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# COPING WITH PAIN AND HEALTH-RELATED QUALITY OF LIFE AMONG ADULTS WITH SICKLE CELL DISEASE

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# COPING WITH PAIN AND HEALTH-RELATED QUALITY OF LIFE AMONG ADULTS WITH SICKLE CELL DISEASE

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## ABSTRACT

### Objectives

The objectives of this dissertation are to: 1) to examine the psychometric properties of the CSQ-SCD among adult sickle cell disease (SCD) patients; 2) to identify psychosocial predictors of health-related quality (HRQOL) among adult SCD patients; and 3) to identify the distinct, multidimensional patterns of strategies for coping with SCD and their association with HRQOL among adult SCD patients in the United States.

### Methods

This cross-sectional study was conducted using a web-based self-administered survey. Adults with SCD were recruited with the help of Rare Patient Voice, a market research company that maintains a panel of SCD patients. Psychometric properties of the CSQ-SCD were assessed in terms of its construct validity and internal consistency reliability using confirmatory factor analysis (CFA) and further exploratory factor analysis was also conducted. Structural equation modeling (SEM) was used to test a theory-driven model to identify psychosocial predictors of HRQOL in the study sample. Finally, unobserved subtypes of coping patterns among adult SCD patients were evaluated using latent class analysis.

### Results

The study sample consisted of 196 adults SCD patients. The CSQ-SCD was found to have less than adequate psychometric properties. The CFA revealed a three-factor model for the CSQ-SCD but had a mediocre model fit. An exploratory factor analysis (EFA) revealed a three-factor model with different subscale loadings, demonstrating a better fit compared to the CFA model. Results from the SEM analysis suggested that crises severity, frequency, affective coping, and self-efficacy were key predictors of HRQOL among adults with SCD. The latent class analysis revealed three groups of underlying coping strategy patterns: cognitive coping, negative thinking/passive adherence coping, and physiological coping.

### Conclusions

The study results indicated that the CSQ-SCD has somewhat poor psychometric properties to assess coping in adults with SCD. Clinicians and caregivers of patients with SCD should aim to mitigate affective coping strategies and encourage more self-efficacy related behaviors while discussing treatment with patients. This study also shows that SCD patients do not utilize one single method of coping, but instead use multiple coping strategies to improve their HRQOL.

## DEDICATION

*This dissertation is dedicated to my beloved parents, Smita and Hemant Salkar, and my dear sister, Rasika Salkar who have always supported and encouraged me to go on every adventure, especially this one*

## LIST OF ABBREVIATIONS AND SYMBOLS

| | |
|---|---|
| AC | Avoidance Coping |
| ACS | Acute Chest Syndrome |
| ACSQ-Me | Adult Sickle Cell Quality of Life Measurement Information System |
| ACT | Acceptance and Commitment Therapy |
| AIC | Akaike's Information Criteria |
| AIDS | Acquired immunodeficiency syndrome |
| AVE | Average Variance Extracted |
| AVN | Avascular Necrosis |
| BIC | Bayesian Information Criteria |
| CA | Catastrophizing |
| CDC | Centers for Disease Control and Prevention |
| CFA | Confirmatory Factor Analysis |
| CFI | Comparative Fit Index |
| CI | Confidence Interval |
| CSQ | Coping Strategies Questionnaire |
| CSS | Calming Self-Statements |
| DA | Diverting Attention |
| EFA | Exploratory Factor Analysis |
| EI | Emotional Impact |
| EOC | Emotion Oriented Coping |
| ER | Emergency Room |
| ESRD | End-Stage Renal Disease |
| FDA | Food and Drug Administration |
| FS | Fear Self-Statements |
| HCM | Heat Cold Massage |
| HIV | Human Immunodeficiency Virus |
| HLA | Human Leukocyte Antigen |
| HRQOL | Health-Related Quality of Life |
| HSCT | Hematopoietic Stem Cell Transplant |
| HU | Hydroxyurea |
| IBA | Increasing Behavioral Activity |
| IPS | Ignoring Pain Sensations |
| IS | Isolation |

| | |
|---|---|
| ISOQOL | International Society for Quality-of-Life Research |
| KMO | Kaiser-Meyer-Olkin |
| LCA | Latent Class Analysis |
| LLCI | Lower-Level Confidence Interval |
| LMR | Lo-Mendell-Rubin |
| LPA | Latent Profile Analysis |
| MEDD | Morphine Equivalent Daily Doses |
| MHC | Medical History Checklist |
| MLE | Maximum Likelihood Estimation |
| MOS-SSS | Medical Outcomes Study- Social Support Survey |
| NHLBI | National Heart, Lung, and Blood Institute |
| NIH | National Institute of Health |
| OR | Odds Ratio |
| PH | Pulmonary Hypertension |
| PI | Pain Impact |
| QOL | Quality of Life |
| RMSEA | Root Mean Square Error of Approximation |
| RPS | Reinterpreting Pain Sensations |
| RS | Resting |
| SCA | Sickle Cell Anemia |
| SCD | Sickle Cell Disease |
| SCM | Self-Care Management |
| SCMSCD | Self-Care Management Sickle Cell Disease |
| SCMVP | Self-Care Management for Vulnerable Populations |
| SCSES | Sickle Cell Self-Efficacy Scale |
| SCT | Sickle Cell Trait |
| SD | Standard Deviation |
| SE | Standard Error |
| SEM | Structural Equation Model |
| SFI | Stiffness Impact |
| SI | Sleep Impact |
| SRMR | Standardized Root Mean Square Residual |
| STI | Stiffness Impact |
| TF | Taking Fluids |
| TLI | Tucker Lewis Index |
| UK | United Kingdom |

| | |
|---|---|
| ULCI | Upper-Level Confidence Interval |
| US | United States |
| VLMR | Vuong-Lo-Mendell-Rubin Likelihood Ratio Test |
| VOC | Vaso-Occlusive Crises |
| WHO | World Health Organization |

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# CHAPTER I

# INTRODUCTION

## STUDY OVERVIEW

Sickle cell disease (SCD) is a group of disorders that affects hemoglobin in the red blood cells.(1) People with this condition have abnormal hemoglobin molecules called hemoglobin S, which can distort red blood cells into a sickle, or crescent, shape.(2) Patients with SCD experience episodes of pain, called vaso-occlusive crises (VOCs) which can vary in intensity and can last for a few hours up to a few weeks.(3) In addition, patients with SCD often suffer from complications such as acute chest syndrome (ACS), chronic pain, stroke, priapism, joint complications and infections including chlamydia, haemophilus influenzae type B, salmonella, and staphylococcus.(1) SCD worsens over time thus placing a significant burden on the health-related quality of life (HRQOL) of patients with the disease.(4)

Existing literature has assessed the HRQOL of patients with SCD. The majority of these studies have reported that SCD affects the physical component of HRQOL of patients rather than the mental component, which was found to be similar to the general population.(5–10) However, many of these studies have disregarded the role of psychosocial variables such as social support, coping, and self-efficacy and their impact on the HRQOL of patients with SCD. Also, only a few of the studies which have evaluated coping among patients with SCD have utilized the only existing sickle cell specific instrument, Coping Strategies Questionnaire-SCD (CSQ-SCD). But the results of the factor structure of the CSQ-SCD measure are inconsistent in the existing

literature. Assessment of the psychometric properties of an instrument is essential to ensure the suitability of the use of an instrument in a particular patient population. Another key aspect of measuring coping is to explore the unobserved coping patterns of SCD patients using a person-centered approach (latent class analysis). This approach could provide more detailed findings compared to the traditional variable-centered approach (factor analysis) as several subpopulations with different coping patterns are examined and explained.(11) Compared to certain specific coping strategies, coping patterns are a better indicator of patient's overall preferences in how they deal with stressors and how the coping patterns affect the HRQOL.

Therefore, the general purpose of this dissertation is to 1) to examine the psychometric properties of the CSQ-SCD among adult SCD patients; 2) to identify psychosocial predictors of HRQOL among adult SCD patients; and 3) to identify the distinct, multidimensional patterns of strategies for coping with SCD and their association with HRQOL among adult SCD patients.

The rest of this chapter will provide a summary of SCD in terms of disease etiology, epidemiology, treatments, comorbidities, economic burden, and impact on patient HRQOL. This chapter also presents an overview of pain coping strategies utilized by patients with SCD, the measures of pain coping strategies as well as the theoretical framework to understand the quality of life in patients with SCD. Chapter 1 explains the need for and the research significance of this dissertation. Chapter 2 provides an evaluation of the psychometric properties of an instrument used to measure coping with pain (i.e., Coping Strategies Questionnaire-SCD [CSQ-SCD]) among adults with SCD. Chapter 3 assesses the psychosocial determinants of HRQOL among adults with SCD by employing a theoretical framework. Chapter 4 evaluates the distinct, multidimensional patterns of strategies for coping with SCD and their association with HRQOL among adults with SCD. Finally, Chapter 5 provides a summary of each of the studies, discusses

directions for future research and reports on supplemental analyses conducted on careless responding.

## Sickle Cell Disease

### *Overview of the disease*

Sickle cell disease (SCD) is one of the most common hereditary, hematological disorders. SCD is characterized by chronic hemolytic anemia and the occurrence of frequent, painful vaso-occlusive events.(12,13) Patients with this disorder have atypical hemoglobin molecules called hemoglobin S, which can alter red blood cells into a sickle, or crescent, shape.(14) Sickle cells die early and painful VOCs can occur when sickled red blood cells, which are stiff and inflexible, get stuck in small blood vessels.(2,14) These crises episodes deprive tissues and organs of oxygen-rich blood and can lead to chronic organ failure including asplenia, stroke, avascular necrosis, chronic lung disease, and chronic renal failure and dysfunction with ageing.(2,15)

### *Epidemiology*

SCD is the most common form of an inherited blood disorder and it affects millions of people worldwide.(16,17) SCD is particularly common among those whose ancestors came from sub-Saharan Africa, South America, the Caribbean, Central America, Saudi Arabia, India and Mediterranean countries such as Turkey, Greece, and Italy.(16,17) It is estimated that more than 300,000 children are born each year with sickle cell anemia (SCA), the most common type of SCD.(17–19) About two-thirds of them are born in Africa; Nigeria, India and the Democratic Republic of Congo take up half the global burden of SCA.(17–19) These numbers are anticipated to climb and by 2050, there will be about 400,000 children born with SCA annually.(17–19)

The (CDC) estimates that SCD affects approximately 100,000 Americans.(16) Furthermore, this number is expected to rise due to immigration trends and heredity effects.(20,21) One out of every 365 African American births (16,20,21) and 1 out of every 16,300 Hispanic-American births suffer from SCD.(16) About 1 in 13 African American neonate is born with sickle cell trait (SCT).(16)

***Disease Etiology***

SCD is caused by an abnormal hemoglobin called hemoglobin "S".(1) Sickle cell hemoglobin, unlike normal hemoglobin are inflexible and can adhere to vessel walls and cause a blockage that slows or stops the flow of blood.(1) Due to this oxygen is unable to reach nearby tissues and can cause sudden attacks of severe pain, called VOCs.(1) Because sickle hemoglobin cells are rigid and cannot move through blood vessels the sickle cells tend to burst apart.(1) Normal red blood cells live about 90 to 120 days, but sickle cells last only 10 to 20 days.(1) Therefore, in patients with SCD the body may have trouble keeping up with how fast the cells are being destroyed.(1) Because of this, the number of red blood cells these patients have is usually lower than normal and can cause lower energy levels.(1) There are three common types of SCD(14):

1) HbSS

In this form of SCD, patients inherit one sickle cell gene ("S") from each parent. This is the most severe form of the disease and is usually called sickle cell anemia.

2) HbSC

In this form of SCD, patients inherit a sickle cell gene ("S") from one parent and a gene for an abnormal hemoglobin called "C" from the other parent. This is generally a milder form of SCD.

3) HbS beta thalassemia

In this form of SCD, patients inherit one sickle cell gene ("S") from one parent and one gene for another type of anemia called beta thalassemia from the other parent. Beta thalassemia is of two types: "0" and "+". Patients with HbS beta 0-thalassemia typically have a severe form of SCD and patients with HbS beta +-thalassemia tend to have a milder form of SCD.

There are also a few rare types of SCD(14):

4) HbSD, HbSE, and HbSO

In these forms of SCD, patients inherit one sickle cell gene ("S") from one parent and another gene from an abnormal type of hemoglobin ("D", "E", or "O") from the other parent. There exists inconsistency in the severity of these types of rare SCD.

In addition, some individuals are classified as having the Sickle Cell Trait (SCT)(14):

5) HbAS

People with SCT inherit one sickle cell gene ("S") from one parent and one normal gene ("A") from the other parent. People with SCT normally do not have any SCD symptoms and live a normal life. But they can pass it on to their offspring.

***Treatment***

Treatment of sickle cell anemia is usually aimed at avoiding VOC's (also called pain crises), alleviating symptoms, and preventing complications. Treatments might include medications and blood transfusions. For a few children and adolescents, stem cell transplant may cure the disease.

*Blood and Bone Marrow Transplant*

Hematopoietic stem cell transplant (HSCT), which requires a human leukocyte antigen (HLA) matched sibling donor is the only cure for SCD today.(1,21,22) The indications for HSCT include stroke, positive transcranial Doppler result, and multiple ACSs or VOCs.(21) Most SCD

transplants are currently performed in children as the risk of infections and immune system problems (graft vs host disease) are higher in adults.(1) The event-free survival in SCD patients receiving HSCT is 85%.(1) Unfortunately, only 14% of SCD patients who have indications for HSCT have an HLA matched donor sibling.(1,21) Even with the high success rate, transplants still have risks including severe infections, seizures, and other clinical problems.(1,21) About 5% of people who have received such transplants have died.(1)

*Blood Transfusions*

Blood transfusions are commonly recommended to treat and prevent certain SCD complications.(21,23) Transfusion therapy may be used transiently in SCD to treat acute manifestations of the disease, such as aplastic crises, splenic sequestration, and ACS or can be used chronically to prevent stroke.(21,23) Even though lifesaving, transfusion also is coupled with iron overload, alloimmunization, and potential infectious complications.(21,23) If transfusion therapy is not used carefully, it is potentially risky due to the hyper viscosity of the sickle hemoglobin.(21)

SCD patients receiving chronic transfusion experience iron overload, typically after 1 year of monthly transfusion.(21) Chelation therapy with deferoxamine or the oral iron chelator deferasirox (Exjade®) should be started at that time.(21) The concerns of untreated iron overload include cardiomyopathy, cirrhosis, diabetes mellitus, and death.(21)

*Medications*

1) Hydroxyurea(1): Hydroxyurea (HU) was the first oral therapy approved by the FDA in 1997 for the treatment of SCD. HU is known to increase the amount of fetal hemoglobin (hemoglobin F) in the blood which provides some protection against the effects of sickle hemoglobin “S”. Studies in children and adults have shown that HU decreases SCD

complications such as reduced number of pain episodes, ACS, anemia, inflammation and dactylitis.

2) Endari (L-glutamine)(4): Endari was approved by the FDA in July 2017 for the treatment of SCD in patients aged 5 years and older. The oral medicine acts by making red blood cells more flexible thus decreasing their risk of getting trapped inside the blood vessels. This improves blood flow and increases the amount of oxygen reaching tissues.
3) Oxbryta (voxelotor)(1): Oxbryta was approved by the FDA in 2019 to treat sickle cell disease in patients age 12 years and older. Oxbryta, an oral medication, prevents red blood cells from forming the sickle shape and sticking together. This may lessen the destruction of some red blood cells, which in turn reduces the risk for anemia and improves blood flow to tissues. Probable side effects include headache, diarrhea, abdominal pain, nausea, fatigue, and fever.
4) Adakveo (crizanluzumab)(1): Adakveo was approved by the FDA in 2019 to reduce the VOCs in SCD patients 16 years and older. This intravenous medicine contains an antibody that blocks a protein in the blood vessels that binds to sickle cells, causing pain and inflammation when the sickle cells block blood flow. Potential side effects include nausea, joint pain, back pain, and fever.
5) Opioids: Opioid analgesics are the recommended treatment for VOC's and pain episodes in SCD.(22–24) A commentary paper by Ruan et al., 2017(25) stated that patients with SCD tend to use more opioids compared to other chronic pain conditions whereas other studies have reported a relatively low opioid use in SCD population in their daily life.(26,27) Two studies using large US claims databases (2009-2014) reported 40%-64% of SCD patients used opioids within 1 year, and the prevalence, dose and duration of

opioid use increased with age.(28,29) Furthermore, Ballas et al. (28) found that SCD patients transitioning into adult care (ages 18-30 years) had a marked increase in inpatient admissions, Morphine Equivalent Daily Doses (MEDD) and opioid days' supply in adults compared to patients below 18 years of age.(28) Moreover, Medicaid patients had a higher number of VOCs, healthcare use and opioid days compared to Commercial patients. Transition into adult care (ages 18-30 years) was associated with a marked increase in opioid utilization, inpatient admissions, and VOCs.

***Comorbidities in Patients with SCD***

As the life span for patients who have HbSS and HbSC has increased, a rise in the number of comorbidities is seen with age.(21,30) People with SCD can suffer both acute and chronic signs, symptoms, and comorbidities.

- Early signs and symptoms: The clinical manifestations of SCD appear during the primary postnatal year.(4,21,30,31) Within the US it is required that all newborns receive screening for SCD.(1) Initial symptoms of SCD may include: A yellow discoloration of the skin, known as jaundice, or whites of the eyes, known as icterus, fatigue from anemia or painful swelling of the hands and feet, referred to as dactylitis.(1)
- Acute comorbidities include VOCs, acute chest syndrome (ACS), stroke, acute renal disorder, priapism, splenic sequestration, hepatobiliary complications and acute ocular conditions and these can occur at any age.(1,4,21,30,31)
- Chronic comorbidities include avascular necrosis (AVN), leg ulcers, pulmonary hypertension (PH), diastolic heart dysfunction, gout, end-stage renal disease (ESRD) and ophthalmologic complications which increase with age.(1,4,21,30,31)

Many patients experience pain daily throughout their lives and acute VOC episodes are the most common symptoms and are major contributors in driving healthcare utilization in the emergency departments and inpatient settings.(30) This pain can even be chronic because of AVN of bone and leg ulcers or because of idiopathic etiology.(30) ACS is the leading cause of death in SCD for both children and adults. Chronic lung pathologies are more common among adults with SCD.(32,33) Repeated episodes of ACS can cause PH.(30,32) Stroke is the main neurological comorbidity in SCD.(1,21,30) SCD causes progressive end-organ damage to the kidneys and will lead to ESRD.(1,21,30) A growing fraction of SCD adult patients become dialysis dependent.(30) Priapism can result in male erectile dysfunction and patients may later require penile implants to revive their function.(1,21,30) Leg ulcers are a major reason of morbidity in SCD and could limit the mobility of adult patients, leading to stigma and reduced social interaction.(1,21,30) Ophthalmologic issues such as SCD retinopathy can lead to vision loss if left uncontrolled, and AVN of femoral head can result in total hip replacement.(1,21,30) Psychological issues are also prevalent amongst the SCD population. One study reported sleep disturbances in over 70 per cent of their cohort.(30,34,35) Sleep disturbances, together with the potential for ischemia-caused cognitive decline, the increased employment absences that may occur due to frequent hospitalizations and the physical difficulties in mobility may contribute to depression.(30) Depression is estimated to be present in at least 20 per cent of the sickle population.(30,34)

***Economic Burden of SCD***

Management of SCD can be very expensive given its chronicity, recurrent hospital admissions for acute VOCs (VOC's), treatment of complications, use of intensive care facilities, and multidisciplinary approach to management.(36) The primary driver of cost for managing

SCD, irrespective of the treatment regimen, is the cost incurred by the frequent inpatient hospitalizations for the VOC episodes.(36–41) VOC's are the most common clinical manifestation of SCD leading to frequent emergency department (ED) visits, hospitalizations, opioid consumption, and increased risk of shorter survival resulting in an estimated $2.4 billion in US health care costs annually.(41) Kauf et al.(37) reported the average lifetime cost of care for a patient with SCD is $460,151 using data from Florida Medicaid Program during 2001-2005.

The study by Bou-Maroun et al.(42) demonstrated that $ 0.9 billion was spent in pediatric SCD related healthcare annually and the median hospitalization cost was $14,337 per stay. The most common secondary diagnosis was VOC, recording 48,698 total hospitalizations and a median length of stay of 3 days.(42) Collectively, pediatric hospitalizations for VOC averaged $0.59 billion in annual expenditures and pediatric hospitalizations for ACS averaged $0.16 billion in annual expenditures.(42) The study concluded that inpatient hospitalizations for secondary manifestations of pediatric SCD were associated with significant healthcare expenditures.(42) Another study found that expenditures of children with SCD were 6 and 11 times greater than those of children without SCD enrolled in Medicaid and private insurance, respectively.(43)

Kauf et al.(37) reported that across the study sample, total health care costs generally rose with age, from $892 in the 0-9 age group to $2,562 in the 50-64 age group per patient-month. Average cost per patient-month was $1,389. Despite high medical utilization by SCD population, the nature, and costs of care, particularly among adults are underexplored. Most healthcare utilization and associated cost studies have focused on a specific ward of care, such as inpatient or ED and have used a state specific Medicaid dataset rather than providing a comprehensive and nationally representative understanding of the costs of SCD and related crises.

The advent of newborn screening mandates antibiotic prophylaxis, newer oral medications and better general medical care in regards of safer blood transfusions and antibiotics will aid in decreasing the rate of recurrence and severity of the SCD related complications and hence decrease the cost for health care.(36) However, these factors may be offset by the increased number and longer lives of patients and the increase in particularly costly complications among older adults such as pulmonary hypertension, renal failure, hemodialysis, iron overload, cardiomyopathy, etc.(36)

***Health-Related Quality of Life (HRQOL)***

The World Health Organization (WHO) defines health as "not merely the absence of disease or infirmity, but as a state of complete physical, mental and social well-being".(44) HRQOL describes "patients' appraisal of their current level of functioning and their satisfaction with it compared with what they perceive to be ideal health".(45) HRQOL is therefore a subjective representation of the patient's health. As patients may not be sensitive to changes in clinical or physiologic disease measures, HRQOL incorporates those physical, mental, social, and emotional aspects of wellbeing and functioning which matter to patients.(46) Moreover, people with comparable disease severities could have different assessments of their HRQOL.(47) Therefore, HRQOL has become an important outcome to be assessed in order to ensure optimal treatment and resource allocation decisions.(48)

Due to medical advances, many SCD patients now live well beyond early adulthood, while a complete cure in adults is not probable.(49) The median life expectancy of adults with sickle cell disease is improving but is still significantly below that of healthy individuals.(50) In SCD, functional status and health-related quality of life (HRQOL) are often deteriorated due to morbid events, such as stroke, chronic anemia, infections owing to splenectomy(5,51). Episodic,

debilitating pain is associated with substantial analgesic use, frequent hospitalization for VOCs, and ultimately organ failure.(5) The relationship of SCD complications to decreased HRQOL has been recognized for frequent sickle pain or opioid usage.(51) However, there are only a few factors that predict the frequency and severity of painful episodes, so the current focus is on acute management.(52) Additionally, the majority of SCD patients are not affected with frequent severe crises requiring hospitalizations (mean estimated overall rate of 0.8 episode per year)(50); instead, they have to live with a disease that impedes with their daily functioning. Brozovic et al. (53) found that 6% of patients accounted for more than 40% of hospital admissions, while Platt et al.(50) reported that 5.2% of patients accounted for almost one-third of all episodes of hospital admissions for pain.

McClish et al.(5) reported that patients with SCD scored significantly worse than US national norms on all subscales of HRQOL except mental health. HRQOL was equal to or poorer than patients with other significant chronic conditions such as cystic fibrosis, asthma, and hemodialysis in many domains.(5) Another study by Anie et al. also reported that adult SCD patients in the UK also had much lower HRQOL scores than general UK population norms.(49)

***Pain Coping Strategies in Patients with SCD***

Recurrent and unpredictable pain attacks are a major problem affecting individuals with SCD. There is great variability in the frequency and severity of these painful episodes.(54) Few patients may experience several painful episodes per month and need frequent hospitalizations and narcotic analgesics for pain relief, whereas others may rarely experience painful episodes.(54) Individuals also differ in their capabilities to cope with pain.(54) A few patients cope well, lead active lives, and are well-adjusted psychologically.(54) Many individuals are also able to manage pain on their own at home by increasing oral fluid intake, resting, and taking oral

analgesics, praying-hoping, and isolation, and less frequently reinterpreting or ignoring pain sensations.(55,56) While others may cope poorly, lead more limited lives, and are often unable to work.(54) Many of these patients have depression, anxiety, and are concerned with their physical symptoms.(57) Individuals may become exceedingly dependent on health care services for their pain management.(54)

Studies with other pain populations have reported that coping strategies are associated with responses to pain even after accounting for medical variables related to disease severity.(12,54,58,59) Literature indicates that coping strategies may be key factors in explaining some of the variation in adjustment to SCD related pain. In a study by Gil et al.(54), in adults with SCD, pain-coping strategies were related to multiple measures of adjustment. Pain-coping strategies described by negative thinking and passive adherence (e.g., catastrophizing, fear self-statements, resting, taking fluids) were associated with more severe pain episodes, less activity during painful episodes, more frequent hospitalizations and emergency room visits, and higher levels of psychological distress. Denial as a defense mechanism has been associated with fewer painful episodes.(60) Elliot et al. report that participation in social and work activities has been related to frequent home management of SCD pain, whereas less social connection has been associated with more frequent hospitalizations and more narcotic intake.(61) In comparison with conventional medical treatment alone, multidisciplinary approaches that include psychosocial components such as coping strategies appear to result in more effective management of SCD pain, with patients experiencing reductions in hospitalizations and emergency room visits.(61)

***Measure of Pain Coping in SCD***

Gil and colleagues (1989)(54) developed a sickle cell specific instrument for measuring coping associated with SCD related pain. These authors used an adaptation of the pain Coping

Strategies Questionnaire (CSQ) developed by Rosenstiel and Keefe (1983)(62), to devise a coping inventory for SCD. This instrument, the Coping Strategies Questionnaire-SCD (CSQ-SCD), is the only sickle cell specific pain coping instrument and consists of 13 subscales. Higher-order factor analysis (first-order factor analysis of scale scores) indicated that these 13 subscales fell into two factors: 'Coping attempts' and 'Negative thinking/passive adherence'.(54) The 'Coping attempts' factor consisted of self-calming statements, diverting attention, ignoring pain sensations, increasing behavioral activity, reinterpreting pain sensations, and praying and hoping.(54) The 'Negative thinking/passive adherence' factor consisted of negative cognitive responses such as catastrophizing and anger self-statements, jointly with 'passive' coping methods usually recommended by physicians, such as resting, heat and cold massages, taking fluids, and isolation.(54) Gil et al.(54) reported that negative thinking/passive adherence was positively related with the severity of pain, though not with the frequency or duration of episodes. Moreover, negative thinking/passive adherence was also associated with utilization of emergency room visits and hospitalizations independently of pain and clinical severity. A prospective study indicated that the negative coping factor was associated longitudinally with hospitalization, indicating that it may play a functional role.(49) A study by McCrae et al.(63) reported that negative thinking/passive adherence was positively associated with pain episode frequency, duration, and severity, after controlling for demographics and disease severity. Negative thinking/passive adherence was also positively related with activity reduction or hospitalization frequency after controlling for pain.(63) Negative thinking/passive adherence is also correlated with poor psychological adjustment.(64) These findings suggest that research on coping associated with SCD-related pain is important in indicating that psychological coping

responses are related to pain, adaptation, and health care utilization independently of clinical indicators of SCD.(49)

***Theoretical framework for understanding QOL in SCD***

The experience of living with a rare genetic condition is more complex than the simple management of its medical features. It can affect every aspect of a patient's quality of life. Quality of life (QOL) refers to "An individual's sense of overall well-being encompassing physical, psychological, emotional, social, and spiritual dimensions."(65) However, there is a lack of clarity as to what dimensions (i.e., physical, psychological, emotional, and social) contribute to QOL from the patient's perspective.(65) Previously, research into genetic conditions such as SCD had been limited to natural history and descriptions of clinical features. However, in recent years, QOL has been increasingly studied in genetic conditions such as SCD. These findings shed light on the personal experiences of individuals living with a genetic condition and the complicated and enormous effects on their QOL. Yet, advancement in this emerging area of research has been hindered by conceptual and methodological issues, and the health literature remains limited in completely representing the perspective of those affected with these conditions.(65) Most of the studies which have assessed predictors of QOL among patients with rare diseases have not utilized a conceptual framework. Using a theoretical framework can help researchers better understand the QOL of patients with SCD and the underlying predictors.

To arrive at a comprehensive understanding of the impact of SCD on patient well-being it becomes imperative to employ a theory-based evaluation. With respect to SCD and HRQOL, variables related to coping strategies, self-efficacy, social support, and socio-demographic appear to be the most significant constructs.(66–68) To address the relationships among these variables, the theoretical model of self-care management for sickle cell disease (SCMSCD) was adapted for

this dissertation. SCMSCD is based on the Theory of Self-Care Management for Vulnerable Populations (SCMVP) by Jenerette et al.(69). SCMVP proposes a method to identify variables that influence self-care management, health status, and QOL among populations who experience health disparities. The SCMSCD proposes that (i) vulnerability factors (socio-demographic and health-need factors) have a negative effect on both health outcomes (health status and QOL) and self-care management resources (assertiveness, self-efficacy, coping behaviors, social support, self-care ability, self-care actions, and communication skills); and (ii) self-care management resources positively mediate the relationship between vulnerability factors and health outcomes. Model relationships have been evaluated in prior published literature in SCD and other chronic illnesses.(67,70) One study (67) tested the SCMSCD model in a sample of 232 African American adults with SCD and stated that vulnerability factors had a negative effect on health outcomes. The study also found that self-care management resources did not mediate the relationship between vulnerability and health care outcomes. However, to satisfy the assumptions of normality as well as criteria for keeping variables for the SEM analysis, this study omitted theorized self-care management resource variables such as coping behaviors and self-care activities. Another study by Matthie et al.(71) examined the adapted SCMSCD model in a sample of 103 young adults (18-30 years) with SCD. The study reported that there was insufficient evidence to support a direct relationship between SCD self-efficacy, social support, years of education, and the number of hospital visits for crises. Additionally, the mediating effect of self-care management, among these variables was also non-significant. These studies (71,72) have not tested the SCMSCD model with coping and self-efficacy as mediators and have analyzed this model in only African American population and young adults. Thus, there is a need for the SCMSCD model to be tested in a more generalized population to enable a better

understanding of the relationships amongst psychosocial variables, vulnerability, and health outcomes such as HRQOL.

**NEED FOR THE STUDY**

1) Need to test the psychometric properties of the coping measure Coping Strategies Questionnaire-SCD (CSQ-SCD) among adult SCD patients.

Factor analyses of the CSQ-SCD in previous sickle cell study samples have produced contradictory results concerning the pattern of coping responses. The maladaptive negative thinking/passive adherence coping factor found by Gil et al.(54) seems to combine two different sets of responses: namely, negative thinking and passive adherence methods commonly recommended by clinicians.(49) However, these do not appear to be logically related as the passive adherence factor includes physiological strategies of coping to manage their pain at home while the negative thinking factor includes negative cognitive strategies which are associated with impaired quality of life. Findings from McCrae and Lumley(63) report that in their factor analysis of the CSQ-SCD that the negative thinking and passive adherence methods loaded on two separate factors. A study by Anie et al.(49) reported a three-factor structure of the CSQ-SCD reflecting active coping, affective coping and passive adherence coping. Gil et al.(54) and McCrae et al.(63) carried out principal component analysis to identify the underlying factor structure of CSQ-SCD in their study samples while Anie et al.(49) performed higher-order factor analysis (first-order factor analysis of scale scores). Given the extensive use of CSQ-SCD, there is a need to confirm the factor structure of CSQ-SCD in a different adult SCD population whilst performing higher-order confirmatory factor analysis.

2) Need to assess psychosocial predictors of HRQOL among adult patients with SCD.

Approximately 90% of the hospitalizations in SCD patients are due to pain crises. It is therefore essential to prevent these crises which necessitates the patient to undertake an active role in their disease management. Literature suggest that further research is needed to examine the self-care management process in the SCD population and to identify factors influencing self-care behaviors. The inter-relationships among variables need to be clearly identified to affect a change in the health outcomes of SCD patients. Therefore, to understand and reduce the hospital visits for crises, there is a need to examine the role of self-care management such as SCD pain-related coping behaviors, self-efficacy, social support; socio-demographic variables, and HRQOL in adults with SCD. Knowledge about these psychosocial factors will not only help healthcare providers and caregivers in improving care and support provided to SCD individuals but will also enable patients to better understand and self-manage their disease condition.

3) Need to identify the distinct, multidimensional patterns of strategies for coping with sickle cell disease (SCD) and their association with health-related quality (HRQOL) among adults.

