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Longitudinal Predictors of Diabetic Ketoacidosis Hospitalizations and Hemoglobin A1c: Examining Adaptation to Type-1 Diabetes in Adolescents

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LONGITUDINAL PREDICTORS OF DIABETIC KETOACIDOSIS HOSPITALIZATIONS AND HEMOGLOBIN A1C: EXAMINING ADAPTATION TO TYPE-1 DIABETES IN ADOLESCENTS

by

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Abstract

Diabetic Ketoacidosis (DKA) and elevated hemoglobin A1c (HbA1c) in youth with type-1 diabetes (T1D) can result in significant morbidity and mortality. Elucidating the risk factors for poor glycemic control and DKA hospitalizations is crucial for the refinement and development of prevention and treatment efforts. Based on a conceptual framework, this study used path analysis to evaluate individual and family characteristics, psychosocial responses, and individual and family responses that prospectively predict number of DKA hospitalizations and HbA1c approximately one year after assessment, accounting for socio-demographics. 174 Youth 12-18 years old with T1D (M = 14.78, SD = 1.65) and their caregivers completed measures assessing demographics, internalizing symptoms, diabetes stress, diabetes-related family conflict, and adherence. Medical records were reviewed to obtain the number of episodes of DKA and the HbA1c closest to 1-year follow-up. Thirty-one participants had at least one episode of DKA based on chart review. Identifying as Black/ African American, a younger age, and higher baseline HbA1c significantly predicted higher HbA1c at follow-up ($p < .05$). For DKA Count, greater duration of diabetes, higher baseline HbA1c, lower income, and identifying as Non-Hispanic White and higher Youth report of internalizing symptoms were significant predictors ($p < 0.05$). Utilizing screeners for internalizing symptoms in endocrinology clinics may be critical for early detection of youth with T1D at risk for DKA.

Table of Contents

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Type 1 Diabetes (T1D) affects 1.25 million individuals (208,000 youth) in the United States and the incidence rate is increasing (Centers for Disease Control and Prevention, 2014; Dabelea et al., 2014). T1D is an autoimmune disorder in which insulin-producing beta cells in the pancreas are destroyed and the pancreas cannot produce sufficient insulin to maintain homeostasis. Thus, patients need to obtain insulin exogenously with either insulin injections (typically 2-4 per day) or an insulin pump to maintain glycemic at levels shown to provide health benefits (average daily glucose ≈ 154 mg/dl or hemoglobin A1c [HbA1c] < 7.5%). Optimal glycemic control or a hemoglobin A1c (HbA1c) < 7.5% significantly reduces risk for future complications, such as retinopathy, neuropathy, and nephropathy (The Diabetes Control and Complications Trial [DCCT], 1993; 1994). An excess of insulin can result in hypoglycemia or low blood sugar; and as such, a range of 6.5 – 7.4% is typically optimal for HbA1c in individuals with T1D. Proper adherence to a complicated medical regimen is especially crucial for youth to decrease risk of macrovascular complications (i.e., coronary artery disease, stroke, and amputations) and microvascular complications (i.e., nephropathy, neuropathy, and retinopathy) in adulthood, and for avoidance of the life-threatening condition of diabetic ketoacidosis (DKA; Donaghue, Chiarelli, Trotta, Allgrove, & Dahl-Jorgensen, 2008; DCCT, 1993; 1995; 2005).

Lack of endogenous insulin, as well as omission and/or suboptimal insulin therapy can result in hyperglycemia (high blood glucose levels) due to decreased ability to utilize glucose, which in turn may lead to DKA (Edge, Ford-Adams, & Dunger, 1999). DKA is a condition that develops from insufficient insulin, which causes the body to breakdown fat and muscle for energy (Wolfsdorf, Glaser, & Sperling, 2006). Consequently, blood acids called ketone bodies

accumulate, resulting in metabolic acidosis. Signs of DKA may include the more common symptoms of untreated T1D, such as vomiting, dehydration, polyuria (frequent urination), and polydipsia (frequent drinking). Kussmaul respirations (hyperventilation or deep gasping breathing) and loss of consciousness may also occur. Approximately 1% of DKA episodes cause cerebral edema (osmotic changes in the brain) and in severe cases coma and death (Glaser et al., 2006).

Despite advancements in diabetes management with the development of continuous glucose monitoring and insulin pumps, rates of DKA remain high both at T1D diagnosis and post diagnosis (Dabelea et al., 2014; Maahs et al., 2015; Wolfsdorf et al., 2009). The rates of DKA at time of T1D diagnosis across five medical centers ranged from 29.1% to 31.1% between 2002 and 2010 among 5,615 youth <19 years of age (Dabelea et al., 2014; Rewers et al., 2008). Post diagnosis, rates of DKA range from 1-10% with risk increasing due to poor glycemic control, insulin omission, and other factors such as lack of access to healthcare (Wolfsdorf et al. 2009). In addition to DKA being life threatening, the estimated annual cost of pediatric DKA admissions in the United States is approximately $90 million (from 2004-2009), with the mean hospital cost of $7,100 per admission (Maahs et al., 2015). In the present study, only post-diagnosis DKA was examined in youth with T1D for at least six months since the typical clinical presentation of T1D at diagnosis can frequently include DKA. Understanding how some youth show diabetes resilience (persistently maintaining optimal glycemic control, no post diagnosis DKA admissions, etc.) and others have poor glycemic control and repeated episodes of DKA, is critical for the enhancement and further development of prevention and intervention programs to promote successful adaptation to T1D (Hilliard, Harris, & Weissberg-Benchell, 2012; Whittemore, Jaser, Guo, & Grey, 2010).

The conceptual framework proposed by Whittemore and colleagues (2010) suggests that successful T1D adaptation is influenced by three broad interacting factors: 1) individual and family characteristics (i.e., socio-demographics), 2) psychosocial responses (i.e., anxiety, depression, stress, etc.), and 3) individual and family responses (i.e., adherence, family conflict, etc.). When integrated with the Hilliard and colleagues (2012) model for diabetes resilience, markers of successful adaptation include optimal glycemic control (HbA1c <7.5% without excessive hypoglycemia), lack of medical hospital admissions for DKA, and adequate to optimal health related quality of life (with the later not discussed due to the focus of the present study on HbA1c and DKA) (Hilliard et al., 2012; Whittemore et al., 2010). Therefore, in the present study by combining the Whittemore and colleagues (2010) model with the Hilliard and colleagues (2012) model, we aim to determine the effects of 1) individual and family characteristics, 2) psychosocial responses, and 3) individual and family responses on diabetes adaptation, which we define as HbA1c and DKA (as reviewed next; Figure 1).

Individual and Family Characteristics

The first set of broad factors that affect risk for maladaptation to T1D (elevated HbA1c and DKA hospitalizations) are *individual and family characteristics*. The characteristics include age, duration of diabetes, sex, socioeconomic status, race/ethnicity, and treatment modality (insulin pumps vs. multiple daily injections). Consistent with the model, the Search for Diabetes in Youth (SEARCH) multi-site study found that in youth <20 years with type 1 diabetes the risk factors for an HbA1c > 9.5% included: older age, longer duration of diabetes, identification as a racial/ethnic minority, a non-two parent household, household income <$25,000, and non-private insurance (Petitti et al., 2009). Lastly, a recent meta-analysis by Benkhadra et al. (2017) showed

that HbA1c was significantly lower in both youth and adults with insulin pumps compared to individuals using only insulin injections ($r = 0.37$; *95% CI*: 0.24 to 0.51).

For DKA, treatment modality and sociodemographics are important individual and family characteristic thought to influence this aspect of T1D adaptation. While insulin pump therapy is associated with decreased HbA1c (Benkhadra et al., 2017), rates of DKA between youth with insulin pumps and individuals using injections did not significantly differ in studies by Plotnick, Clark, Brancati, and Erlinger (2003) and Blackman et al. (2014); however, results have been mixed. Insulin pump use was correlated with more DKA episodes in a population study conducted in Sweden by Hanas, Lindgren, and Lindblad (2009). Similar individual and family characteristics that confer risk for an elevated HbA1c influence rates of DKA. More specifically, the sociodemographics of age (children under 5 and adolescents), minority race/ ethnicity, lack of health insurance, and a lower socioeconomic status have been shown to increase risk for DKA (Dabelea et al., 2014; Wolfsdorf et al., 2009; Cengiz et al., 2013).

Psychosocial Responses

Psychosocial Responses, such as internalizing symptoms and stress, are the second broad category that can adversely affect adaptation to T1D. Depressed mood has been associated with higher HbA1c in youth (Lawrence et al., 2006). A meta-analysis of 14 studies showed that in youth with type 1 diabetes, the pooled prevalence was 30% for symptoms of depression (*95% CI*: 16.33 to 43.74), and up to 32% for symptoms of anxiety (Buchberger et al., 2016). The presence of such symptoms was correlated with poor glycemic control. Previous research has also found that the presence of clinical depression and psychiatric disorders, such as eating disorders, increases the risk for DKA as well (Rewers et al., 2002; cited in Wolfsdorf, Glaser, & Sperling, 2006).

