnic groups (Willi et al., 2015). The small effect size noted in the current study between ethnicity and glycemic control may be attributed to small sample size and the composition of the sample since only 23% of the sample was black and no Hispanic children were enrolled in the study.

The small effect size noted between time-since-diagnosis and glycemic control may be attributed to mixed findings in some studies that glycemic control improves as duration of diagnosis increases (O'Hagan & Harvey, 2010), while other researchers have found that glycemic control in children declines as duration of diagnosis increases (Springer et al., 2006). Other researchers have noted that HbA1c increases following diagnosis, and stabilizes between 2 and 3 years following diagnosis (Palta, Shen, Allen, Klein, & D'Alessio, 1996). These variations in findings between time-since-diagnosis and glycemic control may be attributed to management of diabetes and a learning curve

that is expected following diagnosis with initiation of insulin therapy or change in treatment regimen. In the current study, most children were diagnosed longer than 20 months and no children were considered to be in the "honeymoon" phase following diabetes diagnosis. Since average length of diagnosis in the current sample was 3.5 years, effects of time since diagnosis on glycemic control may have been limited.

Limitations

A primary limitation of this study concerns the sample size and composition. Although the incidence of type 1 diabetes in children has been increasing 2-5% per year worldwide (Maahs et al., 2010), the sample size was small. Because of the small sample size, results presented in the current study must be interpreted with caution and are not generalizable to all prepubertal children with type 1 diabetes. Since participants were enrolled from a convenience sample and the majority of children enrolled in the study were female, sampling bias may impact the results of the current study, as individuals who chose to participate in this study may not be representative of the target population (Polit & Beck, 2012). However, as a pilot study, the current study provides information about methodology and recruitment in children with type 1 diabetes and may be used to inform future research projects. Additionally, several barriers to recruitment and enrollment were identified.

Barriers to enrollment that were identified during recruitment and that may act as limitations in the current study include time restraints of participants. Many potential participants were hesitant to enroll in the study because of time constraints and inability to provide two samples of saliva in the clinic 3 hours apart. To accommodate this barrier

to recruitment and enrollment, the protocol for collection of the first sample of saliva was revised to allow mothers to collect the saliva from their child at home and bring the sample with them to the clinic.

Another barrier to recruitment was contacting potential participants for screening and enrollment in the study. Of the 121 potential participants identified for potential inclusion in the study, 31% were unable to be reached for follow up recruitment and screening. This was attributed to incorrect and incomplete contact information or lack of phone service in the clinic population.

A final barrier that impacted recruitment and enrollment was failure of patients to keep previously scheduled routine endocrinology appointments. The clinic schedules routine appointments for patients with type 1 diabetes every three months to monitor glycemic control and minimize complications of the disease. However, during enrollment and data collection for this study, many patients cancelled, rescheduled or did not attend their appointments. While some parents attributed this to schedule conflicts, other patients and families did not give a reason for missing clinic appointments or had a history of failure to keep scheduled appointments.

In addition to identifying barriers of recruitment and enrollment, several methodological issues were recognized. Specifically, methodological issues that were identified centered on collection of salivary cortisol. While children were instructed not to eat or drink anything other than water 30 minutes prior to collecting cortisol, children were not monitored by research staff. Ingestion of food could alter cortisol levels in saliva. This limitation is heightened as there was a change in protocol allowing some children to collect the first salivary sample at home rather than in clinic.

This change in protocol may have introduced biases in the study since significant differences were noted in cortisol change between children who collected the first salivary sample at home instead of in clinic. Due to the small sample size, it was not possible to evaluate how these differences may have influenced the relationships assessed in the study, or to evaluate data collection site (home versus clinic) as a potential moderator of these associations. Additionally, while parents were instructed on how to collect saliva from their child, the researcher cannot ensure protocol to collect the first salivary sample was followed at home. Considerations also must be made about stressful events happening during the child's clinic appointment. Asking the child if he or she experienced anything upsetting during the clinic appointment or between cortisol collections would be beneficial in future research to help account for elevated late morning or early afternoon levels.

Another limitation was answer bias on surveys for maternal depressive symptomatology. Because depressive symptoms in mothers was assessed in the clinic setting where their child receives care, mothers may have been less likely to indicate depressive symptomatology for fear that others may feel that they are unable to care for their child. While efforts were made to provide privacy, and ensure the mother that the clinician would not receive survey results unless suicide ideality or harm-to-self or others was indicated, it may be beneficial to allow mothers to complete the survey after the child's routine endocrinology appointment to minimize the feeling that the clinician would be biased in the child's care based on the mother's depressive symptomatology.

Conceptual Framework

The results from this study partially support the proposed conceptual framework. Several relationships had effect sizes that met the relevancy threshold and indicated potentially meaningful relationships. Examples of relationships that warrant future investigation include maternal depressive symptoms and glycemic control, child's perceived stress and glycemic control, and cortisol change and glycemic control. While conclusions about the current conceptual framework, including the mediating role that cortisol may have in the relationships, cannot be made at this time, results from the current study support the need for a larger, fully-powered study to examine the proposed framework further.

Implications for Clinical Practice, Policy, and Future Research

Clinically, this study highlighted the fact that many children with type 1 diabetes do not meet clinical recommendations for adequate glycemic control indicated by HbA1c values of 7.5% or less (ADA, 2015b). Moreover, it is interesting to note that children in the current study using pump therapy had significantly higher HbA1c levels. This was an unanticipated finding and may be related to factors besides treatment modality such as SES, child's perceived stress, and cortisol. Additionally, decreased blood glucose monitoring has been associated with poor glycemic control (Rewers et al., 2014). More information is needed to understand why children on pump therapy had higher HbA1c levels to enhance current practice and education aimed at improving glycemic control. Policy changes to lower the cost of blood glucose monitoring supplies, or providing supplies free of charge to individuals with diabetes may help improve glycemic control.

There is reason to believe that children ages 7 to 12 years with type 1 diabetes experience high rates of depressive symptoms and perceived stress, and that their mothers are prone to depressive symptoms. These depressive symptoms and stress may be attributed to responsibility of managing the disease and may be associated with glycemic control. Similar rates of depression and stress have been noted in children with chronic diseases that require routine management (Kub et al., 2009; Lopez-Duran et al., 2015). However, children are not routinely screened for depression and stress in clinical settings. The instruments and surveys used to screen both mothers and children in this study were quick and easy to administer with high reliability in the population. Consideration should be made about including these, or similar, surveys in routine clinical examination of children with type 1 diabetes and their mothers. Additionally, services targeted towards mental health and coping mechanisms could prove beneficial in children with type 1 diabetes and their parents (Grey et al., 2009). Mental health interventions that help children holistically manage diabetes as a chronic illness may not only improve glycemic control, but may also negate other negative outcomes of the disease.

A larger, fully powered study is recommended. While some relationships had small effect sizes and may not prove to be clinically meaningful, further research in a larger study population is necessary to more thoroughly examine the proposed relationships and test hypotheses on the mediation of cortisol between variables of interest. In the current study, effect sizes indicating potential clinical meaningfulness were noted between several variables of interest: maternal depressive symptoms and glycemic control, child's perceived stress and glycemic control, and cortisol change and glycemic control. Moreover, assessment of effect sizes during mediational analysis

indicated potentially meaningful relationships. Therefore, the investigation of the relationship between maternal depressive symptoms, child depressive symptoms, child's perceived stress with glycemic control, and the role cortisol may have as a mediator, is warranted in future studies. Further examination of these variables of interest may help researchers and clinicians better understand the impact mental health and stress have on glycemic control in children with type 1 diabetes.

As a pilot study, the methodology used in this study highlighted protocol revisions that would be beneficial in future recruitment and design procedure. Future research endeavors should aim to enroll equitable numbers of male and female children age 7 to 12 years. Additionally, efforts should be made to include children of all races with type 1 diabetes. Using clinical sites throughout the United States may help to recruit a more diverse and representative sample of prepubertal children with type 1 diabetes. Tools to measure variables of interest may be improved as well.

While all surveys were reliable and easy to use in the current sample, the addition of the Diabetes Stress Questionnaire for Youths (DSQY) (Delamater et al., 2013) in addition to the FBS, would be beneficial to aid in assessment of stress related to diabetes management. Since the DSQY has not been validated in children younger than 10, future studies are needed to examine the validity and reliability for administering the tool to younger children. Moreover, collection of salivary cortisol from school age children could be improved.

Collecting two samples of saliva for cortisol was beneficial in assessing cortisol change from early morning to late morning or afternoon. However, since the goal of research is to examine chronic changes in cortisol rather than the acute cortisol response,

it would be beneficial to assess the child for any stressful occurrence occurring an hour or two before the second saliva collection. Since stressful events may trigger an acute cortisol response and elevate the second cortisol level, elevations in the second cortisol level may be indicative of an acutely stressful event occurring the day of data collection rather than chronic stress alterations. Additionally, it may be beneficial to examine a cortisol awakening response in addition to assessing cortisol change. Even though the second salivary cortisol level should be lower regardless of when the first salivary cortisol was collected, the cortisol awakening response may allow researchers to better assess cortisol rhythms in children (Miller et al., 2016; Törnhage, 2009). Salivary home collection proved beneficial to collect a morning sample of saliva. Parents were able to collect saliva from the child with minimal trouble. However, time of awakening and time of cortisol collection must be noted (Miller et al., 2016). Additionally, considerations of parents following exact protocol must be made. In addition to mailing a paper copy of instructions with collection instruments to parents on how to collect saliva, it was also beneficial to reach out to parents the night before to review the procedure and answer questions. Being accessible to parents, via phone or text, to answer questions that may arise during salivary collection may also prove beneficial.

