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Family Environment and Pediatric Sickle Cell Disease: Patterns of Health Care Utilization and Academic Achievement

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FAMILY ENVIRONMENT AND PEDIATRIC SICKLE CELL DISEASE: PATTERNS OF HEALTH CARE UTILIZATION AND ACADEMIC ACHIEVEMENT

by

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Dissertation Approval Sheet

This dissertation was submitted by Joanna Tsikis under the direction of the Chairperson of the Dissertation committee listed below. It was submitted to the College of Psychology and approved in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Clinical Psychology at Nova Southeastern University.

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ABSTRACT

Sickle cell disease (SCD) is the most common group of genetic, chronic hematologic disorders, and is characterized by chronic pain resulting from vaso-occlusive episodes. As such, youth with SCD utilize a disproportionately high amount of health care resources. Youth with frequent health care utilization (HCU) are at increased risk for psychosocial consequences, including disruptions in family functioning and decreased academic performance. While studies have separately examined HCU, family functioning, and academic achievement in this population, there is a dearth of research examining the association between these variables. The present study aimed to: (1) examine associations between family environment and patterns of HCU, (2) examine associations between patterns of HCU and academic achievement scores in math and reading, and (3) evaluate the indirect effect of family environment on academic achievement scores in math, as explained by patterns of HCU. This study included 41 youth with HbSS or HbSβ-thalassemia. Youth were administered the Woodcock-Johnson III Achievement, and caregivers completed the Family Environment Scale. Sociodemographic characteristics were collected, and medical history information was obtained via retrospective medical chart review. Overall, participants reported a more positive family environment, demonstrated less pain-related ED visits and hospital admissions, and obtained below average scores on academic achievement in math and reading. The present study did not provide evidence of associations between family environment, HCU, and academic achievement. Unique characteristics of the study sample, as well as clinical implications and next steps for future research are discussed.

Keywords: sickle cell disease; family environment; health care utilization; academic achievement

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CHAPTER I

Statement of the Problem

Sickle cell disease (SCD) is the most common group of genetic, chronic hematologic disorders, affecting nearly 100,000 people in the United States, primarily those of African descent (Barakat et al., 2007; Boulet, Yanni, Creary, & Olney, 2010; O'Connor et al., 2014). The most frequent symptom encountered by individuals with SCD is pain resulting from vaso-occlusive crises. While acute pain symptoms are largely unpredictable, they appear to be associated with certain triggers, including environmental stressors (e.g., extreme temperatures), physiological stressors (e.g., strenuous exercise, infection, dehydration, fatigue), and psychological stressors (e.g., academic difficulties, peer conflicts, challenging family environment; Benton, Ifeagwu, & Smith-Whitley, 2007; Lemanek & Ranalli, 2009). While most patients are able to manage their pain through outpatient treatment with infrequent hospitalizations (i.e., zero to one per year), a minority of patients account for the majority of emergency department (ED) visits and hospitalizations (Aisiku et al., 2009; Reese & Smith, 1997). This group of patients with frequent medical utilization are also at increased risk for various psychosocial consequences of SCD, including high rates of school/work absenteeism, decreased academic performance, frequent disruptions in family life, and increased dependency on the family system (Edwards et al., 2005; Logan, Radcliffe, & Smith-Whitley, 2002; Reese & Smith, 1997).

Expanding on the aforementioned variables, families play an important role in SCD management and patient outcomes. Despite its importance, there is limited research on family functioning specific to pediatric SCD populations. Additionally, the research

that does exist is several decades old and has mixed findings. Some studies have documented poor family functioning with less organization and more control (Burlew, Evans, & Oler, 1989), while other studies have found that families of youth with SCD are more cohesive and have less conflict (Anderson, Weitzman, & McMahon, 1986; Midence, McManus, Fuggle, & Davies, 1996).

Academic achievement is another important outcome in this population. Youth with SCD are at increased risk for impaired academic achievement impacted by overt or silent stroke, as well as other hypothesized disease-related factors (e.g., brain damage secondary to chronic anemia, hypoxic damage, etc.; Bonner, Schumacher, Gustafson, & Thompson, 1999; Brown et al., 2000). The indirect effects of social and environmental disadvantages, as well as the consequences of high health care utilization (HCU), may contribute to poor cognitive and academic performance (Schatz, Finke, & Roberts, 2004). While some studies have found that high HCU, associated with increased school absences and disease severity, may contribute to poor academic performance (Schwartz, Radcliffe, & Barakat, 2009), there has been little research published on factors other than disease severity and academic achievement.

There is a great need for research in this area. Current research examining HCU, family environment, and academic achievement could provide evidence supporting the importance of family-based interventions in this population. Further, by attending to the relationships among medical, family, and academic consequences of SCD, clinicians will be able to collaborate more productively with families, ultimately assisting these families in making adaptive decisions about SCD-related disease management.

CHAPTER II

Review of the Literature

SCD occurs in one out of every 365 Black or African American births (Centers for Disease Control and Prevention, 2016), and is a group of autosomal recessive hemoglobinopathies characterized by the production of hemoglobin S, anemia, and acute and chronic tissue damage. Hemoglobin S causes red blood cells to become elongated and sickle-shaped, thus blocking blood flow and interfering with the delivery of oxygen to vital tissues, resulting in tissue damage and the varying symptoms and manifestations of SCD (Boulet et al., 2010). SCD is associated with a lifespan shortened by up to 30 years in diagnosed individuals (Platt et al., 1994). However, the lifespan for children with SCD has increased in the past five decades (Quinn, Rogers, & Buchanan, 2004). Advances in the management of SCD have markedly changed the outlook for patients. In particular, ongoing efforts in clinical research and comprehensive care models have increased life expectancy to 50 years (Claster & Vichinsky, 2003).

The variability in severity of SCD-related complications depends on several factors, including the sickle cell genotype, the influence of other genes present, the existence of comorbid illnesses, knowledge of and adherence to prescribed regimens, and psychosocial factors (Brown, Connelly, Rittle, & Clouse, 2006; Lemanek & Ranalli, 2009). The most common and severe genotype, HbSS, is seen in individuals who inherit two sickle beta globin genes. Other genotypes occur with the inheritance of different mutant forms of the beta gene in combination with the sickle beta gene, including HbSC and HbS beta thalassemia (Brown et al., 2006; Lemanek & Ranalli, 2009). HbSS occurs in approximately 65% of patients, followed by HbSC (25%) and HbS beta thalassemia

(10%). Characteristically, patients with HbSS and HbS beta 0-thal are at greater risk for severe complications compared to those with HbSC or HbS beta +-thal. There is some evidence to suggest that severity of anemia is predictive of overall disease severity, particularly among individuals with HbSS (Brown et al., 2006). However, all types of SCD are variable with respect to the frequency and severity of symptoms, and the variability of complications within and between patients with different types of SCD is high (Brown et al., 2006; Midence et al., 1996; Platt et al., 1991). Youth with SCD are at increased risk of suffering from severe conditions, such as chronic hemolytic anemia, splenic dysfunction, stroke, avascular necrosis, chronic lung disease, chronic renal failure, bacterial infections, and recurrent pain crises (Boulet et al., 2010; Midence et al., 1996; Panepinto, Brousseau, Hillery, & Scott, 2005).

Among the most debilitating effects of SCD are neurological complications, which occur in approximately one-third of children with this chronic illness. Strokes in childhood typically result from stenosis and subsequent occlusion of large intracranial arteries, commonly the middle cerebral and intracranial internal carotid arteries. Pathophysiology involves damage to the vessel wall by sickled red blood cells, causing hyperplasia of the vessel's lining. Thrombogenic and inflammatory processes contribute to further vessel thickening, and complete vascular occlusion occurs with resultant ischemia and neurological damage (Day & Chismark, 2006). Cerebral infarction in SCD ranges from overt stroke, with abrupt onset of neurological deficit, to silent infarcts, which are not acutely clinically apparent but are associated with cognitive impairment (Switzer, Hess, Nichols, & Adams, 2006). The Cooperative Study of Sickle Cell Disease has defined infarct as "an acute neurologic syndrome due to vascular occlusion or

hemorrhage in which neurologic symptoms last more than 24 hours" (Ohene-Frempong et al., 1998). Overt stroke, or cerebrovascular accident (CVA), occurs in approximately five to eight percent of children with SCD (Balkaran et al., 1992; Ohene-Frempong et al., 1998), with an estimated 11% of children experiencing an overt stroke prior to the age of 14 years (Moser et al., 1996). A silent infarct is defined as "an area of abnormally increased signal on intermediate or T-2 weighted pulse sequences on brain magnetic resonance imaging (MRI) with no clinical history of a CVA and a normal neurological exam" (Adams, Ohene-Frempong, & Wang, 2001). Research has indicated that as many as 20 to 30 percent of children with SCD evidence silent stroke (Pegelow et al., 2002; Steen et al., 2003), with an estimated 14% showing evidence of silent infarct prior to the age of 14 years (mean age of onset less than six years; Moser et al., 1996). Children with silent infarcts are at higher risk for further ischemia in terms of both overt and covert cerebrovascular events than are children with SCD and a normal MRI (Miller et al., 2001; Pegelow et al., 2002). Specifically, Miller et al. (2001) demonstrated a 14-fold increase in the risk of clinical infarct for children with evidence of silent infarct on MRI.

SCD necessitates lifelong disease management and ongoing utilization of health care resources (Brown et al., 2006). Management of SCD requires strict daily responsibilities, including taking medications, drinking fluids, avoiding extreme changes in temperature, and eating a well-balanced diet. Whereas management of SCD-related complications has largely focused on symptom control, various treatment approaches have been utilized as preventive strategies (Lemanek & Ranalli, 2009). These include early identification of patients via newborn screening, use of prophylactic penicillin to reduce occurrence of bacterial sepsis and death, supportive care, daily administration of

oral hydroxyurea, and bone marrow transplantation. As a result of lifelong disease management, youth with SCD have often been reported to experience lower health-related quality of life (Barakat, Lutz, Nicolaou, & Lash, 2005).

Vaso-occlusive crises (VOCs) are the most common complication in SCD, and occur when there is compromised vascular flow to affected organs (Aisiku et al., 2009; Panepinto et al., 2005). Pain is a predominant, recurring symptom resulting from vaso-occlusion of small blood vessels by sickle-shaped red blood cells, often resulting in acute care visits and hospitalizations. Severity of disease presentation is defined, in part, by the number of hospitalizations for VOCs (Panepinto et al., 2005). Pain in children may begin as early as four to six months of age (Benjamin, 2008), and can continue in an unpredictable manner throughout the individual's life (Platt et al., 1991). Pain commonly caused by vaso-occlusion may be acute (i.e., due to blocked blood flow) or chronic (i.e., due to damage from tissue ischemia and repeated pain episodes), and varies in location, intensity, quality, and temporal pattern (Lemanek & Ranalli, 2009).

Periodic episodes of severe pain resulting from VOCs are the most frequent symptom encountered by individuals with SCD. Specifically, areas of reported pain often include the abdomen, chest, lower back, joints, and extremities (Platt et al., 1991). On average, pain crises persist for four to five days, although prolonged episodes may last for two to three weeks (Stinson & Naser, 2003). While the acute pain symptoms are largely unpredictable, they appear to be associated with certain triggers, including environmental stressors (e.g., extreme temperatures), physiological stressors (e.g., strenuous exercise, infection, dehydration, fatigue), and psychological stressors (e.g., academic difficulties, peer conflicts, challenging family environment; Benton et al., 2007; Lemanek & Ranalli,

2009). While most patients are able to manage their pain through outpatient treatment with infrequent hospitalizations (i.e., zero to one per year), a small percentage of patients account for the majority of ED visits and hospitalizations (Aisiku et al., 2009; Carroll, Haywood, Fagan, & Lanzkron, 2009; Lanzkron, Haywood, Segal, & Dover, 2006; Reese & Smith, 1997; Shankar et al., 2005). This group of patients with frequent medical utilization are also at increased risk for various emotional and psychological consequences of SCD, including increased reports of depression and anxiety, reduced opportunities for physical recreation, fewer social opportunities, high rates of school/work absenteeism, decreased academic performance, frequent disruptions in family life, and increased dependency on the family system (Edwards et al., 2005; Logan et al., 2002; Reese & Smith, 1997).

Health Care Utilization

As previously mentioned, health care utilization (HCU) is a variable of great importance in the SCD population, and is often used to understand the severity of a particular patient's disease (e.g., number of hospitalizations for VOCs; Panepinto et al., 2005). In addition to pain, patients with SCD experience many associated medical problems, including acute chest syndrome, anemia, infections, and stroke. These complications range in severity across patients, but may lead to frequent emergency room visits and hospitalizations (Panepinto et al., 2005). There are a range of possible reasons for frequent hospitalizations or clinic visits, including the need for medications, symptoms such as weakness and dehydration, and wellness checkups (O'Connor et al., 2014); however, pain crises are responsible for the majority of SCD-related medical care contacts (Aisiku et al., 2009; Shankar et al., 2005). Even in countries in which SCD is a

more recent health concern, pain is the most common reason for ED access and inpatient admission. Data obtained from a retrospective study examining medical charts of children with SCD who had accessed the ED in Italy during an eight-year period indicated that 28 pediatric patients with SCD accounted for 185 ED visits during this time frame. At admission, pain was reported in 96/185 episodes (i.e., 52% of total number of admissions; Po' et al., 2013).

Per the literature, SCD accounts for approximately 113,000 hospital admissions annually in the United States. The majority of these admissions are due to VOCs. The average patient with SCD is admitted to the hospital only 1.5 times per year (Brousseau, Owens, Mosso, Panepinto, & Steiner, 2010). However, data obtained from a longitudinal study following patients from birth to 66 years of age indicated that 5.2% of patients with SCD averaged three to ten episodes of pain a year and accounted for 32.9% of the episodes treated in hospitals (Platt et al., 1991). Individuals with SCD are overrepresented among high utilizers of ED visits and inpatient admissions, even when compared to other serious hemoglobinopathies (Carroll et al., 2009; Yusuf, Atrash, Grosse, Parker, & Grant, 2010). Furthermore, significantly higher rates of hospitalization and emergency care have been found in pediatric patients with SCD compared to a non-SCD Black population (Shankar et al., 2005).

A considerable number of ED visits are made annually by patients with SCD. In a study conducted by Yusuf et al. (2010), data were obtained from the National Hospital Ambulatory Care Surveys from 1999 to 2007. Their findings represent a weighted national estimate of approximately 1,776,000 ED visits made by patients with a diagnosis of SCD. The estimated yearly average number of ED visits by patients with any diagnosis

of SCD was 197,333. Approximately 29% of ED visits resulted in hospital admission. Thirty-seven percent of these admissions were among patients under one to 19 years old. In this study, the most commonly cited reason for the ED visit was pain, including chest pain (11%) and other/unspecified pain (67%). For 97% of ED visits with any diagnosis of SCD, the race of the individual was listed as Black/African American. Aisiku et al. (2009) collected daily diary data over a period of six months from 308 adults (age ≥16 years) diagnosed with SCD. Data indicated that 35% of participants were considered "high utilizers" with an estimated three or more ED visits per year. Three or more hospital admissions per year has been correlated with a lower five-year survival rate (Platt et al., 1991), and high ED utilization has been associated with greater reported pain intensity (Aisiku et al., 2009).

The socioeconomic condition of individuals with SCD may be a factor affecting their HCU and access to care. The majority of youth with SCD live in low-income households (Boulet et al., 2010). As a result, these families often face stressors in addition to chronic health concerns, such as limited access to quality preventive care and poorer health outcomes (Evans, 2004). In addition to poor overall health, children from lower-income families have been shown to receive health services marked by less continuity, more unmet needs, and fewer routine medical visits (Larson & Halfon, 2010). Findings from a few studies indicate that low-income children with SCD have higher levels of hospitalization and ED visits compared to low-income children without SCD (Boulet et al., 2010; Raphael et al., 2009). Parents of children with SCD encounter more challenges in accessing health care services than parents of children without SCD, including long waits at doctors' offices and difficulty obtaining appointments when their

child is sick. During VOCs, these prolonged waiting times in outpatient settings may complicate a child's health condition and result in more frequent and longer periods of hospitalization (Boulet et al., 2010).

In addition to socioeconomic status and healthcare access, HCU may be affected by age. Analyses of data obtained from the Healthcare Cost and Utilization Project Kids' Inpatient Database indicated that older children diagnosed with SCD had more hospitalizations and longer admissions for VOC compared to younger children. Specifically, mean length of stay in this sample was 3.5 days for children zero to four years of age, while mean length of stay was 5.4 days for those youth 15 to 18 years of age (Panepinto et al., 2005). Studies have demonstrated that older individuals with SCD have more frequent VOCs and disease complications, likely resulting in different patterns of HCU than those of younger individuals (Platt et al., 1991; Sanders, Labott, Molokie, Shelby, & Desimone, 2010). Additionally, these findings may reveal that young adults encounter more barriers when seeking outpatient care, thereby coping with their medical issues in the ED (Sanders et al., 2010).