T1D stress may also play a role as increased levels of diabetes-related stress have been linked to glycemic control (Berlin, Hains, Kamody, Kichler, & Davies, 2015), with some variability due to moderating effects of social support and stressor type (Berlin, Rabideau, & Hains, 2012; Hains et al., 2006). For example, Berlin and colleagues (2012) found that diabetes-related stress was positively associated with HbA1c, and particularly so for those with prominent family based diabetes-related stress such as diabetes family conflict. However, the relation between diabetes related stress and DKA has not been widely explored.

Individual and Family Responses

Whittemore and colleagues' third and final broad factor, *individual and family responses*, has been found to contribute to adaptation to T1D. Relevant to the present study, the key variables include adherence and family functioning, such as family conflict. Adhering to treatment through monitoring blood glucoses and following an appropriate insulin regimen are important for glycemic control. A meta-analysis found a moderate sized relation (r = -0.28*, 95% CI*: -0.32 to -0.24) between adherence and glycemic control among youth with T1D such that as adherence increased, HbA1c values decreased (Hood, Peterson, Rohan, & Drotar, 2009). Similar results have been reported in DKA, with regimen adherence (calculated based on insulin dose and insulin prescriptions supplied) inversely related to DKA admissions (r = 0.39) (Morris et al., 1997).

Family functioning (and family conflict in particular) is a critical aspect of *family responses* that has a long history of study and robust prediction of pediatric T1D adaption (Anderson, Miller, Auslander, & Santiago, 1981; Bobrow, AvRuskin & Siller, 1985; Hauser et al., 1990; Miller-Johnson et al., 1994). Family conflict is positively associated with glycemic control in adolescents (Lewin et al., 2006; Rybak et al., 2016; Sander, Odell, & Hood, 2010).

While conflict with parents or caregivers is considered developmentally appropriate during the transition to adolescence, it can significantly complicate diabetes management and adversely affect glycemic control among youth with T1D (Anderson, Ho, Brackett, Finkelstein, & Laffel, 1997). Past research has shown that adherence and glycemic control tend to decline during the adolescent period, which has been associated with greater family conflict. Hilliard, Guilfoyle, Dolan, and Hood (2011) found that diabetes-related family conflict at baseline was associated with less blood glucose monitoring 6 months later, and a higher HbA1c 1 year later. High general family conflict has also been linked to poorer self-care behaviors in youth and a higher HbA1c (Hilliard et al., 2013). Other cross sectional and longitudinal studies have supported the findings by Hilliard, Guilfoyle, Dolan, and Hood (2011) and Hilliard et al. (2013). Diabetes-specific family conflict has been negatively associated with HbA1c and youth report of adherence (Laffel et al., 2003; Williams, Laffel, & Hood, 2009).

There is a relative dearth of research investigating how *family responses* (i.e. family conflict among families with T1D) affect risk for DKA relative to research on glycemic control. One Pre-Diabetes Control and Complications (DCCT) era qualitative case study evaluated 30 youth with recurrent DKA over an 8-year period (White, Kolman, Wexler, Polin, and Winter, 1984). Most patients with recurrent DKA were living in a family environment with high conflict and lack of parenting support with diabetes management. An additional pre-DCCT era study assessed adolescents with DKA and severe hypoglycemia over a period of 8 years and found that baseline family conflict was positively linked to recurrent DKA (Dumont et al. 1994). Yet, episodes of DKA were infrequent with only 28% of the youth having an episode of DKA over the span of 8 years. The DCCT influenced diabetes management in demonstrating that intensive insulin therapy (injections three to four times per day or an insulin pump) was more effective in

decreasing complications compared to conventional therapy (injections one or two times per day) in individuals with T1D (DCCT, 1993). Post-DCCT Standards of Medical Care for type 1 diabetes management is an intensive insulin regimen (American Diabetes Association, 2017). Therefore, more post-DCCT research on the relation between family responses and DKA admissions needs to be conducted since diabetes management has fundamentally changed and treatment specific influences may now have less of an impact on the development of DKA.

The Present Study

Elucidating the risk factors for DKA and suboptimal glycemic control for adolescents with T1D is crucial to decrease morbidity and mortality and reduce the financial cost associated with DKA admissions. Moreover, the identification of specific risk factors for DKA would enable the further development and implementation of effective intervention and screening programs. While multisystematic therapy (MST) has been shown to decrease DKA admissions (Ellis et al., 2008), additional studies leading to alternative and/or more cost-effective interventions are needed. Toward this goal, this study aimed to determine which factors (assessed at baseline) were associated with episodes of DKA over the following year and the HbA1c level closest to one year after baseline among a sample of adolescents with T1D at high risk for poor adaptation (given their age, developmental period, and sociodemographic characteristics).

Consistent with the Whittemore and colleagues (2012) conceptual framework, it was hypothesized that greater internalizing symptoms, increased diabetes related stress, and low levels of adherence would longitudinally predict a higher HbA1c and DKA hospitalizations among a high risk sample of youth with T1D. Moreover, consistent with previous studies examining the family factors associated with high HbA1c levels (Hilliard et al., 2013; Rybak et

al., 2016), it was hypothesized that greater family conflict would prospectively predict a higher HbA1c levels. While family conflict and other risk factors have been studied in relation to HbA1c, few studies have investigated the link between such variables and DKA. In regards to DKA outcomes, it was hypothesized that greater family conflict would also longitudinally predict DKA occurrence. These aforementioned factors are hypothesized to influence adaptation above and beyond the influence of individual and family characteristics (age, gender, race/ethnicity, insulin pump status, and socioeconomic status), which were also included as predictors.

Methods

Participants and Procedures

Data were collected from 174 youth and caregiver dyads from the PRYDE (Predicting Resiliency in Youth with Type 1 Diabetes) study (age: $M = 14.78$, $SD = 1.65$; 47.5% Female; 50% Black/African American; HbA1c: $M = 10.86\%$, $SD = 2.53$; HbA1c time from baseline: ranged from 3 months to 1 year and 2 months ($M = 0.78$ years, $SD = 0.21$ years); median income range = $20,000- $24,999). The PRYDE study is longitudinal and assesses predictors of glycemic control, adherence, and quality of life in youth with T1D. Baseline data were collected (which is analyzed in the present study), as well as data at approximately 6 months and 12 months after the initial study visit. Inclusion criteria for youth and caregiver participation in the study consisted of if they were: English speaking, between 12-18 years old, had T1D for at least 6 months, and were planning to continue to receive care at Le Bonheur for the next year. Youth were excluded if they were pregnant, had a severe developmental disability, legal guardians were unable to provide consent, or if they had cystic fibrosis related diabetes (CFRD), or maturity

onset diabetes of the young (MODY). All caregivers, adult patients, or legally authorized representatives for the youth provided written consent and youth 12-17 provided written assent.

For the present study, baseline data were utilized and participants were excluded for this study if no outcome data (based on clinic visits or hospitalizations) were available in the year after baseline assessment. HbA1c follow-up data was available for 136 youth and DKA count data were available for 150 youth. The Institutional Review Boards at the University of Memphis and the University of Tennessee Health Science Center approved all data collection procedures. Recruitment of participants was conducted at the pediatric endocrinology clinic of Le Bonheur Children's hospital. Youth-caregiver dyads completed questionnaires regarding demographics, regimen adherence, quality of life, social-emotional functioning, and diabetes related stress (youth only). Data were collected over 3 time points: (1) baseline, (2) approximately 6 months post baseline, and (3) approximately 12 months post baseline. Only baseline questionnaire data was used in the present study.

Materials and Measures

Demographics, HbA1c and DKA. Youth and caregivers reported age and sex, and illness duration for youth, and caregivers reported household income. HbA1c levels (which is an average of blood sugars over the previous three months (Sacks et al., 2011) were obtained from medical records at the first clinic appointment (baseline). An additional HbA1c was collected from the clinic visit, hospitalization, or Emergency Room visit closet to one year after baseline. Occurrence of DKA episodes was assessed by retrospective review of medical records. Post diagnosis DKA was identified by either diagnosis of DKA by a physician in the medical note or by using the Diabetes Control and Complications (DCCT) criteria of a bicarbonate (HCO3) < 15 or a venous pH < 7.3. Severity of DKA was classified as mild (venous pH between 7.2 to 7.29,

or bicarbonate between 10-14), moderate (venous pH between 7.10 to 7.19, or bicarbonate between 5-9), or severe (venous pH <7.1, or bicarbonate <5; Figure 2).

Self-Care Inventory- Revised (SCI-R). The SCI-R is a 15-item self-report measuring the perception of youth's adherence to self-care daily T1D specific recommendations, such as blood glucose monitoring, adherence to insulin regimen, diet, and exercise over the previous 1-2 months (Lewin et al., 2009). The revised scale includes questions pertaining to positive self-care related (i.e. "recording blood glucose testing" or "taking the correct dose of insulin") behaviors and negative items (i.e. "skipping meals or "skipping injections) (Helgeson, Siminerio, Escobar, & Becker, 2009); however, only positive items of the SCI-R were assessed. Responses are rated using a 5-point Likert scale from 1: never to 5: always. Higher scores indicate greater self-care behaviors. The internal consistency for the SCI-R is high (α =0.87). Both youths and caregivers were administered the SCI-R. The alphas were good for the present study (Youth SCI-R α = 0.83; Caregiver SCI-R α = 0.87).