Although studies show that people are likely to use a variety of coping strategies at the same time in several settings such as parenting,(73) caring for the mentally ill,(74) older adults,(75) or even for SCD patients,(49,54,63) a conventional variable-centered approach (i.e., factor analysis) still governs the research on coping,(76,77) including coping among SCD patients. The variable-centered approach aims at explaining relations between the variables of interest in a population(11). It often assumes a homogeneous pattern of coping and ignores the probability that people might amalgamate and utilize coping strategies in various ways(75). Literature suggests that this approach does not do a good job at capturing the distinct nature of the population which could lead to less precise and overgeneralized interpretations of study samples.(78) To overcome these shortcomings, a person-centered analytical approach (i.e., latent

class analysis)(79) is proposed in the current study, to explore the unobserved coping patterns of SCD patients. This approach could provide more detailed findings compared to the traditional variable-centered approach as several subpopulations with different coping patterns are examined and explained.(11) Furthermore, compared to certain specific coping strategies, coping patterns are a better indicator of patient's overall preferences in how they deal with stressors(77) We also expect that coping patterns affect the HRQOL. No study has investigated the coping patterns of SCD patients and their impact on HRQOL, but prior studies on other chronic conditions provide some understanding. For example, Kroemeke(76) demonstrated that older adults with chronic conditions showed heterogeneity in coping patterns and their relationship with HRQOL psychological domain changed longitudinally.

**SPECIFIC AIMS AND OBJECTIVES**

1. To examine the psychometric properties of the Coping Strategies Questionnaire- Sickle Cell Disease (CSQ-SCD) among adult SCD patients in the United States
    i. Assess the construct validity (convergent validity, discriminant validity, factorial validity) of the CSQ-SCD instrument; and
    ii. Assess the reliability and floor and ceiling effects of the CSQ-SCD instrument.
2. To evaluate psychosocial predictors of HRQOL among adult SCD patients in the United States
    i. Identify psychosocial determinants of HRQOL in a sample of US adults with SCD by employing a modified version of the Jenerette et al. (2006) model of Theory of Self-Care Management - Sickle Cell Disease (SCM-SCD) that describes variables that influence self-care management, health status, and quality of life. This study

specifically assessed the relationship between disability, social support, coping, self-efficacy, and HRQOL among adult SCD patients using a structural equation model.

3. To identify the distinct, multidimensional patterns of strategies for coping with sickle cell disease (SCD) and their association with health-related quality (HRQOL) among adults.

   i. Characterize the latent subtypes of the coping patterns among adult SCD patients in the United States;

   ii. Examine the significant correlates of these coping patterns; and

   iii. Investigate the relationships between the coping patterns and HRQOL.

# CHAPTER II

# AN ASSESSMENT OF THE PSYCHOMETRIC PROPERTIES OF THE COPING STRATEGIES QUESTIONNAIRE – SICKLE CELL DISEASE (CSQ-SCD) AMONG ADULTS WITH SICKLE CELL DISEASE (SCD) IN THE UNITED STATES

## INTRODUCTION

Sickle cell disease (SCD) is an autosomal recessive genetic disorder of hemoglobin structure characterized by deformed red blood cells.(80) The most common symptomatic manifestations of SCD are acute episodes of ischemic pain, termed vaso-occlusive crises (VOCs) or pain crises.(80) The frequency and severity of VOCs episodes is greatly variable. Some patients experience several episodes per month and need recurrent hospitalizations and narcotic analgesia for pain control, while others only occasionally experience pain crises.(81)

Individuals with SCD also vary in their abilities to cope with SCD-related pain.(54,82) Literature suggests that psychological coping responses defined as behavioral and cognitive efforts made by individuals in attempts to deal with stressful situation, are related to pain, adaptation, and health service utilization after controlling for clinical indicators of sickle cell disease.(12,83–85) A study by Gil et al. reported that after controlling for demographics and disease severity measures, the pain coping strategies factors significantly enhanced their ability to explain the variance in pain severity.(54) While pain severity is a relatively consistent predictor of health service utilization across several studies,(54,83,86–88) coping strategies such as negative thinking and passive adherence coping strategies have also been found to be

associated with greater service utilization.(82) Therefore, coping has evolved as an important factor among patients with SCD.

The Coping Strategies Questionnaire (CSQ-SCD) is a commonly used SCD specific coping measure devised by Gil et al.(54) and consists of 13 subscales. Gil et al.(54) reported that the CSQ-SCD captures information regarding two dimensions of coping, 'Coping attempts' and 'Negative thinking/passive adherence'. Previous factor analyses of the CSQ-SCD have produced inconsistent results concerning the pattern of coping responses. The negative thinking/passive adherence coping factor identified by Gil et al.(54) seems to combine two different sets of responses; namely, negative thinking and adherence to passive techniques commonly recommended by clinicians. However, these do not appear to be logically related as the passive adherence factor includes physiological strategies of coping to manage their pain at home such as resting, taking fluids or heat/cold massage while the negative thinking factor includes negative cognitive strategies such as catastrophizing, fear self-statements, anger self-statements, praying and hoping, and isolation which are associated with impaired quality of life.(83) McCrae and Lumley(63) found in their factor analysis of the seven subscales of 'Negative thinking/passive adherence' that they load onto two separate factors namely negative thinking and passive adherence. Anie et al.(83) conducted higher-order factor analysis on a sample of SCD patients in UK and reported a 3 factor structure of CSQ-SCD (active coping, affective coping and passive adherence coping). McClish et al.(80) followed the methods of Anie et al.(83) and also reported the same three-factor structure of CSQ-SCD in a sample of individuals with SCD in the United States (US).

Although the CSQ-SCD has been used to assess pain coping strategies in SCD patients, there is considerable heterogeneity in the methods used to assess the factor structure of CSQ-

SCD. Studies have previously used principal components analysis(63), exploratory factor analysis (EFA)(54), and higher-order factor analysis (i.e., first-order exploratory factor analysis of scale scores)(80,83). The study by Anie et al.(83) was conducted in a UK population. Even though the study by McClish et al.(80) was done in a US population it does not provide complete information regarding the higher-order factor analysis methods used. Since the factor structure is easily affected by sampled data, repetitive revalidation studies are considered necessary to overcome the sampling bias and to confirm the latent variable structure.(89) Therefore, to obtain evidence about the appropriateness of use of the CSQ-SCD among SCD patients in the US, the aim of this study was to investigate the higher-order factor structure of CSQ-SCD with a new sample of adult SCD patients, to identify the structure of latent variables. The study also evaluated the convergent and discriminant validity, and reliability of the CSQ-SCD instrument.

## METHODS

### Study Design

The current study utilized a cross-sectional design by means of a web-based, self-administered survey distributed to a convenience sample of adults with SCD in the United States. Study approval was obtained from the University of Mississippi Institutional Review Board (Protocol #21x-130).

### Study Sample

For the purposes of the current study, the study sample included adults (≥ 18 years of age) with SCD. The sample was recruited with the help of Rare Patient Voice, a market research company that maintains a panel of SCD patients. Most of the patients in the panel have been recruited at SCD-related conferences and patient advocacy group meetings across the United States. Given the nature of the statistical analysis plan for this study (i.e., structural equation

modeling (SEM)), an a priori sample size of 200 patients with SCD was considered to be adequate.(90)

**Study Methodology**

The survey instrument for the current study included the following measures: CSQ-SCD, Adult Sickle Cell Quality of Life Measurement Information System (ASCQ-Me) pain episode measure, patient demographics, and ASCQ-Me SCD medical history checklist. Study participants were initially sent an email describing the objective and scope of the larger study. This email ensured the respondents that their information would be kept confidential. The email also included a URL link to the survey which was designed and hosted in Qualtrics (Qualtrics Inc, Provo, UT). All respondents were provided $15 Amazon gift cards for participation in the study.

**Study Measures**

***Coping Strategies Questionnaire- Sickle Cell Disease (CSQ-SCD)***

Gil and colleagues (1989) developed the only existing sickle cell specific instrument, the Coping Strategies Questionnaire (CSQ-SCD) consisting of 13 subscales (80 items), for measuring coping associated with SCD related pain.(54) Gil et al. reported that underlying these 13 subscales were two factors: 'Coping attempts' and 'Negative thinking/passive adherence'.(54) According to Gil et al., items from the subscales of self-calming statements, diverting attention, ignoring pain sensations, increasing behavioral activity, reinterpreting pain sensations, and praying and hoping are indicators of the 'Coping attempts' factor while negative cognitive responses such as catastrophizing and anger self-statements, jointly with 'passive' coping methods usually recommended by physicians, such as resting, heat and cold massages, taking fluids, and isolation are indicators of the 'Negative thinking/passive adherence'.(54) Patients can

rate their use of each coping strategy response from 0 = never to 6 = always. Two additional aspects are assessed by single items: perceived ability to control pain, rated from 0 = no control to 6 = complete control, and perceived ability to decrease pain, rated from 0 = can't decrease it at all to 6 = can decrease it completely.(84) Item responses are averaged to produce a mean for each subscale.(84) However, if a subscale consists of less than 2 item responses then the mean for that subscale was not calculated.

***ASCQ-Me Pain Episode Measure***

The ASCQ-Me pain episode measure is a sickle cell specific question set and includes five questions regarding the frequency, timing, and severity of sickle cell pain events. The first question in the set asks about the number of pain attacks in the last 12 months on a scale of 0 = no pain attacks to 4 = 4 or more attacks (Item 1), while the second question (Item 2) asks about the timing of the most recent attack on a scale of 0=never had a panic attack to 7 = I have one right now. The other three questions ask about the severity of the most recent pain attack on a scale from 0 = no pain to 10 = worst imaginable pain (Item 3), the extent to which the pain attack interfered with the respondent's life on a scale from 0 to 5 (Item 4), and the duration of the attack on a scale from 0 to 7 (Item 5). A higher composite score on both severity and frequency questions separately represents more frequency/severity of SCD. In the US setting, the ASCQ-Me has been shown to have excellent internal consistency for each item bank (≥.90) and the item banks differed significantly between SCD severity levels.(68)

***Socio-demographic variables and medical history***

A demographic questionnaire was used in the study to gather information from participants regarding age, sex, race, level of education, employment status, living status and SCD genotype.(67) The questionnaire also included questions on access to opioid medications

and impact of COVID-19 on patients quality of life. The ASCQ-Me SCD Medical history checklist (SCD-MHC), a sickle cell specific checklist, was utilized to determine the conditions associated with SCD. The ASCQ-Me SCD-MHC consists of a list of several treatments and conditions related with SCD, with responses of "yes" or "no" to suggest whether the respondent has that condition or takes that treatment. The score for the checklist is simply the sum of the number of questions with a "yes" response.

**Statistical Analysis**

***Sample description***

Descriptive statistics calculated in the form of frequencies and percentages for categorical variables and means and standard deviations for the continuous variables are reported.

***Item-level descriptives***

Item-level analysis of the CSQ-SCD was conducted in terms of response frequencies as well as means, and standard deviations (SD). The item-response patterns are presented as the frequency and percentage of each response. Missing data was treated as a category with the number of subjects with missing responses included in the calculation of the percentages. Kurtosis and skewness coefficients were also calculated.(90)

***Missing data analysis***

For CFA, which was used to establish the factorial validity of the CSQ-SCD, the total available sample was used for the analysis rather than the listwise deletion approach.(91)

***Factorial validity***

Utilizing the response from adult patients with SCD, the factor structure of the CSQ-SCD instrument was evaluated using higher-order confirmatory factor analysis (CFA), an SEM technique used to assess the fit of a theoretically constructed model. The commonly tested

models for CSQ-SCD are a two-factor (54), second-order factor model (using mean subscale scores as factor indicators) (Gil et al.) and a three-factor (83), second-order factor model (using mean subscale scores as factor indicators) (Anie et al.). However, the Gil et al. study has conducted an exploratory factor analysis while Anie et al. describes to have conducted a higher-order factor analysis.(54,83) The Anie et al. study, however, reports results of an exploratory factor analysis using the mean subscale scores as factor indicators. In the current study, both these models were tested using a higher-order CFA, where the mean subscale scores were used as factor indicators. For the two-factor, second-order model (based on Gil et al. study(54)), the diverting attention (DA), reinterpreting pain sensations (RPS), calming self-statements (CS), ignoring pain sensations (IPS), praying and hoping (PH), and increasing behavioral activity (IBA) subscales were allowed to load on to the coping attempts factor. The remaining 7 subscales of catastrophizing (CA), fear self-statements (FS), anger self-statements (AS), isolation (IS), taking fluids (TF), resting (RS), and heat/cold/massage (HCM) were allowed to load on to the negative thinking/passive adherence factor. Both factors were allowed to correlate. For the three-factor, second-order model (based on Anie et al. study(83)) the subscales IPS, CS, IBA, DA and RPS were allowed to load on to the active coping factor, while the subscales CA, AS, FS, PH and IS were allowed to load on to the affective coping factor.(92) The passive adherence factor consist of the subscales RS, TF and HCM. All three second-order factors were allowed to correlate.(92) Because all the items on the CSQ-SCD are evaluated on a continuous scale, we used maximum likelihood estimation (MLE) to compute the hypothesized relationships.(93) All CFA models were estimated using Mplus version 8.4.(94) The following five fit statistics were assessed for each model: $\chi 2$ statistic, the root mean square error of approximation (RMSEA), the Tucker Lewis Index (TLI), the comparative fit index (CFI), and the standardized root mean

square residual (SRMR). Bagozzi and Yi(95) suggest that for a well-fitting model, the RMSEA, TLI, CFI must be ≤ 0.08, ≥0.92, and ≥0.93 respectively. For a good fitting model, SRMR must be less than 0.08.(96)

***Convergent Validity***

The basic property of convergent validity is that items/subscales which indicate a particular latent construct should correlate strongly with each other or share a high proportion of variance compared to items/subscales from other latent construct.(97) Factor loadings, average variance extracted (AVE), and first-order factor correlations were used to estimate convergent validity among item measures.

The size of the factor loading is an indication of the amount of variance in an item that is explained by the latent construct. For the current study, standardized factor loadings of 0.5 or higher were considered indicative of good construct validity.(98) Statistical significance of the factor loadings was the minimum requirement because a significant loading could be weak or moderate in strength.

For each latent construct the AVE was computed as the total of all squared standardized factor loadings divided by the number of items loading onto that factor. Hair et al. suggests that an AVE of 0.5 or greater is suggestive of good convergent validity because an AVE below 0.5 implies that the error variance remaining in the indicators is greater than the variance explained by the latent factor.(99)

Pearson's correlation between scores of first-order factors (average of subscale scores) underlying the same second-order factor indicated that expected first-order factors under the same second-order factor correlate strongly with each other. Correlations of 0.1-0.29 are considered small, 0.3-0.49 as moderate, and ≥ 0.5 is considered to be strong.(100) A strong

correlation of the IPS, CS, IBA, DA and RPS sub-scales underlying the active coping latent factor was hypothesized. A strong correlation of the CA, AS, FS, PH and IS sub-scales underlying the affective coping latent factor was hypothesized. Similarly, a strong correlation between the RS, TF and HCM sub-scales underlying the passive adherence latent factor was hypothesized.

***Discriminant Validity***

The basic property of discriminant validity is that items/subscales which make up a latent construct should correlate poorly with other latent constructs.(97) In the present study we employed the following methods to assess the discriminant validity of the three coping factors of the CSQ-SCD. First, the fit of the best fitting 3-factor model obtained from the factorial validity analysis was compared to that of a similar model where the latent factor correlation (i.e., correlation between active coping, affective coping, and passive adherence coping) was fixed to 1 (latent construct discriminant validity). This test was carried out using the MODEL TEST option in Mplus.(92,94) A significant difference in the model fit (Wald's $\chi 2$ statistic) was suggestive of discriminant validity.(101) However, this is not a strong test of discriminant validity because even a high very correlation between the two constructs ($\geq 0.90$ or higher but not exactly 1) would indicate adequate discriminant validity.

Second, the difference between the AVE for each latent construct and the square of the correlation estimate between the two constructs was calculated. A positive difference (i.e., the two AVE's exceed the sum of the square of the correlation between the respective latent constructs) suggests that the latent construct explains a greater proportion of the variance in its indicator items as compared to the variance shared with another latent construct, indicating discriminant validity.(102)

Third, correlations of ≤ 0.40 between first-order factors (average of subscale scores) underlying the same second-order factor with first-order factors (average of subscale scores) underlying separate second-order factors was indicative of discriminant validity. It was hypothesized that a weak correlation of the subscales IPS, CS, IBA, DA and RPS with the subscales underlying affective coping and passive adherence coping. Similarly, a weak correlation between the CA, AS, FS, PH and IS sub-scales with subscales underlying active coping and passive adherence coping was hypothesized. Also, a weak correlation between the RS, TF and HCM sub-scales with subscales underlying the active coping and affective coping was hypothesized.

***Internal consistency reliability***

To assess the internal consistency reliability for the CSQ-SCD, Cronbach's alpha (α) and McDonald's omega were calculated for the active coping, affective coping, and the passive adherence coping factors. A Cronbach's $\alpha \geq 0.70$ was suggestive of adequate internal consistency reliability, with values $\geq 0.80$ considered preferable.(103)

**RESULTS**

**Socio-demographic and clinical characteristics**

The final study sample consisted of 196 adults with SCD (Table 2.1). The majority of the study population included patients with Hemoglobin SS (sickle cell anemia) (68.88%), females (86.22%), and were African American (83.67%). Most of the patients lived with someone (71.94%), had more than high school education (75%), and were unemployed (49.49%). Patients also commonly suffered from more than 2 medical health conditions (58.16%), had an average of 3 sickle cell pain attacks (crises) in the past year and for most of them their pain attack (crisis) lasted for 1-3 days (32.65%). The mean sickle cell pain severity

score (51.95) and frequency scores (51.41) were similar to the average score of 50 (for both severity and frequency) in the reference population.(104)

**Table 2.1: Demographic and clinical characteristics of the study sample (N=196)**

| Characteristics | N (%) |
|---|---|
| **SCD Type** | |
| Hemoglobin SS (SCA) | 135 (68.88) |
| Other* | 61 (31.12) |
| **Age, Mean (SD)** | 36 (9.88) |
| **Gender** | |
| Male | 27 (13.78) |
| Female | 169 (86.22) |
| **Race/Ethnicity** | |
| African American/Black | 164 (83.67) |
| Other++ | 13 (6.63) |
| Missing | 19 (9.69) |
| **Living Status** | |
| Living alone | 35 (17.86) |
| Living with someone | 141 (71.94) |
| Missing | 20 (10.20) |
| **Education Level** | |
| High school or less | 30 (15.31) |
| More than high school | 147 (75.00) |
| Missing | 19 (9.69) |
| **Employment Status** | |
| Employed (full time/part-time) | 80 (40.82) |
| Unemployed | 97 (49.49) |
| Missing | 19 (9.69) |
| **Region** | |
| Northeast | 46 (23.47) |
| Midwest | 38 (19.39) |
| South | 69 (35.20) |
| West | 23 (11.73) |
| Missing | 20 (10.20) |
| **Insurance** | |
| Yes | 171 (87.24) |
| No | 25 (12.76) |
| **Insurance Type** | |
| Public | 107 (54.60) |
| Private | 46 (23.47) |
| Both | 19 (9.69) |
| Missing | 24 (12.24) |

| | |
|---|---|
| **Access** | |
| Most of the times | 30 (15.31) |
| Sometimes | 84 (42.86) |
| Never | 58 (26.60) |
| Missing | 24 (12.24) |
| **Impact of COVID-19 on QOL** | |
| Worsened | 57 (29.08) |
| Remained the same/Improved | 120 (61.22) |
| Missing | 19 (9.69) |
| **Medical Health Conditions**[^] | |
| At least 2 | 82 (41.84) |
| More than 2 | 114 (58.16) |
| **Duration of most recent pain attack (crisis)** | |
| 1-23 hours | 35 (17.86) |
| 1-3 days | 64 (32.65) |
| 4-6 days | 36 (18.37) |
| 1-2 weeks | 31 (15.82) |
| More than 2 weeks | 13 (6.63) |
| Missing | 17 (8.67) |
| **Number of sickle cell pain attacks (crises) in the past year, mean (SD)** | 3.12 (1.22) |
| **Sickle cell severity score[%], mean (SD)** | 51.95 (8.10) |
| **Sickle cell frequency score[%], mean (SD)** | 51.41 (9.51) |

SCA= Sickle Cell Anemia; SD=Standard Deviation; QOL=Quality of Life; *Hemoglobin S, Hemoglobin Sβ0 (beta zero) thalassemia, Hemoglobin Sβ+ (beta) thalassemia, Hemoglobin SD; [++]Other includes White/Caucasian, American Indian/Alaskan Native, Asian, Native Hawaiian/Other Pacific Islander, Hispanic, Middle Eastern, Mixed race; [^]Measured using the ASCQ-ME Medical History Checklist; [%]Measured using the ASCQ-ME Pain Episode Measure.

**Subscale distribution**

Table 2.2 shows the mean scores, and skewness and kurtosis coefficients for the 13 subscales of CSQ-SCD instrument. The skewness and kurtosis coefficients for all the CSQ-SCD subscales on were found to be within a range of -1.094 and 0.889. Based on these ranges, the data appear to be normally distributed. Missing data ranged from 0-5 respondents for any of the CSQ-SCD subscales.

**Factorial validity**

Figures 2.1 and 2.2 depict the two CSQ-SCD factor models reported by Gil et al. and Anie et al., respectively, which were tested to examine the factorial validity of the instrument

**Table 2.2: Subscale-level characteristics for the CSQ-SCD among adults with SCD**

| Subscales | N | Missing | Mean (SD) | Skewness | | Kurtosis | |
|---|---|---|---|---|---|---|---|
| | | | | Statistic | Std. error | Statistic | Std. error |
| **Diverting attention (DA)** | 196 | 0 | 3.362 (1.370) | -0.196 | 0.174 | -0.587 | 0.346 |
| **Reinterpreting pain sensations (RPS)** | 193 | 3 | 1.442 (1.269) | 0.889 | 0.175 | 0.399 | 0.348 |
| **Calming self-statements (CSS)** | 193 | 3 | 3.973 (1.013) | -0.113 | 0.175 | -0.350 | 0.348 |
| **Ignoring pain sensations (IPS)** | 191 | 5 | 2.349 (1.057) | 0.184 | 0.176 | -0.193 | 0.350 |
| **Increasing behavioral activity (IBA)** | 195 | 1 | 3.145 (1.043) | 0.229 | 0.174 | -0.175 | 0.346 |
| **Praying and hoping (PH)** | 194 | 2 | 4.134 (1.097) | -0.693 | 0.175 | 0.842 | 0.347 |
| **Catastrophizing (CA)** | 194 | 2 | 2.809 (1.380) | 0.226 | 0.175 | -0.634 | 0.347 |
| **Fear self-statements (FS)** | 193 | 3 | 3.396 (1.146) | 0.110 | 0.175 | -0.496 | 0.348 |
| **Anger self-statements (AS)** | 196 | 0 | 3.024 (1.224) | -0.118 | 0.174 | -0.175 | 0.346 |
| **Isolation (IS)** | 196 | 0 | 3.491 (1.262) | -0.254 | 0.174 | -0.290 | 0.346 |
| **Taking fluids (TF)** | 196 | 0 | 4.732 (1.072) | -1.094 | 0.174 | 1.396 | 0.346 |
| **Resting (RS)** | 194 | 2 | 4.437 (0.980) | -0.830 | 0.175 | 1.324 | 0.347 |
| **Heat/cold/massage (HCM)** | 196 | 0 | 4.057 (1.002) | -0.581 | 0.174 | 0.128 | 0.346 |

among adults with SCD. The model fit indices for the two models can be found in Table 2.3. The two-factor model tested by Gil et al. where all items loaded onto two separate latent coping factors had a poor fit (Chi-square [df] =257.823 [64]; CFI = 0.788; TLI = 0.741; RMSEA [90% CI] = 0.124 [0.109-0.140]; SRMR =0.105). The three-factor model based on the approach used by Anie et al. had a better but mediocre fit among the two models which were tested (Chi-square

[df] = 223.850 [62]; CFI = 0.823; TLI = 0.777; RMSEA [90% CI] = 0.115 [0.099-0.132]; SRMR = 0.090). Based on the modification indices, if the subscale praying and hoping is freely estimated to cross-load on the passive adherence coping latent factor in addition to the subscale loadings already specified in the Anie et al. model., the overall model chi-square is estimated to drop by 25.189 units. This improved the model fit of the final model significantly (Chi-square [df] = 196.797 [62]; CFI = 0.852; TLI = 0.814; RMSEA [90% CI] = 0.105 [0.089- 0.122]; SRMR = 0.071).

**Table 2.3: Summary of model fit indices for the CSQ-SCD higher-order confirmatory factor models**

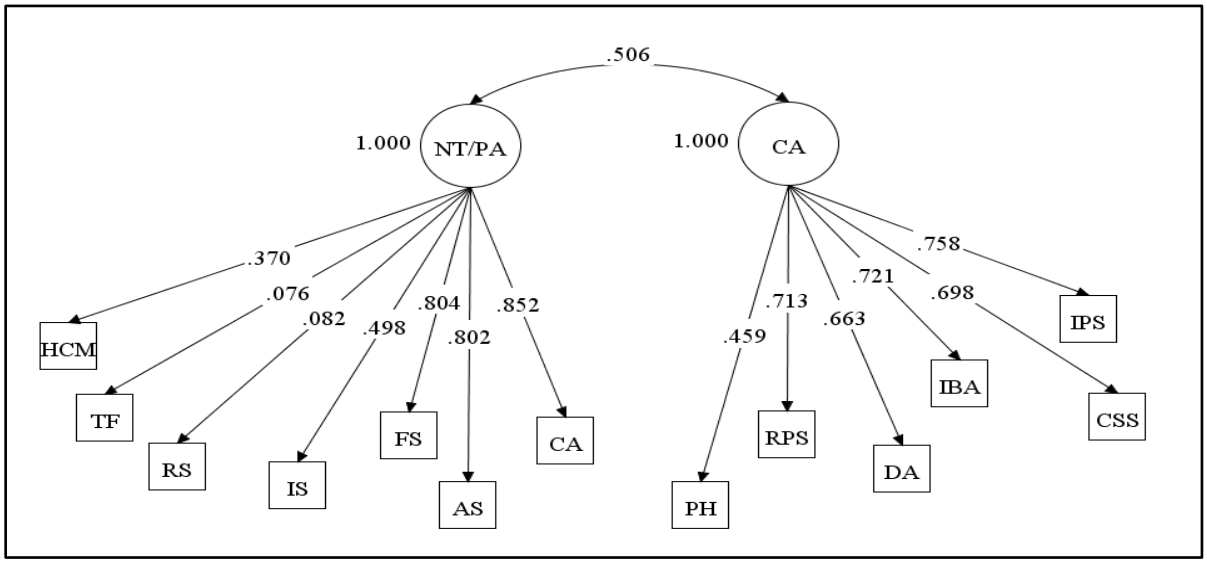
| Fit Statistics | Model 1 | Model 2 |
|---|---|---|
| **Chi-square (df)** | 257.823 (64) | 223.850 (62) |
| **CFI** | 0.788 | 0.823 |
| **TLI** | 0.741 | 0.777 |
| **RMSEA (90% CI)** | 0.124 (0.109-0.140) | 0.115 (0.099-0.132) |
| **SRMR** | 0.105 | 0.090 |

Model 1 – CSQ-SCD CFA model based on Gil et al. (1989) (2-factor model)
Model 2 - CSQ-SCD CFA model based on Anie et al. (2002) (3-factor model)
Note: df, degrees of freedom; CFI, Comparative Fit Index; TLI, Tucker-Lewis Index; RMSEA, Root Mean Square Error of Approximation; SRMR, Standardized Root Mean Square Residual; CI, Confidence Interval.

**Convergent validity**

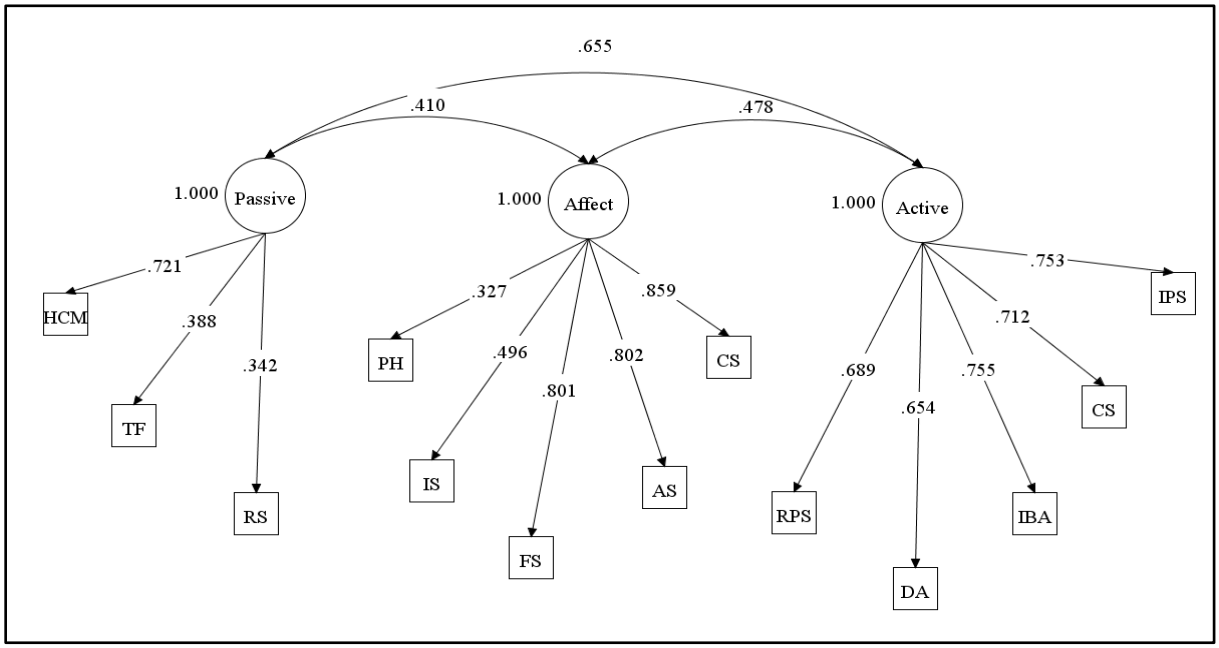
The standardized factor loadings for the final study model have been reported in Table 2.4. All factor loadings were statistically significant at $\alpha = 0.05$. All standardized factor loadings were greater than 0.5 except for the subscales praying and hoping, resting, and taking fluids. The AVE for active coping was found to be 0.713, for affective coping was found to be 0.657, and for passive adherence coping was 0.483. Table 2.5 depicts the first-order (13 subscales) correlation matrix. The correlation between the 13 subscales underlying the same latent factor were moderate to weak (Table 2.5). Subscales underlying the active coping latent factor, namely DA, IPS, CSS, IBA and RPS had moderate correlations with each other compared to the

**Figure 2.1: Two-factor model of CSQ-SCD based on Gil et al. depicting standardized factor loadings**




Note: Negative thinking/Passive adherence (NT/PA), Coping attempts (CA), Diverting attention (DA), Reinterpreting pain sensations (RPS), Calming self-statements (CSS), Ignoring pain sensations (IPS), Increasing behavioral activity (IBA), Praying and hoping (PH), Catastrophizing (CA), Fear self-statements (FS), Anger self-statements (AS), Isolation (IS), Resting (RS), Taking fluids (TF), Heat/cold/massage (HCM).

**Figure 2.2: Three-factor model of CSQ-SCD based on Anie et al. depicting standardized factor loadings**




Note: Passive adherence coping (Passive), Affective coping (Affect), Active coping (Active), Diverting attention (DA), Reinterpreting pain sensations (RPS), Calming self-statements (CSS), Ignoring pain sensations (IPS), Increasing behavioral activity (IBA), Praying and hoping (PH), Catastrophizing (CA), Fear self-statements (FS), Anger self-statements (AS), Isolation (IS), Resting (RS), Taking fluids (TF), Heat/cold/massage (HCM).

**Table 2.4 Standardized factor loadings for the final three-factor model of coping for the CSQ-SCD among adults with SCD**

| Subscales | Estimate^ (SE) |
|---|---|
| **Latent Factor: Active Coping** | |
| Diverting attention (DA) | 0.654 (0.049) |
| Reinterpreting pain sensations (RPS) | 0.689 (0.689) |
| Calming self-statements (CSS) | 0.712 (0.712) |
| Ignoring pain sensations (IPS) | 0.753 (0.753) |
| Increasing behavioral activity (IBA) | 0.755 (0.040) |
| **Latent Factor: Affective Coping** | |
| Praying and hoping (PH) | 0.327 (0.070) |
| Catastrophizing (CA) | 0.859 (0.029) |
| Fear self-statements (FS) | 0.801 (0.033) |
| Anger self-statements (AS) | 0.802 (0.034) |
| Isolation (IS) | 0.496 (0.060) |
| **Latent Factor: Passive Adherence Coping** | |
| Resting (RS) | 0.342 (0.089) |
| Taking fluids (TF) | 0.388 (0.085) |
| Heat/cold/massage (HCM) | 0.721 (0.085) |
| **Latent Factor Correlation** | |
| Latent active coping factor with latent affective coping factor | 0.478 (0.070) |
| Latent active coping factor with latent passive adherence coping factor | 0.655 (0.084) |
| Latent affective coping factor with latent passive adherence coping factor | 0.410 (0.092) |
| **^All factor loadings were significant at $\alpha = 0.05$** | |

subscales underlying the affective coping and passive adherence coping latent factors. While subscales AS, FS, IS and CA were strongly-moderately correlated with the affective coping latent factor and the subscales resting, taking fluids and heat/cold/massage had weak correlations with the passive adherence coping latent factor. However, the subscale praying and hoping was strongly correlated with the subscales DA, RPS, CSS, IPS underlying the active coping latent factor and the subscale HCM underlying the passive adherence coping factor compared to the subscales underlying the affective coping latent factor. Overall, the standardized factor loadings, AVE for each latent factor, and subscale correlations suggested mediocre convergent validity for the CSQ-SCD among adults with SCD.