Summary

This chapter presented a discussion on findings from the study. The aim of the study was to examine the effects sizes of the relationships between maternal depressive symptoms, child depressive symptoms, child's perceived stress, cortisol and glycemic control in prepubertal children with type 1 diabetes and their mothers. As a pilot study,

conclusions about the relationships between variables of interest cannot be made at this time. However, examination of effect sizes between variables of interest supports the need for future research in a larger, more representative sample, including the continued assessment of cortisol as a mediator between maternal depressive symptoms, child depressive symptoms, child's perceived stress, and glycemic control. This study supports the need for the continued investigation of factors, such as child's perceived stress, that influence glycemic control in younger children, as some effect sizes were noteworthy, but may indicate a protective relationship.

REFERENCES

Adams, J. A., & Weaver, J. (1986). Self-esteem and perceived stress in young adolescents with chronic disease. *Journal of Adolescent Health Care, 7,* 173-177.

Aguilera, G. (2011). HPA axis responsiveness to stress: Implications for healthy aging. *Experimental Gerontology, 46,* 90-95.

American Diabetes Association. (2013). Economic costs of diabetes in the U.S. in 2012. Retrieved from http://www.diabetes.org/advocacy/news-events/cost-of-diabetes.html

American Diabetes Association. (2015a). Living with diabetes: complications. Retrieved from http://www.diabetes.org/living-with-diabetes/complications/

American Diabetes Association. (2015b). Standards of medical care in diabetes—2015. *Diabetes Care, 38*, S1-S93.

American Diabetes Association. (2015c). Statistics about diabetes. Retrieved from http://www.diabetes.org/diabetes-basics/statistics/?loc=db-slabnav

Anxiety and Depression Association of America. (2016). Anxiety and depression in children. Retrieved from http://www.adaa.org/living-with-anxiety/children/anxiety-and-depression

Armbruster, D., Mueller, A., Strobel, A., Lesch, K., Brocke, B., Kirschbaum, C. (2012). Children under stress- COMT genotype and stressful life events predict cortisol

increase in an acute social stress paradigm. *International Journal of Neuropsychopharmacology, 15,* 1229-1239.

Ashman, S. B., Dawson, G., Panagiotides, H., Yamada, E., & Wilkinson, C. W. (2002). Stress hormone levels of children of depressed mothers. *Development and Psychopathology, 14,* 333-349.

Auslander, W. F., Thompson, S., Dreitzer, D., White, N. H., & Santiago, J. V. (1997). Disparity in glycemic control and adherence between African-American and Caucasian youths with diabetes. *Diabetes Care, 20*(10), 1569-1575.

Bae, Y. J., Stadelmann, S., Klein, A. M., Jaeger, S., Hiemisch, A., Kiess, W., … & Dohnert, M. (2015). The hyporeactivity of salivary cortisol at stress test (TSST-C) in children with internalizing or externalizing disorders is contrastively associated with a-amylase. *Journal of Psychiatric Research, 71,* 78-88.

Barkmann, C., Erhart, M., Schulte-Markwort, M., & BELLA Study Group. (2008). The German version of the Centre for Epidemiological Studies Depression Scale for Children: psychometric evaluation in a population-based survey of 7 to 17 years old children and adolescents–results of the BELLA study. *European Child & Adolescent Psychiatry*, *17*(1), 116-124.

Baron, R. M., & Kenny, D. A. (1986). The moderator-mediator variable distinction in social psychological research: Conceptual, strategic and statistical considerations. *Journal of Personality and Social Psychology, 51*, 1173-1182.

Batajoo, R. J., Messina, C. R., & Wilson, T. A. (2012). Long-term efficacy of insulin pump therapy in children with type 1 diabetes mellitus. *Journal of Clinical Research in Pediatric Endocrinology, 4*(3), 127-131.

Berlin, K. S., Rabideau, E. M., & Hains, A. A. (2012). Empirically derived patterns of perceived stress among youth with type 1 diabetes and relationships to metabolic control. *Journal of Pediatric Psychology, 37*(9), 990-998.

Betancourt, T., Scorza, P., Meyers-Ohki, S., Mushashi, C., Kayiteshonga, Y., Binagwaho, A., ... & Beardslee, W. R. (2012). Validating the center for epidemiological studies depression scale for children in Rwanda. *Journal of the American Academy of Child & Adolescent Psychiatry*, *51*(12), 1284-1292.

Black, M. J., Anderson, A., Bell, R. A., Dabelea, D., Pihoker, C., Saydah, S., … & Lawrence, J. M. (2011). Prevalence of asthma and its association with glycemic control among youth with diabetes. *Pediatrics, 128(4),* e839-e847. doi:10.1542/peds.2010-3636

Blankfeld, D. F., & Holahan, C. J. (1996). Family support, coping strategies, and depressive symptoms among mothers of children with diabetes. *Journal of Family Psychology, 10,* 173-179.

Blass, A. (2012). Kids with diabetes can be depressed, too. Retrieved from http://www.healthline.com/diabetesmine/kids-with-diabetes-can-be-depressed-too

Brashers, V. L., & Jones, R. E. (2010). Mechanisms of hormonal regulation. In K. L. McCance, S. E. Huether, V. L. Brashers, & N. S. Rote (Eds.) *Pathophysiology: the biological basis for disease in adults and children* (6th ed.) (703-717). Maryland Heights, MO: Mosby Inc.

Brorsson, A. L., Viklund, G., Örtqvist, E., & Lindholm Olinder, A. (2015). Does treatment with an insulin pump improve glycaemic control in children and

adolescents with type 1 diabetes? A retrospective case–control study. *Pediatric Diabetes*, *16*(7), 546-553.

Bulanda, J. R., & Brown, S. L. (2007). Race-ethnic differences in marital quality and divorce. *Social Science Research*, *36*(3), 945-967.

Butler, J. M., Berg, C. A., King, P., Gelfand, D., Fortenberry, K., Foster, C., & Wiebe, D. (2009). Parental negative affect and adolescent efficacy for diabetes management. *Journal of Family Psychology, 23,* 611-614.

Butwicka, A., Zalepa, A., Fendler, W., Szadkowska, A., & Mlynarski, W. (2013). Maternal depressive symptoms predict acute hospitalization among children with type 1 diabetes. *Pediatric Diabetes, 14,* 288-294.

Caputo, J. L., Gill, D. L., Tseh, W., Jamurtas, A. Z. & Morgan, D. W. (2000). Perceived stress and blood pressure in early adolescent children. *Annals of Behavioral Medicine, 22,* 1-7.

Carskadon, M. A., & Acebo, C. (1993). A self-administered rating scale for pubertal development. *Journal of Adolescent Health, 14*(3), 190-195. doi: 10.1016/1054-139X(93)90004-9

Centers for Disease Control and Prevention. (2015a). *Diabetes Report Card 2014.* Atlanta, GA: Centers for Disease Control and Prevention, US Dept of Health and Human Services.

Centers for Disease Control and Prevention. (2015b). *About Child & Teen BMI.* Retrieved from

https://www.cdc.gov/healthyweight/assessing/bmi/childrens_bmi/about_childrens_bmi.html

Centers for Disease Control and Prevention. (2014). *National diabetes statistics report: Estimates of diabetes and its burden in the United States, 2014*. Atlanta, GA: U.S. Department of Health and Human Services.

Centers for Disease Control and Prevention. (2011). *National diabetes fact sheet: national estimates and general information on diabetes and prediabetes in the Unites States, 20*11. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention.

CESD-R. (2008). CESD-R explanation. Retrieved from http://cesd-r.com/cesdr/

CESD-R (2013). About CESD-R. Retrieved from http://cesd-r.com/about-cesdr/

Channanath, A. M., Elkum, N., Al-Abdulrazzaq, D., Tuomilehto, J., Shaltout, A., & Thanaraj, T. A. (2017). Ethnic differences in association of high body mass index with early onset of Type 1 diabetes–Arab ethnicity as case study. *PloS one*, *12*(4), e0175728.

Charmandari, E., Acherman, J. C., Carel, J., Soder, O., & Chrousos, G.P. (2012). Stress response and child health. *Endocrinology, 5*(248), 1-6.

Chrousos, G. P., & Kino, T. (2007). Glucocorticoid action networks and complex psychiatric and/or somatic disorders. *Stress, 10,* 213-219.

Clements, A. D. (2013). Salivary cortisol measurement in developmental research: where do we go from here? *Developmental Psychobiology, 55,* 205-220.

Clayton, K. M., Stewart, S. M., Wiebe, D. J., McConnel, C. E., & Hughes, C. W. (2013). Maternal depressive symptoms predict adolescent healthcare utilization and charges in youth with type 1 diabetes (T1D). *Health Psychology, 32,* 1013-1022. doi:10.1037/a0032761

Cohen, J. (1988). *Statistical power analysis for the behavior sciences*. (2nd ed.). Hillsdale, NJ: Erlbaum.