Although disease severity fails to account for very much of the variance in HCU (Reese & Smith, 1997), frequent ED utilization has been associated with higher clinical severity of the disease, as evidenced by low hematocrit values and need for transfusion treatment (Aisiku et al., 2009). Research has found that youth with HbSS, considered the most severe form of SCD, had significantly higher HCU than their peers with HbSC and HbS beta thalassemia (Barakat et al., 2007; Logan et al., 2002). Additionally, high HCU has been strongly associated with more frequent diagnoses of infections and SCD-related complications (Carroll et al., 2009).

Frequent visits to the ED, hematology acute care unit, or other urgent care centers for pain management, as well as frequent or long hospital stays, are often considered undesirable HCU patterns by providers. Attendance at scheduled clinic appointments for routine care and management of less critical pain symptoms at home are usually viewed as markers of adaptive HCU (Logan et al., 2002). In fact, these may be inversely related, as routine medical care has been associated with reduced inpatient hospitalizations and ED visits (Raphael et al., 2009). In a study assessing ED visits, clinic visits, and hospital admissions among patients with SCD, the authors reported that after proactive efforts (e.g., early intervention with oral and intravenous (IV) pain medication in triage, treatment with intramuscular or subcutaneous pain medication in patients lacking IV access, elimination of meperidine due to increased risk of dependency, administration of outpatient oral medications, and referral for follow-up in clinic after discharge) to improve outcomes, the number of ED visits decreased and clinic utilization increased (Givens, Rutherford, Joshi, & Delaney, 2007). There are many situations in which it would be strongly indicated for SCD patients to seek treatment; therefore, it is not a desirable goal to generally discourage utilization of emergency services. Instead, clinicians should be encouraged to promote more effective utilization of available preventive services (Reese & Smith, 1997).

As previously stated, patients with frequent HCU are at increased risk for psychosocial consequences of SCD. Recurrent SCD-related pain has been associated with frequent and costly health care contacts (e.g., high HCU) and also shown to result in frequent school/work absences, social isolation, poor quality of life, depression and other emotional difficulties (Brown et al., 1993; Midence & Elander, 1994). Of developmental

concern for youth with SCD, frequent hospitalizations for pain interfere with family and peer relationships, acquisition of social skills, and educational achievement (Howard, Thomas, Rawle, Cartwright, & Westerdale, 2008). Although limited research on the psychosocial sequelae of frequent HCU exists, the extant literature, which primarily utilizes small samples and qualitative research designs, suggests that prolonged hospitalizations and absences are barriers to education, ultimately interfering with the development of both academic and social skills (Weisberg, Balf-Soran, Becker, Brown, & Sledge, 2013). In addition to the aforementioned variables, families also play an important role in SCD management and patient outcomes.

Family Functioning

When a child is diagnosed with a chronic medical condition, individuals within the family, their relationships with one another, and the way in which the family functions are affected. Similarly, the family has an important impact on the child's chronic illness (Alderfer & Kazak, 2006). Family functioning refers to the social and structural properties of the global family environment. It includes relationships and interactions within the family, specifically levels of conflict, cohesion, organization, adaptability, and quality of communication (Lewandowski, Palermo, Stinson, Handley, & Chambers, 2010). Healthy and adaptive family functioning occurs within a family environment with clear communication, well-defined roles, strong cohesion, and good emotion regulation. In contrast, poor and generally maladaptive family functioning occurs within families with high levels of conflict, disorganization, and poor emotional and behavioral control (Alderfer et al., 2008). Throughout the literature, family functioning and environment have been measured in various ways. However, the Family

Environment Scale (FES; Moos & Moos, 1981) has been the most widely used measure in the literature on pediatric SCD.

The FES is a 90-item self-report measure designed to assess the social and environmental characteristics of family functioning, particularly interpersonal relationships, personal growth, and family structure/organization. This measure is based on a three-dimensional conceptualization with ten subscales, including (1) Relationship (Cohesion, Expressiveness, Conflict subscales), (2) Personal Growth (Independence, Achievement Orientation, Intellectual-Cultural Orientation, Active-Recreational Orientation, Moral-Religious Emphasis subscales), and (3) System Maintenance (Organization, Control subscales; Moos & Moos, 1981). In a review of family functioning measures used in child health research, the FES was classified as "approaching well-established" in terms of the level of evidence for its reliability and validity (Alderfer et al., 2008). In addition, the Family Relationship Index (FRI; Holahan & Moos, 1982), a subset of scales from the FES comprised of the relationship subscales (Cohesion, Expressiveness, Conflict), was rated as "well-established" (Alderfer et al., 2008). Other measures, such as the Family Assessment Device (FAD; Epstein, Baldwin, & Bishop, 1983; e.g., Barakat et al., 2005) and the Family Adaptability and Cohesion Evaluation Scale (FACES; Olson, Sprenkle, & Russell, 1979; e.g., Brown & Lambert, 1999) have also been used to measure family functioning in the SCD literature, but less widely.

As previously mentioned, family functioning is a multidimensional construct. A subset of variables has been the primary focus of existing literature in pediatric chronic illness and SCD specifically. These include cohesion, expressiveness, organization,

conflict, and control. Cohesion is described as the extent to which family members are concerned and committed to the family, and the degree to which they are helpful and supportive of each other. Expressiveness is the extent to which family members are allowed and encouraged to act openly and to express their feelings directly. Organization is the extent to which order and organization are important in the family in terms of structuring family activities, financial planning, and the explicitness and clarity of rules and responsibilities. Conflict is described as the extent to which the open expression of anger, aggression, and generally conflictual interactions are characteristic of the family. Finally, control is the extent to which the family is organized in a hierarchical manner, the rigidity of rules and procedures, and the extent to which family members "order each other around" (Moos & Moos, 1976, 1981).

Family functioning in pediatric chronic illness and chronic pain. Several outcomes associated with family functioning and environment have been explored in the pediatric chronic illness literature. Prior research has documented less cohesion and/or poorer communication in families of children with a chronic illness (Engstrom, 1999; Janicke, Mitchell, & Stark, 2005; Rodenburg, Meijer, Deković, & Aldenkamp, 2005). Herzer and colleagues (2010) found that approximately 28% of families of children with chronic medical conditions reported poor communication; 36% of these families also reported poor affective involvement (i.e., the degree to which family members are involved in and interested with each other). However, some studies have found no differences regarding the family functioning of youth with chronic illness when compared to their healthy peers (Ievers & Drotar, 1996; Mackner & Crandall, 2006; Rodenburg et al., 2005).

Findings regarding the family environment of youth with chronic pain conditions has also been mixed. For example, adolescents diagnosed with fibromyalgia were found to have poorer overall family environments compared to a healthy control group. Specifically, adolescents with fibromyalgia reported higher levels of conflict, less cohesion, and less organizational structure (Kashikar-Zuck et al., 2008). However, in another study of adolescents with fibromyalgia, both parents and youth reported significantly less conflict than normative samples of parents of both healthy and distressed adolescents. In fact, parents and youth with fibromyalgia endorsed greater cohesion, intellectual-cultural orientation, and moral-religious emphasis than a normative sample of distressed families (Schanberg, Keefe, Lefebvre, Kredich, & Gil, 1998). Additionally, in a few studies comparing family functioning in youth with chronic pain conditions (e.g., recurrent abdominal pain) versus healthy participants, findings do not indicate significant group differences (e.g., cohesion, adaptability; Kaufman et al., 1997; Reid, Lang, & McGrath, 1997).

Family functioning in pediatric SCD. There is limited research on family functioning specific to SCD populations, and much of it was conducted over two decades ago. The extant literature suggests that having a family member with SCD creates stress, which affects the entire family as a system (Evans, Burlew, & Oler, 1988). SCD is thought to affect the well-being of the primary caregiver, alter interpersonal relationships within the family, and change the dynamics of the family environment (Burlew et al., 1989). Similar to the chronic illness literature in general, research on family functioning in pediatric SCD has produced variable results. Over two decades ago, Burlew et al. (1989) documented poor family functioning in youth with SCD. In this study, parents of

children with SCD reported more conflict in the home than the normative comparison group. These parents also reported less organization within the family, and a greater emphasis on control in the home, indicating that parents of youth with SCD may cope with the increased demands or stress placed upon the family by establishing inflexible rules and set ways of doing things. Alternatively, previous research conducted by Anderson et al. (1986) found that families of youth with SCD scored higher on measures of family integration, cooperation, optimism and psychological stability within the family. In addition, Midence and colleagues (1996) found that family relationships in pediatric SCD were marked by increased cohesion and reduced conflict. Finally, some research findings have shown that primary caregivers of youth with SCD did not report any significant differences in family conflict compared to caregivers of healthy youth (Noll et al., 1994).

Research has linked SCD to adjustment difficulties including decreased coping, increased behavior problems, and symptoms of depression and anxiety (Burlew et al., 1989; McClellan & Cohen, 2007; Thompson et al., 1999). Poor adjustment in youth with SCD (e.g., more depressive symptoms, externalizing symptoms) has been linked to poor baseline family functioning, specifically high levels of family conflict, low levels of support, and low levels of cohesion (Brown et al., 1993; Thompson et al., 1999; Thompson et al., 2003). Family functioning has been demonstrated to play a vital role in adjustment to SCD (Burlew et al., 1989; McClellan & Cohen, 2007; Thompson et al., 1999). Cohesive and supportive family environments are related to several dimensions of adaptive functioning (e.g., less symptoms of anxiety and depression, greater self-esteem, effective coping; Billings & Moos, 1982; Burlew, Telfair, Colangelo, & Wright, 2000),

and family functioning characterized by low conflict, high support, moderate organization, and moderate control positively impacts the adjustment of youth with SCD (Barakat et al., 2007; Barbarin, Whitten, Bond, & Conner-Warren, 1999; Thompson et al., 1999).

Improved coping with disease management and complications may be one way in which family functioning results in better adjustment for youth with SCD. Coping with SCD involves confronting many medical, social, interpersonal, and psychological stressors. Research suggests that family factors impact how a child responds to their illness. Particularly, the more psychosocial stressors there are within the family, the less effectively the child copes with having SCD. In contrast, the more social support available to the child from the family, the more likely the child will adjust well to their illness (e.g., comply with their prescribed treatment regimen; Burlew et al., 1989; Wonkam et al., 2014). Further, families characterized by high levels of cohesion may convey a sense of available support to a child and do a better job of meeting the child's needs than families characterized by high levels of disengagement (Kliewer & Lewis, 1995). Families also influence how children interpret stressful events. In a study examining SCD-related coping, children who coped better were those who rejected the sick role and tried to live their lives as fully as possible. It was hypothesized that these children adopted this stance via family influence and early socialization around the illness (Barbarin et al., 1999). Research conducted by Mitchell and colleagues (2007) revealed a positive relationship between patient coping and family functioning. Specifically, higher rates of active coping (e.g., talking with someone, going on despite pain) and passive adherence (e.g., resting, taking medications) were related to better family problem

solving, communication, and overall functioning. Despite mixed findings as to whether family functioning is impaired in SCD compared to families of healthy youth, the existing literature indicates that family functioning plays an important role in youth's adjustment to SCD.

Academic Achievement

Several factors associated with decreased academic performance and low levels of academic achievement have been explored in the pediatric SCD literature. The psychosocial factors previously discussed, including frequent HCU and increased family stress, may operate individually or jointly to affect academic functioning in youth with SCD.

Academic achievement in youth with overt or silent infarcts. Although most children with SCD will not experience a stroke, those who do are at risk for academic difficulties associated with neuropsychological deficits (Bonner et al., 1999). In a sample of youth with SCD, Armstrong et al. (1996) observed significantly lower scores on measures of mathematics and reading in children with clinical infarct compared to those with silent infarct. However, Wang et al. (2001) did not find differences between these two groups. Specifically, in this sample, children with evidence of silent infarct performed significantly worse on neuropsychological testing than their school-age counterparts with normal neuroimaging, but comparably to children with a history of overt stroke. Further, children were compared by age group (i.e., ages 6 to 8, 8 to 10, 10 to 12). Children with silent infarct scored nine to ten points lower than children without infarct in each age group on the Broad Reading and Broad Mathematics clusters of the

Woodcock-Johnson Psychoeducational Test Battery, Revised (WJ-R; Woodcock & Johnson, 1990).

Schatz, Brown, Pascual, Hsu, and DeBaun (2001) compared children with SCD with silent infarct, without infarct, and healthy siblings on measures of academic achievement. In this study, age-adjusted scores were computed for the Broad Reading and Broad Mathematics skill clusters of the WJ-R. Impairments in academic achievement were defined as performing ≥1.5 standard deviations below age expectation on either cluster. Impaired academic achievement scores were observed in 37% of children with silent infarct, 27% of children without infarct, and 6% of healthy siblings. In a study by Nabors and Freymuth (2002), 12 children with HbSS and prior history of stroke, 14 children with HbSS without evidence of stroke, and 13 similar-aged siblings were compared on a measure of academic achievement, the Wide Range Achievement Test-Revised (WRAT-R; Jastak & Jastak, 1978). Children with SCD and history of stroke scored significantly lower on the Spelling and Arithmetic subtests of the WRAT-R when compared to healthy siblings. Additionally, children with SCD and no history of stroke demonstrated intermediate achievement scores on all subtests of the WRAT-R.

In contrast to the aforementioned studies evidencing deficits in academic achievement in children with SCD, some studies have not found an association between neuroimaging results and academic achievement, likely due to limitations of small sample sizes. Results of a study conducted by Brown et al. (2000) did not provide evidence for statistically significant deficits in academic achievement, as measured by the WJ-R, although children with clinical history of CVA performed more poorly than children with silent infarct or those without central nervous system (CNS) pathology.

Similarly, in another study examining predictors of academic achievement in youth with SCD, participants scored within the average range compared to same-age peers on the Woodcock-Johnson III Tests of Achievement (WJ-III Achievement; Woodcock, McGrew, & Mather, 2001) subtests measuring Broad Reading (*M* = 93.28, *SD* = 15.21) and Math Calculation (*M* = 92.40, *SD* = 13.78). Stroke status did not emerge as a significant predictor of academic achievement in this sample (Smith, Patterson, Szabo, Tarazi, & Barakat, 2013). In addition, in a study by Grueneich et al. (2004), the WRAT-R was administered to youth with SCD with no known history of clinical neurological events; however, after recruitment, it was discovered that many of the children evidenced MRI abnormalities, likely representative of silent infarct. Comparisons of the performance of children with more severe genotypes (HbSS and HbS beta 0-thal) with that of children with less severe genotypes (HbSC and HbS beta +-thal) were not statistically significant in any domain of academic achievement (i.e., reading, arithmetic, spelling).

Academic achievement in youth without known neurological disease.

Cognitive deficits have also been reported in children with SCD who have no evidence of overt or silent cerebral infarcts. In children without clinical history of stroke, several factors related to the pathophysiology of cognitive impairment have been hypothesized, including recurrent micro-infarctions of the CNS, brain damage secondary to chronic anemia, hypoxic damage exacerbated by acute events, and chronic nutritional deficiency associated with increased metabolic demands (Brown et al., 2000). In a study by Fowler et al. (1988), children with SCD were compared to a healthy control group, and were found to score lower on individually administered tests of reading and spelling

achievement and on group administered standardized achievement tests. Within the SCD sample, higher scores on the achievement tests were associated with higher maternal education, younger age, and female gender. Similarly, another study compared a sample of youth with SCD with no evidence of overt clinical stroke to their classmates without chronic illnesses matched on gender, race, and age. Children with SCD obtained significantly lower scores on the WRAT-R arithmetic domain, but differences were not significant for the WRAT-R reading and spelling domains (Noll et al., 2001).

Across a variety of studies, similar deficits in the academic achievement of youth with SCD were found despite utilization of different achievement measures. In a study utilizing the Reading and Mathematics subtests of the WJ-R in a sample of youth diagnosed with SCD and their healthy siblings, academic achievement was significantly lower in the HbSS group (Reading cluster, M = 81.52, SD = 12.29; Mathematics cluster, M = 78.43, SD = 11.03) than in the sibling control group (Reading cluster, M = 91.76, SD = 14.78; Mathematics cluster, M = 92.57, SD = 7.81; Swift et al., 1989). Similarly, in a sample of youth with SCD and no known neurological dysfunction, youth with SCD scored lower on mathematics achievement as measured by the WRAT when compared to their healthy siblings (Wasserman, Wilimas, Fairclough, Mulhern, & Wang, 1991). Brown et al. (1993) also compared children with SCD to their healthy siblings on the Arithmetic and Reading Decoding subtests of the Kaufman Assessment Battery for Children (K-ABC; Kaufman & Kaufman, 1983). Results indicated a significant difference between groups in achievement scores on the reading decoding subtest, such that youth with SCD performed more poorly than their healthy siblings. The aforementioned studies all utilize a healthy sibling control group for comparison, which

likely indicates that many factors associated with the family system (e.g., socioeconomic status, maternal education, race/ethnicity) are controlled for.