Pediatric Symptom Checklist (PSC). The PSC is a 17-item measure assessing psychosocial issues regarding attention, internalizing, and externalizing problems in youth. Responses are using a 3-point Likert scale (0: never, 1: sometimes, or 2: often). Higher scores indicate more psychosocial problems. Scores are summed for a total score with higher total scores denoting significant psychosocial problems (Murphy et al., 1996). This study utilized the internalizing subscale. The PSC-17 has high internal consistency (α = .89; Murphy et al., 2016) and the total score correlates with other validated measures of psychological functioning, such as the Columbia Impairment Scale (r =.74), Children's Global Assessment Scale (r = -.64), and the Child Behavior Checklist Score (r = -60) (Gardner, Lucas, Kolko, & Campo, 2007). Both youth

and caregivers were administered the PSC. The alphas were good for the present study (Youth PSC $\alpha = 0.87$; Caregiver PSC $\alpha = 0.90$).

Diabetes Stress Questionnaire (DSQ). The DSQ is a 65-item, self-report measure of diabetes-specific stressors (Delamater, Patiño-Fernández, Smith, & Bubb, 2012) that was administered to youth only. The DSQ contains statements regarding diabetes stressors related to eight subscales: Distress-Worry, Peer Stress, Averse Interpersonal Effects, Parental Stress, Hyperglycemia, Self-Care Regimen, Diet, and Hypoglycemia. Responses are rated on a 4-point Likert scale from 0 = not at all to 3 = very much). The DSQ shows evidence for excellent internal consistency ($\alpha = .97$; Boardway et al., 1993; $\alpha = 0.96$ for the present study), and criterion validity (using anticipated difficulties with adherence: $r = .40$, $p < .01$; Kamody et al., 2014).

The Diabetes Family Conflict Scale (DFCS). The DFCS is a 19-item measure assessing diabetes-specific family conflict related to T1D management over the past month (Hood, Butler, Anderson, & Laffel, 2007). Responses are rated using a 3-point scale (1: never argue, 2: sometimes argue, 3: always argue). The total scores range from 19 to 57 with higher scores representing more family conflict. The DFCS has good internal consistency for both youth report ($\alpha = 0.81$) and parent report ($\alpha = 0.85$). The alphas were excellent for the present study (Youth DFCS $\alpha = 0.96$; Caregiver DFCS $\alpha = 0.96$). Both youths and caregivers were administered the DFCS.

Data Analyses

The outcome variables included were the count of DKA admissions and HbA1c closest to one year after baseline. Caregiver and youth report of psychosocial measures (DFCS, DSQ, SCI, and PSC), demographics (age, gender, race/ ethnicity, family income), treatment modality (insulin pump vs. no insulin pump), and baseline HbA1c were included as predictor variables to

account for previous glycemic control. Given the individually varying assessment of HbA1c, time since baseline was used as a covariate. SPSS (IBM Statistics for Macintosh, Version 22.0, Armonk NY: IBM Corp) was also used to determine the mean and standard deviation of the age and HbA1c of youth with type 1 diabetes (reported previously). Path analyses were conducted using *Mplus* (Version 7.4, Los Angeles, CA: Muthén & Muthén 1998-2015) to model the relation between predictor variables and outcome variables utilizing full information maximum likelihood estimation with robust standard errors, which take into account missing data and non-normal distributions (Muthén & Muthén, 1998–2015). Of the 174 participants included in the original PRYDE study, 136 had HbA1c data and 150 had DKA data available; however, participants with missing HbA1c, and or DKA data did not differ based on demographic or study related variables such as age, income, illness duration.

Based on prevalence data regarding DKA, it was anticipated that the majority of our sample would not have DKA hospitalizations. Thus, analyses to explore the data distribution (i.e. percent of dyads with zero counts for DKA hospitalizations, dispersion, skewness, kurtosis) were conducted to determine our statistical approach to handling count data (zero-inflated vs. not, poisson vs. negative binominal, etc.) (Karazsia & Van Dulmen, 2008). The Bayesian Information Criterion (BIC) was used to compare and determine the most appropriate statistical model that includes count data (Schwarz, 1978), with preference going to the model with the lowest BIC. BIC differences provide evidence of the strength of one model over another (Weak: negative 0-2, Positive: 2-6, Strong: 6-10, and Very Strong: >10) (Kass & Raftery, 1995).

Results

The study sample consisted of 174 youth (136 youth with HbA1c data and 150 youth with DKA data), 31 of whom experienced at least one episode of DKA in the year following

baseline. Of the patients with DKA, 20 had 1 DKA episode, 5 patients had 2 episodes, 2 patients had 3 episodes, 2 patients had 4 episodes, 1 patient had 5 episodes, and 1 patient had 11 episodes of DKA in the year after the baseline report. Based on DCCT criteria, 43.3% of total DKA episodes were mild, 40% were moderate, and 16.6% of episodes were severe respectively

The Poisson regression model had the lowest BIC (7419.17) compared to the zero-inflated Poisson (BIC: 7453.35), negative binomial (BIC: 7423.00), and zero-inflated negative binomial (BIC: 7478.70), as such it was chosen to be most optimal. Path analyses were conducted to determine significant predictors of HbA1c at 1-year follow-up and count of DKA admissions in the Poisson path model (Table 1; Figure 3). As hypothesized, higher HbA1c at baseline predicted higher HbA1c at follow-up (B = 0.58, $SE\ B$ = 0.06, p = 0.001). Identifying as Black/African American (AA) and a younger age also predicted higher HbA1c at follow-up (race: Black/AA: B = 0.84, $SE\ B$ = 0.33, p = 0.01; age: B = -0.20, $SE\ B$ = 0.08, p = 0.008). No other included variables were significant predictors of HbA1c (see Table 1 for complete HbA1c results).

Within this model, analyses were also conducted to determine significant predictors of DKA count (Table 1; Figure 3). Greater duration of diabetes, lower income, and identifying as White were predictors of greater DKA count (duration of diabetes: B = 0.21, $SE\ B$ = 0.06, p = 0.001; income: B = -0.05, $SE\ B$ = 0.01, p = 0.000; race (Black/AA): B = -1.36, $SE\ B$ = 0.54, p = 0.01). Higher HbA1c baseline predicted greater DKA hospitalization count as well (B = 0.38, $SE\ B$ = 0.10, p = 0.001). Greater youth report of internalizing symptoms on the PSC was a predictor of greater DKA hospitalization count (Youth Report: B = 0.87, $SE\ B$ = 0.36, p = 0.015), however the PSC parent report was not a significant predictor of DKA count (Parent Report: B = 0.56, SE

B = 0.43, *p* = 0.19). No other included variables were significant predictors of DKA count (see Table 1 for complete DKA results.)

Follow-up analyses were conducted to explore if the significant direct relation between internalizing symptoms (PSC Youth Report) and DKA hospitalizations was mediated by adherence (SCI), family conflict (DFCS), or stress (DSQ) as suggested by the guiding model (Table 2). Greater PSC youth report of internalizing symptoms predicted less parent report and youth report of adherence based on the SCI (Parent Report: *B* = -0.17, *SE B* = 0.07, *p* = 0.02; Youth Report: *B* = -0.16, *SE B* = 0.07, *p* = 0.03). Greater PSC youth report of internalizing symptoms also predicted greater diabetes stress based on the DSQ youth report and greater diabetes family conflict based on the DFCS Parent Report (Youth Report DSQ: *B* = 0.42, *SE B* = 0.07, *p* = 0.001; Parent Report DFCS: *B* = 0.20, *SE B* = 0.08, *p* = 0.01). Analyses were conducted to assess DFCS Youth Report, DFCS Parent Report, DSQ Youth Report, SCI Parent, and SCI Youth Report as mediators between PSC Youth Report and DKA Count (Table 2). However, there were no significant indirect effects of PSC Youth Report on DKA Count (see Table 2 for complete results).

Discussion

This study investigated predictors of HbA1c and DKA hospitalization in youth with type 1 diabetes by assessing the impact of three broad factors proposed by Whittemore and colleagues' conceptual framework: 1) individual and family characteristics, 2) psychosocial responses, and 3) individual and family responses. Results of this study confirmed that several individual and family characteristics such as greater duration of diabetes, lower income, identifying as White, and higher HbA1c at baseline predict DKA at 1 year follow-up. Also, younger age, identifying as Black or African American, and higher baseline HbA1c predict

HbA1c at follow-up. For psychosocial responses, greater youth report of internalizing symptoms predicted more DKA hospitalizations at 1 year follow-up.

While higher internalizing symptoms were directly associated with more DKA hospitalizations; this effect was not mediated by diabetes related stress, adherence, and diabetes family conflict. More specifically, youth report of more internalizing symptoms did predict more diabetes family conflict, less adherence, and more diabetes stress; however, diabetes related stress, and the individual and family responses of adherence and diabetes family conflict did not predict HbA1c or DKA count. Interestingly, parent report of internalizing symptoms did not predict DKA count. Several studies have suggested that self-report is the most effective type of questionnaire for detecting internalizing symptoms in youth, since such symptoms may present differently than in adults (Beitchman & Corradini, 1988; De Los Reyes & Kazdin, 2005; Pagano, Cassidy, Little, Murphy, & Jellinek, 2000). Therefore, youth may be better at reporting their internalizing symptoms compared to caregiver report.