Crocq, M.-A. (2003). Alcohol, nicotine, caffeine, and mental disorders. *Dialogues in Clinical Neuroscience*, *5*(2), 175–185.

Dabelea, D., Mayer-Davis, E. J., Saydah, S., Imperatore, G., Linder, B., Divers, J., ... & Liese, A. D. (2014). Prevalence of type 1 and type 2 diabetes among children and adolescents from 2001 to 2009. *Journal of the American Medical Association*, *311*(17), 1778-1786.

Davies, D. (2011). *Child Development.* New York, NY: the Guilford Press.

Davis, C. L., Delamater, A. M., Shaw, K. H., LaGreca, A. M., Eidson, M. S., Perez-Rodriguez, J. E., & Nemery, R. (2001). Brief report; Parenting styles, regimen adherence, and glycemic control in 4- to 10-year old children with diabetes. *Journal of Pediatric Psychology, 26*(2), 123-129.

de Heus, P. (2012). R squared effect-size measures and overlap between direct and indirect effect in mediation analysis. *Behavior Research Methods*, *44*(1), 213-221.

Delamater, A. M., de Wit, M., McDarby, V., Malik, J., & Acerini, C. L. (2014). Psychological care of children and adolescents with type 1 diabetes. *Pediatric Diabetes, 15*(s20), 232-244.

Delamater, A. M., Patino-Fernandez, A. M., Smith, K. E., & Bubb, J. (2013). Measurement of diabetes stress in older children and adolescents with type 1 diabetes mellitus. *Pediatric Diabetes, 14*, 50-56.

Delamater, A. M., Shaw, K. H., Applegate, E. B., Pratt, I A., Eidson, M., Lancelotta, G. X., … & Richton, S. (1999). Risk for metabolic control problems in minority youth with diabetes. *Diabetes Care, 22,* 700-705.

DeVries, A. C., Craft, T. K., Glasper, E. R., Neigh, G. N., & Alexander, J. K. (2007). 2006 Curt P. Richter award winner: Social influences on stress responses and health. *Psychoneuroendocrinology, 32,* 587-603. doi: 10.1016/j.psyneuen.2007.04.007

de Wit, M., Delemarre-van de Waal, H. A., Bokma, J. A., Haasnoot, K., Houdijk, M. C., Gemke, R. J., Snoek, F. J. (2007). Self-report and parent- report of physical and psychosocial well-being in Dutch adolescents with type 1 diabetes in relation to glycemic control. *Health Quality Life Outcomes 5(1),* 1.

Diabetes Control and Complications Trial Research Group. (1993). The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *New England Journal of Medicine*, *1993*(329), 977-986.

Diabetes Control and Complications Trial/ Epidemiology of Diabetes Interventions and Complications Study Research Group. (2005). Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *New England Journal of Medicine*, *2005*(353), 2643-2653.

Ducat, L., Rubenstein, A., Philipson, L. H., & Anderson, B. J. (2015). A review of the mental health issues of diabetes conference. *Diabetes Care, 38,* 333-338.

Early, L., Cushway, D., & Cassidy, T. (2006). Perceived stress in young carers: Development of a Measure. *Journal of Child and Family Studies, 15*(2), 169-180.

Eaton, W., Muntaner, C., Smith, C., Tien, A., & Ybarra, M. (2004). Center for Epidemiologic Studies Depression Scale: Review and revision (CESD and CESD-R). In M. E. Maruish (Ed.), *The Use of Psychological Testing for Treatment Planning and Outcomes Assessment* (3rd ed) (pp. 363-377). Mahwah, NJ: Lawrence Erlbaum.

Ertel, K. A., Rich-Edwards, J. W., & Koenen, K. C. (2011). Maternal depression in the United States: Nationally representative rates and risks. *Journal of Women's Health*, *20*(11), 1609-1617.

Essex, M. J., Shirtcliff, E. A., Burk, L. R., Ruttle, P. L., Klein, M. H., Slattery, M. J., Kalin, N. H., & Armstrong, J. M. (2011). Influence of early life stress on later hypothalamic-pituitary-adrenal axis functioning and its covariation with mental health symptoms: A study of the allostatic process from childhood into adolescence. Development and *Psychopathology, 23*, 1039-1058.

Farrell, S. P., Hains, A. A., Davies, W. H., Smith, P., & Parton, E. (2004). The impact of cognitive distortions, stress, and adherence on metabolic control in youths with type 1 diabetes. *Journal of Adolescent Health, 34(*6), 461-467.

Faulstich, M. E., Carey, M. P., Ruggiero, L., Enyart, P., & Gresham, F. (1986). Assessment of depression in childhood and adolescents: An evaluation of the

center for epidemiological studies depression scale for children (CES-DC). *American Journal of Psychiatry, 143,* 1024-1027.

Fendler, W., Baranowska, A. I., Mianoswska, B., Szadkowska, A., Mlynarski, W. (2011). Three-year comparison of subcutaneous insulin pump treatment with multi-daily injections on HbA1c, its variability and hospital burden of children with type 1 diabetes. *Acta Diabetologica,* 49, 363-370.

Fendrich, M., Weissman, M. M., & Warner, V. (1990). Screening for depressive disorder in children and adolescence: validating the Center for Epidemiologic Studies Depression Scale for Children. *The American Journal of Epidemiology, 131(30),* 538-551.

Fernald, L. C. H., Burke, H. M., & Gunnar, M. R. (2008). Salivary cortisol levels in children of low-income women with high depressive symptomatology. *Development and Psychopathology, 20,* 423-436.

Forshee, B. A., Clayton, M. F., & McCance, K., L. (2010). Stress and disease. In K. L. McCance, S. E. Huether, V. L. Brashers, & N. S. Rote (Eds.), *Pathophysiology: the biological basis for disease in adults and children* (6th ed.) (703-717). Maryland Heights, MO: Mosby Inc.

Freese, B. T., Beckman, S. J., Boxley-Harges, S., Bruick-Sorge, C., Harris, S. M., Hermiz, M. E., Meininger, M., & Steinkeler, S. E. (1998). Betty Neuman. In A. Tomey & M. Alligood (Eds.), *Nursing theorists and their work* (4th ed.). St Louis, MO: Mosby.

Gallagher, E. J., Le Roith, D., & Bloomgarden, Z. (2009). Review of hemoglobin A1c in the management of diabetes. *Journal of Diabetes, 1,* 9-17. doi: 10.111/j.1753-0407.2009.00009.x

Gallegos-Macias, A. R., Macias, S. R., Kaufman, E., Skipper, B., & Kalishman, N. (2003). Relationship between glycemic control, ethnicity and socioeconomic status is Hispanic and white non-Hispanic youths with type 1 diabetes mellitus. *Pediatric Diabetes, 4,* 19-23.

Garner, A. S. (2013). Home visiting and the biology of toxic stress: opportunities to address early childhood adversity. *Pediatrics, 132(Supplement 2),* S65-73.

Gold, P. W. (2015). The organization of the stress system and its dysregulation in depressive illness. *Molecular Psychiatry, 20*, 32-47.

Goodyer, I. M., Herbert, J., & Altham, P. M. (1998). Adrenal steroid secretion and major depression in 8- to 16-year-olds, III. Influence of cortisol/DHEA ratio at presentation on subsequent rates of disappointing life events and persistent major depression. *Psychological Medicine, 28*(2):265-73.

Gregg, B., Connor, C. G., Ruedy, K. J., Beck, R. W., Kollman, C., Schatz, D., ... & Lee, J. M. (2015). Body mass index changes in youth in the first year after type 1 diabetes diagnosis. *The Journal of Pediatrics*, *166*(5), 1265-1269.

Grey, M., Whittemore, R., Jaser, S., Ambrosino, J., Lindemann, E., Liberti, L., ... & Dziura, J. (2009). Effects of coping skills training in school-age children with type 1 diabetes. *Research in nursing & health*, *32*(4), 405-418.

Grey, M., Whittemore, R., & Tamborlane, W. (2002). Depression in type 1 diabetes in children: natural history and correlates. *Journal of Psychosomatic Research, 53(4),* 907-911.

Gump, B. B., Reihman, J., Stewart, P., Lonky, E., Darvill, T., Granger, D. A., & Matthews, K. A. (2009). Trajectories of maternal depressive symptoms over her child's life span: Relation to adrenocortical, cardiovascular, and emotional functioning in children. *Development and Psychopathology, 21*, 207-225.

Hannon, T. S., Janosky, J. & Arslanian, S. A. (2006). Longitudinal study of physiologic insulin resistance and metabolic changes of puberty. *Pediatric Research, 60*(6), 759-763.

Hanrahan, K., McCarthy, A. M., Kleiber, C., Lutgendorf, S., Tsalikian, E. (2006). Strategies for salivary cortisol collection and analysis in research with children. *Applied Nursing Research, 19,* 95-101.

Hassan, K., Loar, R., Anderson, B. J., & Heptulla, R. A. (2006). The role of socioeconomic status, depression, quality of life, and glycemic control in type 1 diabetes mellitus. *The Journal of Pediatrics, 149*(4), 526-531.