Similar results have also been obtained on state standardized tests compared to tests often used clinically (e.g., WJ-R, WRAT) described above. In a study conducted by Nettles (1994), a sample of youth diagnosed with SCD (HbSS or HbSC) was compared to a healthy sample of youth matched only by age and race. Reading percentile scores on state achievement tests indicated that the healthy children's scores fell within the 68th percentile, and both the HbSS and HbSC children's scores were within the 26th percentile (below average). Additionally, math scores for both the HbSS and HbSC children fell within the 36th percentile (below average performance). As such, academic achievement for youth with SCD was found to be far below their matched comparison group and below the national average.

Academic achievement and school absenteeism. In addition to the direct impact of SCD on the brain, frequent school absences due to SCD-related complications (e.g., pain crises, ED visits, hospitalizations) may also contribute to poor academic achievement (Herron, Bacak, King, & DeBaun, 2003; Thomas & Taylor, 2002). Research has consistently reported higher school absenteeism among children with SCD. Youth with SCD have been found to miss an average of 20 to 40 school days in one year (Peterson, Palermo, Swift, Beebe, & Drotar, 2005; Schwartz et al., 2009; Shapiro et al., 1995) and to have worse school attendance than their healthy siblings (Ogunfowora, Olanrewaju, & Akenzua, 2005) and controls (Ezenwosu, Emodi, Ikefuna, Chukwu, & Osuorah, 2013; Fowler, Johnson, & Atkinson, 1985; Nettles, 1994). In a study conducted by Nettles (1994), children with SCD experienced excessive absenteeism. Children with

HbSS missed an average of 30 days per year, while those with HbSC missed approximately 20 days per year. As previously mentioned, both groups of youth with SCD obtained reading and mathematics achievement scores that fell within the 26th to 36th percentile, respectively.

Ogunfowora et al. (2005) completed a comparative study of academic performance of children with SCD (without evidence of CVA) and their siblings in Nigeria. The number of school days absent for the SCD group ranged from zero to 32 (M = 9.3, SD = 5.5), while the sibling group ranged from zero to 12 (M = 4.1, SD = 2.9), with the difference between the two means being statistically significant. Academic performance was measured by sessional aggregate score, or the total sum of scores in all subjects offered during the school year. Mean sessional aggregate scores for the SCD group were 62.6 (SD = 15.3), and 64.8 (SD = 14.1) for the sibling group, with no significant difference found between the two groups. Finally, despite the significantly high absence rates reported in the SCD group, no significant correlation was found between school absence and academic performance. Although children in the SCD group were selected based on no evidence of CVA, the authors speculated that the disease itself may have a more direct impact on the intellectual abilities of some children through an undetermined mechanism.

In another study performed with 90 school-aged children with SCD and 90 healthy controls in Nigeria, both school absenteeism and academic achievement were also examined (Ezenwosu et al., 2013). Youth with SCD were absent, on average, 15.85 (SD = 12.30) days, which was significantly higher than the 7.71 (SD = 8.22) days absent for the control group. Per school examination report, the mean of overall academic scores

was 62.71 (*SD* = 19.43) for youth with SCD and 67.47 (*SD* = 16.42) for the control group, both falling within the average range. Additionally, this difference between groups was not statistically significant. However, 32% of youth with SCD and 17% of controls scored in the low (score <50) performance range, with a statistically significant difference. Further, in the SCD group, approximately 62% of the low academic scorers had high rates of absenteeism (>12 days absent), although this association was not statistically significant (Ezenwosu et al., 2013).

Family Functioning and Health Care Utilization

Family factors are posited to affect the coping processes and adjustment outcomes of youth with SCD, yet relatively little is known about the contributions of family factors to HCU in this population. To date, few research studies have focused on the effects of family environment on children's use of health care services. As patterns of health care use are established early in life, and since youth rarely initiate their own health care, investigations of family functioning may help us understand patterns of pediatric HCU.

In the literature, family influences have been associated with HCU in few studies. In a classic study by Weimer, Hatcher, and Gould (1983), families were identified and referred by physicians and nursing staff at a clinic in a Northern California community hospital. Families whose visits to the clinic could not be explained as "routine" were grouped according to their level of HCU, with "high utilizer families" defined as those in which at least one member of the family had clinic visits at more than double the rate of the national average (i.e., four visits per year). "Low utilizer families" were defined as those families in which no member utilized clinic visits more than the national average. All family members (i.e., over the age of 14) in the home were administered the FES and

a structured interview to determine family structure and functioning. Analyses revealed that “high utilizer families” identified as less expressive, more achievement oriented, more organized, and more concerned with control. Additionally, youth from these families reported less independence and greater moral/religious concern within their families.

Family factors, specifically family conflict, have been linked with higher HCU in youth (Riley et al., 1993; Weimer et al., 1983). Additionally, research has found that families who were the least expressive of positive emotions were more likely to miss follow-up clinic visits (Jacobson, Hauser, Willett, Wolfsdorf, & Herman, 1997). In contrast, research conducted by Janicke, Finney, and Riley (2001) found that cohesion, conflict, expressiveness, and organization were not significant predictors of HCU. However, the generalizability of this study may be restricted by the homogeneity of the sample, primarily middle-class families who were members of an HMO. Additional support for a relationship between family functioning and HCU can be inferred from family intervention studies which will be later described.

In addition, evidence for the relationship between family functioning and HCU can be deduced from studies demonstrating the influence of family functioning on disease behaviors and experiences that may impact HCU. In a recent meta-analysis examining family functioning and medical adherence in youth with chronic health conditions, lower family conflict, greater family cohesion, greater family flexibility, more positive communication, and adaptive family problem-solving were each associated with better adherence (Psihogios, Fellmeth, Schwartz, & Barakat, 2019). Additionally, rigidity in family systems has been shown to heighten family members’ susceptibility to illness

(Weimer et al., 1983). Research has also indicated that adolescents who rated themselves as less independent and perceived their families as disorganized and less cohesive were more likely to report somatic complaints (Terre & Ghiselli, 1997). In samples of youth with type 1 diabetes, family dysfunction has been found to negatively impact a child's glycemic control (Anderson, Miller, Auslander, & Santiago, 1981; Hanson, De Guire, Schinkel, & Kolterman, 1995). In fact, Anderson and colleagues (2002) found that youth and parent reports of high family conflict were related to significantly higher HbA1c levels compared to those reporting low levels of family conflict. Still more relevant to SCD, in samples of adolescents with chronic pain, greater levels of family conflict and higher levels of enmeshment have been associated with increased pain-related disability (Larsson & Sund, 2007; Logan, Guite, Sherry, & Rose, 2006). Further, the frequency of family conflict in chronic pain populations has been associated with increased pain occurrence (Kröner-Herwig, Heinrich, & Morris, 2007).

The pediatric diabetes literature has many examples of how positive family environment can also be related to better disease behavior and outcomes. The literature in this population suggests that children with more structured, cohesive, and supportive family environments are in better control of their diabetes (Cohen, Lumley, Naar-King, Partridge, & Cakan, 2004). Researchers have also found that family cohesion and organization are correlated with higher levels of diabetes self-care and adherence, whereas family conflict is correlated with poorer adherence and poorer glycemic control (Klemp & LaGreca, 1987). Hauser et al. (1990) also found that family conflict, cohesion, and organization strongly predicted short-term adherence levels. Further, higher family cohesion predicted better adherence and improved glycemic control (i.e., only among

girls) in children (Cohen et al., 2004). Additionally, families with higher verbal expressiveness had children who had better glycemic control four years later (Jacobson et al., 1994).

The intervention literature provides strong evidence for the relationship between disease outcomes, including HCU, and family functioning. In particular, family-centered interventions have been shown to improve health outcomes in pediatric diabetes (Feldman et al., 2018). In studies examining the effect of behavioral family systems therapy for diabetes (BFST-D) on health outcomes in adolescents with type 1 diabetes, findings indicated an improvement in HbA1C and higher treatment adherence (Harris, Freeman, & Duke, 2015; Wysocki et al., 2007). BFST-D also improved family conflict and treatment adherence significantly, particularly among adolescents with suboptimal metabolic control (Wysocki et al., 2006). Further, studies have sought to determine the effectiveness of multisystemic therapy (MST), an intensive home-based family therapy, on improving regimen adherence and metabolic control among adolescents with poorly controlled type 1 diabetes. Adolescents receiving MST had significant improvements in regimen adherence and metabolic control (Ellis, Frey, et al., 2005; Ellis et al., 2012). An additional study also sought to determine whether MST could reduce rates of ED use and hospital admissions for adolescents related to poor metabolic control. Although no differences were found in the number of ED visits between groups, youth who received MST had a significant decrease in the number of hospital admissions during the study period (Ellis, Naar-King, et al., 2005).

Family functioning constructs have not been studied often in relation to HCU within pediatric SCD. In a study examining the relationship of family functioning with

health outcomes in pediatric SCD, adolescents and their family members completed the FES at the time of consent. Adolescents' health data for the following year was collected via medical chart review. Poor health outcomes (i.e., disease severity, HCU, average hemoglobin level, SCD complications) were associated with poor family functioning (as reported by both teens and caregivers) and disease-related stress in caregivers. In fact, families who endorsed negative aspects of family functioning in this study had the highest disease severity and HCU patterns (Barakat et al., 2007).

Interventions incorporating family members of children with SCD have been less well studied than in pediatric diabetes, but have also provided support for improved health outcomes. For example, when caregivers participated in a developmentally and culturally sensitive family systems intervention for SCD, researchers found that caregivers felt more competent to handle their child's difficulties and the medical care system post-treatment (Kaslow & Brown, 1995). Importantly, there are few studies on family systems interventions that specifically assessed health outcomes in pediatric SCD, including HCU. Results of a study examining an educational intervention provided to caregivers in Lebanon indicated that caregivers greatly benefitted from tailored education and written materials. Although no significant difference was found in the number of ED visits before and after the intervention, the number of hospitalizations decreased significantly (Shahine, Badr, Karam, & Abboud, 2015).

Health Care Utilization and Academic Achievement

Currently, there is little research linking HCU to academic achievement in youth with SCD. Studies that do exist have used varying measures of academic achievement, including educational attainment, parent- and teacher-reported academic difficulties,

statewide readiness assessments, and various achievement assessments. Additionally, these studies have yielded variable results, likely due to the multiple methods used to assess academic achievement.

Frequent HCU for some individuals with SCD can make the process of completing an education even more difficult. In a study examining educational attainment and ED use in young adults with SCD, education level was negatively associated with ED visits. Participants who had greater rates of ED utilization during the previous year attained less education. Specifically, participants in the "no high school" and "high school" groups had a higher mean number of ED visits than the "post-secondary" group. Participants who did not complete high school visited the ED three times as often as those with post-secondary education. Additionally, those who did not complete high school had approximately 1.2 more ED visits than those who completed high school, although this difference was not statistically significant (Jonassaint et al., 2016).

Educational and health-related difficulties in a sample of youth with SCD were also assessed in a study by Mayes, Wolfe-Christensen, Mullins, and Cain (2011). This study utilized both medical chart review and the HOPE Needs Assessment (Peterson et al., 2005), a qualitative measure that assesses learning problems, functional impairment, behavioral concerns, and current services. HCU data was collected for the two years prior to administration of the HOPE Needs Assessment. Medical records indicated that youth visited the ED between zero and 14 times (M = 2.77, SD = 3.17), and were hospitalized between zero and 12 times (M = 2.58, SD = 3.08), with duration of hospital admissions ranging from one to 49 days (M = 6.33, SD = 9.16). Twelve percent of the sample reported educational problems, defined as use of special education services, grade

retention, frequent school absenteeism with subsequent academic difficulty, parent- and teacher-reported concerns regarding academics, or noticeable declines in attention or memory. Thirty-four percent of the sample reported health-related difficulties, defined as history of stroke, two or more hospitalizations within the past two years, functional limitations due to pain or fatigue, or lack of illness-specific accommodations at school. Additionally, 46% of the sample reported both educational and health-related problems, meeting both of the aforementioned criteria. Results of a series of bivariate correlations revealed that length of hospital admission was significantly related to parental concern regarding their child's grades, use of special education services, grade retention, and greater likelihood of being evaluated for learning difficulties.

In study by Finke (2010), a sample of five-year-old children with SCD who were enrolled in kindergarten and first grade in the South Carolina public school system was compared to a demographically-matched sample of healthy controls. Number of ED visits and hospitalizations (from 2003 to 2006) were measured, and the South Carolina Readiness Assessment (SCRA; administered at the beginning and end of both kindergarten and first grade) was used to measure academic achievement, including the domains of English Language Arts and Mathematics. Results did not reveal significant main effects of ED visits or hospitalizations (during the kindergarten academic year) on SCRA domain scores obtained at the beginning of kindergarten. However, when examining the longitudinal effects of ED visits and hospitalizations on academic performance, results indicated a significant effect for number of ED visits on the domains of English Language Arts and Mathematics. As such, children with a higher number of ED visits during kindergarten exhibited lower levels of academic performance on the

SCRA at the end of their kindergarten year. Further exploration indicated a significant interaction effect between time and number of hospitalizations on the domain of English Language Arts. Children who had one hospitalization during this period exhibited significant decreases in scores from kindergarten to first grade. Overall, results of this study indicate that early academic performance is affected by number of ED visits and hospitalizations.

Unlike the previous studies, research conducted by Eaton, Haye, Armstrong, Pegelow, and Thomas (1995) did not yield significant associations between HCU and academic achievement. However, the sample size in this study was much smaller than those in the preceding studies. In this study, two groups of children with HbSS (without evidence of stroke) who differed on frequency of pain-related hospitalizations, school absenteeism, and academic achievement were compared. The high frequency group (n = 11) had four or more pain-related hospitalizations during the preceding two academic years. The low frequency group (n = 11) had no more than one pain-related hospitalization during the preceding two years. In this study, the high frequency group had significantly more absences (M = 35.4, SD = 13.9) over the two-year period than the low frequency group (M = 16.8, SD = 15.9). The groups did not differ on scores obtained on the WRAT-R, although both groups scored between one to 1.5 standard deviations below the established test norms. Frequent pain-related hospitalization was significantly related to the degree of school absence, but neither hospitalization frequency nor school absence was related to academic achievement.

Overall, results of these studies indicate that youth with SCD and higher levels of HCU may be at risk for poor academic achievement. A multidisciplinary approach that

includes parents, students, medical staff, and educators is essential for the early identification and implementation of appropriate educational accommodations (Haridasa, DeBaun, Sanger, & Mayo-Gamble, 2019; Herron et al., 2003). To date, there are only two published studies examining academic or school-based interventions for youth with SCD (King et al., 2006; Koontz, Short, Kalinyak, & Noll, 2004). The study by Koontz and colleagues (2004) focused on the evaluation of a randomized clinical pilot trial comparing routine services with a school intervention program (i.e., providing education about SCD and its management) for children with SCD. Analyses indicated lower rates of school absenteeism for the youth receiving the school intervention program. Given that children with SCD are already at risk for academic difficulties, an intervention that can increase exposure to academic material by decreasing absences is likely to maximize a child's ability to reach his or her academic potential. Another program was also developed to ensure appropriate use of additional education resources (King et al., 2006). Twenty-three children with documented infarct on MRI were included in this study. Outcome measures for the intervention included completion of an IEP for those students who needed one, school absenteeism, and grade retention. At the completion of the intervention, the proportion of students who received IEPs increased from 74% to 87%. No difference in school absenteeism was observed after the intervention, and the intervention was ineffective in decreasing the rates of grade retention for students with SCD and documented infarct. However, neither study examined specific areas of academic achievement impacted in SCD (e.g., reading, mathematics, etc.). As such, these studies may indicate that specific components of school-based interventions for youth with SCD need further study.

Family Functioning and Academic Achievement

The aforementioned studies highlight the relationship between academic achievement and HCU independent of several other well-documented risk factors. Very limited research currently exists examining the role of family environment in relation to academic achievement in youth with SCD. In addition to the previously discussed direct effects related to the disease process, academic performance in youth with SCD may be impacted by other indirect factors, such as increased family stress (Brown, Armstrong, & Eckman, 1993). Family functioning has been shown to play a vital role in adjustment to SCD (McClellan & Cohen, 2007). Furthermore, poor adjustment may manifest as decreased academic performance and low academic achievement. The literature has shown that academic achievement is often impaired in youth with overt or silent stroke, but also in children without evidence of infarct (Noll et al., 2001; Schatz et al., 2001). Therefore, research examining the role of the family environment may further explain deficits in academic achievement in this population.