**Table 2.5 Subscale correlations for the CSQ-SCD among adults with SCD**

| | DA | RPS | CSS | IPS | PH | CA | FS | AS | IBA | IS | TF | RS | HCM |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **DA** | 1 | .449** | .463** | .427** | .440** | .356** | .383** | .250** | .451** | .279** | .216** | .251** | .382** |
| **RPS** | .449** | 1 | .377** | .604** | .361** | .403** | .317** | .325** | .477** | .260** | .094 | .074 | .302** |
| **CSS** | .463** | .377** | 1 | .481** | .316** | .305** | .427** | .305** | .583** | .221** | .228** | .177* | .350** |
| **IPS** | .427** | .604** | .481** | 1 | .302** | .191** | .198** | .232** | .582** | .049 | .055 | .081 | .309** |
| **PH** | .440** | .361** | .316** | .302** | 1 | .287** | .278** | .190** | .141 | .052 | .102 | .230** | .367** |
| **CA** | .356** | .403** | .305** | .191** | .287** | 1 | .701** | .689** | .200** | .395** | -.009 | -.010 | .292** |
| **FS** | .383** | .317** | .427** | .198** | .278** | .701** | 1 | .635** | .172* | .330** | .073 | .080 | .336** |
| **AS** | .250** | .325** | .305** | .232** | .190** | .689** | .635** | 1 | .162* | .504** | .047 | .017 | .236** |
| **IBA** | .451** | .477** | .583** | .582** | .141 | .200** | .172* | .162* | 1 | .187** | .139 | .119 | .340** |
| **IS** | .279** | .260** | .221** | .049 | .052 | .395** | .330** | .504** | .187** | 1 | .126 | .231** | .047 |
| **TF** | .216** | .094 | .228** | .055 | .102 | -.009 | .073 | .047 | .139 | .126 | 1 | .353** | .266** |
| **RS** | .251** | .074 | .177* | .081 | .230** | -.010 | .080 | .017 | .119 | .231** | .353** | 1 | .196** |
| **HCM** | .382** | .302** | .350** | .309** | .367** | .292** | .336** | .236** | .340** | .047 | .266** | .196** | 1 |

Note: Diverting attention (DA), Reinterpreting pain sensations (RPS), Calming self-statements (CSS), Ignoring pain sensations (IPS), Increasing behavioral activity (IBA), Praying and hoping (PH), Catastrophizing (CA), Fear self-statements (FS), Anger self-statements (AS), Isolation (IS), Resting (RS), Taking fluids (TF), Heat/cold/massage (HCM).

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).

**Discriminant Validity**

Three separate tests were employed to examine the discriminant validity of the CSQ-SCD. First the fit of the 3-factor model obtained from the factorial validity analysis was compared to that of a similar model where the latent factor correlation (i.e., correlation between active coping, affective coping, and passive adherence coping) was fixed to 1. We tested for this correlation to be different from 1 which would indicate latent construct discriminant validity. The Wald Chi-Squared Test yielded a significant difference (Wald Chi-Squared Test [df] = 56.015 [1]; $p<0.0001$) which was suggestive of adequate discriminant validity.(99) Second, the difference between the AVE for each latent factor and the square of the latent factor correlation was found to be positive for all three latent factors (Table 2.6). A positive difference was suggestive of adequate discriminant validity.(99) Last, subscales comprising the active coping, affective coping and passive adherence coping latent factors had weak to moderate correlation with subscales not underlying their own latent factor (Table 2.5). However, the subscale praying and hoping was strongly correlated with the subscales DA, RPS, CSS, IPS underlying the active coping latent factor and the subscale HCM underlying the passive adherence coping factor compared to the subscales underlying the affective coping latent factor. Overall, the CSQ-SCD was found to have acceptable discriminant validity among adults with SCD.

**Table 2.6: Discriminant validity assessed by evaluating the difference between the AVE for each latent factor and the square of the latent factor correlation**

| Squared correlations | AVE | Discriminant Validity |
|---|---|---|
| Latent active coping factor with latent affective coping factor = 0.228 | Latent active coping factor = 0.713<br>Latent affective coping factor = 0.657<br>Latent passive adherence coping factor = 0.483 | 0.713-0.228=0.485<br>0.657-0.228=0.429 |
| Latent active coping factor with latent passive adherence coping factor = 0.429 | | 0.713-0.429=0.284<br>0.483-0.429=0.054 |
| Latent affective coping factor with latent passive adherence coping factor = 0.168 | | 0.657-0.168=0.489<br>0.483-0.168=0.315 |

**Internal Consistency Reliability**

The internal consistency reliability for the CSQ-SCD was found to be satisfactory with the Cronbach's alpha value of 0.817 for active coping, 0.780 for affective coping and 0.531 for passive adherence coping (Table 2.7).

**Table 2.7: Reliability analysis for the CSQ-SCD components among adults with SCD**

| Component | Cronbach's alpha | McDonald's Omega | Mean | No. of subscales |
|---|---|---|---|---|
| **Entire scale** | 0.828 | 0.836 | 3.413 | 13 |
| **Active coping** | 0.817 | 0.818 | 2.843 | 5 |
| **Affective coping** | 0.780 | 0.812 | 3.375 | 5 |
| **Passive adherence coping** | 0.531 | 0.552 | 4.404 | 3 |

**Exploratory Factor Analysis**

We considered a follow-up EFA as an adequate fitting higher-order CFA model was only attainable by model re-specification based on the modification indices that are unsupported by theory. Since the results of the CFA, for both the 2-factor as well as the 3-factor model show poor to mediocre model fits, we decided that EFA is more suitable for further "exploration" of the somewhat poor-fitting CFA models. Moreover, results of the convergent and discriminant validity, and reliability also did not show acceptable results.

Before EFA, the Kaiser-Meyer-Olkin (KMO) test and Bartlett's test of sphericity were performed to evaluate the appropriateness of factor analysis. The KMO measure of sampling adequacy was 0.80 and the significance of Bartlett's test of sphericity was less than 0.001, meaning that EFA can be applied to the obtained dataset.(105)

EFA was conducted with the sample data to extract the new factor structure and to examine the construct validity. Mean subscale scores were used as factor indicators and factors were extracted by the maximum likelihood method. The number of factors were decided in

consideration of the scree-plot, the cumulative variance explained, the interpretability of factor loadings, parallel analysis, and model fit indices. Four eigenvalues were greater than 1 and both the parallel analysis and scree plot suggested three factors (Figure 2.3). The percentage of cumulative variance explained by the extracted three factors and four factors was 58% and 67% respectively. Based on the model fit indices (Table 2.8) and interpretability of factor loadings (Table 2.9) we deemed a 3-factor EFA model to be more appropriate for the sample data compared to the four-factor model.

The new factor structure extracted by EFA is similar to the factor structure reported by Anie et al.(83) except that in our analysis the subscale of praying and hoping loads onto the passive adherence coping latent factor. This was also indicated through the modification indices estimated while conducting CFA.

**Figure 2.3: Scree plot based on sample eigenvalues**

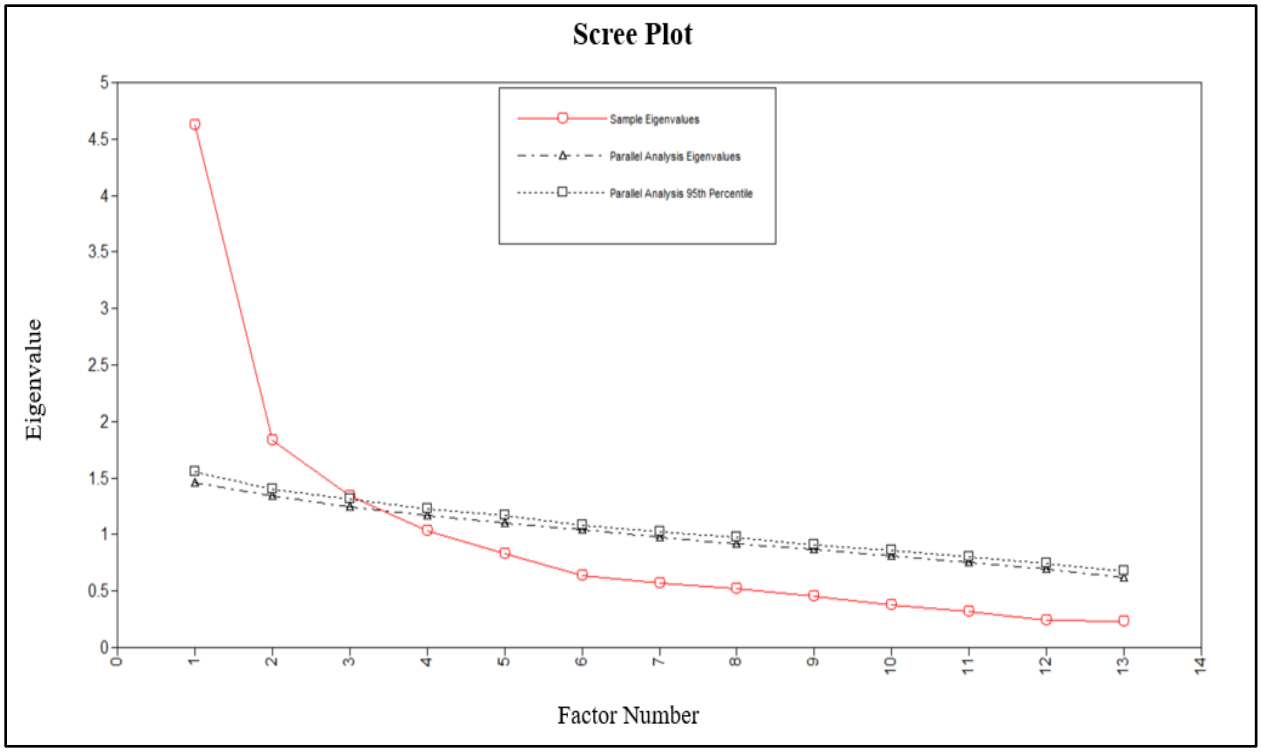


**Table 2.8: Summary of model fit indices for the CSQ-SCD exploratory factor analysis models**

| Fit Statistics | Model 1 | Model 2 |
|---|---|---|
| **Chi-square (df)** | 122.893 (42) | 72.404 (32) |
| **CFI** | 0.911 | 0.956 |
| **TLI** | 0.836 | 0.892 |
| **RMSEA (90% CI)** | 0.099 (0.079-0.120) | 0.080 (0.056-0.105) |
| **SRMR** | 0.043 | 0.031 |

Model 1 – CSQ-SCD EFA 3-factor model
Model 2 - CSQ-SCD EFA 4-factor model
Note: df, degrees of freedom; CFI, Comparative Fit Index; TLI, Tucker-Lewis Index; RMSEA, Root Mean Square Error of Approximation; SRMR, Standardized Root Mean Square Residual; CI, Confidence Interval.

**Table 2.9: Factor loadings for 3-factor exploratory factor analysis model**

| Coping Strategy | Factor 1 | Factor 2 | Factor 3 |
|---|---|---|---|
| **Active coping** | | | |
| Diverting attention (DA) | 0.426 | | |
| Reinterpreting pain sensations (RPS) | 0.636 | | |
| Calming self-statements (CSS) | 0.492 | | |
| Ignoring pain sensations (IPS) | 0.879 | | |
| Increasing behavioral activity (IBA) | 0.703 | | |
| **Affective coping** | | | |
| Catastrophizing (CA) | | 0.876 | |
| Fear self-statements (FS) | | 0.676 | |
| Anger self-statements (AS) | | 0.763 | |
| Isolation (IS) | | 0.342 | |
| **Passive Adherence coping** | | | |
| Praying and hoping (PH) | | | 0.288 |
| Resting (RS) | | | 0.683 |
| Taking fluids (TF) | | | 0.672 |
| Heat/cold/massage (HCM) | | | 0.385 |

## DISCUSSION

In this study, first, in order to investigate whether the factor structure can be replicated in the new sample from 196 SCD patients, CFA was conducted, and several model fits were discussed. After evaluating the model fit, we calculated convergent validity and discriminant validity, along with reliability. We then performed EFA with MLE.

Patient characteristics are similar to what is seen in present literature (Table 1). The mean sickle cell pain severity score (51.95) and frequency scores (51.41) were relatively similar to the average score of 50 (for both severity and frequency) for the ASCQ-Me field test respondents.(106) For the majority of the patients (~33%) the duration of pain attack lasted 1-3 days and the mean number of pain attacks were ~3 in the past 1 year.

To discuss the model fit of CFA, we should consider the criteria of the various model fit indices. It has been suggested that RMSEA values less than 0.05 are good, values between 0.05 and 0.08 are acceptable, values between 0.08 and 0.1 are marginal, and values greater than 0.1 are poor. (33) Therefore, the RMSEA value of 0.115 in this sample indicates a poor fit. The SRMR value (0.09) is closer to 0.08, which shows a mediocre fit. (21) The other fit indices, CFI (0.823) and TLI (0.777), should be over 0.9 for a good fit, but in this sample, the two indices are a little below the criteria. (34) Based on these indices, the factorial validity of the CSQ-SCD found that the three-factor model based on the approach adopted by Anie et al. to have a relatively better, though mediocre, fit in the sample population compared to the two-factor model based on the approach by Gil et al.(54) In a previous study by McCrae and Lumley(63) the factor analysis of the seven subscales of 'Negative thinking/passive adherence' reported that the negative thinking and passive adherence subscale loaded onto two separate factors indicating a three-factor structure of the CSQ-SCD.

Saris et al.(107) demonstrated that the power of the modification index test to identify a particular parameter misspecification (e.g., factor loadings) can be used in conjunction with the expected parameter change for that parameter. Thus, in the current study based on the modification indices, minor modifications driven by data were made wherein the subscale praying and hoping was estimated to load on the passive adherence coping latent factor instead

of the affective coping factor, the rest of subscale loadings remained as already specified in the Anie et al.(83) model. This improved the model fit of the 3-factor model significantly.

The CSQ-SCD was found to have mediocre convergent validity among adults with SCD. Considering the best fitting model (3-factor model), the size of each factor loading for majority of the subscales was greater than 0.5 indicating that the latent factor explained at least 50% of the variance in each observed subscale. The AVE for all three latent factors was close to 0.5 which was indicative of the fact that the latent factors explained a higher proportion of the variance in the observed subscales than the error variance which remained unexplained. The correlation between the 13 subscales underlying the same latent factor were moderate to weak. We did not find evidence of adequate discriminant validity of the CSQ-SCD among adults with SCD. Among the tests conducted to test for discriminant validity, only Wald's Chi-Square test of discriminant validity was suggestive of adequate discriminant validity. The difference between the AVE for each latent factor and the square of the latent factor correlation was found to be positive for all of the subscales suggesting discriminant validity. Additionally, the subscale praying and hoping had strong to moderate correlations with the active coping latent factor. Future studies must examine and assess the reasons for this correlation between the praying and hoping subscale with the active coping latent factor. The internal consistency reliability of the active, affective, and passive adherence coping latent factors was found to be good.

As the CSQ-SCD showed a poor-fitting CFA model, we followed this with an EFA. Our CFA results were backed by our EFA results, wherein we saw the subscale of praying and hoping load onto the passive adherence coping latent factor and this improved the model fit as seen through the modification indices obtained through CFA. Thus, researchers should meticulously consider all options when a hypothesized model does not fit and realize that EFA is

often more suitable for further "exploration" of poor fitting CFA models. Exploratory factor analysis is known as a data-driven technique while CFA as a theory-driven technique.(89) The latent variable structure of a dataset can be explored with EFA. On the other hand, CFA requires an a priori hypothesis or theoretical evidence as CFA is a hypothesis testing method which tests whether the obtained sample data is suitable for a model.(89) Thus, in this study, we used CFA to discuss the model fit of the sample data obtained from SCD patients from a patient panel to the previously extracted CSQ-SCD 3-factor structure. Also, we used EFA to extract the new factor structure. Different from this study, Anie et al.'s model was constructed with a dataset from SCD patients in London who visited the hospital to consult with a clinician regarding their health without any strict exclusion or inclusion criterion.(83) Thus, it was possible for patients, sub healthy, and healthy patients to participate in that study. Additionally, this study had a small sample size of 96 patients. These differences may have resulted in a small difference in factor structure. The results of the current study must be interpreted in the light of certain limitations. The cross-sectional nature of the study prevented us from assessing the predictive validity as well as test-retest reliability of the CSQ-SCD in the study population. Future studies should adopt a longitudinal design to explore these aspects of the psychometric profile of the CSQ-SCD. Adults with SCD who participated in this study are likely to have higher physical functioning because of their ability to participate in survey research. This may limit the generalizability of the study results.

## CONCLUSION

This was the first US-based study to conduct a higher-order CFA of the CSQ-SCD using subscale scores among adults with SCD. Considering that SCD is a rare genetic disorder,

most previous published reports have employed smaller sample sizes or conducted of all races. This study provides evidence about the psychometric properties of the CSQ-SCD among adults with SCD in the US. The scale demonstrated poor factorial, and mediocre convergent and divergent validity. The scale was found to have adequate internal consistency reliability. Overall, the results provide basis for the future development of a coping instrument with acceptable psychometric properties in the SCD population. The CSQ-SCD instrument was developed by Gil et al. in 1989 when the only available treatments options were hydroxyurea, blood and bone marrow transplant or blood transfusions. Owing to medical advances over the past three decades, many patients now live well beyond early adulthood, although complete cure in adults is not possible. Several new FDA approved medications are now available along with research being conducted in genetic therapies with the aim of finding a cure for SCD. Given all these advancements in treatments and the improved life expectancy, it is possible that patients now relatively better manage their disease and have devised different coping strategies to adjust to their condition. Thus, it is best to develop a new coping instrument which is shorter in length compared to CSQ-SCD and with stronger psychometric properties such that the coping information obtained from studies using this instrument can be incorporated into health policy and clinical decision-making studies only in African American patients. To the best of our knowledge, this is the first US-based study to capture the psychosocial construct of coping of a large population of adults with SCD inclusive.

# CHAPTER III

# AN ASSESSMENT OF PSYCHOSOCIAL DETERMINANTS OF HEALTH-RELATED QUALITY OF LIFE AMONG ADULTS WITH SICKLE CELL DISEASE IN THE UNITED STATES

## INTRODUCTION

According to the International Society for Quality of Life Research (ISOQOL), health-related quality of life (HRQOL) is "the health aspect of quality of life that focuses on people's level of ability, daily functioning, and ability to experience a fulfilling life."(108) Functional status and health-related quality of life (HRQOL) may be diminished in patients with sickle cell disease (SCD) due to life-threatening events, such as stroke, or other organ system failures.(5,15,109) Treatment improvements have now altered SCD into a chronic disease suffered by children and adults. Commonly, patients surviving until adulthood experience substantial organ system damage that may include stroke, pulmonary failure and pulmonary hypertension, renal failure, congestive heart failure, leg ulcers, and avascular necrosis of the femoral or humeral heads.(5,15,109)

Compared to the general population, a higher prevalence of depression has also been reported in patients with SCD.(6,69,110) Depression is found to be related with frequent hospitalization for vaso-occlusive pain crises, increased emergency room visits, and recurrent blood transfusions.(111) HRQOL outcomes are reported to be worse in patients with SCD than in unaffected individuals and closely resembles the HRQOL outcomes of patients on dialysis.(5) Because of the grave complications of the disease, and other co-morbid factors patients

experience that influence HRQOL, it is important to understand HRQOL in patients with SCD.(112)

***Need for the Study***

The QOL of patients with SCD is influenced by various complex factors, including the course of the disease itself; coping strategies, stigma, discrimination, and lack of adequate treatment; family life issues; work (or lack of work) issues; social isolation; and disruptions in relationships and social activities.(49,113) Okpala et al.(114) found that early detection of chronic complications and the provision of holistic health care improves QOL in patients with SCD and lessens the number and length of hospitalizations. However, studies have reported that patients with SCD suffer from worse physical HRQOL as compared to the general population.(5–10) The mental health related QOL of patients with SCD was found to be similar to the general population.(5,7,8,10) A literature review study by Edwards et al.(113) demonstrated SCD to be associated with diminished QOL, compromised psychosocial functioning, and altered intra- and interpersonal relationships. McClish et al.(5) observed that QOL scores of SCD patients aged 16 years or older were significantly lesser than those of persons with asthma, cystic fibrosis, and hemodialysis on all the subscales except the mental health subscale.

Even though McClish et al.(5) did not find QOL scores related to mental health to be significantly lower for patients with SCD, SCD is associated with a variety of psychological and psychosocial challenges. Anie et al. reports difficulties with psychological coping as one of the most common complications found in patients with SCD. (115) There is increasing evidence that psychosocial factors contribute substantially to complaints of chronic pain which is the most frequent and disabling concern of patients who have SCD. Social and demographic factors such

as race, gender, age, education, and socioeconomic status, along with psychological factors such as coping style,(49) coping capacity, self-efficacy and social support clarify the differences in disability associated with pain intensity, pain threshold, and pain tolerance.(66,113) Therefore, recognizing and implementing interventions to improve psychosocial factors may be beneficial in the management of the SCD pain.(66)

Despite advancements in pain management and the National Heart, Lung and Blood Institute (NHLBI) recommendations of opioids for pain management in patients with SCD, physicians are often reluctant to give patients adequate dosages of narcotic analgesics because of concerns about addiction, tolerance, and side effects.(22,116) As a result, adults with SCD are often under-treated and this healthcare provider bias may lead to dissatisfaction with care and consequently a reluctance by patients to seek medical attention.(117,118) Dissatisfaction with health-care has a negative effect on health status and quality of life.(67)

Therefore, many adults with SCD primarily manage their pain symptoms at home thus placing a strong emphasis on self-care across the lifespan. The occurrence of pain crises and subsequent hospitalizations may increase without appropriate self-care in the home setting.(71) Moreover, these medical interventions for SCD result in substantial burden, both financially and psychologically.(67) The NHLBI expert panel report recommends guiding providers in supervising persons who take opioids to manage their pain at home.(22) All this makes self-care management of SCD critical to improve and manage pain symptoms, decrease health care costs and utilization, as well as improve the health status and quality of life for persons living with SCD.

Self-care management is central to managing chronic conditions such as SCD.(119) Self-care refers to “one’s perceived ability to participate in general therapeutic activities aimed at

improving health status and quality of life as well as actual performance of those activities".(67) Studies report pain episodes to be most frequent for SCD patients between ages 19 and 39,(120) and health care utilization and re-hospitalization rates being greatest between ages 18 and 30.(38) The transition for patients with SCD from pediatric to adult care occurs in these age ranges.(121) Along with the burden of this transition, young adults lack understanding about the adult SCD care system, do not have financial independence and decision-making capability, and they may also be encountering a change in or loss of healthcare insurance.(122) Furthermore, this chronic condition also experiences a dearth of expert providers to serve this population, especially in low-income areas.(121) Additional constraints include a lack of education, low income status, and unemployment amongst patients with SCD, who may not be able to work due to poor health and frequent pain crises.(123) All of these issues make it difficult for patients with SCD to obtain regular, preventive care, further adding to the importance of self-care.

Sickle cell disease management includes general strategies such as obtaining regular checkups, staying hydrated, eating a healthy diet, getting adequate rest, and preventing extreme temperatures.(124) These general strategies could be deemed as self-care actions which are a vital aspect of pain crisis prevention. In a study assessing self-management strategies used by adult patients with SCD, the reported themes included self-awareness, emotional support, career selection and success factors, nutrition, advocacy, knowledge, physical activity, and complementary and alternative medicine.(125) Another study assessing self-care strategies in middle-aged and older adults reported self-care strategies to be physiologic (warmth, hydration, rest, good food, and avoiding drinking, smoking, and using drugs), psychological (knowledge and understanding of the disease, coping, listening to and learning about the body, prayer, and

social support), and provider-related (knowledgeable health care providers and following providers' orders).(72)

Self-care has many advantages and is correlated with several variables, but the interrelationships between sociodemographic, psychosocial, and HRQOL factors need to be further assessed amongst patients with SCD. Furthermore, the mediating effect of self-care on the relationship between disease severity and crises frequency and quality of life needs evaluation. Knowledge of these factors and how they act together may not only assist healthcare providers and caregivers in improving care provided to individuals with SCD, but also potentially enable patients to better understand and self-manage their condition. Such evaluations can assist clinicians and healthcare policymakers in designing programs aimed at increasing the level of social support provided, fostering the use of adaptive coping strategies such as calming self-statements, increasing activity and diverting attention, and overall ensuring better health among these patients. Therefore, the purpose of this research is to describe socio-demographic, disease severity and crises frequency, and self-care management resources that are associated with HRQOL in persons with SCD. To understand HRQOL, the relationships among self-care management variables (coping strategies, self-efficacy, social support) and socio demographic variables were examined.

***Conceptual Framework***

Employing a theory-based evaluation is essential to arrive at a comprehensive understanding of the impact of SCD on patient well-being. In regard to SCD and HRQOL, coping strategies, self-efficacy, social support, and socio-demographic variables appear to be the most significant constructs.(66–68) To address the relationships among these variables, the theoretical model of self-care management for sickle cell disease (SCMSCD) was adapted. The

theory of SCMSCD is based on the theory of Self-Care Management for vulnerable populations, a middle range theory developed by Jenerette et al.(67), which attempts to understand the relationships among concepts such as vulnerability factors, self-care management resources, and health outcomes. The SCMSCD model shows that (a) vulnerability factors (socio-demographic and health-need factors) have a negative impact on both health outcomes (health status and quality of life) and self-care management resources (self-efficacy, coping strategies, social support), and (b) self-care management resources positively mediate the relationship between vulnerability factors and health outcomes.

The relationships stated in the SCMSCD model have been supported in prior research with individuals with SCD and other chronic illnesses.(67,69,70) The study by Jenerette et al.(67) tested the SCMSCD model in a sample of 232 African American adults with SCD and reported that vulnerability factors had a negative effect on health outcomes and self-care management resources did not mediate the relationship between vulnerability and health care outcomes. However, to meet the assumptions of normality as well as criteria for retaining variables for the SEM analysis, this study excluded theorized self-care management resource variables such as coping behaviors and self-care activities. Another study by Matthie et al.(71) examined the adapted SCMSCD model in a sample of 103 SCD young adults (18-30 years). The study stated that there was no adequate evidence to support a direct relationship between SCD self-efficacy, social support, years of education, and the number of hospital visits for crises. The mediating effect of self-care management, among these variables was also non-significant. Studies in the literature(71,72) have not tested SCMSCD model with coping and self-efficacy as mediators and have analyzed this model in only African American population and young adults. The SCMSCD model needs to be tested in a more generalized population to enable a better

understanding of the relationships amongst these factors (psychosocial, vulnerability and health outcomes factors).

For the purposes of the current study, we adapted the SCMSCD model by looking at the moderating effects of social support. The adapted SCMSCD was employed to identify antecedents and cognitive pathways that influence adaptation responses (i.e., restoring optimal HRQOL) to a chronic disease such as SCD.

***Model Constructs***

*Vulnerability Factors*

Vulnerability factors determine access to health care and health service utilization, which in turn influence health outcomes, including health status and quality of life.(126) In the SCMSCD model, vulnerability factors include socio-demographics (age, income, education level, employment status) and health need factors (complications and SCD severity and frequency of crises). Examining multiple vulnerability factors is preferred to examining individual factors because multiple factors explain reality and enhance our understanding of characteristics that are related to health outcomes.(126)

Socio-demographic variables are important predictors of HRQOL in individuals with SCD.(71) Studies report that HRQOL in adults with SCD is significantly impaired and may be worse than in other chronic diseases.(5,112) Variables affecting HRQOL in SCD include age, gender, family income, education, place of residence, employment status, SCD-related treatments and complications and SCD crises frequency and severity.(71) Age and socio-economic status have a negative effect on HRQOL.(71) Studies demonstrate that African Americans with SCD are more likely to have lower levels of education, have lower income, and are more likely to be unemployed or disabled when compared to African Americans without

SCD.(123) Socio-demographic variables appear to significantly affect patient outcomes.(71) Researchers typically operationalize these variables using age, income, education, and employment or occupation. Further research is needed regarding assessment of and strategies for dealing with socio-demographic problems experienced by patients with SCD.(123)

*Self-Efficacy*

According to Bandura's social learning theory, self-efficacy refers to individuals beliefs that they are able to control certain events and behaviors in their lives as a way to achieve specific outcomes.(127) Self-efficacy is a pre-requisite for effective self-management and behavior changes; and is an underlying mechanism that can affect the outcomes of self-management programs.(128) Consequently, encouraging self-efficacy is an important strategy for attaining self-management skills.(128)

Self-efficacy can be a determining factor in people coping with chronic diseases such as SCD.(69) Perceived self-efficacy helps to foster coping and response to stress producing events.(129) Higher levels of self-efficacy are shown to be correlated with increased use of adaptive coping mechanisms, decreased anxiety, and stress, as well as increased adherence to medical regimens.(130) Studies show that fewer physical and psychosocial symptoms are found in sickle cell patients with higher self-efficacy,(130–132) and patients with low self-efficacy made greater use of health care services compared with their counterparts who had higher self-efficacy.(130) Lenoci et al. also showed a negative relationship between self-efficacy and pain intensity in sickle cell patients.(133) Adolescents with sickle cell disease who are more engaged in self-care behaviors, such as drinking enough fluids, taking medications, and avoiding too much physical activities reported a higher self-efficacy and lower levels of physical and mental ailments.(132) For individuals with chronic diseases, self-efficacy is directly related to

performance,(134) confidence and beliefs of control over outcomes despite accompanying challenges.(135)

In the context of the theoretical framework employed by the current study, self-efficacy was treated as a form of self-management resource. Certain studies in the literature have also found self-efficacy to play the role of a mediator in the vulnerability-HRQOL relationship.(67,71)

*Social Support*

According to Stewart et al., social support is defined as "interactions, with family members, friends, health professionals and peers, that communicate information, reliable alliance, aid and esteem".(136) The quality and availability of social support may impact the health outcomes of individuals with chronic illness and may positively influence self-care behaviors.(137) The different kinds of social support include emotional, instrumental, informational, and appraisal support. Support can be obtained from family, friends, work, healthcare providers and the community.(138)

In chronic disease states, social support from various sources is essential. Family support may decrease depression and increase medication compliance, while support from healthcare providers might increase satisfaction with the healthcare system and decrease perceived discrimination consequently leading to better disease management and HRQOL.(71) Children with family social support were found to have better disease management behaviors.(139) Adults with SCD face stigma, discrimination, loneliness and isolation, and disruptions in relationships, work, and social activities.(68) Negative emotional states can affect the ability of adults with SCD to function in social situations.(68) For example, Thompson et al.(64) stated that adults with poorer psychological adjustment had lower levels of family support and more conflict in

family functioning. In addition, social support was noted to be helpful in adhering to treatment plans.(71,140,141)

*Coping*

Lazarus and Folkman (1984) define coping as "cognitive and behavioral efforts to master, reduce, or tolerate the internal and/or external demands that are created by the stressful situation".(85) There are two types of coping mechanisms: adaptive and maladaptive coping. Adaptive or task-oriented coping aims at managing of the external environment associated with the stressor by seeking information about what to do or holding back from making hasty decisions.(85) Maladaptive coping consists of Emotion-oriented coping (EOC) and Avoidance coping (AC).(85) EOC is concerned with the regulation of the internal affective emotions which are a consequence of the stressor.(85) EOC strategies do not change a damaging situation but they make a person feel better. AC is a strategy where an individual completely avoids or is in denial of the illness and this coping style has been linked to diminished QOL.(85)

The coping strategies used by patients with SCD to deal with pain predict a significant percentage of the variance in adjustment to SCD more than that accounted for by disease severity and demographic variables.(54) Studies have found that pain coping strategies are significant predictors of psychological and physical function.(54,58,62) According to Gil et al.,(54) individuals high on maladaptive coping strategies (Negative Thinking and Passive Adherence) had more severe pain episodes, were less active during painful episodes, had higher levels of psychological distress, and had more frequent hospitalizations and ER visits. Individuals high on the adaptive coping strategies (Coping attempts) were more active during painful episodes.(54) However, the coping strategies factors were not related to pain frequency and duration.(54) Gil

suggests that once pain crises occur, the coping strategies used by the individual appear to be related to overall adjustment.(54)

Another study by Anie et al. reports that maladaptive coping (affective coping) was associated with impaired QOL in terms of physical role limitations, social functioning, mental health and general health perceptions.(49) Poorer QOL may lead to the use of more emotion-focused pain coping responses such as anger, fear and negative thoughts. Such doubtful thoughts and emotions lead to general/mental health problems, and pose limitations on physical and social activities, consequently leading to poor QOL.(49,54,63,82) Thus, knowledge about the way patients respond emotionally is important to the self-management of SCD.