Haugstvedt, A., Wentzel-Larsen, T., Aarflot, M., Rokne, B., & Graue, M. (2015). Assessing fear of hypoglycemia in a population-based study among parents of children with type 1 diabetes–psychometric properties of the hypoglycemia fear survey–parent version. *BMC Endocrine Disorders, 15*(2), 1-8.

Helgeson, V. S., Siminerio, L., Escobar, O., & Becker, D. (2009). Predictors of metabolic control among adolescents with diabetes: a 4-year longitudinal study. *Journal of Pediatric Psychology*, *34*(3), 254-270.

Hellhammer, D. H., Wust, S., & Kudielka, B. M. (2008). Salivary cortisol as a biomarker in stress research. *Psychoneuroendocrinology, 34*, 163-171.

Heneghan, A. M., Silver, E. J., Bauman, L. J. & Stein, R. E. K. (2000). Do pediatricians recognize mothers with depressive symptoms? *Pediatrics, 106*, 1367-1373.

Hilliard, M. E., Yi-Frazier, J. P., Hessler, D., Butler, A. M., Anderson, B. J., & Jaser, S. (2016). Stress and A1c among people with diabetes across the lifespan. *Current Diabetes Reports, 16*(67). doi:10.1007/s11892-016-0761-3

Hinkle, D. E., Wiersma, W., & Jurs, S. G. (2003). *Applied statistics for the behavioral sciences* (5th ed.). Boston, MA: Houghton Mifflin Company.

Hood, K. K., Butler, D., Huestis, S., Volkening, L., Maher, A., & Laffel, L. M. B. (2006). Depressive symptoms in children and adolescents with type 1 diabetes. *Diabetes Care, 29*(6), 1389-1391.

Hood, K. K., Rausch, J. R., & Dolan, L. M. (2011). Depressive symptoms predict change in glycemic control in adolescents with type 1 diabetes: rates, magnitude, and moderators of change. *Pediatric Diabetes, 12(8),* 718-723.

Huether, S. & McCance, K. (2012). *Understanding pathophysiology* (5th ed.). St. Louis: Mosby/Elsevier.

Jaser, S. S., & Grey, M. (2010). A pilot study of observed parenting and adjustment in adolescents with type 1 diabetes and their mothers. *Journal of Pediatric Psychology, 35,* 738-747. doi: 10.1093/jpepsy/jsp098

Jaser, S. S., Whittemore, R., Ambrosino, J. M., Lindemann, E., & Grey, M. (2008). Mediators of depressive symptoms in children with type 1 diabetes and their mothers. *Journal of Pediatric Psychology, 33*, 509-519.

Jenkins, S. K., Rew, L., & Sternglanz, R. W. (2005). Eating behaviors among school-age children associated with perceptions of stress. *Issues in Comprehensive Pediatric Nursing, 28,* 175-191.

Kidshealth.org. (2014). Childhood stress. Retrieved from http://kidshealth.org/parent/emotions/feelings/stress.html

Kongkaew, C., Jampachaisri, K., Chaturongkul, C. A., & Scholfield, C. N. (2013). Depression and adherence to treatment in diabetic children and adolescents: a systematic review and meta-analysis of observational studies. *European Journal of Pediatrics, 173*, 203-212.

Korbel, C. D., Wiebe, D. J., Berg, C. A., & Palmer, D. L. (2007). Gender differences in adherence to type 1 diabetes management across adolescence: The mediating role of depression. *Children's Healthcare, 36*(1), 83-98.

Koss, K. J., George, M. R. W., Davies, P. T., Cicchetti, D., Cummings, E. M., & Sturge-Apple, M. L. (2012). Patterns of children's adrenocortical reactivity to interparental conflict and associations with child adjustment: A growth mixture modeling approach. *Developmental Psychology, 49*(2), 317. doi: 10.1037/a002824

Kub, J., Jennings, J. M., Donithan, M., Walker, J. M., Land, C. L., & Butz, A. (2009). Life Events, Chronic Stressors, and Depressive Symptoms in Low-Income Urban Mothers With Asthmatic Children. *Public health nursing*, *26*(4), 297-306.

Lawrence, J. M., Standiford, D. A., Loots, B., Klingensmith, G. J., Williams, D. E., Ruggiero, A.,… & McKeown, R. E. (2006). Prevalence and correlates of depressed mood among youth with diabetes: The SEARCH for diabetes in youth study. *Pediatrics, 117*(4), 1348-1358.

Lazarus, R. S. (1990). Theory based stress measurement. *Psychological Inquiry, 1*, 3–12.

Levine, T. R. & Hullett, C. R. (2002). Eta squared, partial eta squared, and misreporting of effect size in communication research. *Human Communication Research, 28*(4), 612-625.

Lewis, C. E., Siegel, J. M., & Lewis, M. A. (1984). Feeling bad: Exploring sources of distress among pre-adolescent children. *American Journal of Public Health, 74,* 117-122.

Lopez-Duran, N. L., McGinnis, E., Kuhlman, K., Geiss, E., Vargas, I., & Mayer, S. (2015). HPA-axis stress reactivity in youth depression: evidence of impaired regulatory processes in depressed boys. *Stress*, *18*(5), 545-553.

Lupien, S. J., King, S., Meaney, M. J., & McEwen, B. S. (2000). Child's stress hormone levels correlate with mother's socioeconomic status and depressive state. *Biological Psychiatry, 48,* 976-980.

Maahs, D. M., West, N. A., Lawrence, J. M., & Mayer-Davis, E. J. (2010). Chapter 1: Epidemiology of type 1 diabetes. *Endocrinology and Metabolism Clinics of North America, 39*(1), 481-497. doi:10.1016/j.ecl.2010.05.011

Mackey, E., Struemph, K., Powell, P., Chen, R., Streisand, R., & Holmes, C. (2014). Maternal depressive symptoms and disease care status in youth with type 1 diabetes. *Health Psychology, 33*(8), 783-791. doi:10.1037/hea0000066

Malcarne, V. L., Hamilton, N. A., Ingram, R. E., & Taylor, L. (2000). Correlates of distress in children at risk for affective disorder: Exploring predictors in the offspring of depressed and nondepressed mothers. *Journal of Affective Disorders*, *59*(3), 243-251.

Maldonado, E. F., Fernandez, F. J., Trianes, M. V., Wesnes, K., Petrini, O., Zangara, A., Enguix, A., Ambrosetti, L. (2008). Cognitive performance and morning levels of salivary cortisol and alpha-amylase in children reporting high vs. low daily stress perception. *The Spanish Journal of Psychology, 11,* 3-15.

Malik, F. S., & Taplin, C. E. (2014). Insulin therapy in children and adolescents with type 1 diabetes. *Pediatric Drugs, 16,* 141-150.

Marcovecchio, M. L., & Chiarelli, F. (2012). The effects of acute and chronic stress on diabetes control. *Science Signaling, 5*(247), pt10.

Markowitz, J. T., Volkening, L. K., Butler, D. A., & Laffel, L. M. B. (2015). Youth-perceived burden of type 1 diabetes: Problem area in diabetes survey-pediatric version (PAID-Peds). *Journal of Diabetes Science and Technology, 9*(5), 1080-1085.

McEwen, B. (1998). Stress, adaptation and disease: Allostasis and allostatic load. *Annals of the New York Academy of Sciences, 840,* 33-44.

McEwen, B. S. (2000). Allostasis and allostatic load: Implications for neuropsychopharmacology. *Neuropsychopharmacology, 22,* 108-124.

McEwen, B. S. (2007). Physiology and neurobiology of stress and adaptation: Central role of the brain. *Physiology Review, 87*, 874-904.

McEwen, B. S. & Tucker, P. (2011). Critical biological pathways from chronic psychosocial stress and research opportunities to advance the consideration of stress in chemical risk assessment. *American Journal of Public Health, 101,* S131-S139.

McEwen, M., & Willis, E. M. (2002). *Theoretical basis for nursing*. Philadelphia, PA: Lippincott Williams & Wilkins.

McGrady, M. E., & Hood, K. K. (2010). Depressive symptoms in adolescents with type 1 diabetes: Association with longitudinal outcomes. *Diabetes Research in Clinical Practice, 88*(3), e35-e37.

Meleis, A. I. (2012). *Theoretical nursing: Development and progress* (5th ed.). Philadelphia, PA: Lippincott Williams & Wilkins.

Miller, R., Stalder, T., Jarczok, M., Almeida, D. M., Badrick, E., Bartels, M., ... & Fischer, J. E. (2016). The CIRCORT database: Reference ranges and seasonal changes in diurnal salivary cortisol derived from a meta-dataset comprised of 15 field studies. *Psychoneuroendocrinology, 73,* 16-23.

Moksnes, U. K., Moljord, I. E., Espnes, G. A., & Byrne, D. G. (2010). The association between stress and emotional states in adolescents: The role of gender and self-esteem. *Personality and Individual Differences*, *49*(5), 430-435.

Mosbah, A., Abd-Ellatif, N., & Sorour, E. (2011). Influence of serum cortisol levels on glycemic control in children with type 1 diabetes. *Journal of the Egyptian Society of Parasitology, 41,* 777-784.

Naar-King, S., Idalski, A., Ellis, D., Frey, M., Templin, T., Cunningham, P. B., & Cakan, N. (2006). Gender differences in adherence and metabolic control in urban youth with poorly controlled type 1 diabetes: The mediating role of mental health symptoms. *Journal of Pediatric Psychology, 31*(8), 793-802.