In a study conducted over two decades ago, Devine, Brown, Lambert, Donegan, and Eckman (1998) examined the role of family functioning in predicting academic achievement in youth with SCD. In this sample, caregivers reported average levels of family stress, family adaptability, and family cohesiveness on the FACES-II (Olson, Russell, & Sprenkle, 1983). Additionally, mean academic achievement scores on the Broad Reading and Broad Math clusters of the WJ-R were in the low average range. This study also examined whether family functioning predicted variance in reading and mathematics achievement, beyond that accounted for by illness parameters and socioeconomic status. Family functioning accounted for less than one percent of the

variance in both areas of achievement (non-significant); only socioeconomic status significantly predicted both academic achievement scores.

Most recently, a study by Yarboi et al. (2017) examined the relationship between academic achievement in youth with SCD and their mothers' reports of social-environmental stress and parenting. As family environment was not overtly examined in this sample, home routine, chaos, and positive parenting were used as a proxy. An interview was utilized which included a series of items related to routine and chaos based on a home environment scale (Evans, Gonnella, Marcynyszyn, Gentile, & Salpekar, 2005). The interview was designed to measure the degree of planning and order present in the household. Additionally, two components of positive parenting were assessed – consistent discipline and child monitoring. Children with SCD scored significantly below average on four of the subtests of the WJ-III (Letter-Word Identification, Reading Fluency, Calculations, and Math Fluency), with effect sizes ranging from medium to large. Neither home routine and chaos or positive parenting were significantly related to academic achievement. Notably, this sample included less than five percent of participants who had experienced a silent stroke and no participants with a history of overt stroke. As youth with a history of stroke, particularly overt stroke, are at greatest risk for cognitive impairment (Schatz & McClellan, 2006), and as these cases were underrepresented in this study, the results likely reflect higher-functioning youth with SCD overall.

Another study aimed to evaluate the efficacy of a family-based, group problem-solving intervention, Families Taking Control (FTC), to improve academic functioning for school-age children with SCD (Daniel et al., 2015). The FTC intervention group was

compared to a delayed intervention control (DIC) group. The goal of the intervention was to improve caregiver problem-solving to address disease complications and pursue educational accommodations during elementary school, and improve child problem-solving to promote teacher and peer communication. At baseline, families reported zero to seven school absences for the FTC group, and eight to 14 absences for the DIC group. Academic skills, as measured by the WJ-III Academic Skills Composite score, were in the average range for both groups at baseline. Additionally, caregivers reported strong problem-solving skills in both groups, with a trend for better problem-solving in the FTC group versus the DIC group. Analyses revealed no significant group differences between the FTC and DIC groups on the following outcomes at six-month follow-up – number of school accommodations, presence of an IEP or 504 Plan, school absences, or academic skills. Additionally, there were trends for fewer school absences and fewer school concerns at Time 2 in the FTC group as compared to the DIC group. Further, lack of hypothesized results was attributed to various limitations including limited retention, group differences at baseline despite randomization, and a short follow-up period.

Overall, results of these studies suggest that parent-advocacy efforts incorporated into standard-of-care practices may be beneficial for youth exhibiting academic difficulties. Finally, while the preceding studies all utilized uniform methods for assessing academic achievement, family environment has been examined in various ways. Notably, none of these studies used the FES, which has been widely used and validated in SCD.

Summary and Conclusions

HCU is an important variable to consider in the SCD population, as it is often used to understand the severity of a patient's disease (Panepinto et al., 2005). Although the majority of patients with SCD are hospitalized infrequently and manage their pain at home, a small percentage of patients is frequently admitted to EDs and inpatient units (Carroll et al., 2009; Reese & Smith, 1997). HCU is important to study as patients with frequent HCU are at increased risk for psychosocial consequences of SCD, including frequent school/work absences, social isolation, poor quality of life, depression and other emotional difficulties (Brown, Kaslow, et al., 1993; Midence & Elander, 1994).

To date, few studies have focused on the effects of the family environment on youth's use of health care services. As patterns of HCU are established early in life, and since youth rarely initiate their own health care, investigations of family functioning may help us to understand patterns of pediatric HCU. Since there is minimal research on the family environment of high health care utilizers in SCD, researchers should aim to explore this area. As family functioning is a potentially modifiable construct, by identifying specific family patterns, research may predict the HCU of "at risk" youth with SCD.

Additionally, few studies have been dedicated to examining the effects of HCU and family environment on youth's academic achievement. Results of the existing literature indicate that youth with SCD and higher levels of HCU are at risk for poor academic achievement (Finke, 2010; Jonassaint et al., 2016; Mayes et al., 2011). However, results have been inconclusive in the limited research examining the relationship between family environment and academic achievement. Notably, family

functioning has not been analyzed in a uniform manner, therefore contributing to difficulties in drawing conclusions about this piece of the literature. This is a gap in the literature that must be addressed, as there is evidence that psychosocial stressors (e.g., family environment, academic functioning) impact pain, thereby impacting the pain-related HCU patterns of patients with SCD.

In recent decades, there have been a multitude of changes in the health care system. These changes include implementation of sickle cell day units, community-based interdisciplinary medical teams, and healthcare coverage for youth through age 19 with pre-existing conditions. These changes, coupled with improvements in disease management (e.g., hydroxyurea as an alternative to chronic transfusions for primary stroke prevention) and SCD outcomes (e.g., limited transplant-related complications post-HSCT from HLA identical siblings), necessitate the need for more research to be conducted in this area (American College of Physicians, Inc., 2013; Arnold, Bhatia, Horan, & Krishnamurti, 2016; Cappelli et al., 2015; National Institutes of Health, 2018; Quinn, Rogers, McCavit, & Buchanan, 2010; Ware et al., 2015). Additional research to examine the impact of the family environment on various indices of HCU (e.g., ED utilization, hospital admissions, length of hospital stays), is warranted to clearly link the physical and psychosocial factors that impact HCU. Additionally, there are other factors not thoroughly or explicitly explored in the literature which may be important with respect to HCU, such as academic achievement. By attending to both the medical and psychosocial aspects of SCD, clinicians will be better able to productively collaborate with families, ultimately assisting these families in making adaptive decisions about SCD-related disease management. By determining modifiable psychosocial determinants

of HCU and academic achievement, research can accurately inform the design and implementation of interventions to improve outcomes in pediatric SCD.

Research in this area may also highlight the need for early identification of families more likely to utilize health care services, as well as youth who may be experiencing academic difficulties. For example, youth endorsing difficulties with coping, poor adjustment, and/or lower levels of family functioning may be identified as "at risk." This research could emphasize the importance of utilizing assessment measures, such as the FES, to identify families with lower levels of functioning and discordant family environments, and encourage a shift from the conceptualization of individual difficulties in youth to a focus on larger family systems issues impacting HCU. Further, youth who have evidenced overt or silent infarcts, have high rates of school absenteeism, or those who have exhibited difficulties in academic performance, may also be identified as "at risk." As the etiology of cognitive deficits in this population is not entirely clear, the effects of social and environmental disadvantages, as well as the consequences of frequent ED visits and recurrent hospitalizations, may contribute to poor academic performance (Schatz et al., 2004). Early identification and frequent monitoring of academic skills in children with SCD is critical, as children who are identified as at-risk for academic difficulties merit early intervention to facilitate academic success (Berkelhammer et al., 2007; Schatz, Schlenz, Smith, & Roberts, 2018).

Given consistent findings of high HCU and poor academic achievement in youth with pediatric SCD, preventive clinical approaches that involve ongoing assessment and monitoring of these constructs may be necessary. Research to evaluate the potential benefit of such approaches is needed. Additionally, research and clinical care that involve

the family provide opportunities to improve health outcomes for youth with SCD and their families.

Current Study

The current study aims to examine the relationship among family environment, HCU, and academic achievement in youth with SCD, as the literature has suggested that these variables are of great importance in this population. This ancillary investigation is intended to guide future research and interventions targeted to improve outcomes for youth with SCD. In a sample of youth diagnosed with SCD, this study was designed to achieve the following aims:

Primary aim 1. Examine associations between family environment (at baseline) and patterns of HCU in the following year (from baseline to one-year post-baseline). The hypotheses are represented as follows:

1. It is hypothesized that high scores on the FRI will predict lower frequency of pain-related ED visits in the following year (see Figure 1).
2. It is hypothesized that high scores on the FRI will predict lower frequency of pain-related hospital admissions in the following year (see Figure 2).

Primary aim 2. Examine associations between patterns of HCU in the previous year (from baseline to one-year post-baseline) and academic achievement scores in math (at one-year post-baseline). The hypotheses are represented as follows:

1. It is hypothesized that higher frequency of pain-related ED visits in the previous year will predict lower scores on the Broad Math cluster of the WJ-III Achievement (see Figure 3).

2. It is hypothesized that higher frequency of pain-related hospital admissions in the previous year will predict lower scores on the Broad Math cluster of the WJ-III Achievement (see Figure 4).

Primary aim 3. Examine associations between patterns of HCU in the previous year (from baseline to one-year post-baseline) and academic achievement scores in reading (at one-year post-baseline). The hypotheses are represented as follows:

1. It is hypothesized that higher frequency of pain-related ED visits in the previous year will predict lower scores on the Broad Reading cluster of the WJ-III Achievement (see Figure 5).
2. It is hypothesized that higher frequency of pain-related hospital admissions in the previous year will predict lower scores on the Broad Reading cluster of the WJ-III Achievement (see Figure 6).

Exploratory aim 1. Evaluate the indirect effect of family environment (at baseline) on academic achievement scores in math (at one-year post-baseline), as explained by patterns of HCU (from baseline to one-year post-baseline). The hypotheses are represented as follows:

1. It is hypothesized that frequency of pain-related ED visits (from baseline to one-year post-baseline) will mediate the relationship between family environment (at baseline) and academic achievement scores in math (at one-year post-baseline; see Figure 7).
2. It is hypothesized that frequency of pain-related hospital admissions (from baseline to one-year post-baseline) will mediate the relationship between

family environment (at baseline) and academic achievement scores in math (at one-year post-baseline; see Figure 8).

CHAPTER III

Method

Participants

Participants in this study included 41 youth diagnosed with either HbSS or HbSβ-thalassemia, who were between six and 13-years-old at the time of recruitment for a larger study. Consent was provided by a parent or legal guardian, and the primary caregiver most directly involved with the daily care of the child completed parent-report measures. This person could be a relative who was not the child's parent (i.e., grandmother, aunt, etc.). Youth and their caregiver(s) were recruited from the University of Miami Miller School of Medicine Pediatric Sickle Cell Program outpatient clinic and/or caregiver self-referral.

Youth were not eligible to participate in the larger study if they met one of the following criteria: (1) the child was monolingual in a language other than English, and could not complete standardized testing in English; (2) the caregivers of the child participants were not fluent in English or Spanish; (3) the child had some other developmental disability unrelated to SCD, including Down's syndrome, Autism, Pervasive Developmental Disability, Cerebral Palsy, Seizure Disorder, consequences of severe prematurity, or was diagnosed with a documented closed head injury that resulted in loss of consciousness; and (4) the child had been diagnosed with a significant mental health disorder that was not responsive to behavioral or medical management, including severe depression, schizophrenia, or bipolar disorder.

Measures

Demographics/medical history. The sociodemographic characteristics of the participants, including SCD genotype, age, race/ethnicity, gender, maternal education level, and annual household income were collected via the larger study's Demographics/Medical History Questionnaire. In addition, participants' medical history information was obtained via retrospective medical chart review. Specifically, this information included history of neurobehavioral complications (e.g., history of stroke, silent cerebral infarcts) and treatment (e.g., hydroxyurea, chronic transfusion, etc.).

Health care utilization. Data collection also included a review of participants' medical charts for hospital-based service use, including number of pain-related ED visits, number of pain-related hospital admissions, and duration of pain-related hospital admissions. For each participant, information was collected over the span of one year, beginning at their baseline evaluation.

Family environment. The Family Environment Scale (FES) was completed by caregivers at baseline and was utilized to assess family functioning. The FES is a self-report instrument that focuses on the interpersonal relationships among family members, the directions of personal growth examined in the family, and the family's organizational and system-maintenance characteristics. The FES consists of 90 true-false items and is composed of three composite scales and ten subscales. It includes the Relationship dimension (Cohesion, Expressiveness, Conflict), the Personal Growth dimension (Independence, Achievement, Orientation, Intellectual-Cultural Orientation, Active-Recreational Orientation, Academic Achievement, Moral-Religious Emphasis), and the System Maintenance dimension (Organization, Control). The reported internal

consistency of subscales is moderate (Cronbach's alpha = .61 to 78) and test-retest reliabilities vary (.68 to .86; Moos & Moos, 2002). The FES has been validated as a measure of family environment in diverse families of healthy children, including African American families (Wilson & Tolson, 1990).

To address primary aim 1 and exploratory aim 1, this study utilized a 27-item index, the Family Relationship Index (FRI), which was rated as "well-established" for pediatric populations, including pediatric SCD (Alderfer et al., 2008). The FRI is made up of the three scales from the FES which comprise the relationship domain (i.e., cohesion, expressiveness, and conflict). Cohesion is defined as the extent to which family members are concerned and committed to the family and the degree to which they are helpful and supportive to each other. Expressiveness is defined as the extent to which family members are allowed and encouraged to act openly and to express their feelings directly. Conflict is defined as the extent to which the open expression of anger and aggression and generally conflictual interactions are characteristic of the family. The FRI is calculated by reverse scoring the items in the conflict subscale, then summing scores on the three subscales. Scores on the FRI range from 0 to 27, with higher scores indicative of better family functioning. The FRI has high internal consistency (Cronbach's alpha = .89) and good construct validity (Holahan & Moos, 1983; Moos, 1990). In a normative sample of African American and Latino families, the following subscale scores were found: cohesion (M = 6.90, SD = 1.94), expressiveness (M = 4.97, SD = 1.73), and conflict (M = 3.26, SD = 2.12; Moos & Moos, 1981). These subscale scores translate to the following T-scores for comparison: cohesion (M = 52), expressiveness (M = 47), and conflict (M = 49).

Academic achievement. The Woodcock-Johnson, Third Edition – Tests of Achievement (WJ-III Achievement) is an individually administered achievement test that assesses various areas of academic achievement. This was administered to youth at baseline and one-year post-baseline; however, only scores obtained at one-year post-baseline were utilized for this study. The WJ-III Achievement is considered a standard measure of academic achievement for youth with SCD (Daly, Kral, & Tarazi, 2011). Age-adjusted scores for composite reading and mathematics (Broad Reading and Broad Math) were utilized. The Broad Reading cluster is comprised of the Letter-Word Identification, Reading Fluency, and Passage Comprehension subtests. The Broad Math cluster is comprised of the Calculation, Math Fluency, and Applied Problems subtests. The median reliability coefficients for the standard battery range from .81 to .94. The median cluster reliability is .94 for Broad Reading and .95 for Broad Math (McGrew & Woodcock, 2001). Regarding construct validity, confirmatory factor-analytic models indicate that the WJ-III Achievement is factorially complex. Subtests do not all load solely on a single factor, and there is a moderate inter-correlation between unrelated clusters (.50 to .70; Schrank, McGrew, & Woodcock, 2001).

Procedure

The current study is an ancillary study of a sample recruited for a larger study evaluating an educational support program for caregivers that aimed to improve academic achievement in children with SCD. The larger study was sponsored by the National Institute of Health/National Heart Lung and Blood Institute (US NIH Grant U54HL090569). This retrospective study used information collected between March 2009 and July 2013. Additionally, data from this period was also collected from the

hospital's electronic medical record system. For each participant, data was collected over the span of one year. Approval for the larger study was received from the Institutional Review Board (IRB) at the University of Miami Miller School of Medicine. Additionally, approval for the current study was received from the University of Miami Miller School of Medicine IRB and the Nova Southeastern University IRB.

Recruitment. Youth who met the age and genotype requirements for the larger study were identified prior to routine clinic visits. Caregivers of 116 youth were approached in the clinic by a member of the research team, informed about the study, and offered the chance to participate. The person legally permitted to consent for research participation was identified, and the study was explained in detail in the primary language of that individual (English or Spanish). The primary caregiver provided information related to exclusion criteria: history of developmental disability, history of head trauma resulting in loss of consciousness, history of mental health problems not responsive to treatment, and language proficiency of the primary caregiver. Exclusionary criteria were met by 19 youth, and the primary caregiver was thanked for their time. Of the remaining individuals approached, an additional 15 refused participation in the study and nine requested additional time to consider participation but were ultimately not consented.

If none of the exclusionary criteria were met and the caregiver agreed to participate, written informed consent was obtained for 73 youth. Child assent was obtained for youth aged seven years or older. Primary caregivers provided brief background information, including data about ethnicity, race, preferred language, and parental education. Contact information was obtained from the primary caregiver. After consent, five participants voluntarily withdrew from the study due to economic or

familial stressors, 11 participants were lost to follow-up, and one participant moved out of state.