***Research Hypotheses***

Several hypotheses were tested in this study. First, it was hypothesized that higher levels of disease severity and crises frequency among adults with SCD will be associated with lower HRQOL. Second, it was hypothesized that adults with SCD with higher levels of perceived self-efficacy will have a higher HRQOL. Third, the use of active coping strategies and passive or adherence coping strategies will be associated with better HRQOL among adults with SCD. Fourth, the use of affective coping strategies will be associated with lower HRQOL among adults with SCD. Fifth, the impact of disease severity and crises frequency on HRQOL will be partially mediated by the perceived self-efficacy and the pain coping strategies adopted by adults with SCD. Sixth, at higher levels of perceived social support, the impact of affective coping strategies on HRQOL will be diminished. Seventh, at higher levels of perceived social support, the impact of adaptive coping strategies and passive adherence coping strategies on HRQOL will be enhanced among adults with SCD. Last, at higher levels of perceived social support, the impact of self-efficacy on HRQOL will be enhanced among adults with SCD.

## METHODS

### Study Design

A prospective, cross-sectional design was employed for the current study. An online survey designed using Qualtrics (Qualtrics Inc., Provo, UT) was self-administered to adults with SCD. The study received approval under the exempt status from the University of Mississippi Institutional Review Board (Protocol #21x-130).

### Study Sample

Pain episodes are noted to be most frequent between ages 19 and 39(120,142) and the rates of health care utilization and re-hospitalization are highest between ages 18 and 30.(38) Therefore, the study population for the current study included adult patients (≥ 18 years) with SCD. The online survey for the current study was administered to adults with SCD enrolled with a patient panel maintained by Rare Patient Voice, a market research company.

### Study procedures

An email explaining the nature and purpose of the study was sent out to all potential respondents. Participants were assured about the anonymity and confidentiality of their responses. It was emphasized that study participation is voluntary. The email contained a URL link to the study survey. Amazon gift cards worth $15 were provided to all respondents as a token of appreciation.

### Sample Size

The sample size requirements for the current study were based on the analysis technique used to address the study objectives. The current study used structural equation modeling (SEM) to assess the direct and indirect relationships among the study variables and identify

predictors of HRQOL among adults with SCD. Kline et al.(143) recommends that a sample size of 200 or greater is acceptable for SEM. This study utilized a sample size of 197 SCD patients for this present analysis.

**Study Measures**

*Vulnerability Factors*

- Socio-demographics and Clinical Information

A demographic questionnaire was used in the study to gather information from participants regarding age, sex, race, level of education, employment status, living status and SCD genotype.(67) The questionnaire also included questions on access to opioid medications and impact of COVID-19 on patients quality of life. The ASCQ-Me SCD Medical history checklist (SCD-MHC), a sickle cell specific checklist, was utilized to determine the conditions associated with SCD. The ASCQ-Me SCD-MHC consists of a list of several treatments and conditions related with SCD, with responses of "yes" or "no" to suggest whether the respondent has that condition or takes that treatment. The score for the checklist is simply the sum of the number of questions with a "yes" response.

- Disease severity and Frequency

The disease severity and frequency were obtained using the ASCQ-Me pain episodes measure scale. The ASCQ-Me pain episode measure is a sickle cell specific question set and includes five questions regarding the frequency, timing, and severity of sickle cell pain events. The first two question in the set asks frequency of pain attacks while the other three questions ask about the severity of the pain attacks. A higher composite score on each of these ASCQ-Me scales represents more frequency/severity and more comorbidities associated with SCD. Two separate composite scores were produced by adding information from two questions on the

frequency of pain attacks which results in a raw composite score with a potential range of 0 to 11; and adding information from the three questions on the severity of pain attacks which results in a raw composite score with a potential range of 0 to 22. Because of the differences in the number of responses for each question and number of questions in each composite, we standardized the composite scores into Z-scores and then performed a T-score transformation on the Z-scores. In the US setting, the ASCQ-Me has been shown to have excellent internal consistency for each item bank (≥.90) and the item banks differed significantly between SCD severity levels.(68)

*Self-Efficacy*

SCD self-efficacy was measured using the Sickle Cell Self-Efficacy Scale (SCSES).(144) This scale is a nine-item instrument. It uses a summated rating method to assess an individual's perceived ability to take part in daily functional activities even though they have SCD. The level of measurement for the total scale is interval and responses range from 1 ("not at all sure") to 5 ("very sure"). Item responses were summed to obtain a total score; with higher scores indicating higher self-efficacy.(130) The total score was used in the final analysis. Jenerette et al.(67) reports convergent validity between self-efficacy and self-esteem to be 0.39, sense of mastery to be 0.45, and internal health locus of control to be 0.41 and was assessed by significant correlations and an internal consistency reliability of 0.87. Edwards et al., reported an internal consistency reliability of 0.89.(144)

*Social Support*

Social support, "The internal perception of interpersonal transactions, including expressions of positive affect, affirmation of another's behaviors or views, or giving symbolic or material aid", was measured with the Medical Outcomes Study Social Support Survey (MOS-

SSS).(67,145) This 19-item Likert scale instrument evaluates perceived availability of social support on four subscales: emotional/informational, affectionate, tangible, and positive social interaction.(67,71) The scale measurement is interval with scores ranging from 1 ("none of the time") to 5 ("all of the time"). The responses are computed by calculating the mean of all 19 items, and higher scores reflect greater perceptions of available support.(71) The total score was used for the final analysis in this study. Sherbourne et al. reports the internal consistency reliabilities for the subscales and the total scale are above 0.9.(145) Jenerette et al. reports the reliabilities of the subscales from the parent study to be 0.92 for emotional/informational, 0.82 for affectionate, 0.80 for tangible, and 0.87 for positive social interaction.(67) Sherbourne et al. reports that the overall construct validity as it relates to the correlation of the health measures with social support measures were all significant at $p < 0.01$).(145)

*Coping*

Coping was measured using the Coping Strategy Questionnaire-SCD (CSQ-SCD), originally developed by Rosenstiel and Keefe to measure cognitive and behavioral coping styles in chronic low back pain.(62) This scale was later revised by Gil et al. for patients with SCD together with the addition of items related to strategies particularly relevant to SCD.(54) This adapted CSQ-SCD includes 78 items each rated on Likert scale from 0= Never do that to 6=Always do that. While there are 13 subscales of 6 items each, we followed the methods and results of Anie et al.(49) and also confirmed by our own factor analysis in another study (Paper 1 in this dissertation). We used Anie et al.'s 3 factor structure: active coping (ignoring pain sensations, reinterpreting pain sensations, calming self-statements, diverting attention, and increasing behavioral activities), affective coping (anger, fear, catastrophizing, praying and

hoping, and isolation), and passive adherence coping (taking fluids, resting, and heat/cold/massage).(49) Scale scores are means of the subscales.(5)

*Health-Related Quality of Life (HRQOL)*

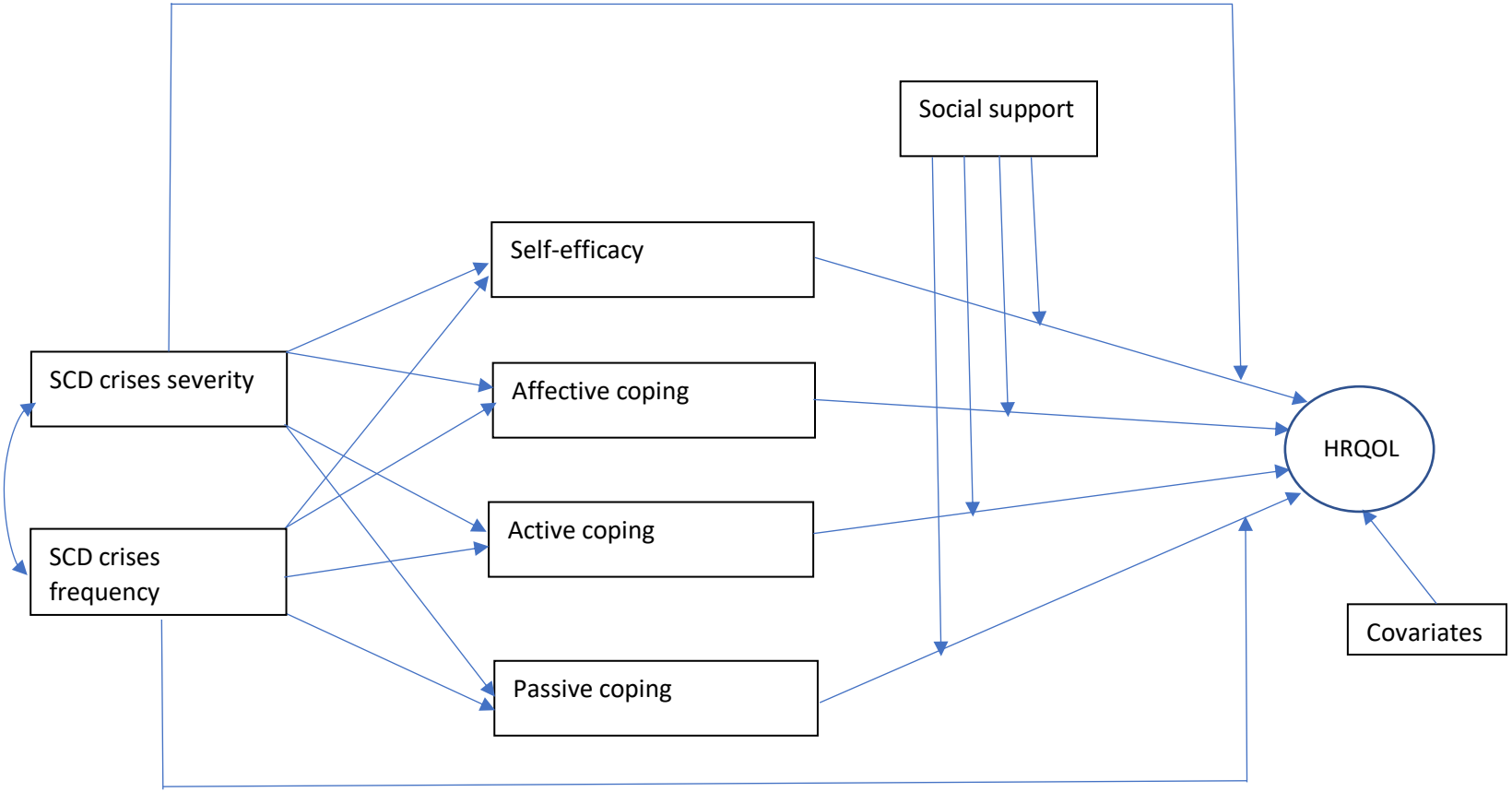
The HRQOL in patients with SCD was measured using a SCD specific instrument, ASCQ-Me Short Form.(146) A 25-item instrument with 5 item banks: Pain impact (5 items); Emotional impact (5 items); Social Functioning impact (5 items); Stiffness impact (5 items); and Sleep impact (5 items). The five item banks are each scored from 5 ("never") to 1 ("always"). Scores on each scale are standardized to have a mean of 50 and a standard deviation of 10. A higher score represents better HRQOL on all item banks. We utilized the online scoring platform HealthMeasures Scoring Service, powered by Assessment Center$^{SM}$ to score ASCQ-Me.(147) In the US setting, the ASCQ-Me has been shown to have excellent internal consistency for each item bank (≥.90) and the item banks differed significantly between SCD severity levels.(68)

**Statistical Analysis**

Descriptive statistics were used to summarize the study variables. Means and percentages were reported for the continuous variables. Frequencies and proportions were reported for summarizing the categorical variables. Correlations were assessed between the study variables using Pearson's correlation coefficient. The assumption of multivariate normality was tested by assessing the absolute skewness and kurtosis indices. To test the proposed theoretical relationships (Figure 3.1), Hayes' PROCESS macro was utilized.(148) This model tested the mediating role of self-efficacy and coping in the relationships between disease severity / crises frequency and HRQOL. To test the moderating effect of social support, interaction terms were created between social support, and coping and self-efficacy. The moderated mediation approach suggested by Hayes was employed for conducting this analysis.(148) HRQOL was

operationalized using five item banks from the ASCQ-Me instrument: Pain impact (PI); Emotional impact (EI); Social Functioning impact (SFI); Stiffness impact (STI); and Sleep impact (SI). Scores measured on each of these item banks were treated as separate dependent variables. Disease severity, crises frequency, perceived social support, active coping, affective coping, passive adherence coping, and self-efficacy were treated as measured variables in the SEM analysis. All analyses were conducted using Hayes' PROCESS macro in IBM SPSS Statistics 27.(148,149)

**Figure 3.1: Hypothesized model for the study**




* HRQOL was measured using the ASCQ-Me five item banks: the latent Pain impact (PI); Emotional impact (EI); Social Functioning impact (SFI); Stiffness impact (SI); and Sleep impact (SLI). Scores measured on each of these item banks were treated as separate dependent variables.

## RESULTS

### Socio-demographic and clinical characteristics

The final study sample consisted of 196 adults with SCD (Table 3.1). The majority of the study population included patients with Hemoglobin SS (sickle cell anemia) (68.88%), who were females (86.22%), and self-identified as African American (83.67%). Most of the patients lived with someone (71.94%), had more than high school education (75%), and were unemployed (49.49%). Patients also commonly suffered from more than 2 health conditions (58.16%), had an average of 3 sickle cell pain attacks (crises) in the past year, which lasted for 1-3 days (32.65%). The mean sickle cell pain severity score (51.95) and frequency scores (51.41) were similar to the average score of 50 (for both severity and frequency) in the reference population.(104)

**Table 3.1: Demographic and clinical characteristics of the study sample**

| Characteristics | N (%) |
|---|---|
| **SCD Type** | |
| Hemoglobin SS (SCA) | 135 (68.88) |
| Other* | 61 (31.12) |
| **Age, Mean (SD)** | 36 (9.88) |
| **Gender** | |
| Male | 27 (13.78) |
| Female | 169 (86.22) |
| **Race/Ethnicity** | |
| African American/Black | 164 (83.67) |
| Other++ | 13 (6.63) |
| Missing | 19 (9.69) |
| **Living Status** | |
| Living alone | 35 (17.86) |
| Living with someone | 141 (71.94) |
| Missing | 20 (10.20) |
| **Education Level** | |
| High school or less | 30 (15.31) |
| More than high school | 147 (75.00) |
| Missing | 19 (9.69) |

| | |
|---|---|
| **Employment Status** | |
| Employed (full time/part-time) | 80 (40.82) |
| Unemployed | 97 (49.49) |
| Missing | 19 (9.69) |
| **Region** | |
| Northeast | 46 (23.47) |
| Midwest | 38 (19.39) |
| South | 69 (35.20) |
| West | 23 (11.73) |
| Missing | 20 (10.20) |
| **Insurance** | |
| Yes | 171 (87.24) |
| No | 25 (12.76) |
| **Insurance Type** | |
| Public | 107 (54.60) |
| Private | 46 (23.47) |
| Both | 19 (9.69) |
| Missing | 24 (12.24) |
| **Access** | |
| Most of the times | 30 (15.31) |
| Sometimes | 84 (42.86) |
| Never | 58 (26.60) |
| Missing | 24 (12.24) |
| **Impact of COVID-19 on QOL** | |
| Worsened | 57 (29.08) |
| Remained the same/Improved | 120 (61.22) |
| Missing | 19 (9.69) |
| **Medical Health Conditions**[^] | |
| At least 2 | 82 (41.84) |
| More than 2 | 114 (58.16) |
| **Duration of most recent pain attack (crisis)** | |
| 1-23 hours | 35 (17.86) |
| 1-3 days | 64 (32.65) |
| 4-6 days | 36 (18.37) |
| 1-2 weeks | 31 (15.82) |
| More than 2 weeks | 13 (6.63) |
| Missing | 17 (8.67) |
| **Number of sickle cell pain attacks (crises) in the past year, mean (SD)** | 3.12 (1.22) |
| **Sickle cell severity score[%], mean (SD)** | 51.95 (8.10) |
| **Sickle cell frequency score[%], mean (SD)** | 51.41 (9.51) |

SCA= Sickle Cell Anemia; SD=Standard Deviation; QOL=Quality of Life; *Hemoglobin S, Hemoglobin Sβ0 (beta zero) thalassemia, Hemoglobin Sβ+ (beta) thalassemia, Hemoglobin SD; [++]Other includes White/Caucasian, American Indian/Alaskan Native, Asian, Native Hawaiian/Other Pacific Islander, Hispanic, Middle Eastern, Mixed race; [^]Measured using the ASCQ-ME Medical History Checklist; [%]Measured using the ASCQ-ME Pain Episode Measure.

The mean HRQOL scale scores for the study sample were: Emotional impact scale, 46.85 (±8.56); Pain impact scale, 44.94 (±8.40); Sleep impact scale, 46.86 (±7.37); Social functioning impact scale, 47.35 (±9.44) and Stiffness impact scale, 46.18 (±7.91). Kurtosis and skewness coefficients were calculated to check for multivariate normality. Absolute values of the skew index and kurtosis index for all study variables were found to be less than 3.0 and less than 10.0 respectively. Therefore, the data were considered to be normally distributed.(143) Descriptive statistics for all study measures have been reported in Table 3.2 below.

**Bivariate Analysis**

Bivariate correlations between study variables were computed using the Pearson's correlation coefficient. Statistically significant correlations were seen between the majority of the variables in the SEM model and the five HRQOL scale scores among adults with SCD. Correlations between passive adherence coping and all HRQOL scale scores (except stiffness impact scale score); and social support and pain impact scores, sleep impact scores and stiffness impact scores were not found to be significant. All bivariate correlations have been reported in Table 3.3 below.

**Psychosocial predictors of HRQOL**

Based on the postulated relationships, a structural equation model was tested. This model tested the mediating role of self-efficacy and coping in the relationship between SCD severity and HRQOL as well as SCD frequency and HRQOL. Additionally, the moderating effect of social support on the relationship between self-efficacy and HRQOL as well as coping and HRQOL was tested (Figure 3.1). Five separate parallel mediation models were run for each HRQOL scale (pain impact, emotional impact, sleep impact, stiffness impact and social functioning impact). In all the five models all the interaction terms testing the moderating role of

social support were not statistically significant at $\alpha = 0.05$. Overall, our hypothesis that social support moderates the relationship between coping and HRQOL and the relationship between self-efficacy and HRQOL was not supported.

To maintain a parsimonious model, we dropped the insignificant interaction terms between social support and self-efficacy as well as between social support and the coping variables from the model and as a post-hoc analysis analyzed the mediating role of self-efficacy and coping between the relationship between SCD severity and frequency and HRQOL.

Table 3.4 contains the parameter estimates for the individual paths and indirect effects on the relationship between SCD severity and HRQOL (measured as emotional impact, pain impact, sleep impact, stiffness impact and social functioning impact) as mediated by active coping, affective coping, passive adherence coping and self-efficacy. With zero in the confidence interval, the total indirect effect of these four mediators was not significant for all HRQOL outcomes except social functioning impact (estimate= -0.101; 95% CI: -0.20, -0.006). However, Preacher and Hayes (2008)(150) reasoned that specific indirect effects should still be studied even in the presence of a non-significant total indirect effect as suppression effects may hide the impact the individual mediators may have.(151) Thus, we also examined the specific indirect effect of each of the four mediators on the relationship between disease severity and the five HRQOL domains. The indirect effect of affective coping was significant for the relationships between SCD severity and emotional impact (estimate= -0.089; 95% CI: -0.186, -0.005) as well as SCD severity and sleep impact (estimate= -0.045; 95% CI: -0.098, -0.002) as demonstrated by confidence intervals that did not contain zero. Affective coping was a significant mediator such that SCD severity were positively related (estimate=0.017) to affective coping, which, in turn, was negatively related to emotional impact (estimate=-5.262). So, two patients that differ by one

**Table 3.2: Descriptive statistics for the variables in the study model**

| | N | Min | Max | Mean | Std. Dev | Skewness | | Kurtosis | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Statistic | Std. Error | Statistic | Std. Error |
| Emotional impact | 177 | 26.8 | 65.5 | 46.85 | 8.56 | 0.36 | 0.18 | -0.18 | 0.36 |
| Pain impact | 179 | 24.8 | 63.8 | 44.94 | 8.40 | 0.49 | 0.18 | 0.65 | 0.36 |
| Sleep impact | 179 | 32.0 | 63.8 | 46.86 | 7.37 | -0.06 | 0.18 | -0.32 | 0.36 |
| Social functioning | 177 | 26.1 | 69.8 | 47.35 | 9.44 | 0.51 | 0.18 | 0.71 | 0.36 |
| Stiffness impact | 177 | 25.0 | 65.4 | 46.18 | 7.91 | 0.18 | 0.18 | 0.55 | 0.36 |
| Severity | 177 | 33.58 | 66.33 | 51.95 | 8.09 | -0.33 | 0.18 | -0.67 | 0.36 |
| Frequency | 171 | 28.53 | 63.51 | 51.41 | 9.51 | -0.81 | 0.19 | -0.10 | 0.37 |
| Active coping | 196 | 0.60 | 6.00 | 2.88 | 0.93 | 0.43 | 0.17 | 0.41 | 0.35 |
| Affective coping | 196 | 0.75 | 5.47 | 3.36 | 0.90 | -0.02 | 0.17 | -0.27 | 0.35 |
| Passive adherence coping | 196 | 0.98 | 5.89 | 4.41 | 0.73 | -0.83 | 0.17 | 2.06 | 0.35 |
| Self-Efficacy | 177 | 9 | 45 | 28.87 | 6.78 | -0.18 | 0.18 | 0.19 | 0.36 |
| Social Support | 177 | 1.00 | 5.00 | 3.58 | 0.98 | -0.38 | 0.18 | -0.81 | 0.36 |

unit on their SCD severity are estimated to differ by -0.089 units on their SCD related emotional impact because of the tendency for those with relatively more severe SCD tend to adopt more of the affective coping strategies (estimate=0.017 is positive), which in turn translates into lower emotional impact (estimate= -5.262), holding all other mediator's constant. Similarly, affective coping was positively related to SCD severity (estimate=0.017) and negatively related to sleep impact (estimate= -2.631). Thus, two patients that differ by one unit on their SCD severity are estimated to differ by -0.045 units on their SCD related sleep impact because of the tendency for those with relatively more severe SCD tend to adopt more of the affective coping strategies (estimate=0.017 is positive), which in turn translates into lower sleep impact (estimate= -2.631), holding all other mediator's constant.

Table 3.5 contains the parameter estimates for the individual paths and indirect effects on the relationship between SCD frequency and HRQOL (measured as emotional impact, pain impact, sleep impact, stiffness impact and social functioning impact) as mediated by active coping, affective coping, passive adherence coping and self-efficacy. With zero in the confidence interval, the total indirect effect of these four mediators was significant for three HRQOL outcomes: pain impact (estimate= -0.083; 95% CI: -0.157, -0.015), social functioning impact (estimate= -0.103; 95% CI: -0.184, -0.024) and stiffness impact (estimate= -0.117; 95% CI: -0.198, -0.035). We also examined the specific indirect effect of each of the four mediators on the relationship between SCD crises frequency and the five HRQOL domains. The indirect effect of self-efficacy was significant for the relationships between SCD crises frequency and emotional impact (estimate= -0.036; 95% CI: -0.076, -0.004), stiffness impact (estimate= -0.059; 95% CI: -0.122, -0.012), social functioning impact (estimate= -0.072; 95% CI: -0.144, -0.017) and pain impact (estimate= -0.043; 95% CI: -0.092, -0.006) as demonstrated by confidence intervals that

**Table 3.3: Correlations among study variables**

| | Emotional impact score | Pain impact score | Sleep impact score | Social functioning score | Stiffness impact score | Severity score | Frequency score | Active coping | Affective coping | Passive adherence coping | Self-Efficacy | Social Support |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Emotional impact score | 1 | | | | | | | | | | | |
| Pain impact score | .657** | 1 | | | | | | | | | | |
| Sleep impact score | .548** | .542** | 1 | | | | | | | | | |
| Social functioning score | .594** | .667** | .445** | 1 | | | | | | | | |
| Stiffness impact score | .631** | .636** | .525** | .592** | 1 | | | | | | | |
| Severity score | -.223** | -.311** | -.290** | -.266** | -.204** | 1 | | | | | | |
| Frequency score | -.200** | -.357** | -.189* | -.312** | -.164* | .071 | 1 | | | | | |
| Active coping | -.332** | -.293** | -.283** | -.195** | -.392** | .059 | .214** | 1 | | | | |
| Affective coping | -.661** | -.395** | -.403** | -.402** | -.504** | .186* | .148 | .455** | 1 | | | |
| Passive adherence coping | -.118 | -.092 | -.053 | -.102 | -.154* | .180* | .081 | .399** | .254** | 1 | | |
| Self-Efficacy | .435** | .365** | .290** | .470** | .401** | -.191* | -.273** | .082 | -.377** | .054 | 1 | |
| Social Support | .218** | .140 | .141 | .165* | .111 | -.020 | -.134 | -.013 | -.183* | .209** | .280** | 1 |

*. Correlation is significant at the 0.05 level (2-tailed).
**. Correlation is significant at the 0.01 level (2-tailed).

did not contain zero. So, for patients that differ by one unit on their SCD crises frequency are estimated to differ by -0.043 units on their SCD related pain impact because of the tendency for those with relatively more frequent SCD crises tend to be less self-efficacious (estimate= -0.162 is negative), which in turn translates into greater pain impact (estimate= 0.267 is positive), holding all other mediator's constant. Similarly, for patients that differ by one unit on their SCD crises frequency are estimated to differ by -0.036 units on their SCD related emotional impact because of the tendency for those with relatively more frequent SCD crises tend to have lower self-efficacy (estimate= -1.162 is negative), which in turn translates into greater emotional impact (estimate= 0.225 is negative), holding all other mediator's constant. Similar inferences can be made for the mediational effect of self-efficacy on the relationship between SCD crises frequency and social functioning impact and stiffness impact.

**Table 3.4: Unstandardized path coefficients for the study model examining psychosocial predictors of health-related quality of life with sickle cell disease severity as the predictor**

| Path | Estimate | SE | Bootstrap 95% Confidence Interval | |
|---|---|---|---|---|
| | | | LLCI | ULCI |
| **Outcome=Emotional Impact[a]** | | | | |
| Individual paths | | | | |
| Severity → Self-efficacy | -0.134 | 0.062 | -0.256 | -0.013 |
| Severity → Active Coping | 0.006 | 0.008 | -0.100 | 0.022 |
| Severity → Affective Coping | 0.017 | 0.008 | 0.002 | 0.032 |
| Severity → Passive Adherence Coping | 0.017 | 0.007 | 0.004 | 0.030 |
| Self-efficacy → Emotional Impact | 0.225 | 0.063 | -0.242 | 0.007 |
| Active Coping → Emotional Impact | -0.918 | 0.745 | -2.389 | 0.553 |
| Affective Coping → Emotional Impact | -5.262 | 0.762 | -6.766 | -3.758 |
| Passive Adherence Coping → Emotional Impact | 1.080 | 0.787 | -0.495 | 2.655 |
| Severity → Emotional Impact | -0.118 | 0.087 | 0.053 | 0.397 |
| Indirect effects | | | | |
| Total Indirect effect | -0.107 | 0.059 | -0.223 | 0.006 |
| Severity → Self-efficacy → Emotional Impact | -0.030 | 0.012 | -0.075 | 0.002 |
| Severity → Active Coping → Emotional Impact | -0.006 | 0.011 | -0.032 | 0.012 |
| Severity → Affective Coping → Emotional Impact | -0.089 | 0.046 | -0.186 | -0.005 |
| Severity → Passive Adherence Coping → Emotional Impact | 0.018 | 0.019 | -0.021 | 0.057 |
| **Outcome=Pain Impact[a]** | | | | |
| Individual paths | | | | |
| Severity → Self-efficacy | -0.134 | 0.062 | -0.256 | -0.013 |
| Severity → Active Coping | 0.006 | 0.008 | -0.010 | 0.022 |
| Severity → Affective Coping | 0.017 | 0.008 | 0.002 | 0.032 |
| Severity → Passive Adherence Coping | 0.017 | 0.007 | 0.004 | 0.030 |
| Self-efficacy → Pain Impact | 0.267 | 0.099 | 0.071 | 0.463 |
| Active Coping → Pain Impact | -2.275 | 0.849 | -0.385 | -0.101 |
| Affective Coping → Pain Impact | -1.439 | 0.868 | -3.951 | -0.599 |
| Passive Adherence Coping → Pain Impact | 1.171 | 0.909 | -0.624 | 2.965 |
| Severity → Pain Impact | -0.243 | 0.072 | -0.385 | -0.101 |
| Indirect effects | | | | |
| Total Indirect effect | -0.055 | 0.042 | -0.139 | 0.023 |
| Severity → Self-efficacy → Pain Impact | -0.036 | 0.024 | -0.090 | 0.002 |
| Severity → Active Coping → Pain Impact | -0.014 | 0.020 | -0.057 | 0.027 |

| | | | | |
|---|---|---|---|---|
| Severity → Affective Coping→ Pain Impact | -0.024 | 0.022 | -0.075 | 0.010 |
| Severity → Passive Adherence Coping→ Pain Impact | 0.020 | 0.021 | -0.024 | 0.062 |
| **Outcome=Sleep Impact[a]** | | | | |
| Individual paths | | | | |
| Severity → Self-efficacy | -0.134 | 0.062 | -0.256 | -0.013 |
| Severity → Active Coping | 0.006 | 0.008 | -0.010 | 0.022 |
| Severity → Affective Coping | 0.017 | 0.008 | 0.002 | 0.032 |
| Severity → Passive Adherence Coping | 0.017 | 0.007 | 0.004 | 0.030 |
| Self-efficacy → Sleep Impact | 0.151 | 0.089 | -0.025 | 0.326 |
| Active Coping→Sleep Impact | -1.364 | 0.760 | -2.865 | 0.138 |
| Affective Coping → Sleep Impact | -2.631 | 0.777 | -4.166 | -1.095 |
| Passive Adherence Coping→Sleep Impact | 1.146 | 0.814 | -0.462 | 2.754 |
| Severity → Sleep Impact | -0.194 | 0.064 | -0.321 | -0.067 |
| Indirect effects | | | | |
| Total Indirect effect | -0.054 | 0.040 | -0.135 | 0.021 |
| Severity → Self-efficacy → Sleep Impact | -0.020 | 0.018 | -0.064 | 0.004 |
| Severity → Active Coping→Sleep Impact | -0.008 | 0.013 | -0.037 | 0.018 |
| Severity → Affective Coping→ Sleep Impact | -0.045 | 0.025 | -0.098 | -0.001 |
| Severity → Passive Adherence Coping→ Sleep Impact | 0.019 | 0.016 | -0.013 | 0.051 |
| **Outcome=Stiffness Impact[a]** | | | | |
| Individual paths | | | | |
| Severity → Self-efficacy | -0.134 | 0.062 | -0.256 | -0.013 |
| Severity → Active Coping | 0.006 | 0.008 | -0.100 | 0.022 |
| Severity → Affective Coping | 0.017 | 0.008 | 0.002 | 0.032 |
| Severity → Passive Adherence Coping | 0.017 | 0.007 | 0.004 | 0.030 |
| Self-efficacy → Stiffness Impact | 0.448 | 0.109 | 0.233 | 0.663 |
| Active Coping→Stiffness Impact | -1.267 | 0.931 | -3.107 | 0.573 |
| Affective Coping → Stiffness Impact | -1.870 | 0.952 | -3.751 | 0.012 |
| Passive Adherence Coping→Stiffness Impact | 0.400 | 0.997 | -1.610 | 2.330 |
| Severity → Stiffness Impact | -0.177 | 0.079 | -0.333 | -0.021 |
| Indirect effects | | | | |
| Total Indirect effect | -0.094 | 0.051 | -0.201 | 0.001 |
| Severity → Self-efficacy → Stiffness Impact | -0.060 | 0.038 | -0.144 | 0.006 |
| Severity → Active Coping→Stiffness Impact | -0.008 | 0.015 | -0.040 | 0.020 |
| Severity → Affective Coping→ Stiffness Impact | -0.032 | 0.027 | -0.097 | 0.007 |

| | | | | |
|---|---|---|---|---|
| Severity → Passive Adherence Coping → Stiffness Impact | 0.006 | 0.019 | -0.037 | 0.042 |
| **Outcome=Social Functioning Impact[a]** | | | | |
| Individual paths | | | | |
| Severity → Self-efficacy | -0.134 | 0.062 | -0.256 | -0.013 |
| Severity → Active Coping | 0.006 | 0.008 | -0.010 | 0.022 |
| Severity → Affective Coping | 0.017 | 0.008 | 0.002 | 0.032 |
| Severity → Passive Adherence Coping | 0.017 | 0.007 | 0.004 | 0.030 |
| Self-efficacy → Social Functioning Impact | 0.364 | 0.100 | 0.186 | 0.541 |
| Active Coping → Social Functioning Impact | -2.781 | 0.769 | -4.300 | -1.262 |
| Affective Coping → Social Functioning Impact | -2.291 | 0.787 | -3.844 | -0.737 |
| Passive Adherence Coping → Social Functioning Impact | 0.264 | 0.824 | -1.363 | 1.891 |
| Severity → Social Functioning Impact | -0.083 | 0.065 | -0.212 | 0.046 |
| Indirect effects | | | | |
| Total Indirect effect | -0.101 | 0.049 | -0.200 | -0.006 |
| Severity → Self-efficacy → Social Functioning Impact | -0.049 | 0.031 | -0.117 | 0.005 |
| Severity → Active Coping → Social Functioning Impact | -0.017 | 0.023 | -0.066 | 0.028 |
| Severity → Affective Coping → Social Functioning Impact | -0.040 | 0.024 | -0.092 | 0.001 |
| Severity → Passive Adherence Coping → Social Functioning Impact | 0.004 | 0.018 | -0.040 | 0.036 |