Nabhan, Z. M., Kreher, N. C., Greene, D. M., Eugster, E. A., Kronenberger, W., & DiMeglio, L. A. (2009). A randomized prospective study of insulin pump vs. insulin injection therapy in very young children with type 1 diabetes: 12-month glycemic, BMI, and neurocognitive outcomes. *Pediatric Diabetes, 10,* 202-208.

National KIDS COUNT. (2017). *Children in Single-parent Families*. Retrieved from http://datacenter.kidscount.org/data/tables/106-children-in-single-parent-families?loc=1&loct=1&gclid=CIjo0_yez9MCFQwVgQodiWYM4Q#detailed/2/2,6-52/false/573,869,36,868,867/any/429,430

Neuman, B. (1995). *The Neuman Systems Model* (3rd ed.). Norwalk, CT: Appleton & Lange.

O'Hagan, M., & Harvey, J. N. (2010). Glycemic control in children with type 1 diabetes in Wales. *Diabetes Care*, *33*(8), 1724-1726.

Orchard, T. J., Nathan, D. M., Zinman, B., Cleary, P., Brillon, D., Backlund, J. Y. C., & Lachin, J. M. (2015). Association between 7 years of intensive treatment of type 1 diabetes and long-term mortality. *The Journal of the American Medical Association*, *313*(1), 45-53.

Palta, M., Shen, G., Allen, C., Klein, R., & D'lessio, D. (1996). Longitudinal patterns of glycemic control and diabetes care from diagnosis in a population-based cohort with type 1 diabetes. *American Journal of Epidemiology*, *144*(10), 954-961.

Paris, C. A., Imperatore, G., Klingensmith, G., Petitti, D., Rodriguez, B., Anderson, A. M., … Pihoker, C. (2009). Predictors of insulin regimens and impact on outcomes in youth with type 1 diabetes: The SEARCH for diabetes youth study. *The Journal of Pediatrics, 155*(2), 183-189.

Petersen, A. C., Crockett, L., Richards, M., & Boxer, A. (1988). A self-report measure of pubertal status: Reliability, validity, and initial norms. *Journal of Youth and Adolescence, 17*(2), 117-133.

Pettitt, D. J., Talton, J., Dabelea, D., Divers, J., Imperatore, G., Lawrence, J. M., ... & Saydah, S. H. (2014). Prevalence of diabetes in US youth in 2009: the SEARCH for diabetes in youth study. *Diabetes Care*, *37*(2), 402-408.

Piganelli, J. (2014). Targeting the autoimmune response to prevent type 1 diabetes. Retrieved from http://www.diabetes.org/research-and-practice/we-are-research-leaders/type-1-research-highlights/targeting-the-autoimmune_response_type1.html

Pinquart, M., & Shen, Y. (2010). Depressive symptoms in children and adolescents with chronic physical illness: an updated meta-analysis. *Journal of Pediatric Psychology, 36*(4), 375-384.

Polit, D., & Beck, C. (2012). *Nursing research: Generating and assessing evidence for nursing practice* (9th ed.). Philadelphia, PA: Lippincott.

Preacher, K. J., & Kelley, K. (2011). Effect size measures for mediation models: quantitative strategies for communicating indirect effects. *Psychological Methods*, *16*(2), 93-115.

Olagunju, A. T., Aina, O. F., Fadipe, B. (2013). Screening for depression with centre for epidemiological studies depression scale revised and its implication for consultation-liaison psychiatry practice among cancer subjects: A perspective from a developing country. *Psycho-Oncology, 22,* 1901-1906.

Radloff, L. S. (1977). The CES-D scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement, 1(3),* 385-401.

Rew, L., Horner, S. D., & Fouladi, R. T. (2010). Factors associated with health behaviors in middle childhood. *Journal of Pediatric Nursing*, *25*(3), 157-166.

Rewers, M., Pihoker, C., Donaghue, K., Hanas, R., Swift, P., & Klingensmith, G. J. (2009). Assessment and monitoring of glycemic control in children and adolescents with diabetes. *Pediatric Diabetes*, *10*(s12), 71-81.

Rodbard, D. (2009). Interpretation of continuous glucose monitoring data: Glycemic variability and quality of glycemic control. *Diabetes Technology & Therapeutics, 11*, s55-s67.

Rohrer, T., Stierkorb, E., Heger, S., Karges, B., Raile, K., Schwab, K. O., & Holl, R. W. (2007). Delayed pubertal onset and development in German children and adolescents with type 1 diabetes: cross-sectional analysis of recent data from the DPV diabetes documentation and quality management system. *European Journal of Endocrinology, 157(5),* 647-653.

Romeo, R. D., & McEwen, B. S. (2006). Stress and the adolescent brain. *Annals of the New York Academy of Sciences, 1094*, 202-214.

Ross, P., Gray, A. R., Milburn, J., Kumarasamy, I. M., Wu, F., Farrand, S., ... & Wheeler, B. J. (2016). Insulin pump-associated adverse events are common, but not associated with glycemic control, socio-economic status, or pump/infusion set type. *Acta Diabetologica*, *53*(6), 991-998.

Rumburg, T. M., Lord, J. H., Savin, K. L., & Jaser, S. S. (2017). Maternal diabetes distress is linked to maternal depressive symptoms and adolescents' glycemic control. *Pediatric Diabetes, 18,* 16-70. doi:10.1111/pedi.12350

Ryan-Wenger, N. A., Wilson, V. L., & Broussard, A. G. (2012). Stress, coping, and health in children. In V. H. Rice (Ed.), *Handbook of stress, coping, and health: Implications for nursing research, theory, and practice* (2nd ed.) (pp. 226-253). Thousand Oaks, CA: Sage.

Salimetrics. (2014). Salivary cortisol. Retrieved from http://www.salimetrics.com/biomarker/cortisol

Shadish, W. R., Cook, T. D., & Campbell, D. T. (2002). *Experimental and quasi-experimental designs for generalized causal inference.* Belmont, CA: Wadswoth.

Shashaj, B. & Sulli, N. (2009). Difference in insulin usage patterns with pubertal development in children with type 1 diabetes during transition from multiple daily injections to continuous subcutaneous insulin infusion (CSII) and through the CSII treatment. *Diabetes Technology & Therapuetics, 11*(12), 767-774.

Spies, L. A., Margolin, G., Susman, E. J., & Gordis, E. B. (2011). Adolescents' cortisol reactivity and subjective distress in response to family conflict: the moderating role of internalizing symptoms. *Journal of Adolescent Health, 49(4),* 386-392. doi: 10.1016/j.jadohealth.2011.01.014

Sprague, J. E. & Arbelaez, A. M. (2011). Glucose conterregulatory responses to hypoglycemia. *Pediatric Endocrinology Review, 9*(1), 463-475.

Springer, D., Dziura, J., Tamborlane, W. V, Steffen, A. T., Ahern, J. H., Vincent, M., & Weinzimer, S. A. (2006). Optimal control of type 1 diabetes mellitus in youth receiving intensive treatment. *The Journal of Pediatrics, 149*(2), 227-232.

Sterline, P., & Eyer, J. (1988). Allostasis: a new paradigm to explain arousal pathology. In S. Fisher & J. Reason (Eds.), *Handbook of Life Stress, Cognition, & Health*. New York, NY: Wiley.

Stewart, J. G., Mazurka, R., Bond, L., Wynee-Edwards, K. E., & Harkness, K. L. (2013). Rumination and impaired cortisol recovery following a social stressor in adolescent depression. *Journal of Abnormal Child Psychology, 41,* 1015-1026.

Stewart, S. M., Rao, U., Emslie, G. J., Klein, D., & White, P. C. (2005). Depressive symptoms predict hospitalization for adolescents with type 1 diabetes. *Pediatrics, 115*(5), 1315-1319.

Storch, E. A., Lewin, A., Silverstein, J. H., Heidgerken, A. D., Strawser, M. S., Baumeister, A., & Geffken, G. R. (2004). Peer victimization and psychosocial adjustment in children with type 1 diabetes. *Clinical Pediatrics*, *43*(5), 467-471.

Suzuki, H., Belden, A. C., Spitznagel, E., Dietrich, R., & Luby, J. L. (2013). Blunted stress cortisol reactivity and failure to acclimated to familiar stress in depressed and sub-syndromal children. *Psychiatry Research, 210*(2), 575-583.

Tabachnick, B. G., & Fidell, L. S. (2013). *Using multivariate statistics* (6th ed). Boston, MA: Pearson Education Inc.

Terzian, M., Moore, K. A., & Nguyen, H. N. (2010). Assessing stress in children and youth: a guide for out-of school time program practitioners. *Child Trends, 22*, 1-5.

Törnhage, C. J. (2009). Salivary cortisol for assessment of hypothalamic-pituitary-adrenal axis function. *Neuroimmunomodulation*, *16*(5), 284-289.

Trast, J. (2014). CE: Diabetes and puberty: a glycemic challenge. *American Journal of Nursing, 114*(7), 26-35.

US Department of Health and Human Services. (2013). Diabetes: Objectives. Retrieved from http://healthypeople.gov/2020/topicsobjectives2020/objectiveslist.aspx?topicId=8

Van Cleave, J., & Davis, M. M. (2006). Bullying and peer victimization among children with special health care needs. *Pediatrics*, *118*(4), e1212-e1219.