Data collection. For the purposes of this study, two time periods were examined: baseline (six months post-consent) and one-year post-baseline. At baseline, caregivers completed the FES and the Demographics/Medical History Questionnaire with a member of the research team. One-year post-baseline, youth completed the WJ-III Achievement. Caregivers were compensated with an incentive of $75 at the completion of the baseline and one-year post-baseline evaluations. As described above, a total of 56 participants completed the evaluation at baseline. Of those participants, ten were lost to follow-up, resulting in 46 who completed an evaluation one year later. In the present study, an additional five participants were removed from the database due to missing data (i.e., FES or WJ-III Achievement), resulting in the final sample of 41 youth.

Analyses

All analyses were performed using IBM SPSS Version 24.0 (IBM Corp., 2016). Descriptive analyses were conducted to describe the sample on demographic and disease-related variables, including means and standard deviations for continuous variables (e.g., age) and frequencies and percentages for categorical variables (e.g., genotype, gender, stroke). Pearson correlation and multiple linear regression analyses were conducted to examine associations between family environment, pain-related ED visits, pain-related hospital admissions, and academic achievement scores in math and reading.

To examine primary aim 1 (hypotheses 1-2), two separate linear regression models (see Figures 1 and 2) were employed with family environment as the independent variable. ED visit frequency was the dependent variable for the first model and hospital

admission frequency was the dependent variable for the second model. In both models, genotype, age, gender, maternal education, and stroke were hypothesized covariates. Additionally, to examine primary aim 2 (hypotheses 1-2), two separate linear regression models (see Figures 3 and 4) were employed, one with ED visit frequency as the independent variable and another with hospital admission frequency as the independent variable. In both models, genotype, age, gender, maternal education, and stroke were hypothesized covariates, and Broad Math scores were the dependent variable. In addition, to examine primary aim 3 (hypotheses 1-2), two separate linear regression models (see Figures 5 and 6) were employed, one with ED visit frequency as the independent variable and another with hospital admission frequency as the independent variable. In both models, genotype, age, gender, maternal education, and stroke were hypothesized covariates, and Broad Reading scores were the dependent variable.

Further, to examine exploratory aim 1 (hypotheses 1-2), mediation analysis using bootstrap methodology was utilized. Two separate mediation models (see Figures 7 and 8) were employed using PROCESS version 3.3 (Hayes, 2018) in SPSS. Mediation analyses were conducted to examine the indirect effect of family environment on Broad Math scores through ED visit frequency and hospital admission frequency.

Additionally, a series of exploratory descriptive analyses was conducted to further characterize participants with no documented ED visits versus those with one or more visits. Further, independent-samples t-tests, chi-square tests for independence, and logistic regression analyses were conducted to examine this dichotomized HCU variable. Pain-related hospital admission frequency was not further analyzed as there were less than 15 individuals with one or more hospital admissions. Given the study's small sample

size, a lack of statistical significance could indicate either a small and trivial effect or a moderate and meaningful effect that would be statistically significant in the context of a larger study. Therefore, effect sizes are provided for all analyses.

CHAPTER IV

Results

Description of Sample

Demographic characteristics. The final sample consisted of 41 youth, ranging in age from 6 to 13-years-old at baseline. Approximately half the sample identified as female (53.7%), and identified as predominately African American and Haitian (70.8%). See Table 1 for a detailed summary of the demographic characteristics of the sample.

Table 1

*Sample Demographic Characteristics (*N = *41*)

Characteristic	Mean/Frequency (SD/%)
Age at baseline (in years)	9.98 (2.05)
Age at one-year post-baseline (in years)	11.13 (2.16)
Gender	
Female	22 (53.7%)
Male	19 (46.3%)
Race/Ethnicity	
Caribbean Black	2 (4.9%)
Black, not of Hispanic origin	7 (17.1%)
Black, of Hispanic origin	2 (4.9%)
Black, of African origin	12 (29.3%)
Haitian	17 (41.5%)
Hispanic, of Caribbean origin	1 (2.4%)
Maternal Education (*n* = 40)	
Less than high school	9 (22.5%)
High school	15 (37.5%)
Some college	11 (27.5%)
College/Post-college	5 (12.5%)
Household Income	
Less than $19,999	19 (46.3%)
$20,000 - $39,999	8 (19.5%)
$40,000 - $59,999	4 (9.8%)
$60,000 or more	1 (2.4%)
Did not want to answer	9 (22%)

Disease-related characteristics. Participants in this study included youth diagnosed with either HbSS (85.4%) or HbSβ-thalassemia (14.6%). Youth had an average of 1.51 (*SD* = 2.77, *range* = 0-16) pain-related ED visits, and an average of 1.02 (*SD* = 2.64, *range* = 0-16) pain-related hospital admissions. More than half of ED visits

(66.13%) resulted in hospital admission. Of those with hospital admissions, mean duration was 13.60 days (*SD* = 22.77, *range* = 2-81). See Table 2 for a summary of disease-related characteristics of the sample.

Table 2

*Sample Disease-Related Characteristics (*N = *41)*

Disease-Related Characteristic	Mean/Frequency (SD/%)
Genotype	
HbSS	35 (85.4%)
HbSβ-thalassemia	6 (14.6%)
Total pain-related HCU	
Pain-related ED visits	1.51 (2.77)
Pain-related hospital admissions	1.02 (2.64)
Pain-related hospital admission duration (*n* = 15)	13.60 (22.77)
History of stroke	5 (12.2%)
Overt	3 (7.3%)
Silent	2 (4.9%)
On chronic transfusion therapy	11 (26.8%)
Treated with hydroxyurea	9 (22.0%)

Health care utilization. Approximately half the sample (*n* = 22, 53.7%) did not have any documented pain-related ED visits. Eight participants (19.5%) had 3 or more ED visits, which in the literature is characterized as being a "high utilizer" (Aisiku et al., 2009). Further, one participant had 16 documented pain-related ED visits during the year following their baseline evaluation. Similarly, the breakdown of pain-related hospital admissions indicated that 63.4% of the sample did not have any documented pain-related hospital admissions. See Figure 9 for a detailed breakdown of pain-related HCU.

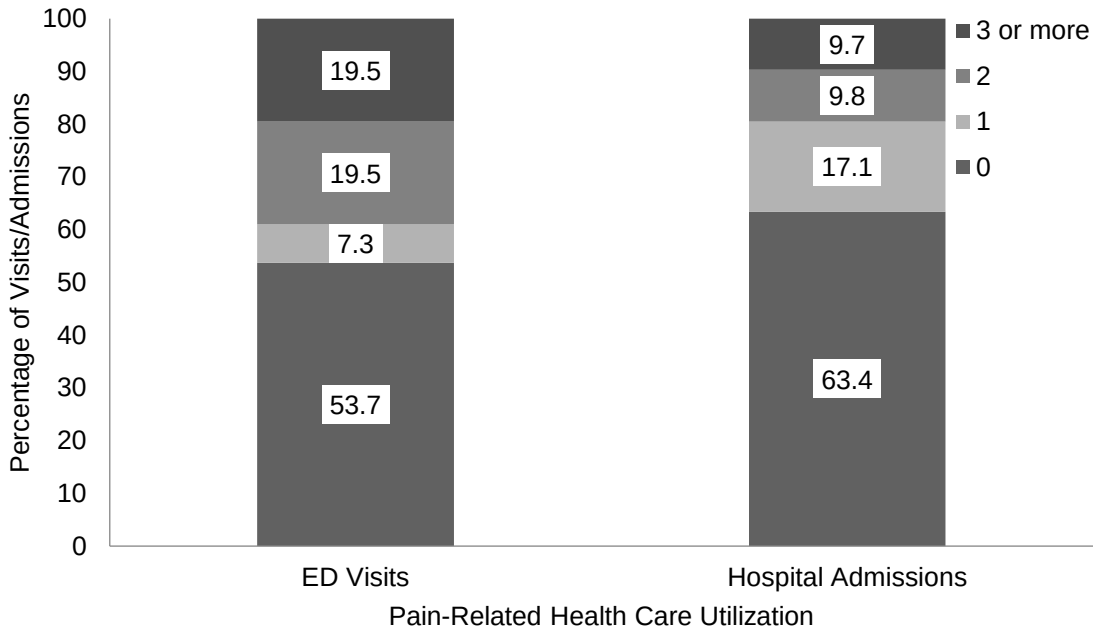

Figure 9. Percentage of total pain-related ED visits and hospital admissions.

Family environment. The FES subscale scores are reported as *T*-scores, which have a mean of 50 and standard deviation of 10. The subscales that make up the FRI are cohesion (*M* = 54.05, *SD* = 8.57, *range* = 25-65), expressiveness (*M* = 47.27, *SD* = 8.49, *range* = 22-65), and conflict (*M* = 44.98, *SD* = 9.43, *range* = 33-70), all of which are in the *average* range. The mean total FRI score for this sample was 19.20 (*SD* = 3.15, *range* = 12-24).

Academic achievement. Academic achievement scores are reported as standard scores, which have a mean of 100 and a standard deviation of 15. The mean score on the Broad Math cluster of WJ-III Achievement at one-year post-baseline was 87.34 (*SD* = 10.88, *range* = 64-118). Additionally, the mean score on the Broad Reading cluster of the WJ-III Achievement at one-year post-baseline was 86.95 (*SD* = 14.74, *range* = 50-113). The mean scores on the Broad Math and Broad Reading clusters were in the *low average* range, with the score ranges falling between *very low* and *high average*.

Primary Analyses

Preliminary analyses were conducted to examine the data for normal distributions and outliers. One participant was excluded from subsequent analyses because of their extreme number of pain-related ED visits and hospital admissions (i.e., 16 ED visits and 16 hospital admissions; see Figure 9 above). Pearson correlation and multiple linear regression analyses were conducted to evaluate variables associated with pain-related ED visits, pain-related hospital admissions, and academic achievement scores in math and reading.

Pearson correlation analyses. Pearson product-moment correlations of primary variables are presented in Table 3. Pain-related HCU, as measured by pain-related ED visit and hospital admission frequency, was not significantly correlated with family environment as measured by FRI score, academic achievement in math as measured by Broad Math score, or academic achievement in reading as measured by Broad Reading score.

Table 3

Pearson Product-moment Correlations

Variable	1	2	3	4	5	6	7	8
1. ED visits	--							
2. Hospital admissions	.82*	--						
3. FRI	-.10	-.09	--					
4. Cohesion	-.01	-.06	.72*	--				
5. Expressiveness	-.15	-.09	.54*	.13	--			
6. Conflict	.06	.06	-.81*	-.43*	-.10	--		
7. Broad Math	-.17	-.03	-.00	-.05	.18	.10	--	
8. Broad Reading	-.12	-.03	-.10	-.13	.00	.09	.62*	--

Note. ED visits = number of total pain-related ED visits; Hospital admissions = number of total pain-related hospital admissions; FRI = Family Relationship Index.
*$p < .01$.

Multiple linear regression analyses. In order to address the proposed hypotheses, a series of multiple linear regression analyses were conducted. A total of six

separate analyses were run. See Figures 1 through 6 in Appendix. To control for inflation of Type I error, a Bonferroni correction (i.e., divide alpha by number of tests within each model) was applied to adjust the alpha level for each test, thus providing a more stringent alpha level. Prior to analysis, the statistical assumptions of multiple regression were assessed, including tests of departure from normality, presence of significant outliers, linearity, homoscedasticity, and independence of residuals. Results from collinearity diagnostics, casewise diagnostics, plotted standardized residuals, and normal probability plots indicated there were no violations of the underlying assumptions for the analyses.

Normality and outliers. The independent and dependent variables in each model were analyzed for departures from normality, and the assumption of normality was met. As described above, an inspection of the studentized deleted residuals was performed to determine whether there were any residuals greater than three standard deviations from the mean of the sample. No outliers were identified.

Linearity and homoscedasticity. In order to assess for linearity, the residuals scatterplots and partial regression plots were examined. Additionally, there was homoscedasticity, as assessed by visual inspection of plots of studentized residuals versus unstandardized predicted values.

Multicollinearity and collinearity. The correlations among the variables were assessed in order to rule out the possibility of multicollinearity. Correlations among the independent variables were checked and not found to be correlated. Additionally, collinearity diagnostics were conducted for each analysis. There was no evidence of multicollinearity, as evidenced by tolerance values greater than 0.1 (Hair, Black, Babin, & Anderson, 2014).

Analyses. None of the hypotheses set forth in the primary research aims were supported by tests of statistical significance. Omnibus tests for the multiple linear regression models were not statistically significant. Small R square values were estimated for models predicting HCU and Broad Reading scores (ranging from .10 to .12), suggesting these models explained little of the variance in pain-related ED visit frequency, hospital admission frequency, and Broad Reading scores. Models predicting Broad Math scores had slightly higher R square values (.24 and .26). The standardized coefficients for the individual covariates and predictors are provided in Tables 4-9. These coefficients were not significantly different from zero in the present analysis, but there was considerable variability in the relative Beta scores (from -.27 to .31). There were relatively small Beta scores for the hypothesized predictors in each model.

Table 4

Regression Analysis Summary for Family Environment and Covariates Predicting Pain-Related ED Visit Frequency

Variable	B	SE B	β	*t*	*p*
FRI	-.07	.09	-.14	-.79	.44
Genotype	-.75	.73	-.18	-1.03	.31
Age	-.04	.13	-.05	-.30	.77
Gender	-.37	.52	-.12	-.70	.49
Maternal education	-.54	.63	-.15	-.86	.40
Stroke	-.63	.80	-.14	-.80	.43

Note. Full model was not statistically significant, $F(6, 32) = .61$, $p = .72$, $R^2 = .10$. FRI = Family Relationship Index.

Table 5

Regression Analysis Summary for Family Environment and Covariates Predicting Pain-Related Hospital Admission Frequency

Variable	B	SE B	β	*t*	*p*
FRI	-.04	.07	-.09	-.51	.61
Genotype	-.60	.53	-.19	-1.14	.27
Age	-.02	.10	-.04	-.23	.82
Gender	.00	.38	.00	.01	.99
Maternal education	-.43	.46	-.16	-.94	.36
Stroke	-.91	.58	-.27	-1.56	.13

Note. Full model was not statistically significant, $F(6, 32) = .73$, $p = .63$, $R^2 = .12$. FRI = Family Relationship Index.

Table 6

Regression Analysis Summary for Pain-Related ED Visit Frequency and Covariates Predicting Broad Math

Variable	B	SE B	β	*t*	*p*
Pain-related ED visits	-.87	1.18	-.13	-.74	.47
Genotype	3.09	5.10	.10	.61	.55
Age	-.82	.85	-.16	-.97	.34
Gender	2.99	3.53	.14	.85	.40
Maternal education	7.54	4.30	.29	1.75	.09
Stroke	-7.84	5.22	-.25	-1.50	.14

Note. Full model was not statistically significant, $F(6, 29) = 1.67$, $p = .16$, $R^2 = .26$.

Table 7

Regression Analysis Summary for Pain-Related Hospital Admission Frequency and Covariates Predicting Broad Math

Variable	B	SE B	β	*t*	*p*
Pain-related hospital admissions	-.33	1.62	-.04	-.20	.84
Genotype	3.45	5.16	.11	.67	.51
Age	-.76	.86	-.15	-.88	.38
Gender	3.25	3.55	.15	.92	.37
Maternal education	7.92	4.36	.31	1.82	.08
Stroke	-7.41	5.44	-.24	-1.36	.18

Note. Full model was not statistically significant, $F(6, 29) = 1.56$, $p = .20$, $R^2 = .24$.

Table 8

Regression Analysis Summary for Pain-Related ED Visit Frequency and Covariates Predicting Broad Reading

Variable	B	SE B	β	*t*	*p*
Pain-related ED visits	-.38	1.73	-.04	-.22	.83
Genotype	3.36	7.18	.09	.47	.64
Age	-.55	1.22	-.08	-.45	.66
Gender	4.79	5.18	.16	.93	.36
Maternal education	8.63	6.14	.25	1.41	.17
Stroke	-1.24	7.76	-.03	-.16	.87

Note. Full model was not statistically significant, $F(6, 30) = .64$, $p = .70$, $R^2 = .11$.

Table 9

Regression Analysis Summary for Pain-Related Hospital Admission Frequency and Covariates Predicting Broad Reading

Variable	B	SE B	β	*t*	*p*
Pain-related hospital admissions	.28	2.37	.02	.12	.91
Genotype	3.85	7.20	.10	.54	.60
Age	-.51	1.22	-.07	-.42	.68
Gender	4.92	5.15	.17	.96	.35
Maternal education	8.92	6.15	.26	1.45	.16
Stroke	-.64	8.00	-.02	-.08	.94

Note. Full model was not statistically significant, $F(6, 30) = .64$, $p = .70$, $R^2 = .11$.