*SE=Standard error; LLCI=Lower-level confidence interval; ULCI=Upper-level confidence interval; [a]The model controls for age, insurance status and frequency of sickle cell crises as covariates.*

**Table 3.5: Unstandardized path coefficients for the study model examining psychosocial predictors of health-related quality of life with sickle cell disease crises frequency as the predictor**

| Path | Estimate | SE | Bootstrap 95% Confidence Interval | |
|---|---|---|---|---|
| | | | LLCI | ULCI |
| **Outcome=Emotional Impact[a]** | | | | |
| Individual paths | | | | |
| Frequency → Self-efficacy | -0.162 | 0.054 | -0.268 | -0.055 |
| Frequency → Active Coping | 0.016 | 0.007 | 0.002 | 0.030 |
| Frequency → Affective Coping | 0.007 | 0.007 | -0.007 | 0.020 |
| Frequency → Passive Adherence Coping | 0.005 | 0.006 | -0.006 | 0.016 |
| Self-efficacy → Emotional Impact | 0.225 | 0.087 | 0.053 | 0.39 |
| Active Coping → Emotional Impact | -0.918 | 0.745 | -2.389 | 0.553 |
| Affective Coping → Emotional Impact | -5.262 | 0.762 | -6.766 | -3.758 |
| Passive Adherence Coping → Emotional Impact | 1.080 | 0.787 | -0.495 | 2.655 |
| Frequency → Emotional Impact | -0.052 | 0.056 | -0.162 | 0.059 |
| Indirect effects | | | | |
| Total Indirect effect | -0.082 | 0.045 | -0.164 | 0.015 |
| Frequency → Self-efficacy → Emotional Impact | -0.036 | 0.019 | -0.076 | -0.004 |
| Frequency → Active Coping → Emotional Impact | -0.014 | 0.017 | -0.057 | 0.008 |
| Frequency → Affective Coping → Emotional Impact | -0.036 | 0.036 | -0.106 | 0.037 |
| Frequency → Passive Adherence Coping → Emotional Impact | 0.006 | 0.014 | -0.009 | 0.045 |
| **Outcome=Pain Impact[a]** | | | | |
| Individual paths | | | | |
| Frequency → Self-efficacy | -0.162 | 0.054 | -0.268 | -0.055 |
| Frequency → Active Coping | 0.016 | 0.007 | 0.002 | 0.030 |
| Frequency → Affective Coping | 0.007 | 0.007 | -0.007 | 0.020 |
| Frequency → Passive Adherence Coping | 0.005 | 0.006 | -0.006 | 0.016 |
| Self-efficacy → Pain Impact | 0.267 | 0.099 | 0.071 | 0.463 |
| Active Coping → Pain Impact | -2.275 | 0.849 | -3.951 | -0.599 |
| Affective Coping → Pain Impact | -1.439 | 0.868 | -3.153 | 0.275 |
| Passive Adherence Coping → Pain Impact | 1.171 | 0.909 | -0.624 | 2.965 |
| Frequency → Pain Impact | -0.212 | 0.064 | -0.338 | -0.086 |
| Indirect effects | | | | |
| Total Indirect effect | -0.083 | 0.036 | -0.157 | -0.015 |
| Frequency → Self-efficacy → Pain Impact | -0.043 | 0.022 | -0.092 | -0.006 |

| | | | | |
|---|---|---|---|---|
| Frequency → Active Coping → Pain Impact | -0.036 | 0.027 | -0.101 | 0.002 |
| Frequency → Affective Coping → Pain Impact | -0.010 | 0.013 | -0.040 | 0.014 |
| Frequency → Passive Adherence Coping → Pain Impact | 0.006 | 0.015 | -0.0.9 | 0.049 |
| **Outcome=Sleep Impact[a]** | | | | |
| Individual paths | | | | |
| Frequency → Self-efficacy | -0.162 | 0.054 | -0.268 | -0.055 |
| Frequency → Active Coping | 0.016 | 0.007 | 0.002 | 0.030 |
| Frequency → Affective Coping | 0.007 | 0.007 | -0.007 | 0.020 |
| Frequency → Passive Adherence Coping | 0.005 | 0.006 | -0.006 | 0.016 |
| Self-efficacy → Sleep Impact | 0.151 | 0.089 | -0.025 | 0.326 |
| Active Coping → Sleep Impact | -1.364 | 0.760 | -2.865 | 0.138 |
| Affective Coping → Sleep Impact | -2.631 | 0.777 | -4.166 | -1.095 |
| Passive Adherence Coping → Sleep Impact | 1.146 | 0.814 | -0.462 | 2.754 |
| Frequency → Sleep Impact | -0.067 | 0.057 | -0.179 | 0.046 |
| Indirect effects | | | | |
| Total Indirect effect | -0.058 | 0.033 | -0.122 | 0.007 |
| Frequency → Self-efficacy → Sleep Impact | -0.024 | 0.017 | -0.065 | 0.001 |
| Frequency → Active Coping → Sleep Impact | -0.021 | 0.019 | -0.067 | 0.004 |
| Frequency → Affective Coping → Sleep Impact | -0.018 | 0.020 | -0.060 | 0.019 |
| Frequency → Passive Adherence Coping → Sleep Impact | 0.006 | 0.012 | -0.008 | 0.038 |
| **Outcome=Stiffness Impact[a]** | | | | |
| Individual paths | | | | |
| Frequency → Self-efficacy | -0.162 | 0.054 | -0.268 | -0.055 |
| Frequency → Active Coping | 0.016 | 0.007 | 0.002 | 0.030 |
| Frequency → Affective Coping | 0.007 | 0.007 | -0.007 | 0.020 |
| Frequency → Passive Adherence Coping | 0.005 | 0.006 | -0.006 | 0.016 |
| Self-efficacy → Stiffness Impact | 0.448 | 0.109 | 0.233 | 0.663 |
| Active Coping → Stiffness Impact | -1.267 | 0.931 | -3.107 | 0.573 |
| Affective Coping → Stiffness Impact | -1.870 | 0.952 | -3.751 | 0.012 |
| Passive Adherence Coping → Stiffness Impact | 0.400 | 0.997 | -1.610 | 2.330 |
| Frequency → Stiffness Impact | -0.183 | 0.070 | -0.321 | -0.045 |
| Indirect effects | | | | |
| Total Indirect effect | -0.103 | 0.050 | -0.184 | -0.024 |
| Frequency → Self-efficacy → Stiffness Impact | -0.072 | 0.033 | -0.144 | -0.017 |
| Frequency → Active Coping → Stiffness Impact | -0.020 | 0.023 | -0.075 | 0.013 |

| | | | | |
|---|---|---|---|---|
| Frequency→ Affective Coping→ Stiffness Impact | -0.013 | 0.017 | -0.052 | 0.016 |
| Frequency→ Passive Adherence Coping → Stiffness Impact | 0.002 | 0.010 | -0.015 | 0.027 |
| **Outcome=Social Functioning Impact[a]** | | | | |
| Individual paths | | | | |
| Frequency → Self-efficacy | -0.162 | 0.054 | -0.268 | -0.055 |
| Frequency → Active Coping | 0.016 | 0.007 | 0.002 | 0.030 |
| Frequency → Affective Coping | 0.007 | 0.007 | -0.007 | 0.020 |
| Frequency→Passive Adherence Coping | 0.005 | 0.006 | -0.006 | 0.016 |
| Self-efficacy → Social Functioning Impact | 0.364 | 0.090 | 0.186 | 0.541 |
| Active Coping→Social Functioning Impact | -2.781 | 0.769 | -4.300 | -1.262 |
| Affective Coping → Social Functioning Impact | -2.291 | 0.787 | -3.844 | -0.737 |
| Passive Adherence Coping→Social Functioning Impact | 0.264 | 0.824 | -1.363 | 1.891 |
| Frequency→ Social Functioning Impact | 0.013 | 0.058 | -0.102 | 0.127 |
| Indirect effects | | | | |
| Total Indirect effect | -0.117 | 0.042 | -0.198 | -0.035 |
| Frequency→Self-efficacy → Social Functioning Impact | -0.059 | 0.028 | -0.122 | -0.012 |
| Frequency →Active Coping → Social Functioning Impact | -0.044 | 0.026 | -0.102 | 0.001 |
| Frequency→ Affective Coping→ Social Functioning Impact | -0.016 | 0.018 | -0.057 | 0.014 |
| Frequency→ Passive Adherence Coping → Social Functioning Impact | 0.001 | 0.010 | -0.011 | 0.031 |

*SE=Standard error; LLCI=Lower-level confidence interval; ULCI=Upper-level confidence interval; [a]The model controls for age, insurance status and severity of sickle cell disease as covariate.*

## DISCUSSION

Although previous studies have examined the relationships stated in the SCMSCD model among individuals with SCD and other chronic illnesses (67,69,119), these studies have mainly focused on self-care management resources such as assertiveness, self-care ability, social support and self-efficacy; vulnerability factors such as lack of sickle cell crisis sign recognition and response, number of complications, number of acute pain episodes per year, and health outcomes such as HRQOL, pain management experience, depressive symptoms, self-esteem, and perceived

health-related stigma. However, many existing studies have overlooked the role of other psychosocial variables such as coping strategies. Coping been identified as one of main factor of HRQOL among patients with SCD and with other diseases.(64,82,152,153) Also, majority of the studies have not used instruments specific to SCD to measure coping strategies, self-efficacy and HRQOL and have conducted studies only in African American or in young adults thus limiting the generalizability of their findings. The current study sought to identify psychosocial predictors of HRQOL by assessing the theory of self-care management for sickle cell disease. The relationships between constructs such as SCD severity, SCD crises frequency, social support, coping strategies adopted, patient self-efficacy, and HRQOL (domains include impact on pain, emotional, social functioning, sleep, and stiffness) were examined in the current study using SEM.

Results from the SEM analysis suggested a direct as well as an indirect effect of SCD severity and SCD crises frequency on HRQOL among adults with SCD. As hypothesized, SCD severity had a significantly negative direct effect on the HRQOL domains such as pain impact, sleep impact and stiffness impact. Similarly, SCD crises frequency also had a significantly negative direct effect on the HRQOL domains such as pain and stiffness. These findings are consistent with the existing literature. A study by Jenerette and Murdaugh also found vulnerability factors such as SCD severity and crises frequency had a significant negative impact on health outcomes.(67) Another study by Rizio et al. reported that patients with SCD who had more frequent or severe VOCs experienced deficits in multiple domains of HRQOL.(154) With respect to the individual domains of HRQOL, the current study suggested that the negative impact of severity on pain was greatest followed by sleep and social functioning. Patients with SCD suffer from repeated VOCs and occurrence of these VOCs has been linked to deficits in

domains of HRQOL such as general health, vitality, and bodily pain.(7) Patients with SCD also report facing sleep disruptions, as well as poor physical and mental well-being.(73) The burden of SCD may also lead to an inability to maintain consistent work or schooling, engage in social or recreational activities, and participate in family life leading to isolation and poor social functioning.(15,154) Considering these limitations placed by SCD on the pain, sleep, and social aspects of the lives of patients, it is reasonable to expect a negative relationship between severity, frequency and HRQOL domains.

The impact of coping on HRQOL among adults with SCD has not been assessed extensively in the existing literature. The findings from the current study suggest that affective coping had a significant negative impact on the pain, sleep, and stiffness domains of HRQOL in SCD adults. A study by Gil et al.(54) reports that individuals with greater use of affective coping had more severe pain episodes, were less active during painful episodes, had higher levels of psychological distress and had more frequent hospitalizations and ER visits. This factor of affective coping appears to detect a pattern of coping with SCD pain that is associated with a varied range of maladaptive responses.(54) As with other pain populations(58,59,62), in SCD irrational perceptions such as catastrophizing, anger and fear self-statements, isolation are associated with greater pain suffering in terms of both psychosocial and functional impairment. Therefore, affective coping strategies are linked to poor pain outcomes.(54) Also, those who report more negative thinking in response to sickle cell pain have also reported to suffer more distress and worse psychological adjustment.(49) Like SCD, in hemophilia patients too, use of affective or maladaptive coping was associated with poor socio-psychological health, lessened participation in daily activities, and reduced social interaction.(156) Santavirta et al. found that among patients with bleeding disorders, the use of affective coping strategies like distraction and

catastrophizing was more than use of active coping strategies such as reinterpreting pain.(157) Also, the use of affective coping strategies was significantly related with poor psychosocial well-being.(157)

In the current study, affective coping also mediated the relationship between SCD severity and the pain and sleep domains of HRQOL. This suggests that an increase in SCD-related severity may lead to a greater adoption of affective coping strategies which in turn would be associated with lower HRQOL in terms of pain and sleep functioning. Similarly, Barakat et al. found that affective coping as a coping strategy mediated the relationship between pain intensity and depression, as well as the relationship between sickle cell diseases pain interference with activities and anxiety among adolescents with SCD.(158) Another study reported a similar finding where coping was found to mediate the relationship between disease severity and psychosocial well-being among adults with hemophilia.(157) Overall, the impact of SCD severity on HRQOL domains may be alleviated with the restricted use of affective coping strategies. Clinicians as well as caregivers of adults with SCD must encourage patients to build better coping mechanisms which could help in the long-term management of their symptoms, possibly reduce SCD disease severity, SCD crises frequency, and improve their HRQOL. Literature suggests that the impact of coping strategies employed may be more effective if supported comprehensively by health care providers.(159) Research shows that just a conversation conveying high-level information about the problem with the healthcare provider was considered most beneficial by the patients in feeling comfortable and had a reassuring effect on the patients.(159) Also, personal contact to the physician proved to be the most wanted source for information.(159) Given, the developments in telemedicine, healthcare providers can now

engage more closely with patients which may help in reducing disease related stress and help in better coping.

A positive effect of self-efficacy on emotional, pain, stiffness, and social functioning domains of HRQOL was observed in this study. Self-efficacy has been found to predict better functional status among patients with sickle cell disease(132) and arthritis.(160,161) Studies that assessed chronic conditions stated that higher levels of self-efficacy were related to reduced pain severity and fewer self-reported symptoms(132) as well as increased use of active/adaptive coping strategies improved adherence to treatments.(130) Lower levels of self-efficacy were associated with more disease symptoms, elevated pain severity, and frequent healthcare visits. In SCD, self-efficacy was negatively correlated with the number of pain crises per year.(162) Moreover, self-efficacy beliefs were inversely related to symptomatology and healthcare utilization, and these beliefs may well predict future changes in SCD symptomatology.(130,132) Similarly, even in chronic conditions like fibromyalgia, arthritis, chronic low back pain, higher levels of self-efficacy were associated with reduced physical symptomatology (e.g., pain severity) and improved psychosocial functioning (e.g., lower levels of depression, stress, and anxiety).(130) Additionally, as hypothesized, we also found that self-efficacy mediated the effect of SCD crises frequency on pain, emotion, stiffness and social functioning domains of HRQOL. In the context of the stress, appraisal and coping framework, self-efficacy served as an important factor in the self-appraisal process which can favorably impact self-reported outcomes of the adaptational process (HRQOL in the present study) more so than other objectively measured outcomes.(153) Several interventions have shown to generate encouraging effects on self-efficacy in other populations.(130) Randomized controlled trials have recommended that short cognitive and behaviorally tailored psychotherapy may improve patient's self-efficacy and

consequently health outcomes in patients with chronic conditions.(130) One study assessing the effects of coping skills training provided via educational videotapes to a sample of patients recovering from coronary artery bypass surgery, improvements in self-efficacy in the intervention group were shown to mediate the effects of the videotapes on length of hospital stay.(163) To our knowledge, the effects of such interventions have not been documented in the population of adults with SCD and future longitudinal studies should aim to implement and study such interventions. Given the availability of interventions that have demonstrated methods to enhance self-efficacy, it may be clinically beneficial to identify at-risk individuals low in self-efficacy to reduce SCD related burden. Effective and low-cost interventions such as psychoeducational groups, individual counseling, or group therapies may facilitate increased self-efficacy beliefs and improved health outcomes, thus increasing patient and provider satisfaction.(130) Family members, caregivers and clinicians should therefore target improving positive strengths such as self-efficacy among adults with SCD. Interventions designed to improve self-efficacy could result in long-term functional and psychosocial benefits in this patient population and diminish the negative impact of disease severity, pain, and SCD related disability on patient HRQOL.

A few limitations must be considered while understanding the results of this study. First, the cross-sectional nature of the study prevents us from making any causal inferences even with the findings of the study being supported by the proposed theoretical model. Future research studies should test the proposed causality of the model using longitudinal studies. The study employed a national convenience sample of SCD patients and recruited patients through an online patient panel. This may limit the generalizability of the study results. Future studies should try to employ probability sampling-based strategies to recruit rare disease patients. To the

best of our knowledge, this is the first US based study to employ such a large sample size of SCD patients to examine mediational role of psychosocial variables. Future studies must also try to assess the role of psychological variables such as depression and anxiety in the relationship between SCD severity, crises frequency and HRQOL among SCD patients. These variables have been shown to be key predictors of patient well-being in previous studies.(164)

## CONCLUSION

The current study builds on existing literature among adults with SCD and employs the SCMSCD framework to identify psychosocial predictors of HRQOL among adults with SCD. Study results revealed the key role played by variables such as affective coping, self-efficacy, and social support in influencing the HRQOL of adults with SCD. It was found that affective coping had a negative influence on social functioning, pain, and sleep domains of HRQOL. Affective coping also mediated the relationship between SCD severity and emotional and sleep domains of HRQOL. Stakeholders must encourage the restricted use of affective coping strategies to minimize its detrimental impact on HRQOL. Self-efficacy had a significant direct positive relationship with pain, social functioning, stiffness, and emotional domains of HRQOL. Self-efficacy also mediated the impact of SCD crises frequency and stiffness, pain, emotional and social functioning domains of HRQOL. We did not find evidence of the moderating role of social support on the relationship between coping and HRQOL as well as self-efficacy and HRQOL. Caregivers, policy makers, and clinicians must pay heed to these modifiable psychosocial variables in providing care to adults with SCD to maximize the benefit which patients may receive from treatment and improve their HRQOL. In general, the results of this study have both pragmatic and theoretic implications. From a pragmatic viewpoint, results from this study can be used to shape interventions to improve social support, increase the use of active

and restrict the use of affective coping strategies, and develop stronger self-efficacy beliefs among adults with SCD. Such interventions could potentially improve functional status, psychosocial well-being and the overall HRQOL in this patient population. From a theoretical perspective we found that the self-care management model specific to sickle cell disease worked well in trying to explain the nature of the relationship between SCD severity, pain crises frequency and HRQOL. This was the first US based study to use an SEM based approach toward identifying the mediating role of psychosocial predictors of HRQOL among adults with SCD. The information from this study can help researchers modify their understanding of HRQOL among SCD patients. In the future, it would be very important to consider the role of psychosocial variables such as coping, self-efficacy and social support while designing studies in which HRQOL is a key outcome parameter. Excluding such important determinants may lead to biased estimates and an incorrect understanding of HRQOL among patients with SCD and other rare diseases.

# CHAPTER IV

# COPING PATTERNS AMONG ADULT SICKLE CELL DISEASE PATIENTS AND HEALTH-RELATED QUALITY OF LIFE - IMPLICATIONS OF A LATENT PROFILE ANALYSIS

## INTRODUCTION

Individuals with sickle cell disease (SCD) are often confronted with unpredictable and repeated attacks of pain. The processes responsible for the onset of these attacks are not clear, and there is no clear physiological sign of painful crises.(165) Few patients rarely experience pain, while some patients have several episodes per month and require regular hospitalizations and narcotics to control their pain.(81) Along with this erratic pain crises occurrence, individuals also show variability in their pain coping ability.(82) Few SCD patients cope well, lead active lives, and are adapted psychologically to their condition.(54) These SCD patients handle pain on their own at home by increasing oral fluid intake, resting, and taking oral analgesics.(56) Others cope poorly, lead more restricted lives, and are frequently unable to work. Many of these patients are depressed, anxious, and are troubled with physical symptoms and some become more dependent than others on health care services for their pain management.(54,57) In other populations of patients who suffer from chronic pain episodes such as those with osteoarthritis and low back pain, coping strategies are related to pain responses even after controlling for disease severity.(54,58,59) Studies indicate that coping strategies may be essential factors in explaining some of the variability in adjustment to SCD pain.(49,54,82)

Thompson et al.(64) demonstrated that uptake of palliative coping methods has been found to be initially effective but become less effective over time when compared to adaptive strategies such as information-seeking and has been related with poorer adjustment to chronic conditions such as SCD. Regarding coping with pain, strategies characterized by negative thinking and passive adherence have been associated with poorer adjustment.(64,82) According to Lazarus and Folkman's (1984)(85) transactional model of stress and coping theory, one potential contributor to these diverse results is that no single coping strategy is adaptive or maladaptive across all stressful situations. Moreover, in any stressful situation, no single strategy is taken solely, but rather, a wide range of coping strategies are employed.(76) Concentrating on only one single coping strategy could lead to misleading inferences.(76)

Even though previous research demonstrates that people are likely to use a variety of coping strategies concurrently in several settings such as parenting,(73) and caring for the mentally ill,(74) older adults,(75) or even for SCD patients(49,63,82), a traditional variable-centered approach (i.e., factor analysis) still dominates the research on coping,(76,77) including coping among SCD patients. This approach focuses on explaining relationships between the variables of interest in a population,(11) and it often assumes a homogeneous pattern of coping, thus overlooking the probability that people might merge and utilize multiple coping strategies in various ways(75). Researchers realized that this approach was not capturing the distinct nature of the population which could lead to less precise and overgeneralized inferences about the study samples.(78)

To overcome these limitations, a person-centered analytical approach called latent profile analysis (LPA) (79) is proposed in the current study, to explore the unobserved coping patterns of SCD patients. This approach could provide more specific results compared to the traditional

variable-centered approach, as several subpopulations with different coping patterns may be elucidated.(11) We hypothesize that there are distinct coping patterns among SCD patients. Coping patterns are a better indicator of patient's overall preferences in how they deal with stressors as compared to certain coping strategies.(77) Additionally, along with the severe physical symptoms and pain related with SCD, psychological and social concerns associated with the condition might also have a considerable impact on patients quality of life (QOL).(49,166,167) Anie et al.(49) reported that patients may benefit from interventions that enhance the use of appropriate pain coping strategies to improve quality of life. Although no study has investigated the coping pattern of SCD patients and their impact on HRQOL, previous studies on other chronic conditions provide some insights. For example, Kroemeke (76) demonstrated that older adults with chronic conditions demonstrated heterogeneity in coping patterns and their association with HRQOL psychological domain changed longitudinally.

The current study aims to (1) characterize the latent subtypes of the coping patterns among adult SCD patients in the United States through a person-centered analytical approach, (2) examine the significant correlates of these coping patterns, and (3) investigate the relationships between the coping patterns and HRQOL.

Our hypotheses are as follows:

1. There are distinct coping patterns among SCD patients while facing disease related-stressors.
2. Predictors of coping patterns include factors related to patient's sociodemographic and clinical information.
3. Coping patterns affect the HRQOL of SCD patients.

## METHODS

### Study Design

For the current study, a prospective, cross-sectional design was employed. An online survey designed using Qualtrics (Qualtrics Inc., Provo, UT) was self-administered to adults with SCD. The study received approval under the exempt status from the University of Mississippi Institutional Review Board (Protocol #21x-130).

### Study Sample

The study population for the current study included adult patients (≥ 18 years) with SCD. The online survey for the current study was administered to adults with SCD enrolled with a patient panel maintained by Rare Patient Voice, a market research company.

### Study procedures

An email explaining the nature and purpose of the study was sent out to all potential respondents. Participants were assured about the anonymity and confidentiality of their responses. It was emphasized that study participation is voluntary. The email contained a URL link to the study survey. We provided $15 Amazon gift cards to all respondents as a token of appreciation for the completion of the survey.

### Sample Size

There are no empirically-analyzed guidelines concerning the minimum sample size needed for conducting a LPA.(168) A comprehensive simulation study by Geiser and Carlson et al.(168) recommends a sample size of N=200 with at least 9-12 moderate quality indicators. Additionally, the study also states that having more indicators is usually advantageous in most cases. This study utilized the 13 coping subscale scores as indicators for the LCA model with a sample size of N=196.

**Study Measures**

*Coping*

Coping was measured using the Coping Strategy Questionnaire-SCD (CSQ-SCD) scale. This scale was originally developed by Rosenstiel and Keefe to measure cognitive and behavioral coping styles in chronic low back pain.(62) This scale was later on revised by Gil et al. for patients with SCD along with the addition of a few items related to strategies particularly relevant to SCD adult population.(54) This scale, the CSQ-SCD, consist of 78 items each measured on a Likert scale from 0 ("Never do that") to 6 ("Always do that"). The scale measures 13 different domains of coping with 6 items for each domain. The 13 domains are (1) ignoring pain sensations, (2) reinterpreting pain sensations, (3) calming self-statements, (4) diverting attention, (5) increasing activities, (6) anger self-statements, (7) fear self-statements, (8) praying and hoping, (9) isolation, (10) taking fluids, (11) resting, and (12) heat/cold/massage.(49) Scores are means of the subscales.(80)

*Health-Related Quality of Life (HRQOL)*

In this study, the HRQOL in patients with SCD was measured using a SCD specific instrument, ASCQ-Me Short Form.(146) This is a 25-item instrument with 5 item banks: Pain impact (5 items); Emotional impact (5 items); Social Functioning impact (5 items); Stiffness impact (5 items); and Sleep impact (5 items). Each item bank is each scored from 5 ("never") to 1 ("always"). A higher score represents better HRQOL on all item banks and scores on each subscale are standardized to have a mean of 50 and a standard deviation of 10. The ASCQ-Me instrument has been shown to have excellent internal consistency for each item bank (≥.90) and the item banks differed significantly between SCD severity levels in the US setting.(68)

*Socio-demographics and Clinical Information*

The following socio-demographic variables were used as covariates: age, gender, race/ethnicity, education status, occupation status, marital status, type of SCD. The survey also included questions on access to opioid prescriptions and impact of COVID-19 on the patients' quality of life.

The ASCQ-Me SCD Medical History Checklist (SCD-MHC) was used to assess the list of treatments and conditions related with SCD. The response options of "yes" or "no" suggest whether the respondent has that condition or takes that treatment. The score for the checklist is simply the sum of the number of questions with a "yes" response.

The ASCQ-Me Pain Episode measure was used to ascertain the severity and frequency of SCD. The items in the Pain Episode measure are, for instance, "In the past 12 months, how many sickle cell pain attacks (crises) did you have?" and, ''When was your last pain attack?". A higher composite score on each of these ASCQ-Me scales represents more frequency/severity and more comorbidities associated with SCD. In the US setting, the ASCQ-Me has been shown to have excellent internal consistency for each item bank (≥.90) and the item banks differed significantly between SCD severity levels.(68,146)

**Statistical Analyses**

This study used latent profile analysis (LPA), a mixture modeling technique which uses continuous indicators to identify relevant, unobserved groups. This technique is referred to as latent class analysis (LCA) when categorical indicators are used.(169–171) The 13 subscales scores from the CSQ-SCD were used as indicators in the current study and treated as continuous variables. The initial step was to identify the most parsimonious model with the best fit. We used a single class model as the baseline model. We ran models with more classes and compared them with the preceding model (e.g., two-class model vs three-class model). The Chi-square ($\chi 2$)

difference test was used to compare if a more complicated model (k classes) was better than a less complicated model (k-1 classes).(169) Mplus 8.4 was used to implement the LPA. To assess relative model fit we implemented the Lo-Mendell-Rubin likelihood ratio test (LMR) and the Vuong-Lo-Mendell-Rubin likelihood ratio test (VLMR).(169) A statistically significant result ($p < 0.05$) ascertained that a more complex model has a better fit.(169,172,173) Furthermore, the Bayesian Information Criterion (BIC) and the sample-size-adjusted BIC (aBIC) were also used.(169) The superior model has the smallest values of information criteria. The entropy statistic, which ranges from 0 to 1 with values nearer to 1 meaning better classification were used to assess the quality of classification.(169,174) In addition, average class assignment probabilities, with a probability (≥.80) indicating high-classification accuracy, is also reported.(169,174) To enable understanding of each subgroup, the sample sizes of each group and standardized parameter estimates are reported.

Once we determined the number of classes, we then examined the associations between coping classification and the sociodemographic and clinical variables (i.e., the predictors of latent class membership) using multinomial logistic regression. The automated R3STEP auxiliary command was used for the 3-step approach for the multinomial logistic regression in MPlus 8.4.(172) A final analysis looked at the relationship between class membership and HRQOL (i.e., using the latent categorical variable as a predictor of a distal outcome) while adjusting for age, severity, frequency and insurance status. As HRQOL is measured using 5 different item banks (i.e., Pain impact, Emotional impact, Social Functioning impact, Stiffness impact, and Sleep impact) that can be treated continuously, multiple regression was used to explore the association between latent subtypes of coping strategy patterns and the HRQOL of SCD patients. Five separate regression models were built wherein the five HRQOL item banks

were treated as continuous distal outcomes. These regression analyses were performed using the BCH manual estimation as proposed by Asparouhov and Muthén in Mplus 8.4.(175) A two-sided p-value less than 0.05 was considered as statistically significant.

## RESULTS

### Socio-demographic and clinical characteristics

The sample characteristics are given in Table 4.1. The current study sample consisted of 196 adults with SCD, with an average age of 36 years (SD=9.88). Majority of the study population included patients with Hemoglobin SS (sickle cell anemia) (68.88%), females (86.22%), and African Americans (83.67%). Most of the patients lived with someone (71.94%), had more than a high school education (75%), and were unemployed (49.49%). Patients also commonly suffered from more than 2 medical health conditions (58.16%), had an average of 3 sickle cell pain attacks (crises) in the past year and for most of them their pain attack (crisis) lasted for 1-3 days (32.65%). The mean sickle cell pain severity score (51.95) and frequency scores (51.41) were similar to the average score of 50 (for both severity and frequency) in the reference population.(104)

**Table 4.1: Demographic and clinical characteristics of the study sample**

| Characteristics | N (%) |
|---|---|
| **SCD Type** | |
| Hemoglobin SS (SCA) | 135 (68.88) |
| Other* | 61 (31.12) |
| **Age, Mean (SD)** | 36 (9.88) |
| **Gender** | |
| Male | 27 (13.78) |
| Female | 169 (86.22) |
| **Race/Ethnicity** | |
| African American/Black | 164 (83.67) |
| Other++ | 13 (6.63) |
| Missing | 19 (9.69) |

| | |
|---|---|
| **Living Status** | |
| Living alone | 35 (17.86) |
| Living with someone | 141 (71.94) |
| Missing | 20 (10.20) |
| **Education Level** | |
| High school or less | 30 (15.31) |
| More than high school | 147 (75.00) |
| Missing | 19 (9.69) |
| **Employment Status** | |
| Employed (full time/part-time) | 80 (40.82) |
| Unemployed | 97 (49.49) |
| Missing | 19 (9.69) |
| **Region** | |
| Northeast | 46 (23.47) |
| Midwest | 38 (19.39) |
| South | 69 (35.20) |
| West | 23 (11.73) |
| Missing | 20 (10.20) |
| **Insurance** | |
| Yes | 171 (87.24) |
| No | 25 (12.76) |
| **Insurance Type** | |
| Public | 107 (54.60) |
| Private | 46 (23.47) |
| Both | 19 (9.69) |
| Missing | 24 (12.24) |
| **Access** | |
| Most of the times | 30 (15.31) |
| Sometimes | 84 (42.86) |
| Never | 58 (26.60) |
| Missing | 24 (12.24) |
| **Impact of COVID-19 on QOL** | |
| Worsened | 57 (29.08) |
| Remained the same/Improved | 120 (61.22) |
| Missing | 19 (9.69) |
| **Medical Health Conditions**[^] | |
| At least 2 | 82 (41.84) |
| More than 2 | 114 (58.16) |
| **Duration of most recent pain attack (crisis)** | |
| 1-23 hours | 35 (17.86) |
| 1-3 days | 64 (32.65) |
| 4-6 days | 36 (18.37) |
| 1-2 weeks | 31 (15.82) |
| More than 2 weeks | 13 (6.63) |
| Missing | 17 (8.67) |

| | |
|---|---|
| **Number of sickle cell pain attacks (crises) in the past year, mean (SD)** | 3.12 (1.22) |
| **Sickle cell severity score[%], mean (SD)** | 51.95 (8.10) |
| **Sickle cell frequency score[%], mean (SD)** | 51.41 (9.51) |

SCA= Sickle Cell Anemia; SD=Standard Deviation; QOL=Quality of Life; *Hemoglobin S, Hemoglobin Sβ0 (beta zero) thalassemia, Hemoglobin Sβ+ (beta) thalassemia, Hemoglobin SD; [++]Other includes White/Caucasian, American Indian/Alaskan Native, Asian, Native Hawaiian/Other Pacific Islander, Hispanic, Middle Eastern, Mixed race; [^]Measured using the ASCQ-ME Medical History Checklist; [%]Measured using the ASCQ-ME Pain Episode Measure.