Van Dam, N. T., & Earleywine, M. (2011). Validation of the center for epidemiologic studies depression scale-revised (CEDS-R): Pragmatic depression assessment in the general population. *Psychiatry Research, 186*, 128-132.

Varni, J. W., Rapoff, M. A., Waldron, S. A., Gragg, R. A., Bernstein, B. H., Lindsley, C. B. (1996). Effects of perceived stress on pediatric chronic pain. *Journal of Behavioral Medicine, 19*(6), 515-528.

Waltz, C. F., Strickland, O. L., & Lenz, E. R. (2010). *Measurement in nursing and health research* (4th ed.). New York, NY: Springer.

Weissman, M.M., Orvaschel, H., Padian, N. (1980). Children's symptom and social functioning self-report scales: Comparison of mothers' and children's reports. *Journal of Nervous Mental Disorders* 168(12):736–740.

Whittemore, R., Liberti, L., Jeon, S., Chao, A., Jaser, S. S., & Grey, M. (2013). Self-management as a mediator of family functioning and depressive symptoms with health outcomes in youth with type 1 diabetes. *Western Journal of Nursing Research, 36*(9), 1254-1271. doi:10.1177/0193945913516546

Wiebe, D. J., Gelfand, D., Butler, J. M., Korbel, C., Fortenberry, K. T., McCabe, J. D., & Berg, C. A. (2011). Longitudinal associations of maternal depressive symptoms, maternal involvement, and diabetes management across adolescence. *Journal of Pediatric Psychology, 36,* 837-846.

Wilkinson, P. O., & Goodyer, I. M. (2011). Childhood adversity and allostatic overload of the hypothalamic-pituitary-adrenal axis: A vulnerability model for depressive disorders. *Development and Psychopathy, 23,* 1017-1037.

Willemen, A. M., Koot, H. M., Ferdinand, R. F., Goossens, F. A., & Schuengel, C. (2008). Change in psycholopathology in referred children: the role of life events and perceived stress. *Journal of Child Psychology and Psychiatry, 49*(11), 1175-1183.

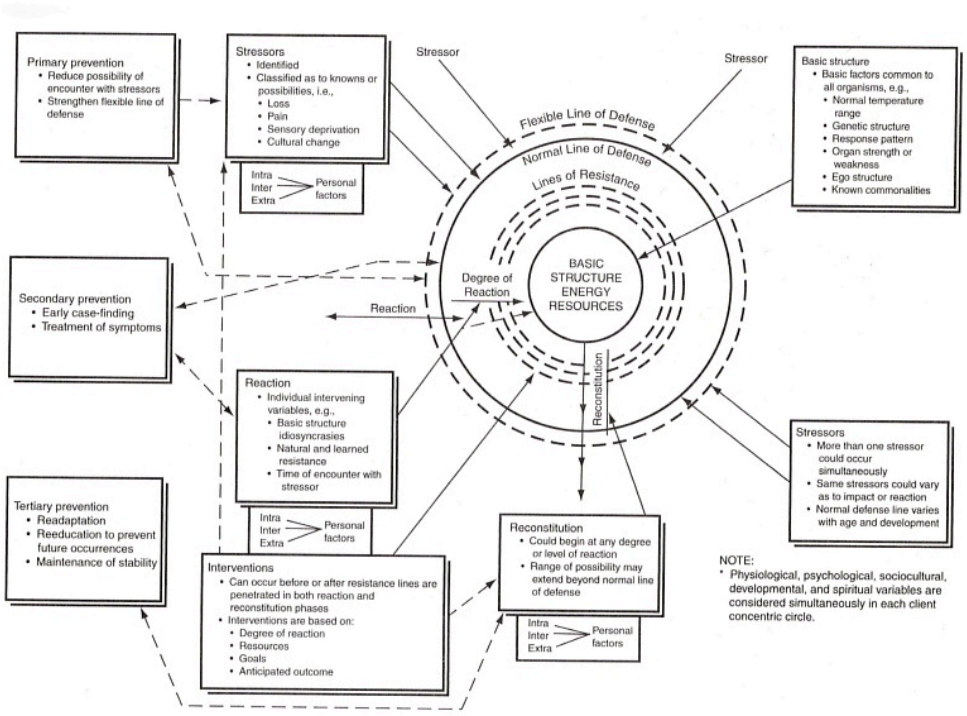
Worrall-Davies, A., Holland, P., Berg, I., Goodyer, I. (1999). The effect of adverse life events on glycaemic control in children with insulin dependent diabetes mellitus. *European Child & Adolescent Psychiatry, 8,* 11-16.

Yarcheski, T. J., Mahon, N. E., Yarcheski, A., & Hanks, M. M. (2010). Perceived stress and wellness in early adolescents using the Neuman Systems Model. *The Journal of School Nursing, 26,* 230-237.

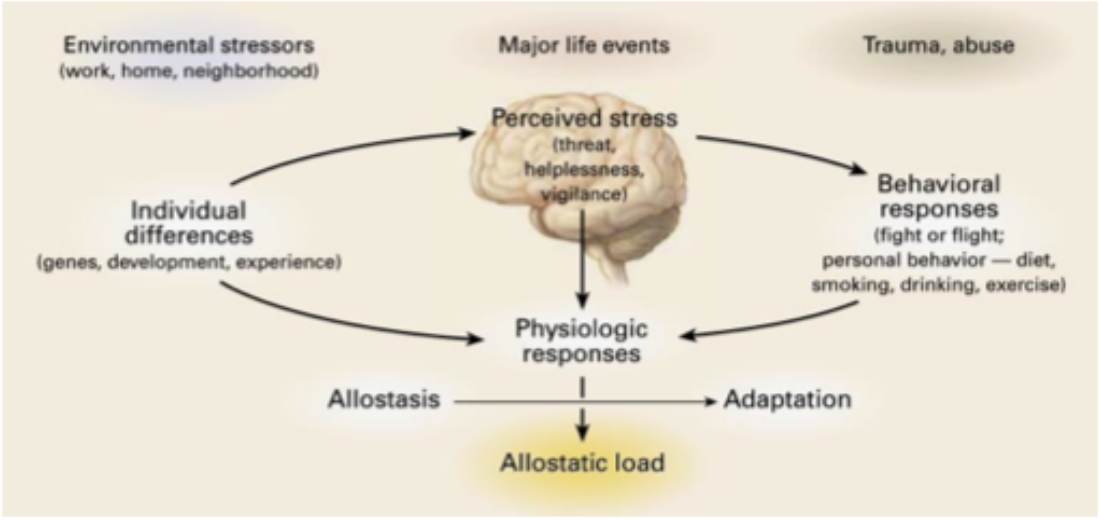
Zimmerman, M. (2012). Tools for depression: Standardized rating scales. *Medscape Education Psychiatry & Mental Health*. Retrieved from http://www.medscape.org/viewarticle/749921

APPENDIX A

THEORETICAL FRAMEWORKS



Neuman's Systems Model (Neuman, 1995)



McEwen's model of stress and allostatic load (McEwen, 2007)

APPENDIX B

SCREENING MATERIALS

Script for Screening

Hello—"I'm calling today because you expressed interest in participating in the research study examining depressive symptoms, stress and glycemic control advertised at USA Children's Specialty Clinic.
Are you still interested in the study?"

If yes—continue to screening.
If no—"Thank you very much for your time"

"To make sure you and your child are a good fit for the study, I need to ask you a few questions. Is this a good time? The interview will take about 15 minutes."
If yes—continue
If no—"Would you like to schedule a time for the screening interview?"

Screening:
"How old is your child?"

If between 7 years and 12 years—continue
If younger than 7 years or older than 12 years— "Thank you very much for your time"

"Has your child been diagnosed with type 1 diabetes?"

If yes—continue.
If no— "Thank you very much for your time"

"How long has your child been diagnosed?"

If longer than 1 year—continue.
If less than 1 year— "Thank you very much for your time"

"Has your child been diagnosed with any other endocrine disorders, such as Cushing's disease or Addison's disease?"

If no—continue.
If yes— "Thank you very much for your time"

"Does your child take any steroid medicines such as prednisone or an inhaled corticosteroid for asthma?"

If no—continue.
If yes— "Thank you very much for your time"

"Does your child have any cognitive deficits or learning delays?"

If no—continue.
If yes— "Thank you very much for your time"

"Does your child read, write, and speak in English?"

If yes—continue.
If no— "Thank you very much for your time"

"Has your child entered puberty?"

If unsure—Use Puberty Rating Scale
If no—continue.

If yes— "Thank you very much for your time"

"Are you the child's biological mother?"
If yes—continue.
If no— "Thank you very much for your time"

"Are you 18 years or older?"
If yes—continue.
If no— "Thank you very much for your time"

"Do you have the most responsibility for helping your child manage his or her diabetes?"
If yes—continue.
If no— "Thank you very much for your time"

"Can you read, write, and speak in English?"
If yes—continue.
If no— "Thank you very much for your time"

"Have you already scheduled a follow up appointment for your child at the endocrinology clinic?"
If yes—"What is the date and time of your next appointment?"
Note appointment date and time for data collection.
If no— "Would you like me to assist you in scheduling an appointment?"
Assist with scheduling an appointment.