Exploratory Analyses

Mediation analyses. In order to address exploratory aim 1 (hypotheses 1-2), two separate mediation analyses were performed (see Figures 7 and 8 in Appendix) using PROCESS version 3.3 (Hayes, 2018) in SPSS. Effects were evaluated at a significance level of $\alpha = .05$. For estimation of the indirect effects, 5,000 bootstrap samples were used to construct confidence intervals to test significance. The seed for the bootstrap samples was fixed to ensure reproducibility of the results. None of the hypotheses set forth in the exploratory research aims were supported by tests of statistical significance. Specifically, family environment did not exert an effect on academic achievement in math indirectly through ED visit frequency or hospital admission frequency. Model coefficients and *p*-

values are provided in Tables 10 and 11, and indirect effects and confidence intervals are provided in Table 12.

Table 10

Regression Coefficients, Standard Errors, and Model Summary Information for the Pain-Related ED Visit Frequency Model

	Consequent					
	M (ED visits)			*Y* (Broad Math)		
Antecedent	Coefficient	*SE*	*p*	Coefficient	*SE*	*p*
X (FRI)	-.080	.088	.369	-.107	.635	.868
M (ED visits)	--	--	--	-1.245	1.210	.311
constant	2.795	1.725	.114	91.106	12.802	<.001*
	Overall model: R^2 = .023 $F(1, 35)$ = .827 , p = .369			Overall model: R^2 = .030 $F(2, 34)$ = .529 , p = .594		

Note. ED visits = number of total pain-related ED visits; FRI = Family Relationship Index.

Table 11

Regression Coefficients, Standard Errors, and Model Summary Information for the Pain-Related Hospital Admission Frequency Model

	Consequent					
	M (Hospital admissions)			*Y* (Broad Math)		
Antecedent	Coefficient	*SE*	*p*	Coefficient	*SE*	*p*
X (FRI)	-.054	.065	.415	-.024	.643	.970
M (Hospital admissions)	--	--	--	-.316	1.652	.850
constant	1.749	1.282	.181	88.178	12.861	<.001*
	Overall model: R^2 = .019 $F(1, 35)$ = .681, p = .415			Overall model: R^2 = .001 $F(2, 34)$ = .018, p = .982		

Note. Hospital admissions = number of total pain-related hospital admissions; FRI = Family Relationship Index.

Table 12

Indirect Effects on Academic Achievement in Math

	Consequent: Broad Math							
Antecedent	*ab*	SE	LLCI	ULCI	*ab**	SE*	LLCI*	ULCI*
M (ED visits)	.099	.175	-.139	.552	.027	.045	-.039	.137
M (Hospital admissions)	.017	.134	-.154	.399	.004	.035	-.042	.103

Note. ED visits = number of total pain-related ED visits; Hospital admissions = number of total pain-related hospital admissions; *Denotes completely standardized effect.

Additional exploratory analyses. Further analyses were conducted following those described above. Given the large proportion of participations in the present sample who had not experienced any documented pain-related ED visits, a series of exploratory analyses was conducted to characterize participants without any documented ED visits versus those with one or more visits. Descriptive statistics were estimated to describe these two groups on demographic and disease-related characteristics. Further, exploratory analyses included independent-samples t-tests, chi-square tests for independence, and logistic regression.

Independent-samples t-tests. Independent-samples t-tests were conducted to compare mean age, family environment, and academic achievement for participants without documented ED visits (n = 22) versus those with one or more ED visits (n = 18). There were no statistically significant differences for the two groups. Effect sizes (Cohen's d) were calculated and interpreted. According to Cohen (1988), an effect size of 0.2 is described as "small," 0.5 as "medium," and 0.8 as "large." Broad Math had a positive, medium effect. Results are presented in Table 13.

Chi-square test for independence. Chi-square tests for independence were conducted to determine whether there was an association between gender, genotype, maternal education, history of stroke, use of chronic transfusion therapy, and use of hydroxyurea for participants without documented ED visits versus those with one or more ED visits. There were no statistically significant associations found between the two groups on any of these variables. Fisher's Exact tests were used when expected cell frequencies were less than five. Effect sizes (phi) were interpreted according to Cohen (1988), such that a value of 0.1 is considered a "small" effect, 0.3 is a "medium" effect,

and 0.5 is a "large" effect. Effect sizes (phi) for genotype, history of stroke, and use of chronic transfusion therapy were small, and gender had a negative, medium effect. Results are presented in Table 13.

Table 13

Summary of Dichotomized Sample Characteristics/Scores by ED Visit Frequency

Characteristic	0 ED Visits (n = 22) Mean/Frequency (SD/%)	≥1 ED Visits (n = 18) Mean/Frequency (SD/%)	p	Effect Size
Age at baseline (in years)	9.85 (2.05)	9.99 (2.09)	.82	.07
Gender			.12	-.25
Female	14 (66.7%)	7 (33.3%)		
Male	8 (42.1%)	11 (57.9%)		
Genotype			.67	-.10
HbSS	18 (52.9%)	16 (47.1%)		
HbSβ-thalassemia	4 (66.7%)	2 (33.3%)		
Maternal Education			1.00	.02
Less than high school	5 (55.6%)	4 (44.4%)		
High school or greater	16 (53.3%)	14 (46.7%)		
History of stroke			.36	-.19
Yes	4 (80.0%)	1 (20.0%)		
No	18 (51.4%)	17 (48.6%)		
Chronic transfusion therapy			.72	-.11
Receiving transfusions	7 (63.6%)	4 (36.4%)		
No transfusions	15 (51.7%)	14 (48.3%)		
Hydroxyurea			1.00	.05
Treated with Hydroxyurea	4 (50.0%)	4 (50.0%)		
No Hydroxyurea	18 (56.3%)	14 (43.8%)		
Family Relationship Index	19.45 (3.28)	19.11 (2.99)	.73	.11
Academic Achievement:				
Broad Math	89.95 (11.50)	84.89 (10.10)	.17	.47
Broad Reading	87.60 (16.16)	86.17 (13.87)	.77	.09

Note. Frequency, percentages, and phi are provided for categorical variables and means, standard deviations, and Cohen's *d* are provided for continuous variables.

Logistic regression. A binomial logistic regression was performed to predict a dichotomous pain-related ED utilization variable (zero ED visits versus one or more ED visits). All covariates and predictors of interest were included: genotype, age, gender, maternal education, history of stroke, and family environment. The logistic regression

model was not statistically significant, $\chi^2(6) = 7.64$, $p = .27$. Of note, males had 4.71 times higher odds of utilizing the ED for pain than females (as shown in Table 14).

Table 14

Summary of Logistic Regression Analysis Predicting Pain-Related ED Utilization

Predictor	*B*	*SE*	*OR*	95% CI	Wald statistic	*p*
FRI	-.14	.13	.87	[.67, 1.13]	1.05	.31
Genotype	-.81	.99	.44	[.06, 3.13]	.66	.42
Age	.18	.19	1.20	[.82, 1.75]	.88	.35
Gender	1.55	.78	4.71	[1.02, 21.83]	3.92	.048*
Maternal education	-.14	.90	.87	[.15, 5.08]	.03	.88
Stroke	-1.81	1.35	.16	[.01, 2.28]	1.82	.18

Note. CI = confidence interval for odds ratio (*OR*). FRI = Family Relationship Index. Genotype is for HbSβ-thalassemia compared to HbSS. Gender is for males compared to females. Maternal education is for high school or greater compared to less than high school. Stroke is for positive history of stroke compared to no history of stroke.

*$p < .05$.

CHAPTER V

Discussion

The goal of the present study was to examine relationships between family environment, health care utilization (HCU), and academic achievement in youth with SCD. The existing literature has highlighted the importance of these variables, given that individuals with frequent HCU are also at risk for an array of difficulties related to SCD, including disruptions in family functioning, increased dependency on the family system, and decreased academic performance (Edwards et al., 2005; Logan et al., 2002; Reese & Smith, 1997). Further, the goal of many interventions, some which have been explicitly conducted with the SCD population, has been to reduce HCU and improve health outcomes (Kaslow & Brown, 1995; Shahine et al., 2015).

Predicting Health Care Utilization

The first aim of the present study sought to examine associations between family environment and patterns of HCU in the following year. To date, few research studies have focused on the effects of family environment on children's use of health care services within the context of pediatric SCD. However, greater family environment has been associated with improved health outcomes in youth with chronic health conditions (Psihogios, Fellmeth, Schwartz, & Barakat, 2019). Additionally, within the SCD literature, decreased family functioning has been associated with poor health outcomes, including greater HCU (Barakat et al., 2007). As such, it was hypothesized that high scores on the Family Relationship Index (FRI) would be associated with lower frequency of pain-related ED visits and pain-related hospital admissions in the following year. Contrary to these hypotheses, results from the present study indicated that family

environment was not associated with either pain-related ED visits or hospital admissions. Similarly, genotype, age, maternal education, and stroke status did not predict pain-related ED visits or hospital admissions. Lack of significant findings may be due to a variety of factors. Unique characteristics of the present study's sample may, in part, explain the unexpected findings. Specifically, participants in this sample reported a more positive family environment, demonstrated less pain-related ED visits and hospital admissions, were less likely to have a history of stroke, and were younger in age.

Caregivers of youth in the present study reported average levels of cohesion, expressiveness, and conflict. In the literature, cohesive and supportive family environments have been associated with effective coping, and family functioning characterized by low conflict and high support has been shown to positively impact the adjustment of youth with SCD (Barakat et al., 2007; Barbarin, Whitten, Bond, & Conner-Warren, 1999; Billings & Moos, 1982; Burlew, Telfair, Colangelo, & Wright, 2000; Thompson et al., 1999). In the present study, scores obtained on the FRI were indicative of higher cohesion, lower conflict, and similar expressiveness when compared to a normative sample of African American and Latino families (Moos & Moos, 1981). In addition, the present study's sample predominantly identified as African American or Haitian. There are several important differences to be noted within Haitian culture, particularly regarding family environment. In Haitian families, youth must show respect for their elders and must not talk back, argue, or disagree with them. Additionally, togetherness and support among family members is characteristic of most Haitian families (McEachern & Kenny, 2002). In the present study, there was limited variability in scores on the FRI and, overall, scores were indicative of a more positive family

environment. Given the large number of Haitian families endorsing more positive family relationships, this may have impacted the ability to detect significant findings when examining the relationship between family environment and HCU in the present study.

With regard to HCU, there was significant lack of variability in the frequency of pain-related ED visits and hospital admissions in the present study. Specifically, approximately half of the sample (53.7%) did not have any documented pain-related ED visits, and more than half of the sample (63.4%) did not have any documented pain-related hospital admissions. The amount of youth without any documented HCU is greater than what has been described in the literature (e.g., Brousseau et al., 2010). Existing research demonstrates that routine medical care has been associated with reduced ED visits and hospital admissions (Raphael et al., 2009). Perhaps, due to the larger study's recruitment methods (e.g., participants recruited from clinic), the sample obtained was one of patients who accessed routine medical care, thereby ultimately having a sample of youth with reduced ED visits and hospital admissions. While family-focused interventions for youth attending routine clinic visits may be important for addressing other outcomes, focusing on family environment may not lead to significant changes in ED visits and hospitalizations for youth with reduced HCU to begin with.

Additionally, in the present study, more than one-quarter of the sample (26.8%) was receiving chronic transfusion therapy and approximately one-quarter (22%) was being treated with hydroxyurea. In the literature, chronic transfusion and hydroxyurea treatments have been shown to decrease pain, thereby likely suppressing the variability of pain-related HCU in the present sample. In a study by Mize and colleagues (2014), individuals placed on chronic blood transfusions for pain crises had a significant

reduction in ED visits and hospitalizations. Further, results obtained from the Pediatric Hydroxyurea Phase III Clinical Trial (BABY HUG) indicate that hydroxyurea has been associated with significantly lower rates of initial and recurrent pain episodes and associated hospitalizations (Thornburg et al., 2012; Wang et al., 2011). The proportion of individuals accessing treatments that have been shown to reduce the occurrence of pain may also be partially responsible for the present sample's reduced number of ED visits and hospitalizations.

Results of the present study did not yield significant associations between history of stroke and HCU. Incidence of overt stroke was reported in the medical record for 7.3% of this sample, which falls within the range reported in the literature. Specifically, overt stroke has been reported to occur in approximately 5-8% of children with SCD (Balkaran et al., 1992; Ohene-Frempong et al., 1998). Further, 4.9% of youth in the present study sample demonstrated silent stroke per medical record review. This finding, however, is vastly different from the literature, which has indicated that as many as 20-30% of children with SCD evidence silent stroke (Pegelow et al., 2002; Steen et al., 2003). This large discrepancy may be attributable to the fact that silent strokes are clinically covert and can only be detected through brain imaging. As such, they are almost always incidentally found well after their onset (Dowling et al., 2009). Notably, data obtained pertaining to stroke history is limited and may not accurately reflect all silent strokes experienced by participants in the present study. Further, the use of chronic transfusion therapy and hydroxyurea has been shown to reduce the likelihood of occurrence or recurrence of stroke. As a result, history of stroke in this sample may be indicative of a sample with overall decreased risk.

While the existing literature has highlighted associations between age and HCU, results of the present study did not yield significant associations between these variables. Lack of significant findings may be due to limited variability within the study sample, as the present study consisted of youth between the ages of six and 13-years-old and did not include older adolescents or young adults. Specifically, older children have been found to have more frequent pain crises and disease complications, likely resulting in more hospitalizations and longer admissions compared to younger children (Panepinto et al., 2005; Platt et al., 1991; Sanders, Labott, Molokie, Shelby, & Desimone, 2010). In the literature, the lowest rates of HCU have been documented in youth aged five to nine years (Shankar et al., 2005), whereas rates of HCU are highest for youth between the ages of 10 and 19 years (Shankar et al., 2005) and those between the ages of 18 and 30 years (Brousseau et al., 2010).

As previously discussed, participants in the present study demonstrated more positive family environment and decreased pain-related HCU overall. In order to parse out potential group differences, participants were characterized by those with no documented ED visits versus those with one or more visits. This method of dichotomizing HCU has been used in previous studies (e.g., Aisiku et al., 2009; Eaton et al., 1995). Interestingly, gender was found to predict pain-related ED visit frequency, such that males had 4.71 times higher odds of utilizing the ED for pain than females. This finding is consistent with that of previous research, which suggests that males have more difficulty coping with SCD compared to females (Brown et al., 1993; Lemanek & Ranalli, 2009), and males are more likely to visit the ED than females (Yusuf et al., 2010). This may be due to the co-occurrence of alpha-thalassemia in SCD, which is

caused by mutations in the ATRX gene located on the X chromosome (Steinberg, Benz, Adewoye, & Ebert, 2018). Specifically, alpha-thalassemia has been shown to decrease disease severity by reducing the amount of sickled red blood cells, increasing the fetal hemoglobin level, and decreasing the intracellular hemoglobin S level (Sheehan et al., 2013). In the literature, SCD associated with two alpha-thalassemia alleles has been associated with decreased pain and lower ED visit rate (Abuamer et al., 2017; Rumaney et al., 2014).

In the present study, when examining subsamples based on frequency of pain-related ED visits, individuals in both groups obtained approximately the same mean score on the FRI (see Table 13). Notably, due to the present study's small sample size, the ability to dichotomize the HCU variable in other ways was limited. Perhaps youth with three or more documented ED visits (characterized as "high utilizers") are meaningfully different with regard to their family environment. Given that there were only eight participants with three or more documented ED visits, this could not be further examined.

Predicting Academic Achievement

The second and third aims of the present study intended to examine associations between patterns of HCU and academic achievement scores in math and reading one year later. Currently, there is little research linking HCU to academic achievement in youth with SCD, with existing studies using various measures of academic achievement (e.g., parent- and teacher-reported academic difficulties, statewide readiness assessments, and various achievement measures). In the literature, greater number of ED visits has been associated with lower levels of academic performance in kindergarten-aged youth with SCD (Finke, 2010). Additionally, youth with greater disease severity are more likely to

have been retained a grade, have increased parent-reported academic difficulties, and have greater likelihood of being evaluated for learning difficulties and receiving formal school-based accommodations (Mayes, 2011). As such, it was hypothesized that higher frequency of pain-related ED visits and hospital admissions in the previous year would be associated with lower scores on the Broad Math and Broad Reading clusters of the WJ-III Achievement. Contrary to these hypotheses, results indicated that neither pain-related ED visit frequency nor hospital admission frequency were associated with academic achievement in math or reading. Similarly, genotype, age, gender, and stroke status did not predict academic achievement scores in math or reading.

In addition, the exploratory aim of the present study sought to evaluate the indirect effect of family environment on academic achievement in math, as explained by patterns of HCU. While the literature that does exist is quite limited, family environment has not been found to be associated with academic achievement. However, as previously reviewed, decreased family functioning has been associated with poor health outcomes (Barakat et al., 2007). Additionally, youth with greater HCU and disease severity have evidenced lower levels of academic performance and decreased academic achievement (Finke, 2010; Mayes 2011). Taken together, it may be that psychosocial stressors (e.g., family environment) impact pain, thereby impacting pain-related HCU patterns, which, in turn, impact academic achievement. As such, it was hypothesized that frequency of pain-related ED visits and hospital admissions would mediate the relationship between family environment and academic achievement scores in math. Contrary to these hypotheses, results indicated that there was not an indirect effect of family environment on academic achievement through ED visit or hospital admission frequency.