The present study found that more internalizing symptoms of anxiety and depression predicted risk for DKA hospitalizations. The current results are consistent with a previous study reporting that more depressive symptoms increased risk for hospitalizations for diabetes related complications in youth with T1D (Stewart, Rao, Emslie, Klein, & White, 2005). However, the study by Stewart et al. (2005) reported a lower prevalence of hospitalizations (11% total compared to 21% total in the present study) over a longer span of time (2 years compared to 1 year in the present study). Furthermore, the present study specifically examined admissions for DKA, while the study by Stewart et al. (2005) investigated diabetes related hospitalizations overall.

Youth report of more internalizing symptoms predicted less adherence. A meta-analysis by DiMatteo, Lepper, and Croghan (2000) of medical treatment adherence suggested three main reasons why depression (a facet of internalizing) may result in poor adherence. Dimatteo et al. (2000) asserts that depression is commonly characterized by hopelessness, which could interfere with patients' positive beliefs about the efficacy of treatment. DiMatteo et al. (2000) also hypothesized that social isolation in depression may adversely affect treatment adherence as well, since social support (specifically family support in youth) has been shown to improve adherence and disease outcomes. Moreover, less social support due to family conflict and lack of family cohesiveness has been linked to DKA hospitalizations (Dumont et al., 1995). Although the present study found that internalizing symptoms internalizing predicted less adherence, adherence did not predict DKA. As such, future studies further assess the effect of adherence as a mediator between internalizing symptoms and DKA hospitalizations since depression (a facet of internalizing symptoms) has been specifically associated with poor treatment adherence in youth with diabetes and other chronic illnesses.

Fewer studies have investigated the relation between anxiety and adherence in youth. In youth following liver or kidney transplant, Wu, Aylward, and Steele (2010) showed that higher state anxiety (emotional arousal) was linked to more medication adherence. However, in youth with type 1 diabetes, more state anxiety symptoms was associated with less adherence (Herzer & Hood, 2010). The discrepancy between the two studies could be explained by the Yerkes-Dodson bell-shaped curve in which moderate levels of state anxiety may be protective and improve adherence, while low and high levels of state anxiety interfere with performance (Herzer & Hood, 2010; Yerkes & Dodson, 1908). Therefore, while this study looked at

internalizing symptoms in general, determining the specific effects of anxiety compared to depression in predicting both adherence and DKA hospitalizations is crucial.

Certain individual and family characteristics were found in the current study that longitudinally predicted DKA count and HbA1c. A lower income, greater duration of diabetes, identification as Non-Hispanic white, and greater HbA1c at baseline all predicted more DKA hospitalizations. For HbA1c at follow-up, a higher baseline HbA1c, younger age, and identification as Black or African American predicted a greater HbA1c. The DKA findings regarding individual and family characteristics are generally consistent with previous studies. Low income and higher HbA1c have been previously shown to predict DKA (Cengiz et al., 2013). The present study found that a longer duration of diabetes increases risk for DKA. The finding is interesting since DKA post diagnosis occurs most frequently from poor glycemic control and insulin omission and youth with longer duration of T1D should be able to avoid DKA through more experience with diabetes management. Although a study by Dabelea et al. (2014) determined that a younger age at diagnosis increased risk for DKA, duration of illness and age of onset are not precisely the same construct. With regard to predictors of elevated HbA1c in the present study, the primary finding was that a younger age predicted a higher HbA1c. Studies by Petitti et al. (2009) and Delamater, Albrecht, Postellon, and Gutai (1991) showed an older age predicted a higher HbA1c. However, the study by Petitti et al. (2009) had a broader age range for inclusion, <20 years. Consistent with previous studies, Black/African American children in the current study were at greater risk for elevated HbA1c compared to non-Hispanic white youth (Borschuk & Everhart, 2015; Delamater, Albrecht, Postellon, & Gutai, 1991; Delamater et al., 1999; Kirk et al., 2006). Yet, white youth had increased risk for DKA hospitalizations compared to Black/African American youth. The specific mechanisms for the

finding remain unclear. Results of studies on DKA and health disparities have been inconsistent. While one study showed that African American youth had greater hospitalizations for DKA compared to white youth (Delamater et al., 1991), another found no differences among African American, White, and Hispanic youth in DKA hospitalizations (Delamater et al., 1999). However, the results of the present study could be driven by a Non-Hispanic White outlier participant with 11 DKA hospitalizations. Moreover, the current study also controlled for income differences, which could have altered the effect of race on the results given that previous studies have reported a wealth and income gap between White and Black families (Oliver & Shapiro, 2006; Shapiro, Meschede, Osoro, 2013).

Even though the present study found that some psychosocial responses and individual and family characteristics predicted HbA1c and DKA counts, individual and family responses were not significant (self and caregiver report of adherence, self and caregiver report of diabetes related family conflict). Previous studies have found that greater adherence is linked to a lower HbA1c and less risk for DKA (Hood et al., 2009; Morris et al., 1997). However, in the present study even though youth report of internalizing symptoms was associated with adherence, the self and caregiver report of adherence was not a predictor of HbA1c or DKA count. Therefore, individuals in the study may be overstating or understating how often they or their child engage in positive self-care related behaviors, such as blood glucose monitoring, adherence to insulin regimen, and eating healthy. Further investigation of the relation between internalizing symptoms, adherence measured by alternative methods such as frequency of self-monitoring blood glucose or blood glucose meter/ insulin pump data downloads, and diabetes outcomes (DKA count/ HbA1c) is necessary to determine if self-report bias is contributing to the results or if the items listed in the Self Care Inventory (SCI) are less relevant to the prevention of DKA.

Therefore, although not observed in the present study, adherence assessed in a more objective way in fact may still be an important mediator between internalizing symptoms and DKA count.

Also in regard to Individual and Family Responses, diabetes related family conflict was not a prospective predictor of elevated HbA1c or DKA hospitalizations in a model controlling for illness duration, treatment modality, income, and other sociodemographic variables. Yet, previous studies have reported that diabetes related conflict is a risk factor for a higher HbA1c (Hilliard et al., 2013; Hilliard, Guilfoyle, Dolan, and Hood, 2011). The discrepancies between the present study and the study by Hilliard et al. (2013) could be partially due to the differences between the study participants. The study by Hilliard et al. (2013) studied predominately white (70%) early adolescents (11-14 years of age) with better glycemic control (M =8.8%, SD = 1.6%), while the present study studied a broader age range (12-18 years of age) and a more diverse sample (50% Black/African American) with worse glycemic control (M =10.86%, SD = 2.53). The present study also found that youth or caregiver report of diabetes family conflict did not predict DKA hospitalization. However, more research needs to be conducted regarding family conflict and DKA, since there is a relative dearth of research about the role of family conflict in DKA.

Despite the novelty of the current investigation in assessing risk factors for DKA as opposed to solely HbA1c, the study had some limitations. The sample size was relatively small (N=174) and only 18% of subjects had DKA. Of the 174 youth in the original sample, 136 subjects had follow-up HbA1c and 150 had outcome data regarding DKA. Therefore, some data were lost to attrition. Also, some youth with T1D could have had DKA hospitalizations, but were treated at another medical facility. Additionally, the present study's finding that Black/ African American youth had lower DKA rates should be confirmed by future studies since the results of

the study may have been driven by an outlier participant. Predicting DKA severity using the bicarbonate level would be ideal, but there were too few subjects in the mild, moderate, and severe DKA categories to conduct an analysis with adequate power. Moreover, the BIC values did not clearly favor two-part (zero-inflated) models which are of substantive interest (predictor those with vs. without DKA, and the rates of DKA for those who had experienced it). Lastly, self-report questionnaires were completed by caregivers and youth, which can be biased.

Future studies should investigate why youth reporting more internalizing symptoms are at increased risk for DKA hospitalizations. Differentiating between the effects of anxiety and depression on diabetes outcomes and DKA will be useful for intervention. For instance, while the effects of anxiety on diabetes outcomes may be more parabolic based on Yerkes Dodson law, the effects of depression may be more linear. Moreover, utilizing more objective reports of variables in the study may explain some of the present study's results. Self-report of adherence and stress can be inherently biased. Also, diabetes related stress could be assessed more objectively by collecting biological markers such as the stress hormone cortisol in saliva or hair since individuals with anxiety, dysphoria, and increased stress reactivity have also shown to have neuroendocrine dysregulation and elevated cortisol (Carrasco & Van de Kar 2003). Comparing self-report measures to more objective measures could also be useful for determining validity and reliability.

In summary, the findings of this study have important clinical significance, suggesting that self report of more internalizing symptoms using the PSC-17 brief screener predicted DKA hospitalizations in youth with T1D. The present study's findings also suggest that youth report may have more utility than caregiver report of internalizing symptoms. Utilizing screeners for internalizing symptoms in endocrinology clinics may be critical for early detection of at risk

youth with T1D. Implementing psychological interventions focused on ameliorating symptoms of depression and anxiety may be important in pediatric endocrinology clinics. Ultimately, such early detection and corresponding intervention could decrease risk for costly DKA hospitalizations that cause significant morbidity and mortality in youth with T1D.