"Thank you very much for your time. I look forward to working with you and your child. Please feel free to call me at 251-447-4870 if you have any questions or concerns regarding the research study."

Reminder the day before data collection

"I'm calling because you expressed interest in participating in the research study examining depressive symptoms, stress and glycemic control advertised at USA Children's Specialty Clinic. I have you scheduled for your endocrinology appointment and data collection tomorrow. Are you still interested in participating in the study?"
If yes—continue.
If no— "Thank you very much for your time"

"I would like to remind you to arrive an hour before your appointment so we can collect a saliva sample and complete a few short surveys with you and your child. We also ask that your child does not eat, smoke, or drink anything except water 1 hour prior to arriving in the clinic. We will provide your child with a snack after information is collected. Do you have any questions about tomorrow?"
If yes—Answer any questions related to research study.
If no— "Thank you very much for your time. We look forward to working with you in the morning"

A Self-Administered Rating Scale for Pubertal Development

Question	Response Options	Value
1. Would you say that growth in height:	has not yet begun to spurt[2]	1
	has barely started	2
	is definitely underway	3
	seems completed	4
	I don't know	

2. And how about the growth of body hair?
("Body hair" means hair any place other than your head, such as under your arms.)

Would you say that body hair growth:	has not yet begun to grow	1
	has barely started to grow	2
	is definitely underway	3
	seems completed	4
	I don't know	

3. Have you noticed any skin changes, especially pimples?

skin has not yet started changing	1
skin has barely started changing	2
skin changes are definitely underway	3
skin changes seem complete	4
I don't know	

FORM FOR BOYS:

4. Have you noticed a deepening of his voi

voice has not yet started changing	1
voice has barely started changing	2
voice changes are definitely underway	3
voice changes seem complete	4
I don't know	

5. Has he begun to grow hair on his face?

facial hair has not yet started growing	1
facial hair has barely started growing	2
facial hair growth has definitely started	3
facial hair growth seems complete	4
I don't know	

FORM FOR GIRLS:

4. Have you noticed that her breasts have begun to grow?

have not yet started growing	1
have barely started growing	2
breast growth is definitely underway	3
breast growth seems complete	4
I don't know	

5a. Has she begun to menstruate (started to have her period)?

yes	4
no	1

5b. If yes, how old was she when she started to menstruate?

age in years

APPENDIX C

INSTRUMENTS AND SURVEYS

Demographic Data Sheet

Child's Information

Child's date of birth: _____

Gender (circle): MALE FEMALE

School Grade: _____

Child's race (circle): WHITE BLACK HISPANIC ASIAN BI/MULTI RACIAL

Child's Health History (circle): DIABETES ASTHMA DEPRESSION

LEARNING DELAY/DISABILITY ENDOCRINE DISORDER

Date of type 1 diabetes diagnosis: _____

Medications taken daily or as needed: _____

How long has your child been on his or her current insulin regiment (treatment)?

_____

Mother's Information

Mother's Health History (circle): DIABETES DEPRESSION LEARNING DELAY/DISABILITY

Mother's use of: alcohol YES NO If yes, how often_____

smoking YES NO If yes, how often_____

drugs YES NO If yes, how often_____

Mother's highest level of education (circle): SOME HIGHSCHOOL

HIGH SCHOOL GRADUATE/GED COLLEGE GRADUATE BEYOND COLLEGE

Parent's relationship status (circle):

MARRIED DIVORCED REMARRIED UNMARRIED SINGLE

Annual household income (circle):

Less than $30,000

$30,001-50,000

$50,001-70,000

$70,001-100,000

above $100,000

Demographic Data Sheet

Family Structure
How many brothers and sisters does your child have? Who lives in the home with your child (mother, father, siblings, grandparents, aunts/uncles, etc)? Have there been any major changes in the household (parental divorce, move, etc.) in the last year?

Center for Epidemiologic Studies Depression Scale – Revised (CESD-R)

Below is a list of the ways you might have felt or behaved. Please check the boxes to tell me how often you have felt this way in the past week or so.	Last Week				Nearly every day for 2 weeks
	Not at all *or* Less than 1 day	1 - 2 days	3 - 4 days	5 - 7 days	
My appetite was poor.	0	1	2	3	4
I could not shake off the blues.	0	1	2	3	4
I had trouble keeping my mind on what I was doing.	0	1	2	3	4
I felt depressed.	0	1	2	3	4
My sleep was restless.	0	1	2	3	4
I felt sad.	0	1	2	3	4
I could not get going.	0	1	2	3	4
Nothing made me happy.	0	1	2	3	4
I felt like a bad person.	0	1	2	3	4
I lost interest in my usual activities.	0	1	2	3	4
I slept much more than usual.	0	1	2	3	4
I felt like I was moving too slowly.	0	1	2	3	4
I felt fidgety.	0	1	2	3	4
I wished I were dead.	0	1	2	3	4
I wanted to hurt myself.	0	1	2	3	4
I was tired all the time.	0	1	2	3	4
I did not like myself.	0	1	2	3	4
I lost a lot of weight without trying to.	0	1	2	3	4
I had a lot of trouble getting to sleep.	0	1	2	3	4
I could not focus on the important things.	0	1	2	3	4

REFERENCE: Eaton, W. W., Smith, C., Ybarra, M., Muntaner, C., Tien, A. (2004). Center for Epidemiologic Studies Depression Scale: review and revision (CESD and CESD-R). In ME Maruish (Ed.). *The Use of Psychological Testing for Treatment Planning and Outcomes Assessment* (3rd Ed.), Volume 3: Instruments for Adults, pp. 363-377. Mahwah, NJ: Lawrence Erlbaum.

Center for Epidemiological Studies Depression Scale for Children (CES-DC)

Number _____

Score _____

INSTRUCTIONS

Below is a list of the ways you might have felt or acted. Please check how *much* you have felt this way during the *past week*.

DURING THE PAST WEEK	Not At All	A Little	Some	A Lot
1. I was bothered by things that usually don't bother me.	____	____	____	____
2. I did not feel like eating, I wasn't very hungry.	____	____	____	____
3. I wasn't able to feel happy, even when my family or friends tried to help me feel better.	____	____	____	____
4. I felt like I was just as good as other kids.	____	____	____	____
5. I felt like I couldn't pay attention to what I was doing.	____	____	____	____

DURING THE PAST WEEK	Not At All	A Little	Some	A Lot
6. I felt down and unhappy.	____	____	____	____
7. I felt like I was too tired to do things.	____	____	____	____
8. I felt like something good was going to happen.	____	____	____	____
9. I felt like things I did before didn't work out right.	____	____	____	____
10. I felt scared.	____	____	____	____

DURING THE PAST WEEK	Not At All	A Little	Some	A Lot
11. I didn't sleep as well as I usually sleep.	____	____	____	____
12. I was happy.	____	____	____	____
13. I was more quiet than usual.	____	____	____	____
14. I felt lonely, like I didn't have any friends.	____	____	____	____
15. I felt like kids I know were not friendly or that they didn't want to be with me.	____	____	____	____

DURING THE PAST WEEK	Not At All	A Little	Some	A Lot
16. I had a good time.	____	____	____	____
17. I felt like crying.	____	____	____	____
18. I felt sad.	____	____	____	____
19. I felt people didn't like me.	____	____	____	____
20. It was hard to get started doing things.	____	____	____	____

Code Number _____

Feel Bad Scale

Instructions: The following is a list of things that some kids say make them feel bad, nervous, or make them worry. For each item, mark an "X" in the box next to the best phrase showing how you would feel *if this happened to you*, or if this has happened to you, how you felt. There is no wrong or right answer.

1.	**Having parents separate**	Not bad ☐	A Little Bad ☐	Pretty Bad ☐	Real Bad ☐	Terrible ☐
2.	**Being pressured to try something new**	Not bad ☐	A Little Bad ☐	Pretty Bad ☐	Real Bad ☐	Terrible ☐
3.	**Having your parents argue in front of you**	Not bad ☐	A Little Bad ☐	Pretty Bad ☐	Real Bad ☐	Terrible ☐
4.	**Not spending enough time with your mom or dad**	Not bad ☐	A Little Bad ☐	Pretty Bad ☐	Real Bad ☐	Terrible ☐
5.	**Feeling sick**	Not bad ☐	A Little Bad ☐	Pretty Bad ☐	Real Bad ☐	Terrible ☐
6.	**Fighting with parents about house rules**	Not bad ☐	A Little Bad ☐	Pretty Bad ☐	Real Bad ☐	Terrible ☐
7.	**Not having homework done on time**	Not bad ☐	A Little Bad ☐	Pretty Bad ☐	Real Bad ☐	Terrible ☐
8.	**Moving from one place to another**	Not bad ☐	A Little Bad ☐	Pretty Bad ☐	Real Bad ☐	Terrible ☐
9.	**Not getting along with your teacher**	Not bad ☐	A Little Bad ☐	Pretty Bad ☐	Real Bad ☐	Terrible ☐
10.	**Being overweight or bigger than others your age**	Not bad ☐	A Little Bad ☐	Pretty Bad ☐	Real Bad ☐	Terrible ☐