Lack of significant findings across aims may be due to a variety of factors. Some of the same unique characteristics of the sample described above (i.e., demonstrating limited variability regarding family environment and HCU, decreased history of stroke) may, in part, explain the lack of significant findings. Additionally, other characteristics specific to this sample will be discussed below, including socioeconomic status (i.e., maternal education, household income) and race/ethnicity.

In the present study, mean scores on the Broad Math (*M* = 87.34, *SD* = 10.88, *range* = 64-118) and Broad Reading (*M* = 86.95, *SD* = 14.74, *range* = 50-113) clusters were in the low average range. These results are consistent with those of other studies (Nettles, 1994; Schatz et al., 2002; Swift et al., 1989), indicating that youth with SCD exhibit below average performance on tests of academic achievement. Additionally, when examining subsample scores based on frequency of pain-related ED visits in the present study, individuals without any documented ED visits scored approximately five points higher on Broad Math than youth with one or more ED visits. This had a moderate effect size, although it did not reach statistical significance. Interestingly, although the present study sample endorsed a more positive family environment, displayed low rates of pain-related HCU, was less likely to have a history of stroke, and excluded individuals with history of developmental disability or head trauma, mean academic achievement scores were still in the low average range. Despite the sample not including youth with likely risk factors, academic achievement was still negatively impacted, with scores extending as low as the “very low” range.

Some of the existing literature has also documented deficits in academic achievement in youth without known neurological disease (Fowler et al., 1988; Noll et

al., 2001; Swift et al., 1989). Previous studies have consistently found reduced hemoglobin levels (i.e., used as a proxy for reduced oxygen delivery to the brain) to be a risk factor for neurocognitive dysfunction in individuals with SCD (Hogan, Pit-ten Cate, Vargha-Khadem, Prengler, & Kirkham, 2006; Steen et al., 2005). Additionally, youth without history of stroke, but with elevated cerebral blood flow velocity on transcranial Doppler (TCD) ultrasonography, have demonstrated neurocognitive deficits. In a study by Kral et al. (2003), TCD values were classified according to the Stroke Prevention Trial in Sickle Cell Anemia (STOP; Adams et al., 1998). Although not statistically significant, youth with conditional TCD values (170-200 cm/sec) performed more poorly than youth with normal TCD values (<170 cm/sec) on measures of academic achievement in math and reading. As such, individuals with SCD who are neurologically asymptomatic are still at risk for neurocognitive deficits. Although the present study did not obtain data on hemoglobin or TCD values, decreased scores in academic achievement in this sample may be attributed to these reasons.

Academic achievement scores in math and reading were also examined as dependent variables in four of the multiple linear regression models. While controlling for all other independent variables, maternal education was found to have a medium size effect in each model (see Tables 6-9). Additionally, maternal education was significantly, moderately correlated with academic achievement scores in math. These findings are consistent with those in the literature, which indicate that higher maternal education is associated with improved academic achievement (Fowler et al., 1988; Smith et al., 2013; Tarazi et al., 2007).

In the present study sample, maternal education consisted of less than high school (22.5%), high school (37.5%), and at least some college or greater (40%). Additionally, almost half (46.3%) of the present study sample reported an annual household income of less than $19,999. An additional 19.5% of the sample reported an annual household income between $20,000 and $39,999. According to the federal poverty guidelines during the time which data was collected (i.e., between 2009 and 2013), the poverty level ranged between $14,000 (two-person family) and $22,000 (four-person family) per year (US Department of Health and Human Services, 2019). As such, much of the present study sample had a very low household income, likely indicative of living at or below poverty level. Another unique characteristic of the present study sample relates to race/ethnicity, as approximately 41.5% of the sample identified as Haitian. Lower maternal education may also be a result of immigration and differences in education systems, which may contribute to decreased academic achievement.

Strengths and Limitations

The present study has several qualities that make it a unique contribution to previous research. Strengths include a longitudinal study design, allowing for hypotheses with temporal predictions. Additional strengths include methods of assessment. Specifically, family environment was evaluated with a well-established measure in pediatric psychology, and academic achievement was assessed using a gold-standard measure of reading and math ability. Additionally, the use of medical chart review is considered an objective and standard measure of HCU in the literature.

There are also several limitations of the present study that should be considered. The most significant limitation is the sample size. This study's small sample size likely

limited statistical power and required greater effect sizes in order to find statistical significance. Sample size may have been limited for several reasons, including method of recruitment, attrition, and use of pre-existing data. The method of recruitment for the larger study consisted of a member of the research team approaching caregivers of pre-selected youth in clinic. As such, families who did not attend clinic or who were unable to schedule evaluations and were lost to follow-up were not included in the sample. Additionally, the present study used pre-existing data obtained from the larger, longitudinal study. As there was data missing throughout the dataset, the present study removed participants that did not have all variables of interest. By removing these participants, there may have been characteristics specific to these individuals that were not included, potentially limiting the generalizability of the findings. While longitudinal data is a strength of the present study, it may also have resulted in attrition over time, ultimately decreasing the size of the prospective sample. Notably, these are not just limitations because they lead to a smaller sample size, but also because they contribute to having a select sample that may not actually be representative of all youth with SCD. Because of this limitation, the present study sample's unique characteristics were described above.

Another limitation pertains to measures used in this study. The Family Environment Scale (FES), which was used to ascertain family environment in this study, relied entirely on caregiver report. This may be viewed as a limitation given that the existing research promotes the use of data obtained from multiple informants. Results obtained from youth on family functioning may have been different from that obtained from caregivers. Additionally, while medical chart review is considered an objective and

standard measure of HCU in the literature, reliance on this may present disadvantages in terms of lacking complete documentation of all instances of HCU. Instances of HCU were collected from one healthcare system, however, some participants may have visited other healthcare systems for pain-related ED visits or hospitalizations during the same time frame. As the researchers were only able to obtain data from one healthcare system, inclusion of multiple healthcare systems within the same area may have provided additional variability of results. While it is expected that these participants received emergency care at the same location they received their routine care, there is no way of confirming this. Perhaps a combination of methodologies, including self-report and medical chart review, would present a more complete assessment of HCU at any given point in time.

Conclusions, Clinical Implications, and Future Directions

The present study did not provide evidence of associations between family environment, HCU, and academic achievement. Unique characteristics of the present sample and limitations of the present study have been described as potentially contributing to these findings. The results of the current study do, however, suggest possible clinical implications and beneficial next steps for future research. Characteristics of the present study sample suggest that individuals with poorer health outcomes (i.e., high HCU, history of stroke) may have not been included in this study. It is notable that, despite this, difficulties with academic achievement remained. As such, there is a continued need for further research and policy changes.

Clinical implications. As previously discussed, the amount of youth in the present study without any documented pain-related HCU was greater than what has been

described in the literature. The most recent guidelines published by the NHLBI recommend that all infants, children, and adolescents with SCD be offered treatment with hydroxyurea to reduce SCD-related complications (National Heart, Lung, and Blood Institute, 2014). In addition to decreasing pain, hydroxyurea has also been recently shown to improve cognitive and academic functioning. In a study conducted by Wang et al. (2017), hydroxyurea treatment over a one-year period in children with SCD was associated with a significant improvement in IQ score. With regard to academic achievement, youth treated with hydroxyurea demonstrated improved reading comprehension on the WJ-III Achievement. While only 22% of the present sample was currently taking hydroxyurea,, these findings highlight the potential benefits of hydroxyurea in SCD, regardless of clinical severity.

The present study sample included families who primarily identified as African American or Haitian, as well as families with very low annual household income. Additionally, higher maternal education was found to be associated with increased academic achievement. These cultural and socioeconomic variables may be important in the context of academic achievement for several reasons. Previous research indicates that family involvement in school is important, particularly for youth from lower income and less educated families. These youth may be easily identified based on annual household income and maternal education, and may benefit from early identification, monitoring, or intervention to promote increased academic achievement. These youth may also benefit from higher levels of family involvement in the school system. However, barriers to involvement may exist, such as lack of parental familiarity in navigating the school system and difficulty obtaining appropriate school-based accommodations for their

children. As such, intervention studies focused on increasing parental involvement and supporting parents in developing strategies to improve academic outcomes may be beneficial. Intervention studies like that of the larger study may ultimately lead to improved outcomes. The larger study implemented a parent-focused intervention to improve academic success in youth with SCD. As part of the intervention, youth received neurodevelopmental evaluations, and parents were provided with relevant recommendations. These included recommendations to request school meetings in order to implement informal academic support in the classroom. Additionally, for youth whose performance indicated the need for formal special education services, a member of the research team was available to attend meetings at the school to facilitate accommodations based on recommendations made in the evaluation.

In addition, while family environment was not associated with pain-related HCU in the present study sample, there may be other reasons why family environment may likely be an important target of intervention for youth with SCD. Family-centered interventions have been shown to improve health outcomes in pediatric diabetes, particularly among adolescents with suboptimal metabolic control (Feldman et al., 2018; Wysocki et al., 2006). While family-based interventions have been less well studied in pediatric SCD, they also provide support for improved health outcomes (Kaslow & Brown, 1995; Shahine et al., 2015). Particularly, these interventions may not be applicable with a sample of individuals that has more positive family environment, lower HCU, and is younger in age. However, intervention studies focused on high health care utilizers, as well as adolescents and young adults may be beneficial.

Future directions. The present study leads us to several recommendations for future research. For example, future studies should include a larger sample, use of a managed care sample or large national database, or use of different recruitment methods. Access to a larger study sample would allow for the examination of HCU in different ways. Given the lack of variability among HCU and the large number of youth without any documented ED visits or hospital admissions in this study, it may be worthwhile to focus on individuals with high HCU in future studies. It may be that these individuals are meaningfully different with regard to their family environment and academic achievement. In the present study, due to the small sample size, it was not possible to dichotomize the HCU variable in ways that would have allowed for the examination of this. Researchers interested in continuing to study HCU may also aim to include a wider age range in their sample, including adolescents and young adults with SCD, as the literature has demonstrated that these individuals experience more frequent pain crises, disease complications, and HCU.

Although the use of large national databases would provide a much larger sample size and access to a wealth of data, these databases would likely not include information on other potentially relevant variables, including family environment and academic achievement. However, including this information in these databases could still be accomplished with the use of less comprehensive or reliable measures (e.g., giving a brief family environment measure, asking about grades in school). Additionally, there is a great need for continued funding of large multi-centered repositories of data, particularly those that have been developed in an interdisciplinary manner and consider multiple facets of an individual's environment, including family and school. Research conducted

as part of multi-centered studies would be particularly useful as this would specifically allow for the examination of youth classified as “high health care utilizers.” With regard to using different methods of recruitment, participants recruited in settings other than clinic (i.e., recruited from emergency departments or during inpatient hospital admissions) may result in a sample with more variable or representative HCU utilization.

Challenges with recruitment and attrition in the larger study from which this ancillary study was developed may be linked to the larger literature on engaging racial and ethnic minorities in research. Addressing the challenges of engaging racial and ethnic minorities in research ought to be a focus of future research. According to Yancey et al. (2006), there are low levels of participation of minority populations in health-related research. Perception of trust and mistrust of researchers and academic institutions has been found to be a central barrier to recruitment, particularly among African Americans. Specifically, mistrust has been cited as a barrier to study enrollment among the SCD community (Stevens et al., 2016). As such, additional research is needed to address differences related to culture and race/ethnicity. Given that our sample uniquely included a large number of African American and Haitian families, future research may want to expand upon this by including these populations in their study samples. Additionally, given the increased rate of immigration, more individuals with SCD are now living in the United States. In a recent study focused on families of children with SCD who emigrated from Africa, several factors were outlined that may likely lead to improved outcomes (Thornburg & Ware, 2018). These factors include acknowledging and addressing cultural differences, differences in medical history and experience, as well as differences in communication with schools to improve academic outcomes.

In conclusion, while the present study's hypotheses were not supported, research that considers other systems (e.g., family and school systems) that influence and are impacted by HCU remains important. Ultimately, future research aimed at determining modifiable psychosocial determinants of HCU and academic achievement in youth with SCD may help to accurately inform the design and implementation of much-needed interventions to improve outcomes in pediatric SCD.

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Appendix

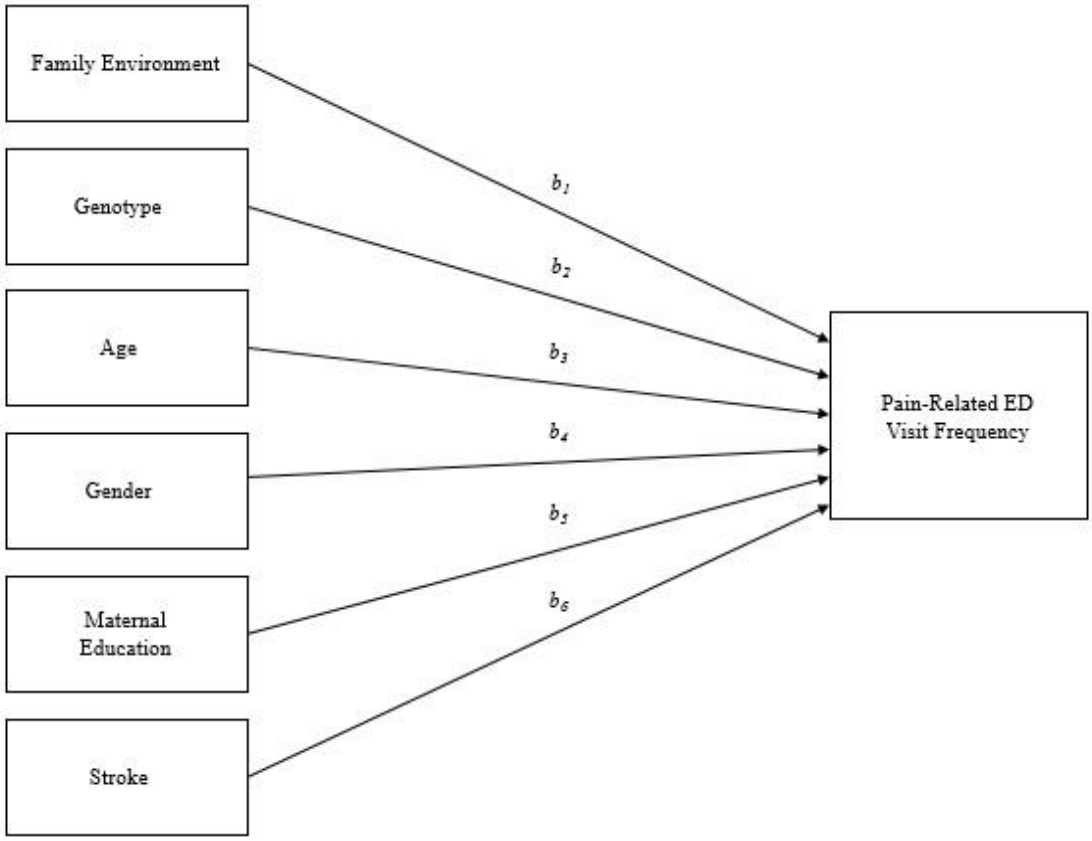

Figure 1. Proposed multiple regression model displaying family environment (at baseline), genotype, age, gender, maternal education, and stroke status predicting pain-related ED visit frequency in the following year.