The first objective was to determine the number of classes. Model fit indices of the LPA models are given in Table 4.2. Comparisons of fit indices across models showed the AIC, BIC and aBIC reached its lowest value in the four-class solution. However, compared to the three-class model, adding one more class did not significantly improve the model (LMR test=123.57, p-value=0.473; VLMR=125.25, p-value=0.468). Additionally, the entropy statistic indicated that the three-class model (0.86) had a better accuracy of classification compared to the four-class model (0.83). Finally, the three-class model had smaller values of BIC and aBIC, higher entropy, and had significantly better fit compared to the two-class model (LMR test = 164.83, p = 0.05; VLMR test = 167.06, p = 0.05). As a result, the three-class model was used for the subsequent analysis. The average class probabilities were 0.915, 0.945 and 0.946 for class 1, 2 and 3, indicating well-separated classes.

The mean scores of the classification indicators for each of the three classes can be found in Table 4.3. Class 1 (14.0%) was characterized with the highest probability of adopting a variety of cognitive coping strategies very frequently (i.e., reinterpreting pain sensations, diverting attention, calming self-statements, ignoring pain sensations, praying, and hoping, catastrophizing, fear self-statements and anger self-statements) when facing SCD related stressors such as pain crises compared to the other two coping patterns. As a result, this class was named the "high use of variety of cognitive coping skills" group (referred to as "cognitive strategies" group hereafter). For Class 2 (56.0%), a similar pattern as that of Class 1 was

observed, but they had relatively less frequent usage of different coping skills, and slightly higher usage of some negative thinking and passive adherence coping skills such as catastrophizing, fear self-statements and anger self-statements, resting, heat/cold massage and taking fluids. As a result, this class was named as the "negative thinking/passive adherence" group. For Class 3 (30.0%), most of the respondents tended to rely on physiological strategies such as taking fluids and resting while having a low probability of usage of other coping strategies. On subscales such as "reinterpreting pain sensations" and "catastrophizing" this group had the lowest mean indicating not using such strategies at all. As such, this class was named as the "physiological strategies" group.

**Table 4.2: Fit indices of latent profile models**

| No. of classes | Npar | AIC | BIC | aBIC | Entropy | LMR | LMR p-value | VLMR | VLMR p-value |
|---|---|---|---|---|---|---|---|---|---|
| 2 | 40 | 7504.2 | 7635.3 | 7508.6 | 0.8 | 391.1 | 0.03 | 396.4 | 0.03 |
| **3** | **54** | **7365.1** | **7542.2** | **7371.1** | **0.9** | **164.8** | **0.05** | **167.1** | **0.05** |
| 4 | 68 | 7267.9 | 7490.8 | 7275.4 | 0.8 | 123.6 | 0.47 | 125.3 | 0.47 |

Notes: Bold means the final model selected in this study. Npar, numbers of parameter to be estimated; BIC, Bayesian Information Criterion; aBIC, sample-size-adjusted Bayesian Information Criterion; LMR, Lo–Mendell–Rubin likelihood ratio test; VLMR, Vuong–Lo-Mendell–Rubin likelihood ratio test.

We first ran univariable multinomial logistic regressions to assess the significant predictors of group membership. Only predictors found to be significant in the univariable approach were then included as predictors in the multivariable multinomial logistic regression model. The univariable model demonstrated age, severity score, frequency score, and insurance to be significant predictors of class membership. The multinomial logistic regression results suggested that compared to the cognitive strategies coping group, a one-unit increase in sickle cell patients' age (odds ratio [OR] = 1.122, 95% confidence interval [CI] 1.046–1.204, p = 0.001) significantly increases the likelihood of being in the physiological strategies group by

approximately 12%. Similarly, compared to the cognitive coping strategies group, a one-unit increase in SCD severity (OR = 0.221, 95% confidence interval [CI] 0.064–0.763, $p = 0.017$) and a one unit increase in SCD crises frequency (OR = 0.929, 95% confidence interval [CI] 0.896–0.993, $p = 0.029$) significantly decreases the likelihood of being in the physiological strategies group by approximately 78% and 7.1% respectively. Compared to the cognitive coping strategies group, a one-unit increase in SCD severity (OR = 0.270, 95% confidence interval [CI] 0.088-0.830, $p = 0.022$) significantly decreases the likelihood of being in the negative thinking/passive adherence group by approximately 73%. Table 4.4 provides the detailed multinomial logistic regression results.

**Table 4.3: Profiles of coping classes in patients with SCD**

| | **Class 1 (Cognitive strategies)** N=28 (14%) | **Class 2 (Negative thinking/passive adherence strategies)** N=109 (56%) | **Class 3 (Physiological strategies)** N=59(30%) |
|---|---|---|---|
| | **Means** | **Means** | **Means** |
| **Diverting Attention** | 4.874 | 3.535 | 2.322 |
| **Reinterpreting pain sensations** | 3.083 | 1.463 | 0.661 |
| **Calming self-statements** | 5.253 | 3.989 | 3.365 |
| **Ignoring pain sensations** | 3.400 | 2.387 | 1.796 |
| **Praying and hoping** | 4.881 | 4.311 | 3.459 |
| **Catastrophizing** | 4.511 | 3.093 | 1.490 |
| **Fear self-statements** | 4.892 | 3.555 | 2.405 |
| **Anger self-statements** | 4.271 | 3.264 | 1.986 |
| **Increasing behavioral activity** | 4.337 | 3.101 | 2.646 |
| **Isolation** | 4.675 | 3.533 | 2.848 |
| **Taking fluids** | 5.247 | 4.639 | 4.656 |
| **Resting** | 4.899 | 4.372 | 4.341 |
| **Heat/cold Massage** | 5.001 | 4.164 | 3.408 |

**Table 4.4: Multinomial Logistic Regression of the Latent Coping Pattern Subtypes**

| Characteristics | Physiological vs. Cognitive coping strategies | | | Negative thinking/passive adherence vs. Cognitive coping strategies | | | Physiological vs. Negative thinking/passive adherence coping strategies | | |
|---|---|---|---|---|---|---|---|---|---|
| | *OR* | *95% CI* | *p* | *OR* | *95% CI* | *p* | *OR* | *95% CI* | *p* |
| **Age** | 1.122 | 1.046-1.204 | 0.001 | 1.056 | 0.989-1.127 | 0.105 | 1.063 | 1.016-1.112 | 0.008 |
| **Severity** | 0.221 | 0.064-0.763 | 0.017 | 0.270 | 0.088-0.830 | 0.022 | 0.819 | 0.347-1.935 | 0.649 |
| **Frequency** | 0.929 | 0.869-0.993 | 0.029 | 0.954 | 0.899-1.013 | 0.127 | 0.973 | 0.932-1.016 | 0.217 |
| **Insurance** | 12.232 | 0.490-30.539 | 0.127 | 7.718 | 0.456-27.515 | 0.157 | 1.585 | 0.071-15.271 | 0.771 |

Note: CI = confidence interval; OR = odds ratio

Results of the multivariable regression analyses looking at the relationship between class membership and HRQOL (i.e., using the latent categorical variable as a predictor of a distal outcome HRQOL) while controlling for covariates (only covariates found significant in the univariable regression analysis were included in the multivariable regression model) are presented in Table 4.5. In these regression analyses we constrained the relationships between the covariates and the outcome (HRQOL) to be the same across all classes. Here, the intercept is an adjusted mean, representing the average value of the dependent variable considering the covariate and its relationship to the independent variable. The intercept represents the average value of the distal outcome HRQOL when all predictors are equal to zero. For instance, for latent class 1: Cognitive coping strategies, the intercept (=37.660) represents the mean (or expected) value of pain impact score for patients who were insured (coded as 0 in the dataset) and when age (=36.17), severity score (=51.95) and frequency scores (=51.41) were set to their average value in the study (mean centered). Table 4.5 reports the adjusted means for the three latent classes across all the distal outcomes. Table 4.6 reports an omnibus test (Wald test statistic)

which suggests that there are overall significant differences among the latent classes across all the distal outcomes (HRQOL): pain impact (Value=19.454, $p<0.05$), emotional impact (Value =77.355, $p<0.05$), sleep impact (Value=29.666, $p<0.05$), social functioning impact (Value =10.625, $p<0.05$) and stiffness impact (Value=46.228, $p<0.05$) as well as reports the pairwise comparisons of the latent classes for all the distal outcomes (HRQOL) to see which latent classes are significantly different. The pairwise comparisons of the distal outcome (HRQOL) adjusted means demonstrate that there are significant differences across all the latent classes ($p<0.05$).

**Table 4.5: Multivariable Regression of the Latent Coping Pattern Classes on HRQOL^**

| Parameter | Pain Impact | | Emotional Impact | | Sleep Impact | | Social Functioning Impact | | Stiffness Impact | |
|---|---|---|---|---|---|---|---|---|---|---|
| | *Estimate* | *P-value* | *Estimate* | *P-value* | *Estimate* | *P-value* | *Estimate* | *P-value* | *Estimate* | *P-value* |
| **Cognitive coping strategies** | | | | | | | | | | |
| **Intercept (adjusted means)** | | | | | | | | | | |
| ***Latent class 1:*** | | | | | | | | | | |
| **Cognitive coping strategies** | 39.070 | <0.001 | 37.660 | <0.001 | 40.911 | <0.001 | 42.568 | <0.001 | 37.346 | <0.001 |
| ***Latent class 2:*** | | | | | | | | | | |
| **Negative thinking/passive adherence coping strategies** | 44.427 | <0.001 | 44.766 | <0.001 | 46.245 | <0.001 | 46.098 | <0.001 | 44.848 | <0.001 |
| ***Latent class 3:*** | | | | | | | | | | |
| **Physiological coping strategies** | 48.006 | <0.001 | 53.457 | <0.001 | 50.548 | <0.001 | 50.716 | <0.001 | 51.358 | <0.001 |
| **Age*** | 0.047 | 0.502 | 0.005 | 0.942 | -0.026 | 0.611 | 0.009 | 0.895 | -0.014 | 0.801 |
| **Severity score*** | -0.101 | 0.180 | -0.233 | 0.004 | -0.177 | 0.011 | -0.206 | 0.020 | -0.078 | 0.237 |
| **Frequency score*** | -0.057 | 0.404 | -0.254 | 0.001 | -0.080 | 0.190 | -0.247 | 0.002 | -0.039 | 0.523 |
| **Insurance (Yes)** | 2.178 | 0.251 | 1.885 | 0.475 | 3.226 | 0.068 | 4.100 | 0.123 | 3.575 | 0.279 |

^ Five HRQOL item banks (i.e., Pain impact, Emotional impact, Social Functioning impact, Stiffness impact, and Sleep impact) were treated as continuous distal outcomes, *Variables are mean centered.

**Table 4.6: Pairwise Comparisons of the Distal HRQOL^ Outcome Means across Latent Coping Pattern Classes**

| **Parameter** | **Pain Impact** | | **Emotional Impact** | | **Sleep Impact** | | **Social Functioning Impact** | | **Stiffness Impact** | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Value | P-value | Value | P-value | Value | P-value | Value | P-value | Value | P-value |
| **Omnibus test*** | 19.454 | 0.0001 | 77.355 | <0.0001 | 29.666 | <0.0001 | 10.625 | 0.0049 | 46.228 | <0.0001 |
| **Pairwise comparisons** | **Estimate** | **P-value** | **Estimate** | **P-value** | **Estimate** | **P-value** | **Estimate** | **P-value** | **Estimate** | **P-value** |
| **Cognitive coping strategies vs Negative thinking/passive adherence coping strategies** | 5.357 | 0.001 | 7.107 | <0.0001 | 5.333 | 0.001 | 3.529 | 0.100 | 7.502 | <0.0001 |
| **Cognitive coping strategies vs Physiological coping strategies** | 8.937 | <0.001 | 15.798 | <0.0001 | 9.637 | <0.0001 | 8.148 | 0.002 | 14.012 | <0.0001 |
| **Negative thinking/passive adherence coping strategies vs Physiological coping strategies** | 3.580 | 0.029 | 8.691 | <0.0001 | 4.304 | 0.002 | 4.619 | 0.012 | 6.510 | <0.0001 |

^ Five HRQOL item banks (i.e., Pain impact, Emotional impact, Social Functioning impact, Stiffness impact, and Sleep impact) were treated as continuous distal outcome; *Wald test statistics.

## DISCUSSION

Through a person-centered analytical approach, the current study demonstrated that there are three groups of underlying coping strategy patterns among patients with SCD in the US: cognitive coping, negative thinking/passive adherence coping, and physiological coping strategies. Patients in the cognitive coping strategies group used a variety of coping strategies including diverting attention, reinterpreting pain sensations, calming self-statements, ignoring pain sensations, praying, and hoping, catastrophizing, fear self-statements and anger self-statements. Patients in the negative thinking/passive adherence coping group had slightly higher dependence on maladaptive and passive adherence coping strategies such as catastrophizing, fear self-statements, anger self-statements, resting, taking fluids and heat/cold massages. Lastly, patients in the physiologic coping strategies group relied mainly on strategies like heat/cold massages, taking fluids and resting. Furthermore, this was also the group with the lowest probability of using cognitive and negative thinking/passive adherence coping strategies. This study is the first to use latent class methods to provide insights on the complexity of coping strategies in SCD patients.

Previous studies have looked at coping patterns among caregivers, elderly patients with chronic conditions or minority adolescents. Lin et al. (75) reported there are unpatterned, emotional, and hybrid coping patterns among caregivers of frail older adults. While a study by Yuan et al. (77) reported three groups of coping patterns-high coping (highest probability of adopting a variety of coping strategies), medium coping and low coping, among caregivers of persons with dementia. The study among minority adolescents reported three distinct coping profiles: adolescents who used several specific coping strategies at a low level (low generic copers), adolescents who emphasized active/approach strategies (active copers), and adolescents

who emphasized avoidant/passive strategies (avoidant copers).(176) Such differences among the reported patterns of coping strategies might be due to the differences in the study populations of the mentioned studies i.e., the current study focused on SCD patients and the other studies focused on caregivers and adolescents. The differences could also be due to the assessment tools used. The present study utilized the sickle cell specific instrument CSQ-SCD, while other studies have used COPE, Brief COPE, and a self-developed list of coping strategies.(75,77,176) Factors influencing the coping patterns of our sample were mainly related to patients age, insurance status and clinical characteristics such as severity and frequency of SCD. The present study found that increase in age significantly increases the likelihood of using physiologic coping strategies compared to cognitive strategies. As SCD is a disease that worsens over time with increase in pain severity, studies report that patients with the worst pain are more likely to resort to responses such as rest and the application of heat.(49) An increase in SCD severity and crises frequency significantly decreases the likelihood of employing physiological coping strategies as at these times patients may benefit more from using active coping strategies as well as using opioids to manage the pain.

Findings from this study also extend to Lazarus and Folkman's traditional transactional model of stress and coping in additional ways.(85) Previous studies indicated that individuals who adopt coping strategies such as emotional support seeking, problem-solving, and acceptance-based coping tend to have better health outcomes(177), while those who adopt more wishful thinking, avoidance, and denial coping are related with poorer health(77,177–179). However, individuals depend on multiple coping strategies, and these strategies could include both active and passive coping strategies or both problem-solving and emotional coping strategies. Additionally, when several coping strategies are used, the established findings of the

relationship between one specific coping strategy and health outcomes may no longer be relevant, indicating potential research gaps and the need of more research here. In this study, patients with physiological coping strategies had the highest mean HRQOL scores (highest scores on emotional, stiffness, social functioning, and sleep impact scales) as compared to patients with the other two coping patterns. As most SCD patients manage their pain condition at home, may be daily physiologic coping strategies of heat/cold massage, taking enough fluids and resting help in improving their SCD symptoms and in turn their HRQOL. However, due to the cross-sectional nature of this study, future longitudinal studies are still needed to further assess this hypothesis.

The current findings provide valuable new information on coping among SCD patients, and these findings have meaningful implications. First, unlike existing studies focused on specific coping strategies,(49,54,80) our study suggests that patients with SCD combine a variety of coping strategies in different ways and have distinct coping patterns while facing disease stressors. Second, our study suggests that patients with cognitive coping strategies had lower mean pain scores suggesting better pain management. As such, it is vital to identify the driving force behind such a coping pattern and to develop tailored interventions to improve pain management. Third, patients with negative thinking/passive adherence coping strategies had higher mean pain scores indicating more pain severity and crises episodes. Patients in this group could benefit from practicing more acceptance based coping strategies. Acceptance and Commitment Therapy (ACT) is an "evidence-based psychotherapy that targets the struggles with symptoms that may be most prominent and troublesome in chronic disorders."(41) It enables disengagement from self-critical thoughts and fosters psychological adaptability.(43) Studies suggest that ACT might be helpful to situations that are unalterable, such as chronic pain,

(180,181) or loss of psychological function in aging,(182) or lifelong diseases such as SCD. If SCD patients engaging in negative thinking learn to be more accepting of their life-long condition, it can help them adapt better and consequently help improve their HRQOL. Future studies can investigate if ACT can be a viable and effective intervention for patients with SCD.

To the best of our knowledge, this is the first study in the US that used a person-centered analytical approach to explore the coping pattern among patients with SCD in the US. There was another study that had used similar analytical strategies among SCD patients; however, its focus was on classifying patients based on their pain profiles. The benefit of such an approach is that it is able to capture the heterogeneity of the study sample, and as a result, it provides additional understandings that traditional variable-centered approaches alone cannot.(79,183) Increasingly, researchers are starting to combine the use of these two approaches to understand a single issue.(184) For future studies, researchers could investigate the generalizability of the coping patterns among SCD patients elsewhere and the rationale behind each coping pattern.

There are some limitations to the current study. First, the study focused on SCD patients in US, also patients who participated in filling out the study survey could be in better health which might limit the generalizability of the study findings. Also, we are uncertain whether the investigated coping patterns reported in this study also exist among SCD patients elsewhere, as SCD patients at different places may have different characteristics. Nonetheless, researchers could use the same analytical strategies to investigate coping patterns of SCD patients elsewhere. Second, because self-reported measures were used, there might be recall bias in the data collection. More specifically, the results of the ASCQ-Me HRQOL might be affected by frequency and severity of crises experienced and remembered at the time of administration. Third, as SCD is a rare disease, our study had a relatively small sample size which might lead to

less accurate predictions of the associations,(185) therefore future studies should aim to conduct similar analyses using a larger sample size for more accurate estimates. Lastly, the current study used a cross-sectional design, which precluded us from drawing a conclusion on causal relationships (e.g., HRQOL and coping patterns). Future studies can also employ a longitudinal study design to identify the distinct, multidimensional patterns of strategies for coping with SCD and their association with changes in HRQOL.

## CONCLUSION

The current study observed three distinct coping patterns among SCD patients in the US while facing stressful events from the condition, namely, cognitive coping strategies, negative thinking/passive adherence coping strategies, and physiological coping strategies. These coping patterns are featured by the frequency and variety of coping strategies used by patients, and different coping patterns could lead to different HRQOL. SCD patients with the physiological coping strategies had better HRQOL. Factors influencing coping patterns were age, insurance status, and clinical factors such as severity and frequency of the condition. Future research should investigate the underlying reasons for different coping patterns, further test the relationships between coping patterns, caregiving burden, and health outcomes, and examine whether an acceptance-based intervention would be helpful for SCD patients.

# CHAPTER V

## INTRODUCTION

Based on our proposed methods for this dissertation, we collected data from two patient organizations and a patient panel, Rare Patient Voice. However, for the analyses conducted and reported in this dissertation, we only utilized the data collected from Rare Patient Voice. This chapter discusses the issues we came across while analyzing the data from the two patient organizations, how we tackled them and the reasons behind the informed decision we took of not including the data from the two patient organizations based on our findings. In addition, this chapter also summarizes the three studies reported in this dissertation as well as directions for future research.

## DATA COLLECTION FOR THIS DISSERTATION: CARELESS RESPONDING ANALYSIS

### Background

For this dissertation study, in addition to the data collect from the patient panel, Rare Patient Voice, we also collected data from two SCD patient organizations. An online survey designed using Qualtrics (Qualtrics Inc., Provo, UT) was self-administered to adults (≥ 18 years) with SCD in these two patient organizations. An email explaining the nature and purpose of the study was sent out to all potential respondents. Participants were assured about the anonymity and confidentiality of their response, and it was emphasized that study participation is voluntary. The email contained a URL link to the study survey and all respondents were provided $15 Amazon gift cards as a token of appreciation for the completion of the survey.

Upon completion of data collection, we ran descriptive statistics calculated in the form of frequencies and percentages for categorical variables and means and standard deviations for the continuous variables (Table 5.1). Our sample descriptives showed us some inconsistency in the race/ethnicity proportions for the data obtained from the two patient organizations. Sickle cell disease is predominantly prevalent in African Americans/Blacks. Existing studies reporting national estimates of SCD have reported the prevalence of SCD to be ~87-91% in African Americans/Blacks and ~1-2% in Whites.(1,186–188) However, our sample descriptives for the two patient organizations showed the proportions of African Americans/Blacks=22.18% only and Whites=54.03%. Based on the SCD epidemiology literature(1,187,188) and the discrepant sample descriptives observed, we were positive that our data from the two patient organizations showed preliminary evidence of careless responding. Therefore, to further identify careless respondents in the data obtained from the two patient organizations, we employed several data

screening techniques recommended by DeSimone et al.(189) for careless responding and aimed to identify specific low-quality response patterns.

**Table 5.1: Demographic and clinical characteristics of the data from the two patient organizations and Rare Patient Voice**

| Characteristics | Patient Organization N=540 (100%) | Rare Patient Voice N=196 (100%) |
|---|---|---|
| **SCD Type** | | |
| Hemoglobin SS (SCA) | 193 (35.74) | 135 (68.88) |
| Hemoglobin SC | 109 (20.19) | 42 (21.43) |
| Hemoglobin Sβ0 (beta zero) thalassemia | 88 (16.30) | 5 (2.55) |
| Hemoglobin Sβ+ (beta) thalassemia | 69 (12.78) | 12 (6.12) |
| Hemoglobin SD | 33 (6.11) | 2 (1.02) |
| Hemoglobin SE | 30 (5.56) | 0 |
| Hemoglobin SO | 18 (3.33) | 0 |
| **Age, Mean (SD)** | 33 (8.20) | 36 (9.88) |
| **Gender** | | |
| Male | 286 (52.96) | 27 (13.78) |
| Female | 254 (47.04) | 172 (86.22) |
| **Race/Ethnicity** | | |
| African American/Black | 110 (22.18) | 164 (92.66) |
| American Indian/Alaska Native | 50 (10.08) | 0 (0.00) |
| Asian | 10 (2.02) | 1 (0.56) |
| Hispanic | 49 (9.88) | 4 (2.26) |
| Native Hawaiian/Other Pacific Islander | 5 (1.01) | 2 (1.13) |
| Caucasian/White | 268 (54.03) | 2 (1.13) |
| Mixed Race | 1 (0.20) | 3 (1.69) |
| Middle Eastern | 0 (0.00) | 1 (0.56) |
| Other | 3 (0.30) | 0 (0.00) |
| Missing | 44 (8.15) | 19 (9.69) |
| **Living Status** | | |
| Living alone | 23 (4.62) | 35 (19.89) |
| Living with family/partner | 424 (85.14) | 131 (74.43) |
| Living with friends | 49 (9.84) | 4 (2.27) |
| Living with kids | 0 (0.00) | 6 (3.41) |
| Other | 2 (0.40) | 0 (0.00) |
| Missing | 42 (7.77) | 20 (10.20) |
| **Education Level** | | |
| Less than high school | 6 (1.20) | 2 (1.13) |
| High school/GED | 67 (13.45) | 28 (15.82) |
| Some college | 154 (30.92) | 57 (32.20) |
| 2-year college degree | 93 (18.67) | 28 (15.82) |
| 4-year college degree | 146 (29.32) | 35 (19.77) |

| | | |
|---|---|---|
| Professional Degree | 25 (5.02) | 3 (1.69) |
| Master's degree | 4 (0.80) | 24 (13.56) |
| Doctoral Degree | 3 (0.60) | 0 (0.00) |
| Missing | 42 (7.77) | 19 (9.69) |
| **Employment Status** | | |
| Employed/ self-employed full time | 252 (50.60) | 55 (31.07) |
| Employed part-time | 155 (31.12) | 25 (14.12) |
| Retired | 24 (4.82) | 9 (5.08) |
| Homemaker | 24 (4.82) | 19 (10.73) |
| Student | 16 (3.21) | 23 (12.99) |
| Seeking work | 25 (5.02) | 11 (6.21) |
| Unemployed | 0 (0.00) | 6 (3.39) |
| Disabled | 1 (0.20) | 27 (15.25) |
| Other | 1 (0.20) | 2 (1.13) |
| Missing | 42 (7.77) | 19 (9.69) |
| **Region** | | |
| Northeast | 97 (20.21) | 46 (26.14) |
| Midwest | 136 (28.33) | 38 (21.59) |
| South | 156 (32.50) | 69 (39.20) |
| West | 91 (1.96) | 23 (13.07) |
| Missing | 60 (11.11) | 20 (10.20) |
| **Insurance** | | |
| Yes | 445 (82.41) | 171 (87.24) |
| No | 95 (17.59) | 25 (12.76) |
| **Insurance Type** | | |
| Public | 208 (46.85) | 107 (62.21) |
| Private | 178 (40.09) | 46 (26.74) |
| Both | 58 (13.06) | 19 (11.05) |
| Missing | 96 (17.77) | 24 (12.24) |
| **Access** | | |
| Always | 26 (5.83) | 9 (5.23) |
| Often | 103 (23.09) | 21 (12.21) |
| Sometimes | 165 (37.00) | 41 (23.84) |
| Rarely | 100 (22.42) | 43 (25.00) |
| Never | 52 (11.66) | 58 (33.72) |
| Missing | 94 (17.41) | 24 (12.24) |
| **Impact of COVID-19 on QOL** | | |
| Worsened | 159 (32.38) | 57 (29.08) |
| Remained the same | 202 (41.14) | 105 (53.57) |
| Improved | 130 (26.48) | 15 (7.65) |
| Missing | 49 (9.07) | 19 (9.70) |
| **Medical Health Conditions**[^] | | |
| Less than 2 | 152 (28.15) | 50 (25.51) |
| Equal to 2 | 81 (15.00) | 32 (16.08) |
| More than 2 | 307 (56.85) | 114 (57.29) |

| | | |
|---|---|---|
| **Duration of most recent pain attack (crisis)[%]** | 404 (74.81) | 35 (17.86) |
| 1-23 hours | 52 (9.81) | 64 (32.65) |
| 1-3 days | 40 (7.55) | 36 (18.37) |
| 4-6 days | 19 (3.58) | 31 (15.82) |
| 1-2 weeks | 15 (2.83) | 13 (6.63) |
| More than 2 weeks | 10 (1.85) | 17 (8.67) |
| Missing | | |
| **Number of sickle cell pain attacks (crises) in the past year, mean (SD)[%]** | 1.91 (1.04) | 3.12 (1.22) |
| **Sickle cell severity score[%], mean (SD)** | 40.22 (7.31) | 51.95 (8.10) |
| **Sickle cell frequency score[%], mean (SD)** | 42.55 (7.47) | 51.41 (9.51) |

SCA= Sickle Cell Anemia; SD=Standard Deviation; QOL=Quality of Life; [++]; [^]Measured using the ASCQ-ME Medical History Checklist; [%]Measured using the ASCQ-ME Pain Episode Measure.

**Methods and Results**

To identify careless respondents, we employed archival and statistical techniques. Archival screening methods focus on patterns of response behavior throughout the course of responding to the survey.(189) Statistical screening methods depend on statistical techniques to detect deviant response patterns.(189) A brief description of each of the techniques used under archival and statistical categories is reported in Table 5.2.

**Table 5.2: Brief description of data screening techniques**

| Technique | Category | Intended to screen respondents who: |
|---|---|---|
| **Response time** | Archival | Respond too quickly |
| **Long string** | Archival | Respond the same way to all items |
| **Personal reliability index** | Statistical | Respond inconsistently within each measure |

- Response time

It relies on the notion that there is a minimum amount of time that respondents must spend on an item to answer accurately. Even though differences in respondents reading speed and item length make cutoff scores tricky to rationalize, it is "unlikely for participants to respond

to survey items faster than the rate of 2 seconds per item".(189,190) The dissertation study survey consisted of a total 158 items and 5 instruction statements for the respondent (excluding the screener items and survey information prior to beginning the survey). We therefore employed a cut-off of 326 secs [(158 items+5 instructions) x 2secs] for the response time. Respondents with response time less than 326 secs were considered as careless respondents (Table 5.3).

- Long string

The long string technique relies on the assumption that too many consecutive invariant responses may indicate a lack of effort and may be suggestive of low-quality data.(189) Researchers have recommended screens based on 6 to 14 long string or invariant responses in a row.(189–191) To be considered as a careless respondent we employed a long string cut off of $\geq$10 invariant responses in a row (Table 5.3).

- Personal reliability index (even-odd consistency index)

The personal reliability method assesses each respondent's consistency within each measure. To calculate personal reliability index, we divided the CSQ-SCD and ASCQ-Me measures into even and odd items and calculated the two average scores for each respondent on each measure. Next, we correlated one set of halves (even items) with the other set of halves (odd items) and corrected for test length using the Spearman–Brown prophesy formula.(189,192,193) Response consistency within each measure will result in a high value of the personal reliability index and we employed a cut off of <0.3 as recommend by researchers.(194) Respondents with personal reliability index less than 0.3 were considered as careless respondents (Table 5.3).

**Table 5.3: Results on the proportion of likely careless respondents**

| Technique | Likely Careless Respondents, N (%) |
|---|---|
| **Response time** | 88 (16.30) |
| **Long string** | 17 (3.15) |
| **Personal reliability index** | 363 (64.22) |

Furthermore, to determine the discrepancies in careless responding between African American/Blacks and Caucasians/Whites we ran cross tabulations between race/ethnicity and careless responding measures (Tables 5.4, 5.5 and 5.6). We also report cross-tabulations between race/ethnicity and region (Table 5.7). However, results show us that the proportion of potential careless responders are nearly similar between African Americans/Blacks and Whites.