Code Number _____

11.	**Changing schools**	Not bad ☐	A Little Bad ☐	Pretty Bad ☐	Real Bad ☐	Terrible ☐
12.	**Not having enough money to spend**	Not bad ☐	A Little Bad ☐	Pretty Bad ☐	Real Bad ☐	Terrible ☐
13.	**Not being able to dress the way you want to**	Not bad ☐	A Little Bad ☐	Pretty Bad ☐	Real Bad ☐	Terrible ☐
14.	**Feeling left out of a group**	Not bad ☐	A Little Bad ☐	Pretty Bad ☐	Real Bad ☐	Terrible ☐
15.	**Having nothing to do**	Not bad ☐	A Little Bad ☐	Pretty Bad ☐	Real Bad ☐	Terrible ☐
16.	**Pressured to get good grades**	Not bad ☐	A Little Bad ☐	Pretty Bad ☐	Real Bad ☐	Terrible ☐
17.	**Not being good enough at sports**	Not bad ☐	A Little Bad ☐	Pretty Bad ☐	Real Bad ☐	Terrible ☐
18.	**Being late for school**	Not bad ☐	A Little Bad ☐	Pretty Bad ☐	Real Bad ☐	Terrible ☐
19.	**Feeling like your body is changing**	Not bad ☐	A Little Bad ☐	Pretty Bad ☐	Real Bad ☐	Terrible ☐
20.	**Being smaller than others your age**	Not bad ☐	A Little Bad ☐	Pretty Bad ☐	Real Bad ☐	Terrible ☐

Code Number _____

Instructions: Now please indicate if any of these things has happened to you in the past year, and if so, how often. There is no wrong or right answer.

1.	**Having parents separate**	Never ☐	Once or Twice ☐	Sometimes ☐	Often ☐	All the time ☐
2.	**Being pressured to try something new**	Never ☐	Once or Twice ☐	Sometimes ☐	Often ☐	All the time ☐
3.	**Having your parents argue in front of you**	Never ☐	Once or Twice ☐	Sometimes ☐	Often ☐	All the time ☐
4.	**Not spending enough time with your mom or dad**	Never ☐	Once or Twice ☐	Sometimes ☐	Often ☐	All the time ☐
5.	**Feeling sick**	Never ☐	Once or Twice ☐	Sometimes ☐	Often ☐	All the time ☐
6.	**Fighting with parents about house rules**	Never ☐	Once or Twice ☐	Sometimes ☐	Often ☐	All the time ☐
7.	**Not having homework done on time**	Never ☐	Once or Twice ☐	Sometimes ☐	Often ☐	All the time ☐
8.	**Moving from one place to another**	Never ☐	Once or Twice ☐	Sometimes ☐	Often ☐	All the time ☐
9.	**Not getting along with your teacher**	Never ☐	Once or Twice ☐	Sometimes ☐	Often ☐	All the time ☐
10.	**Being overweight or bigger than others your age**	Never ☐	Once or Twice ☐	Sometimes ☐	Often ☐	All the time ☐

Code Number _____

11.	**Changing schools**	Never ☐	Once or Twice ☐	Sometimes ☐	Often ☐	All the time ☐
12.	**Not having enough money to spend**	Never ☐	Once or Twice ☐	Sometimes ☐	Often ☐	All the time ☐
13.	**Not being able to dress the way you want to**	Never ☐	Once or Twice ☐	Sometimes ☐	Often ☐	All the time ☐
14.	**Feeling left out of a group**	Never ☐	Once or Twice ☐	Sometimes ☐	Often ☐	All the time ☐
15.	**Having nothing to do**	Never ☐	Once or Twice ☐	Sometimes ☐	Often ☐	All the time ☐
16.	**Pressured to get good grades**	Never ☐	Once or Twice ☐	Sometimes ☐	Often ☐	All the time ☐
17.	**Not being good enough at sports**	Never ☐	Once or Twice ☐	Sometimes ☐	Often ☐	All the time ☐
18.	**Being late for school**	Never ☐	Once or Twice ☐	Sometimes ☐	Often ☐	All the time ☐
19.	**Feeling like your body is changing**	Never ☐	Once or Twice ☐	Sometimes ☐	Often ☐	All the time ☐
20.	**Being smaller than others your age**	Never ☐	Once or Twice ☐	Sometimes ☐	Often ☐	All the time ☐

APPENDIX D

PERMISSIONS TO USE RESEARCH TOOLS

JUDITH SIEGEL
To: Sara Laubinger Davis
Re: Feel Bad Scale- Permission to use in research

June 25, 2015 at 7:45 PM
Inbox - Exchange

JS

Hello Sara,

Feel free to use the Feel Bad Scale in your research. Good luck.

****
Judith M. Siegel, Ph.D., M.S.Hyg.
Professor
Department of Community Health Sciences
UCLA Fielding School of Public Health

See More from Sara Laubinger Davis

Sara Laubinger Davis
To: jmsiegel@ucla.edu
Feel Bad Scale- Permission to use in research

June 24, 2015 at 2:51 PM
Sent - Exchange

SL

Good afternoon Dr. Siegel-

I hope this email finds you well.

My name is Sara Davis and I am a PhD student at the University of Alabama at Birmingham. I am writing you to request permission to use the Feel Bad Scale in my pilot and dissertation study. I am interested in the relationship between child's perceived stress, maternal depressive symptoms, and glycemic control in children with type 1 diabetes. Two of my peers have used the scale successfully in their research and I feel it would work well with my population.

Thank you for your time and consideration.

Respectfully,

Sara Davis

APPENDIX E

IRB APPROVAL

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Institutional Review Board for Human Use

Form 4: IRB Approval Form
Identification and Certification of Research
Projects Involving Human Subjects

UAB's Institutional Review Boards for Human Use (IRBs) have an approved Federalwide Assurance with the Office for Human Research Protections (OHRP). The Assurance number is FWA00005960 and it expires on January 24, 2017. The UAB IRBs are also in compliance with 21 CFR Parts 50 and 56.

Principal Investigator:	DAVIS, SARA LAUBINGER
Co-Investigator(s):	
Protocol Number:	**X150728006**
Protocol Title:	*Effects of Maternal and Child Depressive Symptoms and Perceived Stress on Glycemic Control as Mediated by Cortisol in Prepubertal Children with Type-1 Diabetes*

The IRB reviewed and approved the above named project on 8-24-16. The review was conducted in accordance with UAB's Assurance of Compliance approved by the Department of Health and Human Services. This Project will be subject to Annual continuing review as provided in that Assurance.

This project received EXPEDITED review.

IRB Approval Date: 8-24-16

Date IRB Approval Issued: 8-24-16

IRB Approval No Longer Valid On: 8-24-17

HIPAA Waiver Approved?: N/A

Partial HIPAA Waiver Approved?: Yes

Marion Dobs

Expedited Reviewer
Member - Institutional Review Board
for Human Use (IRB)

Investigators please note:

The IRB approved consent form used in the study must contain the IRB approval date and expiration date.

IRB approval is given for one year unless otherwise noted. For projects subject to annual review research activities may not continue past the one year anniversary of the IRB approval date.

Any modifications in the study methodology, protocol and/or consent form must be submitted for review and approval to the IRB prior to implementation.

Adverse Events and/or unanticipated risks to subjects or others at UAB or other participating institutions must be reported promptly to the IRB.

470 Administration Building
701 20th Street South
205.934.3789
Fax 205.934.1301
irb@uab.edu

The University of
Alabama at Birmingham
Mailing Address:
AB 470
1720 2ND AVE S
BIRMINGHAM AL 35294-0104

irb@southalabama.edu

UNIVERSITY OF SOUTH ALABAMA

TELEPHONE: (251) 460-6308
CSAB 138 · MOBILE, AL. 36688-0002

INSTITUTIONAL REVIEW BOARD
January 19, 2017

Principal Investigator:	Sara Davis, MSN, RN		
IRB # and Title:	IRB PROTOCOL: 15-220 [659969-6] Effects of maternal and child depressive symptoms and perceived stress on glycemic control as mediated by cortisol in prepubertal children with type-1 diabetes		
Status:	APPROVED	Review Type:	Expedited Review
Approval Date:	November 4, 2016	Submission Type:	Amendment/Modification
Initial Approval:	October 30, 2015	Expiration Date:	October 29, 2017
Review Category:	Category: 45 CFR 46.110 (3): Prospective collection of biological specimens for research purposes by noninvasive means.		
DHHS/FDA Subpart D:	45 CFR 46.404: FDA 50.51 - Research not involving greater than MINIMAL RISK to children		

This panel, operating under the authority of the DHHS Office for Human Research and Protection, assurance number FWA 00001602, and IRB Database #00000286, has reviewed the submitted materials for the following:

1. *Protection of the rights and the welfare of human subjects involved.*
2. *The methods used to secure and the appropriateness of informed consent.*
3. *The risk and potential benefits to the subject.*

The regulations require that the investigator not initiate any changes in the research without prior IRB approval, except where necessary to eliminate immediate hazards to the human subjects, and that **all problems involving risks and adverse events be reported to the IRB immediately!**

Subsequent supporting documents that have been approved will be stamped with an IRB approval and expiration date (if applicable) on every page. Copies of the supporting documents must be utilized with the current IRB approval stamp unless consent has been waived.

Notes:

Expedited review and approval for amendment to include a home collection of saliva