References

Anderson, B. J., Miller, J. P., Auslander, W. F., & Santiago, J. V. (1981). Family characteristics of diabetic adolescents: relationship to metabolic control. *Diabetes Care*, *4*(6), 586-594.

Anderson, B., Ho, J., Brackett, J., Finkelstein, D., & Laffel, L. (1997). Parental involvement in diabetes management tasks: relationships to blood glucose monitoring adherence and metabolic control in young adolescents with insulin-dependent diabetes mellitus. *The Journal of pediatrics*, *130*(2), 257-265. doi: http://dx.doi.org/10.1016/S0022-3476(97)70352-4

American Diabetes Association. (2016). Standards of medical care in diabetes—2016 abridged for primary care providers. *Clinical diabetes: a publication of the American Diabetes Association*, *34*(1), 3.

Berg, C. A., Butler, J. M., Osborn, P., King, G., Palmer, D. L., Butner, J., ... & Swinyard, M. (2008). Role of parental monitoring in understanding the benefits of parental acceptance on adolescent adherence and metabolic control of type 1 diabetes. *Diabetes Care*, *31*(4), 678-683.

Beitchman, J. H., & Corradini, A. (1988). Self-report measures for use with children: A review and comment. *Journal of Clinical Psychology*, *44*(4), 477-490.

Benkhadra, K., Alahdab, F., Tamhane, S. U., McCoy, R. G., Prokop, L. J., & Murad, M. H. (2017). Continuous subcutaneous insulin infusion versus multiple daily injections in individuals with type 1 diabetes: a systematic review and meta-analysis.

Berlin, K. S., Hains, A. A., Kamody, R. C., Kichler, J. C., & Davies, W. H. (2015). Differentiating peer and friend social information-processing effects on stress and

glycemic control among youth with type 1 diabetes. *Journal of pediatric psychology*, *40*(5), 492-499.

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*, jss080.

Blackman, S. M., Raghinaru, D., Adi, S., Simmons, J. H., Ebner-Lyon, L., Chase, H. P., ... & Raman, V. (2014). Insulin pump use in young children in the T1D Exchange clinic registry is associated with lower hemoglobin A1c levels than injection therapy. *Pediatric diabetes*, *15*(8), 564-572.

Boardway, R. H., Delamater, A. M., Tomakowsky, J., & Gutai, J. P. (1993). Stress management training for adolescents with diabetes. *Journal of Pediatric Psychology*, *18*(1), 29-45.

Bobrow, E. S., AvRuskin, T. W., & Siller, J. (1985). Mother-daughter interaction and adherence to diabetes regimens. *Diabetes Care*, *8*(2), 146-151.

Borschuk, A. P., & Everhart, R. S. (2015). Health disparities among youth with type 1 diabetes: A systematic review of the current literature. *Families, Systems, & Health*, *33*(3), 297.

Buchberger, B., Huppertz, H., Krabbe, L., Lux, B., Mattivi, J. T., & Siafarikas, A. (2016). Symptoms of depression and anxiety in youth with type 1 diabetes: A systematic review and meta-analysis. *Psychoneuroendocrinology*, *70*, 70-84.

Carrasco, G. A., & Van de Kar, L. D. (2003). Neuroendocrine pharmacology of stress. *European journal of pharmacology*, *463*(1), 235-272.

Cengiz, E., Xing, D., Wong, J. C., Wolfsdorf, J. I., Haymond, M. W., Rewers, A., ... & Miller, K. M. (2013). Severe hypoglycemia and diabetic ketoacidosis among youth with type 1 diabetes in the T1D Exchange clinic registry. *Pediatric diabetes*, *14*(6), 447-454.

Centers for Disease Control and Prevention. 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; 2014.

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. *Jama*, *311*(17), 1778-1786.

Dabelea, D., Rewers, A., Stafford, J. M., Standiford, D. A., Lawrence, J. M., Saydah, S., ... & Pihoker, C. (2014). Trends in the prevalence of ketoacidosis at diabetes diagnosis: the SEARCH for diabetes in youth study. *Pediatrics*, *133*(4), e938-e945. doi: http://dx.doi.org/10.1542/peds.2013-2795

Delamater, A. M., Albrecht, D. R., Postellon, D. C., & Gutai, J. P. (1991). Racial differences in metabolic control of children and adolescents with type I diabetes mellitus. *Diabetes Care*, *14*(1), 20-25.

Delamater, A. M., Patiño-Fernández, 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*(1), 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*(5), 700-705.

De Los Reyes, A., & Kazdin, A. E. (2005). Informant discrepancies in the assessment of childhood psychopathology: a critical review, theoretical framework, and recommendations for further study. *Psychological bulletin*, *131*(4), 483.

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. *N Engl j Med*, *1993*(329), 977-986. doi: http://dx.doi.org/10.1056/NEJM199309303291401

Diabetes Control and Complications Trial (1994). Effect of intensive diabetes treatment on the development and progression of long-term complications in adolescents with insulin-dependent diabetes mellitus. *The Journal of pediatrics*, *125*(2), 177-188.

Diabetes Control and Complications Trial Research Group. (1995). The relationship of glycemic exposure (HbA1c) to the risk of development and progression of retinopathy in the diabetes control and complications trial. *Diabetes*, *44*(8), 968-983.

Diabetes Control and Complications Trial. (2005). Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *N Engl J Med*, *2005*(353), 2643-2653.

DiMatteo, M. R., Lepper, H. S., & Croghan, T. W. (2000). Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. *Archives of internal medicine*, *160*(14), 2101-2107.

Donaghue, K. C., Chiarelli, F., Trotta, D., Allgrove, J., & Dahl-Jorgensen, K. (2007). Microvascular and macrovascular complications. *Pediatric diabetes*, *8*(3), 163-170.

Dumont, R. H., Jacobson, A. M., Cole, C., Hauser, S. T., Wolfsdorf, J. I., Willett, J. B., ... & Wertlieb, D. (1995). Psychosocial predictors of acute complications of diabetes in youth. *Diabetic Medicine*, *12*(7), 612-618. doi: http://dx.doi.org/10.1111/j.1464-5491.1995.tb00551.x

Edge, J. A., Ford-Adams, M. E., & Dunger, D. B. (1999). Causes of death in children with insulin dependent diabetes. 1990–96. *Archives of disease in childhood*, *81*(4), 318-323. doi: http://dx.doi.org/10.1136/adc.81.4.318

Ellis, D., Naar-King, S., Templin, T., Frey, M., Cunningham, P., Sheidow, A., ... & Idalski, A. (2008). Multisystemic therapy for adolescents with poorly controlled type 1 diabetes. *Diabetes Care*, *31*(9), 1746-1747.

Ellis, D. A., Podolski, C. L., Frey, M., Naar-King, S., Wang, B., & Moltz, K. (2007). The role of parental monitoring in adolescent health outcomes: Impact on regimen adherence in youth with type 1 diabetes. *Journal of Pediatric Psychology*, *32*(8), 907-917.

Gardner, W., Lucas, A., Kolko, D. J., & Campo, J. V. (2007). Comparison of the PSC-17 and alternative mental health screens in an at-risk primary care sample. *Journal of the American Academy of Child & Adolescent Psychiatry*, *46*(5), 611-618.

Glaser, N. S., Wootton-Gorges, S. L., Buonocore, M. H., Marcin, J. P., Rewers, A., Strain, J., ... & Kuppermann, N. (2006). Frequency of sub-clinical cerebral edema in children with diabetic ketoacidosis. *Pediatric diabetes*, *7*(2), 75-80. doi: http://dx.doi.org/10.1111/j.1399-543X.2006.00156.x

Gonder-Frederick, L. A., Cox, D. J., & Ritterband, L. M. (2002). Diabetes and behavioral medicine: the second decade. *Journal of consulting and clinical psychology*, *70*(3), 611.

Gonder-Frederick, L. A., Fisher, C. D., Ritterband, L. M., Cox, D. J., Hou, L., DasGupta, A. A., & Clarke, W. L. (2006). Predictors of fear of hypoglycemia in adolescents with type 1 diabetes and their parents. *Pediatric diabetes*, *7*(4), 215-222.

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.

Hains, A. A., Berlin, K. S., Hobart Davies, W., Smothers, M. K., Sato, A. F., & Alemzadeh, R. (2006). Attributions of adolescents with type 1 diabetes related to performing diabetes care around friends and peers: the moderating role of friend support. *Journal of Pediatric Psychology*, *32*(5), 561-570.

Hanna, K. M., & Decker, C. L. (2010). A concept analysis: assuming responsibility for self-care among adolescents with type 1 diabetes. *Journal for Specialists in Pediatric Nursing*, *15*(2), 99-110.

Hanas, R., Lindgren, F., & Lindblad, B. (2009). A 2-yr national population study of pediatric ketoacidosis in Sweden: predisposing conditions and insulin pump use. *Pediatric diabetes*, *10*(1), 33-37.