**Table 5.4: Cross-tabulation of duration by race/ethnicity**

| **Frequency** |
|---|
| **Row Pct** |
| **Col Pct** |

| **Duration** | **Race/Ethnicity** | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Black** | **White** | **American Indian/Alaska Native** | **Asian** | **Hispanic** | **Native Hawaiian /PI** | **Mixed Race** | **Other** | **Missing** | **Total** |
| **Less than 326 sec (Maybe careless responders)** | 18 | 52 | 7 | 1 | 3 | 1 | 0 | 0 | 6 | 88 |
| | 16.36 | 19.40 | 14.00 | 10.00 | 6.12 | 20.00 | 0.00 | 0.00 | 13.64 | 16.30 |
| | 20.45 | 59.09 | 7.95 | 1.14 | 3.41 | 1.14 | 0.00 | 0.00 | 6.82 | |
| **More than 326 sec** | 92 | 216 | 43 | 9 | 46 | 4 | 1 | 3 | 38 | 452 |
| | 83.64 | 80.60 | 86.00 | 90.00 | 93.88 | 80.00 | 100 | 100 | 86.36 | 83.70 |
| | 20.35 | 47.79 | 9.51 | 1.99 | 10.18 | 0.88 | 0.22 | 0.66 | 8.41 | |

*PI=Pacific Islander*

**Table 5.5: Cross-tabulation of long string by race/ethnicity**

| |
|---|
| **Frequency** |
| **Row Pct** |
| **Col Pct** |

| **Long String** | **Race/Ethnicity** | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Black** | **White** | **American Indian/Alaska Native** | **Asian** | **Hispanic** | **Native Hawaiian /PI** | **Mixed Race** | **Other** | **Missing** | **Total** |
| **At least 10 (Maybe careless responders)** | 2 | 6 | 0 | 0 | 0 | 0 | 0 | 1 | 8 | 17 |
| | 1.82 | 2.24 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 33.33 | 18.18 | 3.15 |
| | 11.76 | 35.29 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 5.88 | 47.06 | |
| **Less than 10** | 108 | 262 | 50 | 10 | 49 | 5 | 1 | 2 | 36 | 523 |
| | 98.18 | 97.76 | 100.00 | 100.00 | 100.00 | 100.00 | 100.00 | 66.67 | 81.82 | 96.85 |
| | 20.65 | 50.10 | 9.56 | 1.91 | 9.37 | 0.96 | 0.19 | 0.38 | 6.88 | |

*PI=Pacific Islander*

**Table 5.6: Cross-tabulation of personal reliability index by race/ethnicity**

| |
|---|
| **Frequency** |
| **Row Pct** |
| **Col Pct** |

| **Personal reliability index** | **Race/Ethnicity** | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Black** | **White** | **American Indian/Alaska Native** | **Asian** | **Hispanic** | **Native Hawaiian /PI** | **Mixed Race** | **Other** | **Missing** | **Total** |
| **Less than 0.3 (Maybe careless responders)** | 81 | 173 | 35 | 6 | 30 | 4 | 0 | 3 | 31 | 363 |
| | 73.64 | 64.55 | 70.00 | 60.00 | 61.22 | 80.00 | 0.00 | 100.00 | 70.45 | 67.22 |
| | 22.31 | 47.66 | 9.64 | 1.65 | 8.26 | 1.10 | 0.00 | 0.83 | 8.54 | |
| **At least 0.3** | 29 | 95 | 15 | 4 | 19 | 1 | 1 | 0.00 | 13 | 177 |
| | 26.36 | 35.45 | 30.00 | 40.00 | 38.78 | 20.00 | 100.00 | 0.00 | 29.55 | 32.78 |
| | 16.38 | 53.67 | 8.47 | 2.26 | 10.73 | 0.56 | 0.56 | 0.00 | 7.34 | |

*PI=Pacific Islander*

**Table 5.7: Cross-tabulation of region by race/ethnicity**

| |
|---|
| **Frequency** |
| **Percent** |
| **Row Pct** |
| **Col Pct** |

| **Region** | **Race** | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Missing** | **Black** | **American Indian/ Alaska Native** | **Asian** | **Hispanic** | **Native Hawaiian/ PI** | **White** | **Mixed Race** | **Other** | **Total** |
| **Missing** | 47 | 8 | 1 | 1 | 1 | 0 | 9 | 0 | 0 | 67 |
| | 8.59 | 1.46 | 0.18 | 0.18 | 0.18 | 0.00 | 1.65 | 0.00 | 0.00 | 12.25 |
| | 70.15 | 11.94 | 1.49 | 1.49 | 1.49 | 0.00 | 13.43 | 0.00 | 0.00 | |
| | 92.16 | 7.27 | 2.00 | 10.00 | 2.04 | 0.00 | 3.36 | 0.00 | 0.00 | |
| **North-east** | 0 | 19 | 17 | 0 | 11 | 0 | 49 | 0 | 1 | 97 |
| | 0.00 | 3.47 | 3.11 | 0.00 | 2.01 | 0.00 | 8.96 | 0.00 | 0.18 | 17.73 |
| | 0.00 | 19.59 | 17.53 | 0.00 | 11.34 | 0.00 | 50.52 | 0.00 | 1.03 | |
| | 0.00 | 17.27 | 34.00 | 0.00 | 22.45 | 0.00 | 18.28 | 0.00 | 33.33 | |
| **Mid-west** | 3 | 22 | 22 | 5 | 9 | 3 | 72 | 0 | 0 | 136 |
| | 0.55 | 4.02 | 4.02 | 0.91 | 1.65 | 0.55 | 13.16 | 0.00 | 0.00 | 24.86 |
| | 2.21 | 16.18 | 16.18 | 3.68 | 6.62 | 2.21 | 52.94 | 0.00 | 0.00 | |
| | 5.88 | 20.00 | 44.00 | 50.00 | 18.37 | 60.00 | 26.87 | 0.00 | 0.00 | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **South** | 1 | 30 | 7 | 4 | 9 | 2 | 101 | 0 | 2 | 156 |
| | 0.18 | 5.48 | 1.28 | 0.73 | 1.65 | 0.37 | 18.46 | 0.00 | 0.37 | 28.52 |
| | 0.64 | 19.23 | 4.49 | 2.56 | 5.77 | 1.28 | 64.74 | 0.00 | 1.28 | |
| | 1.96 | 27.27 | 14.00 | 40.00 | 18.37 | 40.00 | 37.69 | 0.00 | 66.67 | |
| **West** | 0 | 31 | 3 | 0 | 19 | 0 | 37 | 1 | 0 | 91 |
| | 0.00 | 5.67 | 0.55 | 0.00 | 3.47 | 0.00 | 6.76 | 0.18 | 0.00 | 16.64 |
| | 0.00 | 34.07 | 3.30 | 0.00 | 20.88 | 0.00 | 40.66 | 1.10 | 0.00 | |
| | 0.00 | 28.18 | 6.00 | 0.00 | 38.78 | 0.00 | 13.81 | 100.00 | 0.00 | |
| **Total** | 51 | 110 | 50 | 10 | 49 | 5 | 268 | 1 | 3 | 547 |
| | 9.32 | 20.11 | 9.14 | 1.83 | 8.96 | 0.91 | 48.99 | 0.18 | 0.55 | 100.00 |

*PI=Pacific Islander*

## Conclusions

Our preliminary findings demonstrate presence of careless responding in the data obtained from the two patient organizations, even though the proportions of careless respondents did not differ between African Americans/Blacks and Whites. These findings along with the sample descriptives highlighted aberrant behavior in the collected data. Therefore, to obtain reliable and meaningful findings we decided to not use the data obtained from the two patient organizations. We only utilized the data obtained from Rare Patient Voice for all our analyses presented in this dissertation.

## Lessons Learned

A few lessons learned through my preliminary research on careless responding are:

- During the survey development phase identify the forms of careless responding most likely to be exhibited by respondents and identify the data screening techniques most appropriate for the identification of careless respondents.
- If needed, add in bogus/instructed items, identify, or create semantic synonym/antonym pairs to identify careless respondents.
- Add in screener items at various points throughout the survey to detect gaps in respondent effort.
- Time respondents while they are filling the survey.
- Once data is collected calculate the careless responding indices and report the findings.

## STUDY SUMMARY

Sickle cell disease is a group of disorders wherein people with this condition have abnormal hemoglobin molecules called hemoglobin S, which can distort red blood cells into a sickle, or crescent, shape.(1,2) Patients with SCD experience pain episodes or vaso-occlusive crises (VOCs) which are variable in pain intensity and can last from a few hours to a few weeks.(3) Patients with SCD often suffer from other complications too such as acute chest syndrome (ACS), chronic pain, stroke, priapism, joint complications and infections.(1) SCD worsens over time thus placing a significant burden on the health-related quality of life (HRQOL) of patients with the disease.(4)

The majority of the studies in the existing literature have assessed HRQOL of patients with SCD but most of these studies have reported that SCD affects the physical component of HRQOL of patients rather than the mental component.(5–10) But, many of these studies have not considered the role of psychosocial variables such as social support, coping, and self-efficacy and their impact on the HRQOL of patients with SCD. Also, few of the studies which have evaluated coping among patients with SCD have utilized the only existing sickle cell specific instrument, Coping Strategies Questionnaire-SCD (CSQ-SCD). However, the factor structure of the CSQ-SCD has inconsistent results in the existing literature. Measurement of the psychometric properties of an instrument is necessary to confirm the suitability of the use of an instrument in a particular patient population. Self-care management processes in SCD patients can reduce the severity and frequency of pain crises and consequently lead to improved HRQOL. Therefore, to understand and reduce pain crises, there is a need to examine the role of self-care management such as SCD pain-related coping behaviors, self-efficacy, social support; socio-demographic variables, and HRQOL in adults with SCD. Another important aspect of measuring

coping is to explore the unobserved coping patterns of SCD patients using a person-centered approach (latent class analysis) rather than a variable-centered approach (factor analysis). The person-centered approach can provide more detailed results as compared to the traditional variable-centered approach as it will examine and explain several subpopulations with different coping patterns.(11) Compared to certain specific coping strategies, coping patterns are a better indicator of patient's overall preferences in how they deal with stressors and how the coping patterns affect the HRQOL.

**Study 1**

Studies have demonstrated that psychological coping responses are related to pain, adaptation, and health service utilization after controlling for clinical indicators of sickle cell disease.(12,83,84) Thus, coping has emerged as an important psychosocial factor among patients with SCD. The CSQ-SCD is a commonly used SCD specific coping measure, however, there is considerable heterogeneity in the factor structure reported and the methods used to assess the factor structure.(54,63,83) In order to obtain evidence about the appropriateness of use of the CSQ-SCD among SCD patients, it is necessary to test its psychometric properties in terms of its validity and reliability. This study provides evidence about the psychometric properties, in terms of validity (factorial validity, convergent and discriminant validity) and reliability of the CSQ-SCD among adults with SCD in the US. The higher-order factor analysis revealed a 3-factor structure as proposed by Anie et al.(83) to have a relatively better, though mediocre fit when compared to the 2-factor structure proposed by Gil et al.(15 ) The scale demonstrated mediocre convergent and discriminant validity. The scale was found to have adequate internal consistency reliability. The study also reports a follow-up EFA, as an adequate fitting higher-order CFA model was only achievable by model re-specification based on the modification indices that were

not supported by theory. Based on the model fit indices and interpretability of factor loadings we deemed a 3-factor EFA model to be more appropriate for the sample data compared to the four-factor model. The new factor structure extracted by EFA is like the factor structure reported by Anie et al.(83) except that in our analysis the subscale of praying and hoping loads onto the passive adherence coping latent factor. Overall, the results provide basis for the future development of a new coping instrument which has stronger psychometric properties such that the coping information obtained from studies using this instrument can be incorporated into health policy and clinical decision making.

**Study 2**

While a few previous studies have emphasized on clinical and psychosocial determinants of HRQOL, this was the first US-based study which critically shifted focus to an assessment of psychosocial predictors such as coping among patients with SCD. In regard to SCD and HRQOL, coping strategies, self-efficacy, social support, and socio-demographic variables appear to be the most significant constructs. (18,23,34). An adapted version of the theoretical model of self-care management for sickle cell disease (SCMSCD) was employed to examine the relationships between constructs such as SCD severity, SCD crises frequency, social support, coping strategies adopted, patient self-efficacy, and HRQOL using SEM. Study results suggest a direct as well as an indirect effect of SCD severity and SCD crises frequency on HRQOL among adults with SCD. Affective coping had a significant negative impact on the pain, sleep, and stiffness domains of HRQOL in SCD adults and it mediated the relationship between SCD severity and the pain and sleep domains of HRQOL. In addition, a positive direct effect of self-efficacy on emotional, pain, stiffness, and social functioning domains of HRQOL was observed in this study. As hypothesized, that self-efficacy mediated the effect of SCD crises frequency on

pain, emotion, stiffness, and social functioning domains of HRQOL. Results from this study can be used to shape interventions to improve social support, increase the use of active and restrict the use of affective coping strategies, and develop stronger self-efficacy beliefs among adults with SCD. Such interventions could potentially improve functional status, psychosocial well-being and the overall HRQOL in this patient population. Knowledge about these psychosocial factors will not only assist healthcare providers and caregivers in improving care provided to individuals with SCD but will also enable patients to better understand and self-manage their disease condition.

**Study 3**

Studies have demonstrated that individuals adopt several different coping strategies at the same time in different settings.(54,63,73–75,83) However, even then a conventional variable-centered approach (i.e., factor analysis) still governs the research on coping,(76,77) including coping among SCD patients. Literature suggests that this approach does not fare well at capturing the distinctive nature of the population which could lead to less accurate and overgeneralized understandings of study samples.(78) To overcome these shortcomings, a person-centered analytical approach (i.e., latent class analysis)(79) was utilized in current study, to explore the unobserved coping patterns of SCD patients. The study also examined the significant correlates of these coping patterns and investigated the relationships between the coping patterns and HRQOL. Three underlying coping-strategies patterns were observed among patients with SCD in the US: cognitive coping, negative thinking/passive adherence coping, and physiological coping. Factors influencing the coping patterns were mainly related to patients age, insurance status and clinical characteristics such as severity and frequency of SCD. In the multivariable analysis, we saw that those in the physiological coping strategies class had

significantly higher adjusted means for emotional, social functioning, stiffness, and sleep domains, indicating better HRQOL compared to the cognitive or negative thinking/passive adherence coping classes. Patients employing cognitive coping strategies had significantly lower adjusted means for pain domain indicating that cognitive coping strategies are helpful in reducing the pain impact compared to those employing physiological or negative thinking/passive adherence coping. Overall, the results provide basis for the utilization for multiple coping strategies to improve HRQOL.

This dissertation is an important addition to the existing pool of literature relating to coping and HRQOL among patients with SCD. The findings of the psychometric validation of the CSQ-SCD lays the groundwork for future development of a new sickle cell specific instrument with superior psychometric properties for use among adults with SCD. Also, the evidence that affective coping and self-efficacy mediate the relationship between pain crises severity, frequency and HRQOL, respectively, is a key for clinical management of SCD. In addition, we also observed three mutually exclusive underlying coping strategies pattern among SCD patients thus providing evidence that patients utilize multiple coping strategies to improve HRQOL.

## DIRECTIONS FOR FUTURE RESEARCH

The findings from this dissertation project paves the way for future research.

**Study 1**

Future studies should adopt a longitudinal design to explore the predictive validity and test-retest reliability of the CSQ-SCD among adults with SCD. Future studies should adopt a longitudinal design to explore any response shift in the HRQOL of adults with SCD over a period. Future studies should also consider using a disease specific HRQOL measure to ascertain the convergent and discriminant validity of the SF-12v2 in this patient population. Future studies can also assess measurement invariance of CSQ-SCD.

**Study 2**

Future research studies should test the proposed causality of the model using longitudinal studies. To improve the generalizability of the study results to all US adults with SCD, future studies should consider utilizing a probability-based sampling technique to recruit patients with rare diseases. Future studies must also try to assess the role of psychological variables such as depression and anxiety in the relationship between SCD severity, crises frequency and HRQOL among SCD patients. Future studies can also assess the coping and its relationship on the HRQOL of caregivers of SCD patients.

**Study 3**

Future research should aim to explore patterns of coping using a larger sample size for better generalizability and more accurate sample estimates. Future studies can also employ a

longitudinal study design to identify the distinct, multidimensional patterns of strategies for coping with SCD and their association with changes in HRQOL.

# LIST OF REFERENCES

1. Sickle Cell Disease | National Heart, Lung, and Blood Institute (NHLBI) [Internet]. [cited 2020 Feb 24]. Available from: https://www.nhlbi.nih.gov/health-topics/sickle-cell-disease

2. Sickle Cell Disease. Genetics Home Reference-NIH [Internet]. U.S. National Library of Medicine. [cited 2020 Feb 24]. Available from: https://ghr.nlm.nih.gov/condition/sickle-cell-disease

3. Sickle cell anemia - Symptoms and causes [Internet]. Mayo Clinic. [cited 2020 Feb 24]. Available from: https://www.mayoclinic.org/diseases-conditions/sickle-cell-anemia/symptoms-causes/syc-20355876

4. CDC. Complications and Treatments of Sickle Cell Disease | CDC [Internet]. Centers for Disease Control and Prevention. 2019 [cited 2020 Feb 24]. Available from: https://www.cdc.gov/ncbddd/sicklecell/treatments.html

5. McClish DK, Penberthy LT, Bovbjerg VE, Roberts JD, Aisiku IP, Levenson JL, et al. Health related quality of life in sickle cell patients: The PiSCES project. Health Qual Life Outcomes. 2005 Aug 29;3:50.

6. Adam SS, Flahiff CM, Kamble S, Telen MJ, Reed SD, De Castro LM. Depression, quality of life, and medical resource utilization in sickle cell disease. Blood Adv. 2017 Oct 12;1(23):1983–92.

7. Dampier C, LeBeau P, Rhee S, Lieff S, Kesler K, Ballas S, et al. Health-related quality of life in adults with sickle cell disease (SCD): a report from the comprehensive sickle cell centers clinical trial consortium. Am J Hematol. 2011 Feb;86(2):203–5.

8. Ahmed AE, Alaskar AS, Al-Suliman AM, Jazieh A-R, McClish DK, Salamah MA, et al. Health-related quality of life in patients with sickle cell disease in Saudi Arabia. Health Qual Life Outcomes. 2015 Dec;13(1):1–9.

9. Nwogoh B, Ofovwe C, Omoti C. Health-related quality of life in sickle cell disease subjects in Benin City, Nigeria. J Med Health Sci. 2016 Jul 1;15(2):80.

10. Almeida Matos M, Dias Malheiros C, Matos S. Health related quality of life of patients with sickle cell disease. J Blood Disord Transfus. 2016;07(02).

11. Howard M, Hoffman MS. Variable-centered, person-centered, and person-specific approaches: where theory meets the method. Organ Res Methods. 2018 Oct;21(4):846–76.

12. Jonassaint CR, Jonassaint JC, Stanton MV, De Castro LM, Royal CD. Clinical and sociodemographic factors predict coping styles among adults with sickle cell disease. J Natl Med Assoc. 2010 Nov 1;102(11):1045–9.

13. Renoux C, Romana M, Joly P, Ferdinand S, Faes C, Lemonne N, et al. Effect of age on blood rheology in sickle cell anaemia and sickle cell haemoglobin C disease: a cross-sectional study. PLoS ONE. 2016 Jun 29;11(6).

14. CDC. What is Sickle Cell Disease? | CDC [Internet]. Centers for Disease Control and Prevention. 2016 [cited 2020 Feb 26]. Available from: https://www.cdc.gov/ncbddd/sicklecell/facts.html

15. Fuggle P, Shand PA, Gill LJ, Davies SC. Pain, quality of life, and coping in sickle cell disease. Arch Dis Child. 1996 Sep 1;75(3):199–203.

16. CDC. Data & Statistics on Sickle Cell Disease | CDC [Internet]. Centers for Disease Control and Prevention. 2016 [cited 2020 Feb 24]. Available from: https://www.cdc.gov/ncbddd/sicklecell/data.html

17. Mburu J, Odame I. Sickle cell disease: reducing the global disease burden. Int J Lab Hematol. 2019;41(S1):82–8.

18. Thein MS, Thein SL. World sickle cell day 2016: a time for appraisal. Indian J Med Res. 2016 Jun;143(6):678–81.

19. Aygun B, Odame I. A global perspective on sickle cell disease. Pediatr Blood Cancer. 2012 Aug;59(2):386–90.

20. Oliver-Carpenter G, Barach I, Crosby LE, Valenzuela J, Mitchell MJ. Disease management, coping, and functional disability in pediatric sickle cell disease. J Natl Med Assoc. 2011 Feb;103(2):131–7.

21. Driscoll MC. Sickle Cell Disease. Pediatr Rev. 2007 Jul 1;28(7):259–68.

22. National Heart, Lung, and Blood Institute. Evidence-based management of sickle cell disease: expert panel. Bethesda, MD: National Heart. Lung, and Blood Institute. 2014. :1–161.

23. Yawn BP, John-Sowah J. Management of sickle cell disease: recommendations from the 2014 expert panel report. Am Fam Physician. 2015 Dec 15;92(12):1069–76.

24. Steinberg MH. Management of sickle cell disease. N Engl J Med. 1999 Apr 1;(340(13):):1021–30.

25. Ruan X, Wu H, Wang D. A comment on pattern of opioid use in sickle cell disease. Am J Hematol. 2017;92(4):E42–3.

26. Smith, WR, McClish, DK, Dahman, BA, Levenson, JL, Aisiku, IP, Citero, V de A, et al. Daily home opioid use in adults with sickle cell disease: The PiSCES project. J Opioid Manag. 2015 May 1;11(3):243.

27. Ballas SK, Bauserman RL, McCarthy WF, Castro OL, Smith WR, Waclawiw MA. Utilization of analgesics in the multicenter study of hydroxyurea in sickle cell anemia: effect of sex, age, and geographical location. Am J Hematol. 2010;85(8):613–6.

28. Ballas SK, Kanter J, Agodoa I, Howard R, Wade S, Noxon V, et al. Opioid utilization patterns in United States individuals with sickle cell disease. Am J Hematol. 2018;93(10):E345–7.

29. Han J, Zhou J, Saraf SL, Gordeuk VR, Calip GS. Characterization of opioid use in sickle cell disease. Pharmacoepidemiol Drug Saf. 2018;27(5):479–86.

30. Ogu UO, Billett HH. Comorbidities in sickle cell disease: adult providers needed! Indian J Med Res. 2018 Jun;147(6):527–9.

31. Ballas SK. Comorbidities in aging patients with sickle cell disease. Connes P, editor. Clin Hemorheol Microcirc. 2018 Mar 28;68(2–3):129–45.

32. Platt OS, Brambilla DJ, Rosse WF, Milner PF, Castro O, Steinberg MH, et al. Mortality in sickle cell disease -- life expectancy and risk factors for early death. N Engl J Med. 2010 Jan 15;

33. Gladwin MT. Cardiovascular complications and risk of death in sickle-cell disease. The Lancet. 2016 Jun 18;387(10037):2565–74.

34. Wallen GR, Minniti CP, Krumlauf M, Eckes E, Allen D, Oguhebe A, et al. Sleep disturbance, depression and pain in adults with sickle cell disease. BMC Psychiatry. 2014 Jul 21;14:207.

35. Pecker LH, Darbari DS. Psychosocial and affective comorbidities in sickle cell disease. Neurosci Lett. 2019 Jul 13;705:1–6.

36. Ballas SK. The cost of health care for patients with sickle cell disease. Am J Hematol. 2009;84(6):320–2.

37. Kauf TL, Coates TD, Huazhi L, Mody-Patel N, Hartzema AG. The cost of health care for children and adults with sickle cell disease. Am J Hematol. 2009;84(6):323–7.

38. Brousseau DC, Owens PL, Mosso AL, Panepinto JA, Steiner CA. Acute care utilization and rehospitalizations for sickle cell disease. JAMA. 2010 Apr 7;303(13):1288–94.

39. Davis H, Moore RM, Gergen PJ. Cost of hospitalizations associated with sickle cell disease in the United States. Public Health Rep. 1997;112(1):40–3.

40. Woods K, Karrison T, Koshy M, Patel A, Friedmann P, Cassel C. Hospital utilization patterns and costs for adult sickle cell patients in Illinois. Public Health Rep. 1997;112(1):44–51.

41. Lanzkron S, Haywood C, Segal JB, Dover GJ. Hospitalization rates and costs of care of patients with sickle-cell anemia in the state of Maryland in the era of hydroxyurea. Am J Hematol. 2006;81(12):927–32.

42. Bou-Maroun LM, Meta F, Hanba CJ, Campbell AD, Yanik GA. An analysis of inpatient pediatric sickle cell disease: incidence, costs, and outcomes. Pediatr Blood Cancer. 2018 Jan;65(1):e26758.

43. Amendah DD, Mvundura M, Kavanagh PL, Sprinz PG, Grosse SD. Sickle cell disease–related pediatric medical expenditures in the U.S. Am J Prev Med. 2010 Apr 1;38(4):S550–6.

44. World Health Organization Constitution [Internet]. [cited 2020 Apr 16]. Available from: https://www.who.int/about/who-we-are/constitution

45. Cella D, Tulsky D. Measuring quality of life today: methodological aspects. Oncology (Williston Park). 1990 May;4(5):29.

46. Bullinger M, von Mackensen S. Quality of life assessment in haemophilia. Haemophilia. 2004 Mar;10(s1):9–16.

47. Guyatt GH, Feeny DH, Patrick DL. Measuring health-related quality of life. Ann Intern Med. 1993 Apr 15;118(8):662–9.

48. Fischer K, Van Der Bom JG, Van Den Berg HM. Health-related quality of life as outcome parameter in haemophilia treatment. Haemophilia. 2003 May;9(s1):75–82.

49. Anie KA, Steptoe A, Bevan DH. Sickle cell disease: pain, coping and quality of life in a study of adults in the UK. Br J Health Psychol. 2002 Sep;7(3):331–44.

50. Platt OS, Thorington BD, Brambilla DJ, Milner PF, Rosse WF, Vichinsky E, et al. Pain in sickle cell disease. N Engl J Med. 1991 Jul 4;325(1):11–6.

51. Kambasu DM, Rujumba J, Lekuya HM, Munube D, Mupere E. Health-related quality of life of adolescents with sickle cell disease in sub-Saharan Africa: a cross-sectional study. BMC Hematol. 2019 Dec;19(1):1–9.

52. Davies SC, Oni L. Management of patients with sickle cell disease. BMJ. 1997 Sep 13;315(7109):656–60.

53. Brozović M, Davies SC, Brownell AI. Acute admissions of patients with sickle cell disease who live in Britain. Br Med J Clin Res Ed. 1987 May 9;294(6581):1206–8.

54. Gil KM, Abrams MR, Phillips G, Keefe FJ. Sickle cell disease pain: relation of coping strategies to adjustment. J Consult Clin Psychol. 1989;57(6):725–31.

55. Ezenwa MO, Yao Y, Molokie RE, Wang ZJ, Mandernach MW, Suarez ML, et al. Coping with pain in the face of healthcare injustice in patients with sickle cell disease. J Immigr Minor Health. 2017 Dec 1;19(6):1449–56.

56. Rosse W. Diagnosis and treatment of the painful episode in sickle cell disease. N C Med J. 1983 Jul 1;44(7):419–20.

57. Whitten CF, Fischhoff J. Psychosocial effects of sickle cell disease. Arch Intern Med. 1974 Apr 1;133(4):681–9.

58. Keefe FJ, Caldwell DS, Queen KT, Gil KM, Martinez S, Crisson JE, et al. Pain coping strategies in osteoarthritis patients. J Consult Clin Psychol. 1987;55(2):208–12.

59. Turner JA, Clancy S. Strategies for coping with chronic low back pain: relationship to pain and disability. Pain. 1986 Mar 1;24(3):355–64.

60. Nadel C, Portadin G. Sickle cell crises: psychological factors associated with onset. N Y State J Med. 1977;77(7):1075–8.

61. Vichinsky EP, Johnson R, Lubin BH. Multidisciplinary approach to pain management in sickle cell disease. J Pediatr Hematol Oncol. 1982 Oct;4(3):328–33.

62. Rosenstiel AK, Keefe FJ. The use of coping strategies in chronic low back pain patients: relationship to patient characteristics and current adjustment. Pain. 1983 Sep 1;17(1):33–44.

63. McCrae JD, Lumley MA. Health status in sickle cell disease: examining the roles of pain coping strategies, somatic awareness, and negative affectivity. J Behav Med. 1998 Feb 1;21(1):35–55.

64. Thompson RJ, Gil KM, Abrams MR, Phillips G. Stress, coping, and psychological adjustment of adults with sickle cell disease. J Consult Clin Psychol. 1992;60(3):433–40.

65. Cohen JS, Biesecker BB. Quality of life in rare genetic conditions: a systematic review of the literature. Am J Med Genet A. 2010 May;152A(5):1136–56.

66. Mann-Jiles V, Morris DL. Quality of life of adult patients with sickle cell disease. J Am Acad Nurse Pract. 2009 Jun;21(6):340–9.

67. Jenerette CM, Murdaugh C. Testing the theory of self-care management for sickle cell disease. Res Nurs Health. 2008 Aug;31(4):355–69.

68. Treadwell M, Hassell K, Levine R, Keller S. Adult sickle cell quality-of-life measurement information system (ASCQ-Me): conceptual model based on review of the literature and formative research. Clin J Pain. 2014 Oct;30(10):902–14.

69. Jenerette CM, Phillips RCS. An examination of differences in intra-personal resources, self-care management, and health outcomes in older and younger adults with sickle cell disease. South Online J Nurs Res. 2006;7(3):1–24.

70. Dorsey C, Phillips KD, Williams C. Adults sickle cell patients' perceptions of nurses' caring behaviors. ABNF J. 2001 Sep 1;12(5):95–100.

71. Matthie N, Jenerette C, McMillan S. The Role of self-care in sickle cell disease. Pain Manag Nurs Off J Am Soc Pain Manag Nurses. 2015 Jun;16(3):257–66.

72. Jenerette CM, Brewer C, Leak AN. Self-care recommendations of middle-aged and older adults with sickle cell disease. Nurs Res Pract. 2011;2011:1–5.

73. Kistin CJ, Radesky J, Diaz-Linhart Y, Tompson MC, O'Connor E, Silverstein M. A qualitative study of parenting stress, coping, and discipline approaches among low-income traumatized mothers. J Dev Behav Pediatr JDBP. 2014 Apr;35(3):189–96.

74. Azman A, Singh PSJ, Sulaiman J. Caregiver coping with the mentally ill: a qualitative study. J Ment Health. 2017 Mar 4;26(2):98–103.

75. Lin I-F, Wu H-S. Patterns of coping among family caregivers of frail older adults. Res Aging. 2014 Sep;36(5):603–24.

76. Kroemeke A. Coping flexibility and health-related quality of life among older adults: the compensatory effect of co-rumination. Front Psychol. 2019 Jan 23;10(59).

77. Yuan Q, Wang P, Tan TH, Devi F, Poremski D, Magadi H, et al. Coping patterns among primary informal dementia caregivers in singapore and its impact on caregivers—implications of a latent class analysis. The Gerontologist. 2020 Jun 27;

78. Eye AV, Bergman LR. Research strategies in developmental psychopathology: dimensional identity and the person-oriented approach. Dev Psychopathol. 2003 Sep;15(3):553–80.

79. Scotto Rosato N, Baer JC. Latent class analysis: a method for capturing heterogeneity. Soc Work Res. 2012 Mar 1;36(1):61–9.

80. McClish DK, Smith WR, Levenson JL, Aisiku IP, Roberts JD, Roseff SD, et al. Comorbidity, pain, utilization, and psychosocial outcomes in older versus younger sickle cell adults: the PiSCES project. BioMed Res Int. 2017 Mar 28;2017.

81. Rucknagel DL. The genetics of sickle cell anemia and related syndromes. Arch Intern Med. 1974 Apr 1;133(4):595–606.

82. Gil KM. Coping with Sickle Cell Disease Pain. Ann Behav Med. 1989 Jan 1;11(2):49–57.

83. Anie KA, Steptoe A, Bevan DH. Sickle cell disease: Pain, coping and quality of life in a study of adults in the UK. Br J Health Psychol. 2002 Sep;7(3):331–44.

84. Midence K, McManus C, Fuggle P, Davies S. Psychological adjustment and family functioning in a group of British children with sickle cell disease: Preliminary empirical findings and a meta-analysis. Br J Clin Psychol. 1996;35(3):439–50.

85. Lazarus RS, Folkman S. Coping and adaptation. The handbook of behavioral medicine 282325; 1984. 282–325 p.

86. Porter LS, Gil KM, Carson JW, Anthony KK, Ready J. The role of stress and mood in sickle cell disease pain: an analysis of daily diary data. J Health Psychol. 2000 Jan;5(1):53–63.

87. Porter LS, Gil KM, Sedway JA, Ready J, Workman E, Thompson RJ. Pain and stress in sickle cell disease: an analysis of daily pain records. Int J Behav Med. 1998 Sep;5(3):185–203.

88. Sanders KA, Labott SM, Molokie R, Shelby SR, Desimone J. Pain, coping and health care utilization in younger and older adults with sickle cell disease. J Health Psychol. 2010 Jan;15(1):131–7.

89. Kim H, Ku B, Kim JY, Park Y-J, Park Y-B. Confirmatory and Exploratory Factor Analysis for Validating the Phlegm Pattern Questionnaire for Healthy Subjects. Evid-Based Complement Altern Med ECAM. 2016;2016:2696019.

90. Kline RB. Principles and Practice of Structural Equation Modeling, Fourth Edition. Guilford Publications; 2015. 553 p.

91. Asparouhov T, Muthén B. Weighted least squares estimation with missing data. Mplus Tech Append. 2010 Aug;2010:1–10.

92. Brown TA. Confirmatory factor analysis for applied research, second edition. Guilford Publications; 2015. 482 p.

93. Muthén B. A general structural equation model with dichotomous, ordered categorical, and continuous latent variable indicators. Psychometrika. 1984 Mar 1;49(1):115–32.

94. Muthen, Linda K, Muthen B. Muthén & Muthén, Mplus [Internet]. Los Angeles, CA; [cited 2020 Apr 28]. Available from: https://www.statmodel.com/

95. Bagozzi RP, Yi Y. Specification, evaluation, and interpretation of structural equation models. J Acad Mark Sci. 2012 Jan 1;40(1):8–34.

96. Hu L, Bentler PM. Cutoff criteria for fit indexes in covariance structure analysis: conventional criteria versus new alternatives. Struct Equ Model Multidiscip J. 1999 Jan 1;6(1):1–55.

97. Moritz DJ, Kasl SV, Berkman LF. The health impact of living with a cognitively impaired elderly spouse: depressive symptoms and social functioning. J Gerontol. 1989 Jan 1;44(1):S17–27.

98. Hair JF, Black W, Babin B, Anderson R, Tatham R, editors. Multivariate data analysis. 7. ed. Upper Saddle River, NJ: Prentice Hall; 1998. 734 p.

99. Hair JF, Anderson R, Tatham R, Black W, River N. Multivariate data analysis. 2010.

100. Cohen J. Statistical Power Analysis for the Behavioral Sciences. Academic Press; 2013. 459 p.

101. Anderson JC, Gerbing DW. Structural equation modeling in practice: a review and recommended two-step approach. Psychol Bull. 1988;103(3):411–23.

102. Fornell C, Larcker DF. Structural Equation Models with Unobservable Variables and Measurement Error: Algebra and Statistics. J Mark Res. 1981;18(3):382–8.