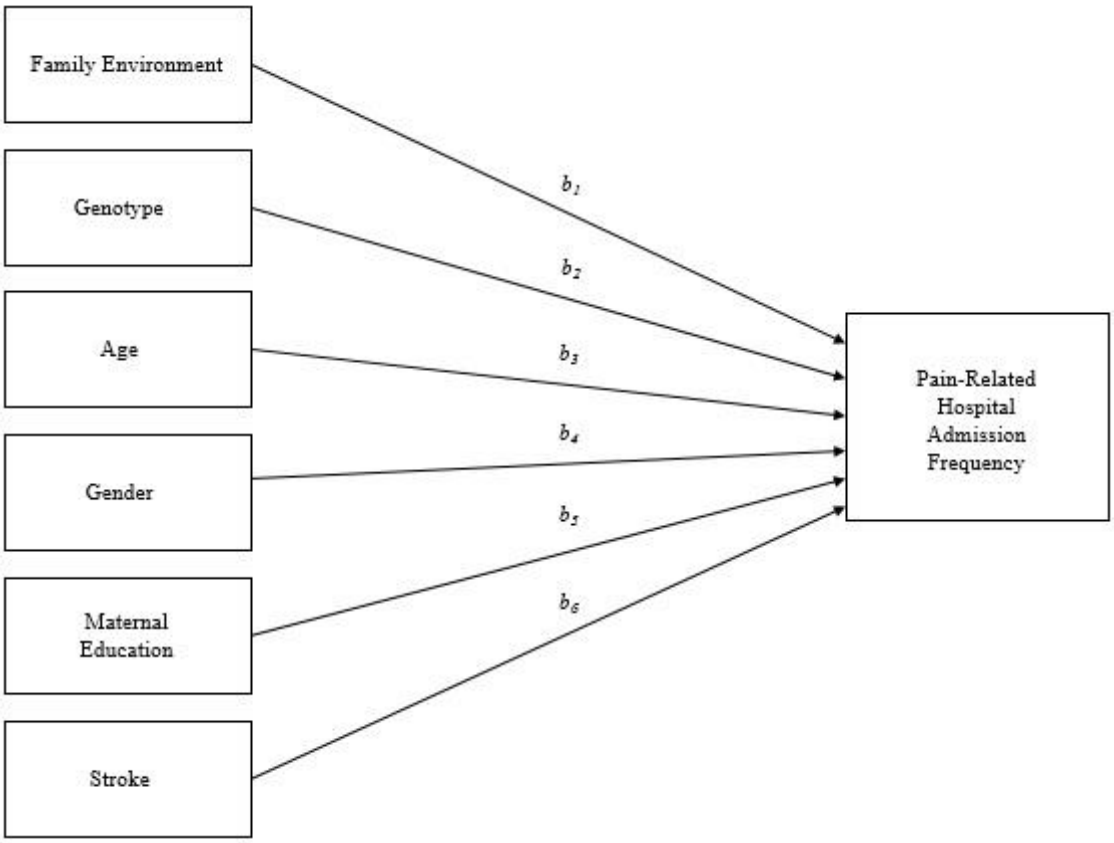

Figure 2. Proposed multiple regression model displaying family environment (at baseline), genotype, age, gender, maternal education, and stroke status predicting pain-related hospital admission frequency in the following year.

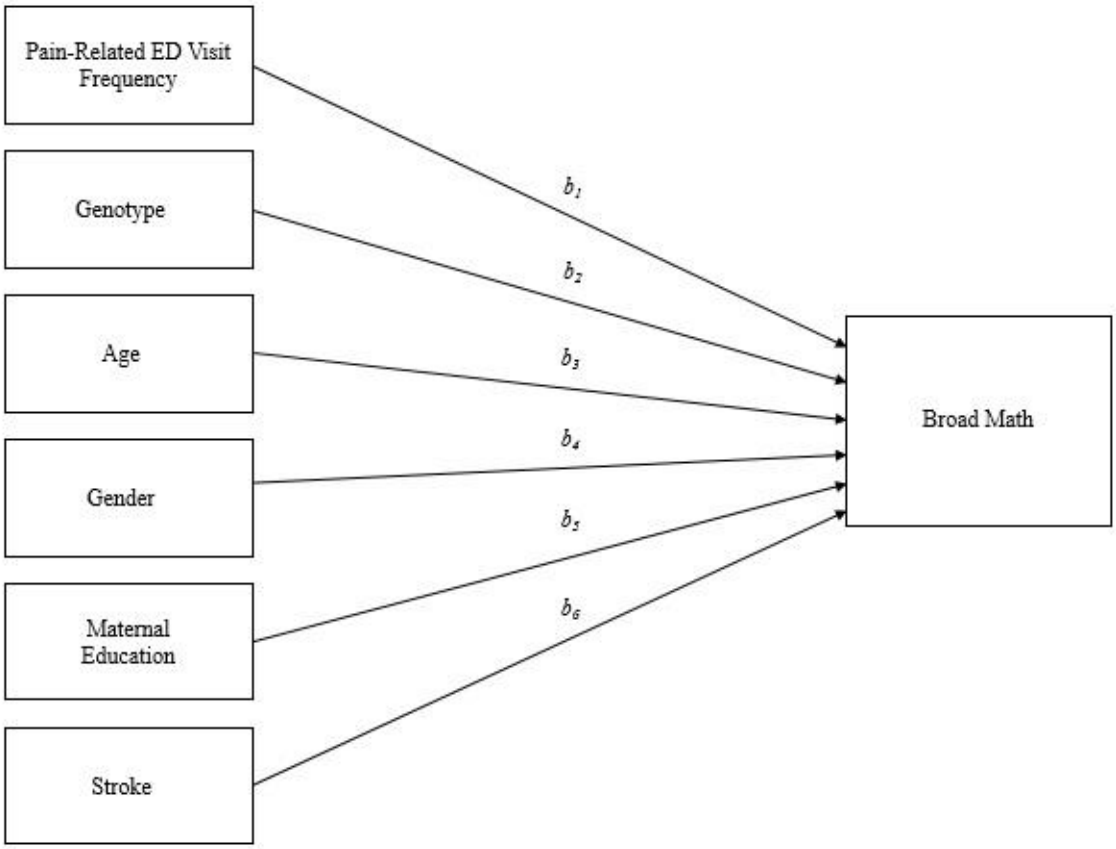

Figure 3. Proposed multiple regression model demonstrating pain-related ED visit frequency (in the previous year), genotype, age, gender, maternal education, and stroke status predicting Broad Math scores one-year post-baseline.

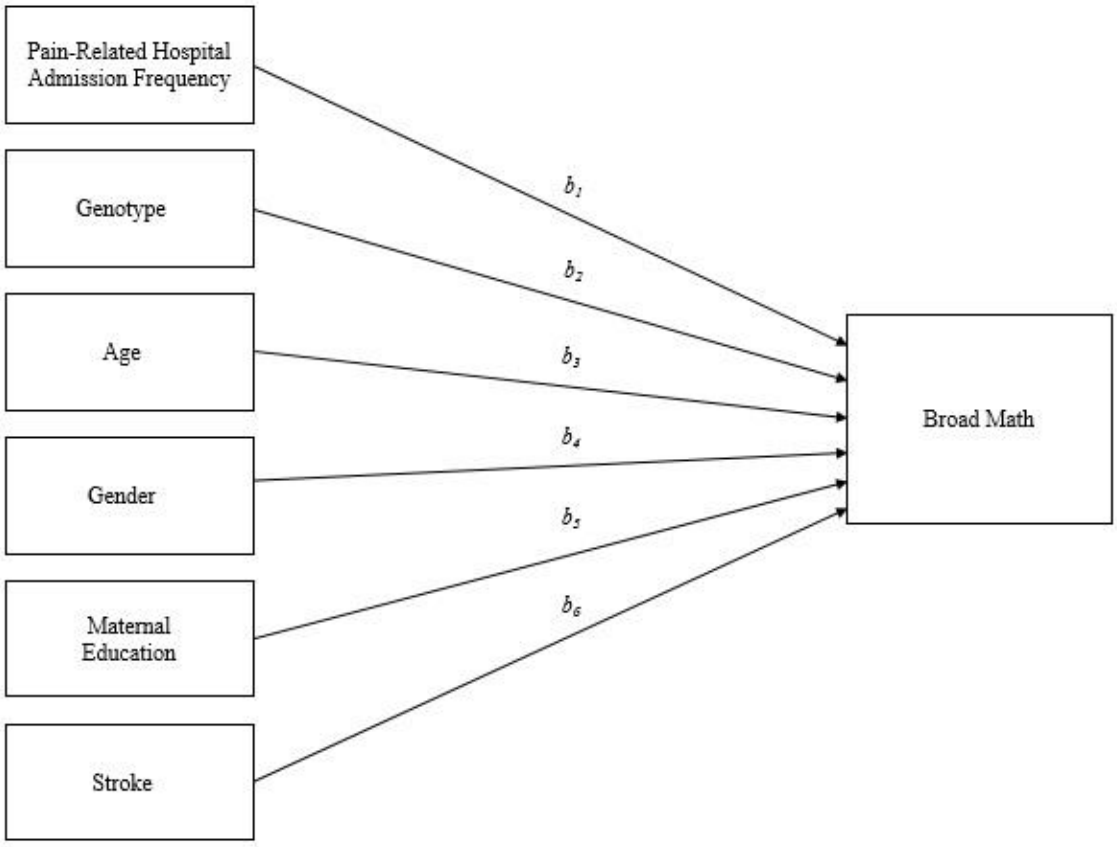

Figure 4. Proposed multiple regression model demonstrating pain-related hospital admission frequency (in the previous year), genotype, age, gender, maternal education, and stroke status predicting Broad Math scores one-year post-baseline.

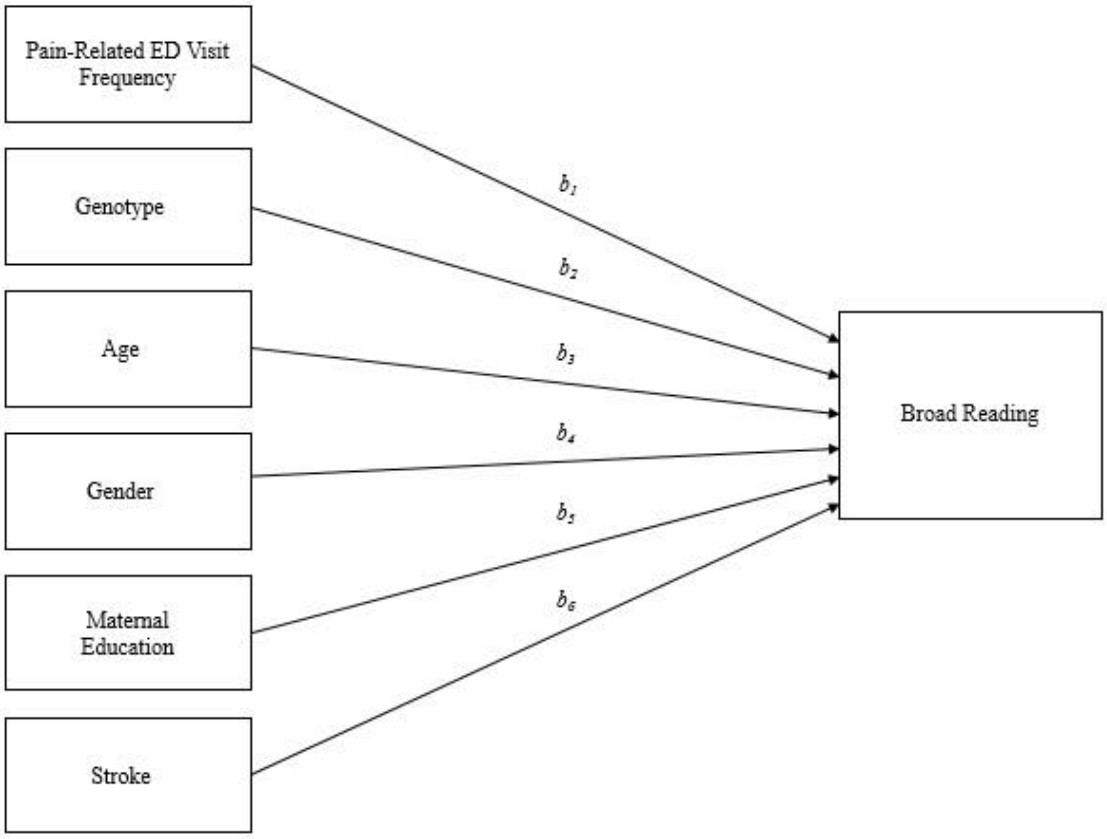

Figure 5. Proposed multiple regression model representing pain-related ED visit frequency (in the previous year), genotype, age, gender, maternal education, and stroke status predicting Broad Reading scores one-year post-baseline.

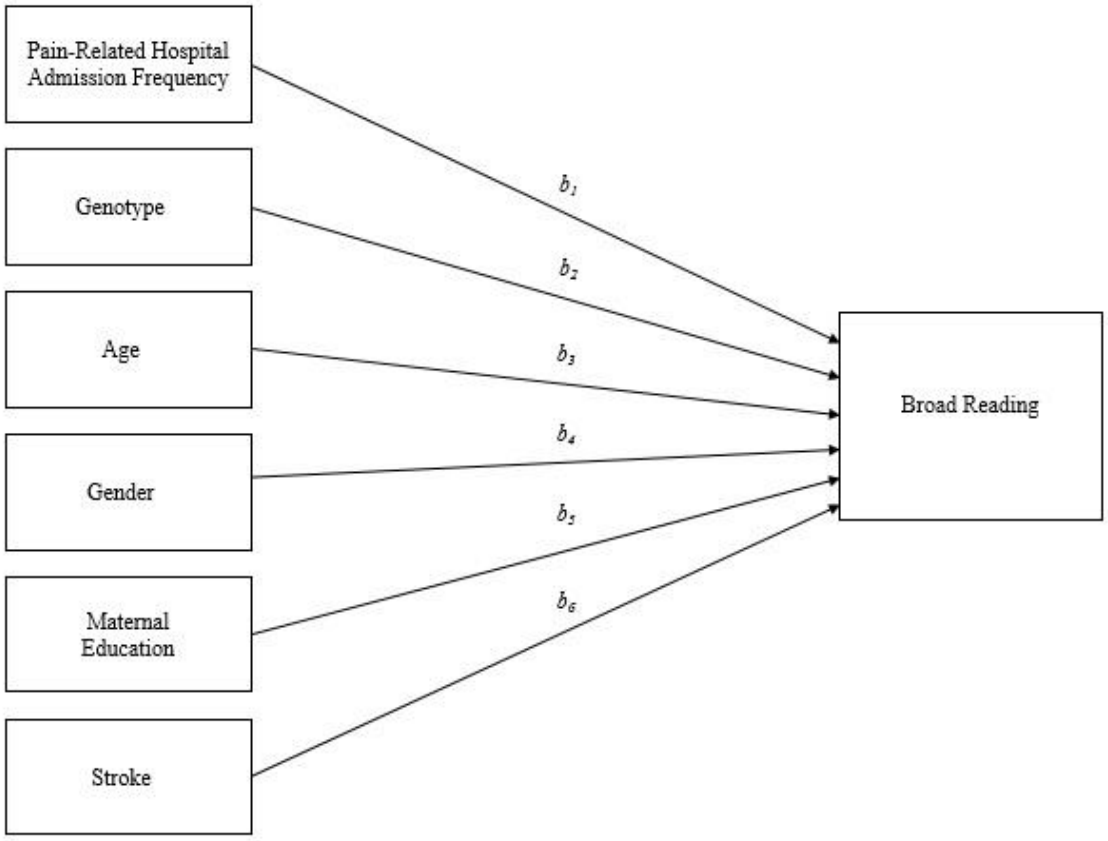

Figure 6. Proposed multiple regression model representing pain-related hospital admission frequency (in the previous year), genotype, age, gender, maternal education, and stroke status predicting Broad Reading scores one-year post-baseline.

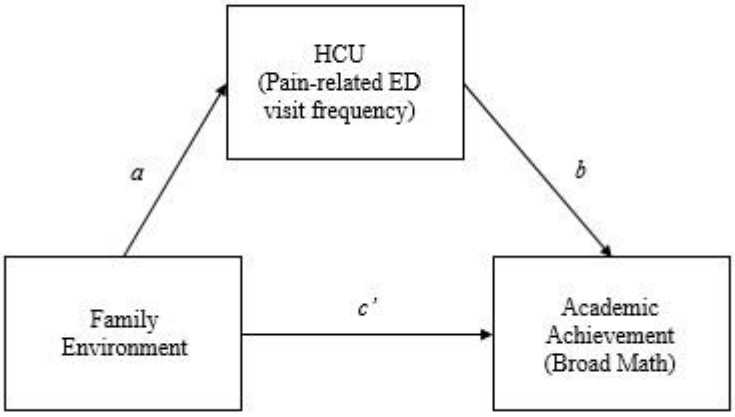

Figure 7. Proposed model of the relationship of family environment (at baseline) and academic achievement in math (one-year post-baseline), with HCU (pain-related ED visit frequency; between baseline and one-year post-baseline) as a mediator.

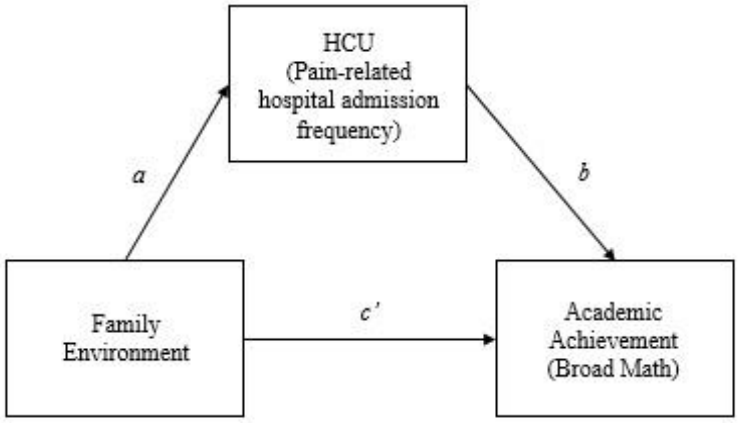

Figure 8. Proposed model of the relationship of family environment (at baseline) and academic achievement in math (one-year post-baseline), with HCU (pain-related hospital admission frequency; between baseline and one-year post-baseline) as a mediator.