Hauser, S. T., Jacobson, A. M., Lavori, P., Wolfsdorf, J. I., Herskowitz, R. D., Milley, J. E., ... & Stein, J. (1990). Adherence among children and adolescents with insulin-dependent diabetes mellitus over a four-year longitudinal follow-up: II. Immediate and long-term linkages with the family milieu. *Journal of Pediatric Psychology*, *15*(4), 527-542.

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.

Herzer, M., & Hood, K. K. (2009). Anxiety symptoms in adolescents with type 1 diabetes: association with blood glucose monitoring and glycemic control. *Journal of pediatric psychology*, *35*(4), 415-425.

Hilliard, M. E., Guilfoyle, S. M., Dolan, L. M., & Hood, K. K. (2011). Prediction of adolescents' glycemic control 1 year after diabetes-specific family conflict: the mediating role of

blood glucose monitoring adherence. *Archives of pediatrics & adolescent medicine*, *165*(7), 624-629. doi: http://dx.doi.org/10.1001/archpediatrics.2011.86

Hilliard, M. E., Harris, M. A., & Weissberg-Benchell, J. (2012). Diabetes resilience: A model of risk and protection in type 1 diabetes. *Current diabetes reports*, *12*(6), 739-748.

Hilliard, M. E., Holmes, C. S., Chen, R., Maher, K., Robinson, E., & Streisand, R. (2013). Disentangling the roles of parental monitoring and family conflict in adolescents' management of type 1 diabetes. *Health Psychology*, *32*(4), 388. doi: http://dx.doi.org/10.1037/a0027811

Hood, K. K., Butler, D. A., Anderson, B. J., & Laffel, L. M. (2007). Updated and revised diabetes family conflict scale. *Diabetes care*, *30*(7), 1764-1769.

Hood, K. K., Peterson, C. M., Rohan, J. M., & Drotar, D. (2009). Association between adherence and glycemic control in pediatric type 1 diabetes: a meta-analysis. *Pediatrics*, *124*(6), e1171-e1179.

Kamody, R. C., Berlin, K. S., Hains, A. A., Kichler, J. C., Davies, W. H., Diaz-Thomas, A. M., & Ferry, R. J. (2014). Assessing measurement invariance of the Diabetes Stress Questionnaire in youth with type 1 diabetes. *Journal of pediatric psychology*, jsu076.

Karazsia, B. T., & Van Dulmen, M. H. (2008). Regression models for count data: Illustrations using longitudinal predictors of childhood injury. *Journal of pediatric psychology*, *33*(10), 1076-1084. doi: http://dx.doi.org/10.1093/jpepsy/jsn055

Kass, R. E., & Raftery, A. E. (1995). Bayes factors. *Journal of the american statistical association*, *90*(430), 773-795.

Kirk, J. K., D'Agostino, R. B., Bell, R. A., Passmore, L. V., Bonds, D. E., Karter, A. J., & Narayan, K. V. (2006). Disparities in HbA1c levels between African-American and non-Hispanic white adults with diabetes. *Diabetes care*, *29*(9), 2130-2136.

Kordonouri, O., Danne, T., Enders, I., & Weber, B. (1998). Does the long-term clinical course of type I diabetes mellitus differ in patients with prepubertal and pubertal onset? Results of the Berlin Retinopathy Study. *European journal of pediatrics*, *157*(3), 202-207.

Laffel, L. M., Connell, A., Vangsness, L., Goebel-Fabbri, A., Mansfield, A., & Anderson, B. J. (2003). General quality of life in youth with type 1 diabetes. *Diabetes care*, *26*(11), 3067-3073.

La Greca, A. M., Auslander, W. F., Greco, P., Spetter, D., Fisher Jr, E. B., & Santiago, J. V. (1995). I get by with a little help from my family and friends: Adolescents' support for diabetes care. *Journal of Pediatric Psychology*, *20*(4), 449-476.

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.

Lewin, A. B., Heidgerken, A. D., Geffken, G. R., Williams, L. B., Storch, E. A., Gelfand, K. M., & Silverstein, J. H. (2006). The relation between family factors and metabolic control: the role of diabetes adherence. *Journal of pediatric psychology*, *31*(2), 174-183.

Lewin, A. B., LaGreca, A. M., Geffken, G. R., Williams, L. B., Duke, D. C., Storch, E. A., & Silverstein, J. H. (2009). Validity and reliability of an adolescent and parent rating scale of type 1 diabetes adherence behaviors: The Self-Care Inventory (SCI). *Journal of pediatric psychology*, *34*(9), 999-1007.

Maahs, D. M., Hermann, J. M., Holman, N., Foster, N. C., Kapellen, T. M., Allgrove, J., ... & Beck, R. W. (2015). Rates of diabetic ketoacidosis: international comparison with 49,859 pediatric patients with type 1 diabetes from England, Wales, the US, Austria, and Germany. *Diabetes Care*, *38*(10), 1876-1882.

Miller-Johnson, S., Emery, R. E., Marvin, R. S., Clarke, W., Lovinger, R., & Martin, M. (1994). Parent-child relationships and the management of insulin-dependent diabetes mellitus. *Journal of consulting and clinical psychology*, *62*(3), 603.

Morris, A. D., Boyle, D. I., McMahon, A. D., Greene, S. A., MacDonald, T. M., Newton, R. W., & DARTS/MEMO Collaboration. (1997). Adherence to insulin treatment, glycaemic control, and ketoacidosis in insulin-dependent diabetes mellitus. *The Lancet*, *350*(9090), 1505-1510.

Muthén, B. O., & BO, M. (1998). Muthén & Muthén. *Los Angeles, CA*, *2012*.

Murphy, J. M., Ichinose, C., Hicks, R. C., Kingdon, D., Crist-Whitzel, J., Jordan, P., ... & Jellinek, M. S. (1996). Utility of the Pediatric Symptom Checklist as a psychosocial screen to meet the federal Early and Periodic Screening, Diagnosis, and Treatment (EPSDT) standards: a pilot study. *The Journal of pediatrics*, *129*(6), 864-869.

Murphy, J. M., Bergmann, P., Chiang, C., Sturner, R., Howard, B., Abel, M. R., & Jellinek, M. (2016). The PSC-17: subscale scores, reliability, and factor structure in a new national sample. *Pediatrics*, e20160038.

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.

Noser, A. E., Huffhines, L., Clements, M. A., & Patton, S. R. (2016). Diabetes conflict outstrips the positive impact of self-efficacy on youth adherence and glycemic control in type 1 diabetes. *Pediatric Diabetes*, doi: http://dx.doi.org/10.1111/pedi.12471

Pagano, M. E., Cassidy, L. J., Little, M., Murphy, J. M., & Jellinek, M. S. (2000). Identifying psychosocial dysfunction in school-age children: The Pediatric Symptom Checklist as a self-report measure. *Psychology in the Schools*, *37*(2), 91.

Petitti, D. B., Klingensmith, G. J., Bell, R. A., Andrews, J. S., Dabelea, D., Imperatore, G., ... & Mayer-Davis, E. (2009). Glycemic control in youth with diabetes: the SEARCH for diabetes in Youth Study. *The Journal of pediatrics*, *155*(5), 668-672.

Plotnick, L. P., Clark, L. M., Brancati, F. L., & Erlinger, T. (2003). Safety and effectiveness of insulin pump therapy in children and adolescents with type 1 diabetes. *Diabetes care*, *26*(4), 1142-1146.

Oliver, M. L., & Shapiro, T. M. (2006). *Black wealth, white wealth: A new perspective on racial inequality*. Taylor & Francis.

Rewers, A., Chase, H. P., Mackenzie, T., Walravens, P., Roback, M., Rewers, M., ... & Klingensmith, G. (2002). Predictors of acute complications in children with type 1 diabetes. *Jama*, *287*(19), 2511-2518.

Rewers, A., Klingensmith, G., Davis, C., Petitti, D. B., Pihoker, C., Rodriguez, B., ... & Dabelea, D. (2008). Presence of diabetic ketoacidosis at diagnosis of diabetes mellitus in youth: the Search for Diabetes in Youth Study. *Pediatrics*, *121*(5), e1258-e1266.

Rybak, T. M., Ali, J. S., Berlin, K. S., Klages, K. L., Banks, G. G., Kamody, R. C., ... & Diaz-Thomas, A. M. (2016). Patterns of Family Functioning and Diabetes-Specific Conflict in Relation to Glycemic Control and Health-Related Quality of Life Among Youth With

Type 1 Diabetes. *Journal of Pediatric Psychology*, jsw071. doi: http://dx.doi.org/10.1093/jpepsy/jsw071

Sacks, D. B., Arnold, M., Bakris, G. L., Bruns, D. E., Horvath, A. R., Kirkman, M. S., ... & Nathan, D. M. (2011). Position statement executive summary: guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. *Diabetes care*, *34*(6), 1419-1423.

Sander, E. P., Odell, S., & Hood, K. K. (2010). Diabetes-specific family conflict and blood glucose monitoring in adolescents with type 1 diabetes: mediational role of diabetes self-efficacy. *Diabetes Spectrum*, *23*(2), 89-94.

Schwarz, G. (1978). Estimating the dimension of a model. *The annals of statistics*, *6*(2), 461-464.

Skinner, T. C., John, M., & Hampson, S. E. (2000). Social support and personal models of diabetes as predictors of self-care and well-being: a longitudinal study of adolescents with diabetes. *Journal of Pediatric psychology*, *25*(4), 257-267.

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

Shapiro, T., Meschede, T., & Osoro, S. (2013). The roots of the widening racial wealth gap: Explaining the black-white economic divide. *Research and policy brief*.

Vries, L., Oren, L., Lazar, L., Lebenthal, Y., Shalitin, S., & Phillip, M. (2013). Factors associated with diabetic ketoacidosis at onset of Type 1 diabetes in children and adolescents. *Diabetic Medicine*, *30*(11), 1360-1366.

White, K., Kolman, M. L., Wexler, P., Polin, G., & Winter, R. J. (1984). Unstable diabetes and unstable families: a psychosocial evaluation of diabetic children with recurrent ketoacidosis. *Pediatrics*, *73*(6), 749-755. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/6427749

Whittemore, R., Jaser, S., Guo, J., & Grey, M. (2010). A conceptual model of childhood adaptation to type 1 diabetes. *Nursing outlook*, *58*(5), 242-251. doi: http://dx.doi.org/10.1016/j.outlook.2010.05.001.

Wiebe, D. J., Chow, C. M., Palmer, D. L., Butner, J., Butler, J. M., Osborn, P., & Berg, C. A. (2014). Developmental processes associated with longitudinal declines in parental responsibility and adherence to type 1 diabetes management across adolescence. *Journal of pediatric psychology*, *39*(5), 532-541. doi: http://dx.doi.org/10.1093/jpepsy/jsu006

Williams, L. B., Laffel, L. M. B., & Hood, K. K. (2009). Diabetes-specific family conflict and psychological distress in paediatric type 1 diabetes. *Diabetic Medicine*, *26*(9), 908-914.

Wolfsdorf, J., Craig, M. E., Daneman, D., Dunger, D., Edge, J., Lee, W., ... & Hanas, R. (2009). Diabetic ketoacidosis in children and adolescents with diabetes. *Pediatric diabetes*, *10*(s12), 118-133.

Wolfsdorf, J., Glaser, N., & Sperling, M. A. (2006). Diabetic ketoacidosis in infants, children, and adolescents. *Diabetes care*, *29*(5), 1150-1159.

Wu, Y. P., Aylward, B. S., & Steele, R. G. (2010). Associations between internalizing symptoms and trajectories of medication adherence among pediatric renal and liver transplant recipients. *Journal of pediatric psychology*, *35*(9), 1016-1027.

Wysocki, T., Taylor, A., Hough, B. S., Linscheid, T. R., Yeates, K. O., & Naglieri, J. A. (1996). Deviation from developmentally appropriate self-care autonomy: association with diabetes outcomes. *Diabetes Care*, *19*(2), 119-125.

Yerkes, R. M., & Dodson, J. D. (1908). The relation of strength of stimulus to rapidity of habit-formation. *Journal of comparative neurology*, *18*(5), 459-482.

Appendix A: Tables and Figures

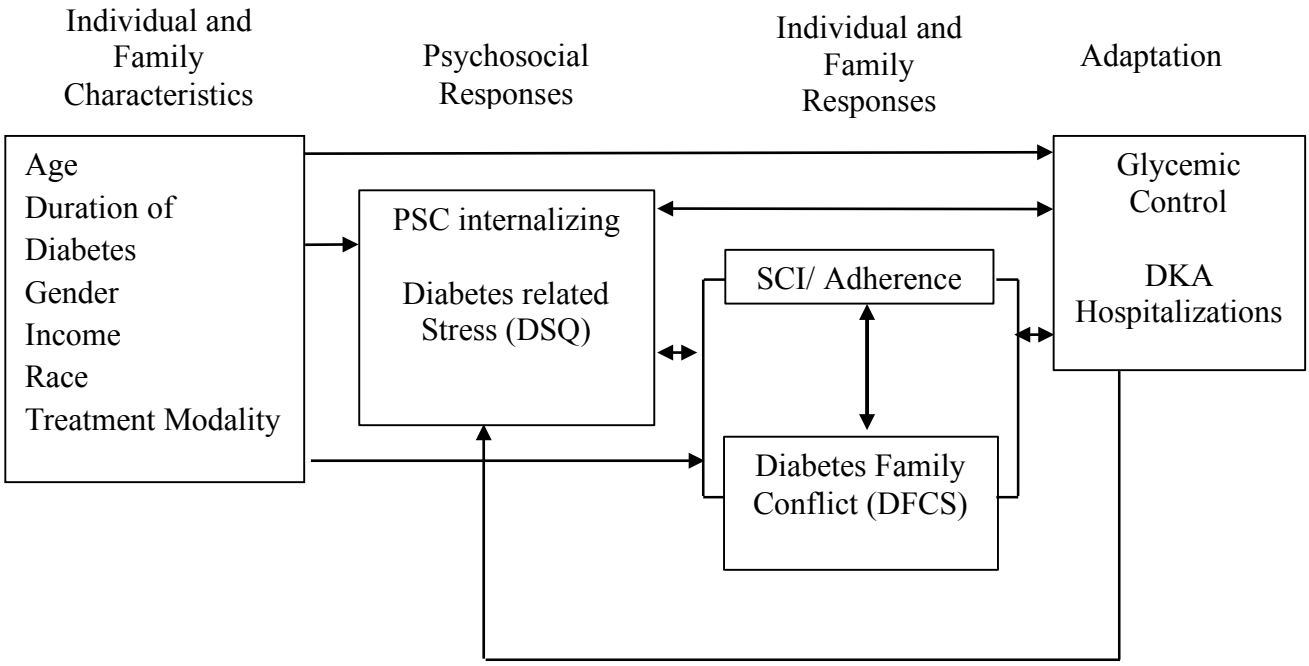

Figure 1. A modified version of Whittemore, Jaser, Guo, & Grey (2010)'s model of adaptation to type 1 diabetes. The model illustrates proposed individual characteristics, psychosocial responses, and individual responses, which may be associated with indicators of adaptation in the present study (DKA hospitalizations and glycemic control).

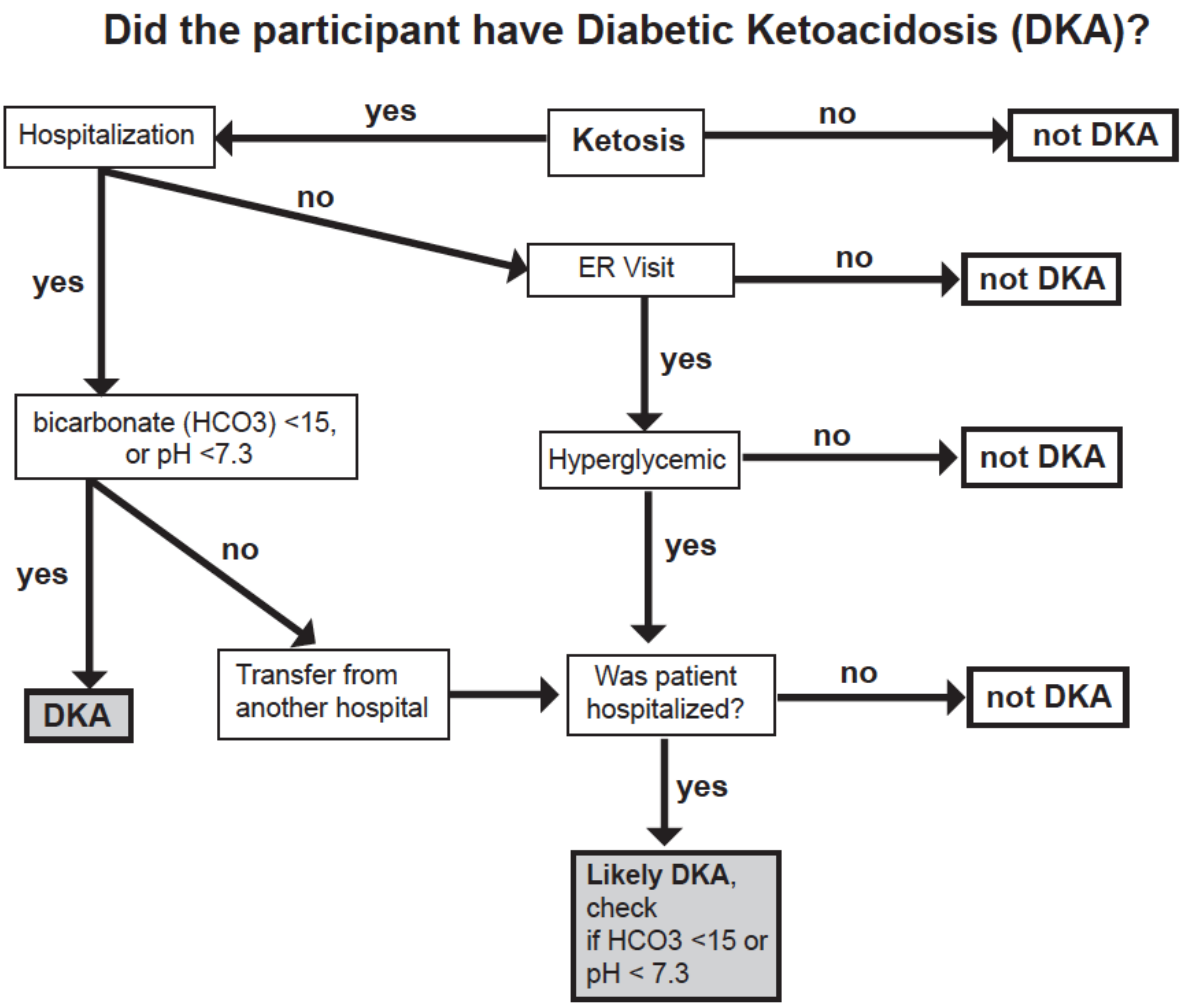

Figure 2. Decision tree used to determine if participants experienced a diabetic ketoacidosis (DKA) hospitalization. DCCT criteria of bicarbonate < 15 and pH < 7.3 or a physician diagnosis of DKA determined the classification.

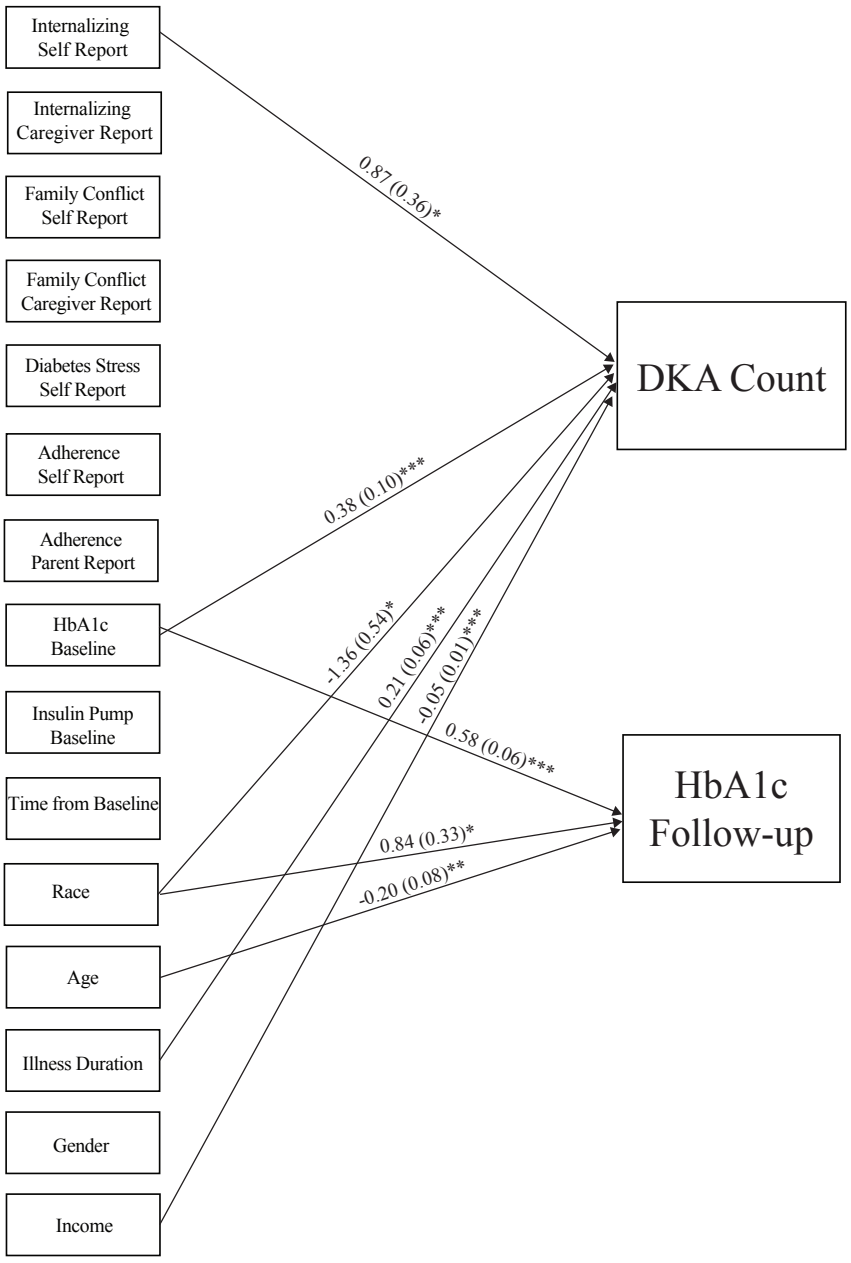

Figure 3. Path analysis model of Poisson regression illustrating the unstandardized estimates and S.E. of significant predictors of DKA count and HbA1c at one year follow-up (*p < .05, **p < .01, ***p < .001).

Table 1.

Summary of Path Analyses Predicting HbA1c and DKA Count at 1 Year Follow-up

Variable	Estimate	S.E.	Est./ S.E.	*p*-value
HbA1c				
Age	-0.2001	0.075	-2.65473	0.008*
Duration of Diabetes	-0.015	0.039	-0.388	0.698
Gender	0.212	0.298	0.711	0.477
Income	-0.002	0.004	-0.451	0.652
Race: Black/AA	0.839	0.327	2.564	0.010*
Baseline Pump	-0.357	0.272	-1.312	0.190
Baseline HbA1c	0.581	0.061	9.506	0.001*
Time from Baseline	-0.060	0.489	-0.123	0.902
PSC Youth Report	0.098	0.233	0.419	0.675
PSC Parent Report	0.050	0.289	0.172	0.864
DSQ Youth Report	0.093	0.256	0.361	0.718
SCI Youth Report	0.043	0.245	0.176	0.860
SCI Parent Report	-0.125	0.207	-0.604	0.546
DFCS Youth Report	0.054	0.228	0.238	0.812
DFCS Parent Report	0.374	0.284	1.315	0.188
DKA Count				
Age	-0.256	0.132	-1.936	0.053
Duration of Diabetes	0.212	0.056	3.781	0.001*
Gender	-0.317	0.421	-0.753	0.452
Income	-0.048	0.014	-3.512	0.001*
Race: Black/AA	-1.355	0.540	-2.509	0.012*
Baseline Pump	0.526	0.415	1.267	0.205
Baseline HbA1c	0.380	0.100	3.804	0.001*
Time from Baseline	0.652	0.819	0.796	0.426
PSC Youth Report	0.872	0.359	2.428	0.015*
PSC Parent Report	0.558	0.427	1.305	0.192
DSQ Youth Report	-0.039	0.397	-0.099	0.921
SCI Youth Report	0.189	0.282	0.670	0.503
SCI Parent Report	-0.126	0.276	-0.455	0.649
DFCS Youth Report	0.121	0.260	0.465	0.642
DFCS Parent Report	0.291	0.341	0.854	0.393

Note. Estimates, S.E., Est./ S.E., and p-values (*p < .05) for Youth and Parent Report of Pediatric Symptoms Checklist (PSC), Diabetes Stress Questionnaire (DSQ) (Youth only), Self-Care Inventory (SCI), Diabetes Family Conflict Scale (DFCS), and youth demographics as predictors of 1 year HbA1c and the number of DKA hospitalizations at 1 year post baseline.

Table 2.

Summary of the direct and indirect effects of Youth Report of Internalizing Symptoms on DKA Count through Family Conflict, Adherence, and Diabetes Stress

	Estimate	S.E.	Est./S.E.	*p*-value
Direct Effects of Internalizing Symptoms				
DFCS Youth Report	0.130	0.083	1.557	0.120
DFCS Parent Report	0.196	0.078	2.505	0.012*
SCI Youth Report	-0.163	0.074	-2.206	0.027*
SCI Parent Report	-0.165	0.069	-2.374	0.018*
DSQ Youth Report	0.424	0.065	6.511	0.001*
DKA Count	0.867	0.361	2.404	0.016*
Direct Effects of Mediators on DKA Count				
DFCS Youth Report	0.020	0.068	0.294	0.769
DFCS Parent Report	0.090	0.079	1.134	0.257
SCI Youth Report	0.066	0.083	0.794	0.427
SCI Parent Report	-0.034	0.088	-0.390	0.697
DSQ Youth Report	-0.017	0.102	-0.170	0.865
Indirect Effects of Internalizing Symptoms on DKA Through Specific Mediators				
DFCS Youth Report	0.011	0.039	0.288	0.774
DFCS Parent Report	0.075	0.074	1.015	0.310
SCI Youth Report	-0.046	0.061	-0.753	0.452
SCI Parent Report	0.024	0.065	0.371	0.711
DSQ Youth Report	-0.031	0.184	-0.171	0.864

Note. Estimates, S.E., Est./ S.E., and p-values for Diabetes Stress Questionnaire (DSQ) (Youth only), Self-Care Inventory (SCI), and Diabetes Family Conflict Scale (DFCS) as mediators of the relation between Youth Report of Pediatric Symptoms Checklist (PSC) and DKA Count.