103. Nunnally JC. Psychometric Theory 2nd ed. Mcgraw hill book company; 1978.

104. National Cancer Institute. Adult Sickle Cell Quality of Life Measurement Information System. In: Definitions [Internet]. Qeios; 2020 [cited 2021 Aug 9]. Available from: https://www.qeios.com/read/definition/32800

105. An index of factorial simplicity | SpringerLink [Internet]. [cited 2021 Aug 9]. Available from: https://link.springer.com/article/10.1007%2FBF02291575

106. Keller S, Evensen C, Yang M. Adult Sickle Cell Quality of Life Measurement Information System: ASCQ Me User's Manual. Bethesda, MD: National Heart. Lung and Blood Institute.; 2011.

107. Saris WE, Satorra A, van der Veld WM. Testing Structural Equation Models or Detection of Misspecifications? Struct Equ Model Multidiscip J. 2009 Oct 6;16(4):561–82.

108. What Is QOL? | ISOQOL [Internet]. [cited 2020 May 13]. Available from: https://www.isoqol.org/what-is-qol/

109. Andong AM, Ngouadjeu EDT, Bekolo CE, Verla VS, Nebongo D, Mboue-Djieka Y, et al. Chronic complications and quality of life of patients living with sickle cell disease and receiving care in three hospitals in Cameroon: a cross-sectional study. BMC Hematol. 2017 Dec;17(1):1–7.

110. Comer E. Integrating the health and mental health needs of the chronically ill: a group of individuals with depression and sickle cell disease. Soc Work Health Care. 2004 May 22;38(4):57–76.

111. Hasan SP, Hashmi S, Alhassen M, Lawson W, Castro O. Depression in sickle cell disease. J Natl Med Assoc. 2003 Jul;95(7):533–7.

112. Panepinto JA, Bonner M. Health-related quality of life in sickle cell disease: Past, present, and future. Pediatr Blood Cancer. 2012 Aug;59(2):377–85.

113. Edwards CL, Scales MT, Loughlin C, Bennett GG, Harris-Peterson S, Castro LMD, et al. A brief review of the pathophysiology, associated pain, and psychosocial issues in sickle cell disease. Int J Behav Med. 2005 Sep 1;12(3):171–9.

114. Okpala I, Thomas V, Westerdale N, Jegede T, Raj K, Daley S, et al. The comprehensive care of sickle cell disease. Eur J Haematol. 2002 Mar;68(3):157–62.

115. Anie KA. Psychological complications in sickle cell disease. Br J Haematol. 2005 Jun;126(6):723–9.

116. Yale SH, Nagib N, Guthrie T. Approach to vaso-occlussive crisis in adults with sickle cell disease. Am Fam Physician. 2000 Mar 1;61(5):1349–56.

117. Maxwell K, Streetly A, Bevan D. Experiences of hospital care and treatment seeking for pain from sickle cell disease: qualitative study. BMJ. 1999 Jun 12;318(7198):1585–90.

118. Elander J, Lusher J, Bevan D, Telfer P. Pain management and symptoms of substance dependence among patients with sickle cell disease. Soc Sci Med. 2003 Nov 1;57(9):1683–96.

119. Druye A, Robinson B, Nelson K. Self-management recommendations for sickle cell disease: a Ghanaian health professionals' perspective. Health Sci Rep. 2018;1(11):e88.

120. Yusuf HR, Atrash HK, Grosse SD, Parker CS, Grant AM. Emergency department visits made by patients with sickle cell disease: a descriptive study, 1999–2007. Am J Prev Med. 2010 Apr 1;38(4, Supplement):S536–41.

121. Sobota A, Neufeld EJ, Sprinz P, Heeney MM. Transition from pediatric to adult care for sickle cell disease: results of a survey of pediatric providers. Am J Hematol. 2011 Jun;86(6):512–5.

122. Jordan L, Swerdlow P, Coates TD. Systematic review of transition from adolescent to adult care in patients with sickle cell disease. J Pediatr Hematol Oncol. 2013 Apr;35(3):165–9.

123. Laurence B, George D, Woods D. Association between elevated depressive symptoms and clinical disease severity in African-American adults with sickle cell disease. J Natl Med Assoc. 2006 Mar;98(3):365–9.

124. CDC. Living Well with Sickle Cell Disease | CDC [Internet]. Centers for Disease Control and Prevention. 2020 [cited 2020 Oct 3]. Available from: https://www.cdc.gov/ncbddd/sicklecell/healthyliving-living-well.html

125. Tanabe P, Porter J, Creary M, Kirkwood E, Miller S, Ahmed-Williams E, et al. A qualitative analysis of best self-management practices: sickle cell disease. J Natl Med Assoc. 2010 Nov 1;102(11):1033–41.

126. Shi L. The convergence of vulnerable characteristics and health insurance in the US. Soc Sci Med. 2001 Aug;53(4):519–29.

127. Bandura A. Self-efficacy: toward a unifying theory of behavioral change. Psychol Rev. 1977 Mar;84(2):191–215.

128. Ahmadi M, Shariati A, Jahani S, Tabesh H, Keikhaei B. The effectiveness of self-management programs on self-efficacy in patients with sickle cell disease. Jundishapur J Chronic Dis Care. 2014 Jul;3(3):e21702.

129. Bandura A. Self-Efficacy Mechanism in Human Agency. Am Psychol. 1982 Feb;37(22):122.

130. Edwards R, Telfair J, Cecil H, Lenoci J. Self-efficacy as a predictor of adult adjustment to sickle cell disease: one-year outcomes. Psychosom Med. 2001 Oct;63(5):850–8.

131. Anie KA, Telfair J. Multi-site study of transition in adolescents with sickle cell disease in the United Kingdom and the United States. Int J Adolesc Med Health. 2005 Jun;17(2):169–78.

132. Clay OJ, Telfair J. Evaluation of a disease-specific self-efficacy instrument in adolescents with sickle cell disease and its relationship to adjustment. Child Neuropsychol J Norm Abnorm Dev Child Adolesc. 2007 Mar;13(2):188–203.

133. Lenoci JM, Telfair J, Cecil H, Edwards RFR. Self-care in adults with sickle cell disease. West J Nurs Res. 2002 Apr;24(3):228–45.

134. Rapley P, Fruin DJ. Self-efficacy in chronic illness: the juxtaposition of general and regimen-specific efficacy. Int J Nurs Pract. 1999 Dec;5(4):209–15.

135. Adegbola M. Spirituality, self-efficacy, and quality of life among adults with sickle cell disease. South Online J Nurs Res. 2011 Apr;11(1).

136. Stewart MJ. Integrating social support in nursing. SAGE Publ Inc. 1993 Jun 9;

137. Chlebowy DO, Garvin BJ. Social support, self-efficacy, and outcome expectations. Diabetes Educ. 2006 Sep;32(5):777–86.

138. Ngamvitroj A, Kang D-H. Effects of self-efficacy, social support and knowledge on adherence to PEFR self-monitoring among adults with asthma: a prospective repeated measures study. Int J Nurs Stud. 2007 Aug 1;44(6):882–92.

139. Sin M-K, Kang D-H, Weaver M. Relationships of asthma knowledge, self-management, and social support in African American adolescents with asthma. Int J Nurs Stud. 2005 Mar 1;42(3):307–13.

140. Loeb SJ, Penrod J, Falkenstern S, Poon LW. Supporting older adults living with multiple chronic conditions. West J Nurs Res. 2003;8–29.

141. Cox LE. Social support, medication compliance and HIV/AIDS. Soc Work Health Care. 2002 Aug 20;35(1–2):425–60.

142. Jacob E. The pain experience of patients with sickle cell anemia. Pain Manag Nurs. 2001 Sep 1;2(3):74–83.

143. Kline RB. Principles and practice of structural equation modeling. Methodology in the Social Sciences. Vol. 2. 2005. 366 p.

144. Edwards R, Telfair J, Cecil H, Lenoci J. Reliability and validity of a self-efficacy instrument specific to sickle cell disease. Behav Res Ther. 2000 Sep;38(9):951–63.

145. Sherbourne CD, Stewart AL. The MOS social support survey. Soc Sci Med 1982. 1991;32(6):705–14.

146. Cooper O, McBain H, Tangayi S, Telfer P, Tsitsikas D, Yardumian A, et al. Psychometric analysis of the adult sickle cell quality of life measurement information system (ACSQ-Me) in a UK population. Health Qual Life Outcomes. 2019 Dec;17(1):1–11.

147. HealthMeasures Scoring Service [Internet]. [cited 2021 Oct 24]. Available from: https://www.assessmentcenter.net/ac_scoringservice

148. Hayes AF. Introduction to Mediation, Moderation, and Conditional Process Analysis, Second Edition: A Regression-Based Approach. Guilford Publications; 2017. 713 p.

149. IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp.

150. Preacher KJ, Hayes AF. Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. Behav Res Methods. 2008 Aug 1;40(3):879–91.

151. MacKinnon DP, Krull JL, Lockwood CM. Equivalence of the Mediation, Confounding and Suppression Effect. :9.

152. Luszczynska A, Sarkar Y, Knoll N. Received social support, self-efficacy, and finding benefits in disease as predictors of physical functioning and adherence to antiretroviral therapy. Patient Educ Couns. 2007 Apr;66(1):37–42.

153. McKnight PE, Afram A, Kashdan TB, Kasle S, Zautra A. Coping self-efficacy as a mediator between catastrophizing and physical functioning: treatment target selection in an osteoarthritis sample. J Behav Med. 2010 Jun;33(3):239–49.

154. Rizio AA, Bhor M, Lin X, McCausland KL, White MK, Paulose J, et al. The relationship between frequency and severity of vaso-occlusive crises and health-related quality of life and work productivity in adults with sickle cell disease. Qual Life Res. 2020 Jun 1;29(6):1533–47.

155. Wallen GR, Minniti CP, Krumlauf M, Eckes E, Allen D, Oguhebe A, et al. Sleep disturbance, depression and pain in adults with sickle cell disease. BMC Psychiatry. 2014 Jul 21;14(1):207.

156. Binnema M, Schrijvers LH, Bos R, Schuurmans MJ, Fischer K. Coping in adult patients with severe haemophilia. Haemoph Off J World Fed Hemoph. 2014 Jul;20(4):513–8.

157. Santavirta N, Björvell H, Solovieva S, Alaranta H, Hurskainen K, Konttinen YT. Coping strategies, pain, and disability in patients with hemophilia and related disorders. Arthritis Rheum. 2001 Feb;45(1):48–55.

158. Barakat LP, Schwartz LA, Simon K, Radcliffe J. Negative Thinking as a Coping Strategy Mediator of Pain and Internalizing Symptoms in Adolescents with Sickle Cell Disease. J Behav Med. 2007 Jun 1;30(3):199–208.

159. Aust H, Rüsch D, Schuster M, Sturm T, Brehm F, Nestoriuc Y. Coping strategies in anxious surgical patients. BMC Health Serv Res. 2016 Jul 12;16(1):250.

160. Marks R, Allegrante JP, Lorig K. A review and synthesis of research evidence for self-efficacy-enhancing interventions for reducing chronic disability: implications for health education practice (part I). Health Promot Pract. 2005 Jan;6(1):37–43.

161. Maly MR, Costigan PA, Olney SJ. Self-Efficacy Mediates Walking Performance in Older Adults with Knee Osteoarthritis. J Gerontol Ser A. 2007 Oct 1;62(10):1142–6.

162. Jenerette CM, Valrie CR. The influence of maternal behaviors during childhood on self-efficacy in individuals with sickle cell disease. J Fam Nurs. 2010 Nov;16(4):422–34.

163. Mahler HI, Kulik JA. Effects of preparatory videotapes on self-efficacy beliefs and recovery from coronary bypass surgery. Ann Behav Med Publ Soc Behav Med. 1998;20(1):39–46.

164. Shah RM. Measuring And Understanding Health-Related Quality Of Life Among Adult Patients With Hemophilia. :204.

165. Fabry ME, Benjamin L, Lawrence C, Nagel RL. An objective sign in painful crisis in sickle cell anemia: the concomitant reduction of high density red cells. Blood. 1984 Aug 1;64(2):559–63.

166. Claster S. Managing sickle cell disease. BMJ. 2003 Nov 15;327(7424):1151–5.

167. Ballas SK. Sickle cell disease: current clinical management. Semin Hematol. 2001 Oct 1;38(4):307–14.

168. Geiser C, Carlson I. Testing the limits of latent class analysis (2012). In.

169. Lee K, Bentley J, Hsu H-YM. Using characteristics of serious leisure to classify rock climbers: a latent profile analysis. J Sport Tour. 2017 Oct 2;21(4):245–62.

170. Pastor DA, Barron KE, Miller BJ, Davis SL. A latent profile analysis of college students' achievement goal orientation. Contemp Educ Psychol. 2007 Jan;32(1):8–47.

171. Oberski D. Mixture Models: latent Profile and latent class analysis. In Modern Statistical Methods for HCI. Mod Stat Methods HCI. 2016;275–87.

172. Asparouhov T, Muthén B. Auxiliary variables in mixture modeling: three-step approaches using Mplus. Struct Equ Model Multidiscip J. 2014 Jul;21(3):329–41.

173. Lo Y, Mendell NR, Rubin DB. Testing the number of components in a normal mixture. Biometrika. 2001 Oct 1;88(3):767–78.

174. Geiser C. Data Analysis with Mplus. Guilford Press; 2012. 321 p.

175. Asparouhov T, Muthen B. Auxiliary Variables in Mixture Modeling: Using the BCH Method in Mplus to Estimate a Distal Outcome Model and an Arbitrary Secondary Model. :80.

176. Aldridge AA, Roesch SC. Developing Coping Typologies of Minority Adolescents: A Latent Profile Analysis. J Adolesc. 2008 Aug;31(4):499–517.

177. Li R, Cooper C, Bradley J, Shulman A, Livingston G. Coping strategies and psychological morbidity in family carers of people with dementia: A systematic review and meta-analysis. J Affect Disord. 2012 Jun;139(1):1–11.

178. Gilhooly KJ, Gilhooly MLM, Sullivan MP, McIntyre A, Wilson L, Harding E, et al. A meta-review of stress, coping and interventions in dementia and dementia caregiving. BMC Geriatr. 2016 May 18;16(1):106.

179. Taylor BJ, Irish LA, Martire LM, Siegle GJ, Krafty RT, Schulz R, et al. Avoidant coping and poor sleep efficiency in dementia caregivers. Psychosom Med. 2015;77(9):1050–7.

180. Esteve R, Ramírez-Maestre C, López-Martínez AE. Adjustment to chronic pain: The role of pain acceptance, coping strategies, and pain-related cognitions. Ann Behav Med. 2007 Jun;33(2):179–88.

181. McCracken LM, Eccleston C. Coping or acceptance: what to do about chronic pain? PAIN. 2003 Sep;105(1):197–204.

182. Wetherell JL, Afari N, Ayers CR, Stoddard JA, Ruberg J, Sorrell JT, et al. Acceptance and Commitment Therapy for Generalized Anxiety Disorder in Older Adults: A Preliminary Report. Behav Ther. 2011 Mar;42(1):127–34.

183. Nurius PS, Macy RJ. Heterogeneity among violence-exposed women: Applying person-oriented research methods. J Interpers Violence. 2008;23(3):389–415.

184. Meeusen C, Meuleman B, Abts K, Bergh R. Comparing a Variable-Centered and a Person-Centered Approach to the Structure of Prejudice. Soc Psychol Personal Sci. 2018 Aug;9(6):645–55.

185. Bolck A, Croon M, Hagenaars J. Estimating Latent Structure Models with Categorical Variables: One-Step Versus Three-Step Estimators. Polit Anal. 2004;12(1):3–27.

186. Brousseau DC, Panepinto JA, Nimmer M, Hoffmann RG. The number of people with sickle-cell disease in the United States: national and state estimates. Am J Hematol. 2010;85(1):77–8. 187. Hassell KL. Population Estimates of Sickle Cell Disease in the U.S. Am J Prev Med. 2010 Apr 1;38(4):S512–21.

188. Reeves S, Garcia E, Kleyn M, Housey M, Stottlemyer R, Lyon-Callo S, et al. Identifying Sickle Cell Disease Cases using Administrative Claims. Acad Pediatr. 2014;14(5 Suppl):S61–7.

189. DeSimone JA, Harms PD, DeSimone AJ. Best practice recommendations for data screening. J Organ Behav. 2015;36(2):171–81.

190. Huang JL, Curran PG, Keeney J, Poposki EM, DeShon RP. Detecting and Deterring Insufficient Effort Responding to Surveys. J Bus Psychol. 2012 Mar 1;27(1):99–114.

191. Costa PT, McCrae RR. The revised NEO personality inventory (NEO-PI-R). SAGE Handb Personal Theory Assess Vol 2 - Personal Meas Test. 2008 Jan 1;179–98.

192. Brown W. Some Experimental Results in the Correlation of Mental Abilities1. Br J Psychol 1904-1920. 1910;3(3):296–322.

193. Spearman C. Correlation calculated from faculty data. Br J Psychol [Internet]. 1910 [cited 2021 Oct 25]; Available from: https://bpspsychub.onlinelibrary.wiley.com/doi/10.1111/j.2044-8295.1910.tb00206.x

194. Johnson JA. Ascertaining the validity of individual protocols from Web-based personality inventories. J Res Personal. 2005 Feb 1;39(1):103–29.

# APPENDIX

## APPENDIX A: COVER LETTER

Respected Sir/Madam,

You are being invited to participate in an online survey, conducted by researchers at the University of Mississippi, School of Pharmacy, to assess the disease burden, coping strategies and quality of life of people who have been diagnosed with sickle cell disease. This study is part of a Ph.D. student's research project.

**Who's eligible?:** Adult (18 years of age and older) patients who have been diagnosed with sickle cell.

**How long does it take?:** The survey should take no longer than 30 minutes to complete.

**What can you expect?:** Upon completion of the survey, you will be asked to provide an email address so that the research team can send you a $15 Amazon gift card and the summary of the findings on completion of the study. Your email address will not be linked with your survey responses or used for any other purposes than those stated above. Your participation in the study is anonymous. We do not expect any risks associated with participation in this study.

This questionnaire is voluntary, and you may withdraw from the study, without consequence, at any time. **Click on the following link or Copy and Paste it in your internet browser to complete the survey:**

https://uofmississippi.qualtrics.com/jfe/form/SV_ezGPmYP5ps4eQxn

THANK YOU in advance for your time and participation in this survey. If you have any questions or need more information, please contact Monika Salkar in the Department of Pharmacy Administration, University of Mississippi at **msalkar@go.olemiss.edu**.

**This study has been reviewed by The University of Mississippi's Institutional Review Board (IRB). If you have any questions, concerns, or reports regarding your rights as a participant of research, please contact the IRB at (662) 915-7482 or irb@olemiss.edu.**

Sincerely,


**Monika Salkar, MS**
Ph.D. Candidate
Pharmacy Administration
The University of Mississippi
School of Pharmacy

**Dr. John P. Bentley, PhD**
Professor,
Pharmacy Administration
The University of Mississippi
School of Pharmacy

**Dr. Meagen Rosenthal, PhD**
Associate Professor,
Pharmacy Administration
The University of Mississippi
School of Pharmacy

# APPENDIX B: STUDY SURVEY

Thank you for your willingness to participate in this survey.

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Start of Block: Introduction

Q41
You have been selected to take part in a research study conducted by the University of Mississippi. This study is asking individuals across the United States to complete an online survey.

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Q43
**Welcome to the research study!**

**The purpose of this study**

We want to know about how adults with sickle cell disease feel about their quality of life, how you cope with sickle cell disease related pain, perceptions of how you can manage your own health, and about your social connections. Finally, there are some 'demographic' questions, like age, education, income, and what kind of health insurance you have.

**Time required for this study**

The survey should take you approximately 20 minutes to complete.

**Possible risks from your participation**

Answering survey questions about your health may be stressful for you. The questions that are being asked are not that different from those that a doctor or nurse may ask. Please see the Confidentiality section for information on how we minimize the risk of a breach of confidentiality.

**Benefits from your participation**

You should not expect benefits from participating in this study. However, you might experience satisfaction from contributing to scientific knowledge. We hope that data from this survey will contribute to a better understanding of health and coping with pain among adults with sickle cell disease.

**Incentives**

Upon completion of the surveys, you will receive an honorarium worth $15 as a token of our appreciation for your time and participation.

**Confidentiality**

All information in the study will be collected from you anonymously: Researchers at the University of Mississippi will not have access to your name or any other personal information.

**Right to Withdraw**

Your participation in this research is voluntary. You have the right to withdraw at any point during the study, for any reason, and without any prejudice. If you would like to contact the Principal Investigator in the study to discuss this research, please e-mail Ms. Monika Salkar at msalkar@go.olemiss.edu

**IRB Approval**

This study has been reviewed by The University of Mississippi's Institutional Review Board (IRB). The IRB has determined that this study fulfills the human research subject protections obligations required by state and federal law and University policies. If you have any questions or concerns regarding your rights as a research participant, please contact the IRB at (662) 915-7482 or irb@olemiss.edu.

By clicking the button below, you acknowledge that your participation in the study is voluntary, you are 18 years of age, and that you are aware that you may choose to terminate your participation in study at any time and for any reason.

Please note that this survey will be best displayed on a laptop or desktop computer. Some features may be less compatible for use on a mobile device.

- ○ I consent, begin the study
- ○ I do not consent, I do not wish to participate

End of Block: Introduction

Start of Block: Screener

Q217

**Thank you for your willingness to participate in this survey!**

**GENERAL INSTRUCTIONS**: For each of the following questions please check the most appropriate response. Please note that there are no right or wrong answers to any of the following questions.

Q218 **Are you 18 years of age or older?**

- ○ Yes
- ○ No

Q219 **With which type of Sickle Cell Disease were you diagnosed?**

- ○ Hemoglobin SS (sickle cell anemia)
- ○ Hemoglobin SC
- ○ Hemoglobin Sβ0 (beta zero) thalassemia
- ○ Hemoglobin Sβ+ (beta) thalassemia
- ○ Hemoglobin SD
- ○ Hemoglobin SE
- ○ Hemoglobin SO
- ○ Other (please specify) _____

Q220
Have you participated in a similar study asking questions related to sickle cell disease quality of life, coping with pain, perceptions of how you can manage your own health, and about your social connections from researchers at **University of Mississippi**?

- ○ Yes
- ○ No

End of Block: Screener

Start of Block: Section I Part B: Your coping strategies

Q29 **INSTRUCTIONS:** This section asks for your sickle cell disease coping strategies. This information will help understand the different coping strategies you use when in sickle cell disease related pain crises (vaso-occlusive crises). For each of the following questions, please select the option that best describes your answer.

Individuals who experience pain have developed a number of ways to cope or deal with their pain. These include saying things to themselves when they experience pain, or engaging in different activities. Below are a list or things that patients have reported doing when they feel pain. For each activity, I want you to indicate, using the scale below, how much you engage in that activity when you feel pain, where 0 indicates you never do that when you are experiencing pain, a 3 indicates you sometimes do that when you are experiencing pain, and a 6 indicates you always do it when you are experiencing pain. Remember, you can use any point along the scale.

Q31 **When I feel pain...**

| | Never do that 0 | 1 | 2 | Sometimes do that 3 | 4 | 5 | Always do that 6 |
|---|---|---|---|---|---|---|---|
| I try to get some sleep | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I imagine that the pain is outside my body | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I take a hot or cold bath | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I think of things I enjoy doing | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I try to think years ahead, what everything will be like after I have gotten rid of the pain | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I read | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I avoid people | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I realize that most people don't really care | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I don't like to be with people | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I try to think of something pleasant | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

| Q32 **When I feel pain...** | Never do that 0 | 1 | 2 | Sometimes do that 3 | 4 | 5 | Always do that 6 |
|---|---|---|---|---|---|---|---|
| I drink twice as much as I usually do | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I rub the parts of body that hurt | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I increase my fluid intake | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I tell myself it doesn't hurt | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| It is awful and I feel that it overwhelms me | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I try to drink some water or juice every hour | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I think it is not fair that I have to live this way | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I do something I enjoy, such as watching TV or listening to music | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I try to drink a lot of water | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| I worry that I am having a heart attack or some other physical problem | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

Page Break

Q33 **When I feel pain...**

| | Never do that 0 | 1 | 2 | Sometimes do that 3 | 4 | 5 | Always do that 6 |
|---|---|---|---|---|---|---|---|
| It is terrible and I feel it is never going to get any better | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I take a hot or cold shower | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I think no one wants to hear about my problems | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I go off by myself | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I go to bed | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I try to be alone | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I rely on my faith in God | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I count numbers in my head or run a song through my mind | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I worry that my disease is getting worse | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I know I need to get away from everyone | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

Page Break

Q34 **When I feel pain...**

| | Never do that 0 | 1 | 2 | Sometimes do that 3 | 4 | 5 | Always do that 6 |
|---|---|---|---|---|---|---|---|
| I pretend it is not a part of me | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I massage painful areas | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I use ice packs to help relieve the pain | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I play mental games with myself to keep my mind off the pain | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I go to a quiet place where I won't be bothered | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I think of people I enjoy doing things with | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| Although it hurts, I just keep on going | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I think that if I can't be healthy then no one else should be | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I tell myself that I can overcome the pain | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I ignore it | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

Q15 **When was your <u>last pain attack</u> (crisis)?**

- ○ I have never had a pain attack (crises)
- ○ More than 5 years ago
- ○ 1-5 years ago
- ○ 7-11 months ago
- ○ 1-6 months ago
- ○ 1-3 weeks ago
- ○ Less than a week ago
- ○ I have one right now

Q35 **When I feel pain...**

| | Never do that 0 | 1 | 2 | Sometimes do that 3 | 4 | 5 | Always do that 6 |
|---|---|---|---|---|---|---|---|
| I try to be around other people | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I have faith in doctors that someday there will be a cure for my pain | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I think that I don't deserve this | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I just go on as if nothing happened | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I tell myself to be brave and carry on despite the pain | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I worry all the time whether it will end | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I just think of it as some other sensation, such as numbness | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I know others don't understand | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I don't pay any attention to it | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| I drink five or more glasses of water or juice a day | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

Page Break

Q36 **When I feel pain...**

| | Never do that 0 | 1 | 2 | Sometimes do that 3 | 4 | 5 | Always do that 6 |
|---|---|---|---|---|---|---|---|
| I worry that I am really going to get sick | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I relax my muscles | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I do anything to get my mind off the pain | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I am afraid I am going to die | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I lay down on the bed or couch in order to relax | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I try not to think of it as my body but rather as something separate from me | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I feel I can't go on | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I pretend it is not there | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I pray to God it won't last long | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I feel I can't stand it anymore | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

Page Break

Q37 **When I feel pain...**

| | Never do that 0 | 1 | 2 | Sometimes do that 3 | 4 | 5 | Always do that 6 |
|---|---|---|---|---|---|---|---|
| I replay in my mind pleasant experiences in the past | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I do something active like household chores or projects | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I try to feel distant from the pain, almost as if the pain was is somebody else's body | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I drink as much juice or water as I can | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I know I'll have to go to the hospital or see my doctor | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I spend time resting | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I know someday someone will be here to help me and it will go away for awhile | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I don't think about the pain | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| I leave the house and do something, such as going to the movies or shopping | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I try to relax | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 14 | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

Page Break

Q38 **When I feel pain...**

| | Never do that 0 | 1 | 2 | Sometimes do that 3 | 4 | 5 | Always do that 6 |
|---|---|---|---|---|---|---|---|
| No matter how bad it gets I know I can handle it | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I am sure there is something wrong | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I tell myself I can't let the pain stand in the way of what I have to do | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I use a heating pad | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I see it as a challenge and don't let it bother me | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I feel my life isn't worth living | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I pray for the pain to stop | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| I don't think of it as pain but rather as a dull or warm feeling | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

Page Break

Q39 **Based on all the things you do to cope or deal with your pain, on an average day, how much control do you feel you have over it? Please select the appropriate number. Remember, you can select any number along the scale.**

- ○ No control 0
- ○ 1
- ○ 2
- ○ Some control 3
- ○ 4
- ○ 5
- ○ Complete control 6

Q40 **Based on all the things you do to cope or deal with your pain, on an average day, how much are you able to decrease it? Please select the appropriate number. Remember, you can select any number along the scale.**

- ○ Can't decrease it at all 0
- ○ 1
- ○ 2
- ○ Can decrease it somewhat 3
- ○ 4
- ○ 5
- ○ Can decrease it completely 6

Page Break

End of Block: Section I Part B: Your coping strategies

Start of Block: Clinical Information

Q57 **In the past 12 months, how many sickle cell pain attacks (crises) did you have?**

- ○ I did not have a pain attack (crises) in the past 12 months
- ○ 1
- ○ 2
- ○ 3
- ○ 4 or more

---

Q59 **When was your last pain attack (crisis)?**

- ○ I have never had a pain attack (crises)
- ○ More than 5 years ago
- ○ 1-5 years ago
- ○ 7-11 months ago
- ○ 1-6 months ago
- ○ 1-3 weeks ago
- ○ Less than a week ago
- ○ I have one right now

---

Page Break

Q61 **Using any number from 0 to 10, where 0 is no pain and 10 is the worst pain imaginable, how severe was your pain during your last pain attack (crisis)?**

- ○ No pain 0
- ○ 1
- ○ 2
- ○ 3
- ○ 4
- ○ 5
- ○ 6
- ○ 7
- ○ 8
- ○ 9
- ○ Worst Imaginable pain 10
- ○ I have never had a pain attack (crises)

Q63 **How much did your <u>last pain attack</u> (crisis) interfere with your life?**

- ○ I've never had a pain attack (crisis)
- ○ Not at all, I did everything I usually do
- ○ I had to cut down on some things I usually do
- ○ I could not do most things I usually do
- ○ I could not take care of myself and needed some help from family or friends
- ○ I could not take care of myself and needed constant care from family, friends, doctors, or nurses

---

X→

Q65 **About how long did your <u>most recent pain attack</u> (crisis) last?**

- ○ I have never had a pain attack (crises)
- ○ Less than 1 hour
- ○ 1-12 hours
- ○ 13-23 hours
- ○ 1-3 days
- ○ 4-6 days
- ○ 1-2 weeks
- ○ More than 2 weeks

---

Q67 **Please answer the following questions**

| | Yes | No |
|---|---|---|
| Have you ever had open sores on your legs or feet (leg ulcers)? | ○ | ○ |
| Has a doctor or nurse ever told you that you have lung damage? | ○ | ○ |
| Has a doctor or nurse ever told you that you have kidney damage? | ○ | ○ |
| Has a doctor or nurse ever told you that you have eye damage called retinopathy? | ○ | ○ |
| Has a doctor or nurse ever told you that you have damage to your hip or shoulder due to sickle cell disease? | ○ | ○ |
| Has a doctor or nurse ever told you that you have had a stroke? | ○ | ○ |
| Has your spleen either been removed or seriously damaged due to sickle cell disease? | ○ | ○ |
| Do you get regular blood transfusions for your sickle cell disease? | ○ | ○ |
| Do you take pain medicine every day for your sickle cell disease? | ○ | ○ |

**End of Block: Clinical Information**

**Start of Block: Section I Part C: Information about you and your well being**

Q41
**INSTRUCTIONS**: This section asks for your views about your health. This information will help keep track

of how you feel and how well you are able to do your usual activities. For each of the following questions, please select the option that best describes your answer.

Q42 **In the <u>past 7 days</u>,...**

| | Never | Rarely | Sometimes | Often | Always |
|---|---|---|---|---|---|
| how often did you stay up most of the night because you could not fall asleep? | ○ | ○ | ○ | ○ | ○ |
| how often was it very easy for you to fall asleep? | ○ | ○ | ○ | ○ | ○ |
| how often did you have a lot of trouble falling asleep? | ○ | ○ | ○ | ○ | ○ |
| how often did you stay up all night because you could not fall asleep? | ○ | ○ | ○ | ○ | ○ |
| how often did you stay up half of the night because you could not fall asleep? | ○ | ○ | ○ | ○ | ○ |
| how often did you have pain so bad that you could not do anything for a whole day? | ○ | ○ | ○ | ○ | ○ |
| how often did you have pain so bad that you could not get out of bed? | ○ | ○ | ○ | ○ | ○ |
| how often did you have very severe pain? | ○ | ○ | ○ | ○ | ○ |
| how often did you have pain so bad that you had to stop what you were doing? | ○ | ○ | ○ | ○ | ○ |

| | | | | | |
|---|---|---|---|---|---|
| how often did you have pain so bad that it was hard to finish what you were doing? | ○ | ○ | ○ | ○ | ○ |

Page Break

Q47 **In the <u>past 7 days</u>,...**

| | Never | Rarely | Sometimes | Often | Always |
|---|---|---|---|---|---|
| how often how often did you feel completely hopeless because of your health? | ○ | ○ | ○ | ○ | ○ |
| how depressed were you about your health problems? | ○ | ○ | ○ | ○ | ○ |
| how lonely did you feel because of your health problems? | ○ | ○ | ○ | ○ | ○ |
| how much did you worry about getting sick? | ○ | ○ | ○ | ○ | ○ |
| how often were you very worried about needing to go to the hospital? | ○ | ○ | ○ | ○ | ○ |
| how often were your joints very stiff when you woke up? | ○ | ○ | ○ | ○ | ○ |
| how often were your joints very stiff during the day? | ○ | ○ | ○ | ○ | ○ |
| how often were your joints so stiff during the day that you could not move? | ○ | ○ | ○ | ○ | ○ |
| how often did you wake up so stiff that you could not move? | ○ | ○ | ○ | ○ | ○ |

| | | | | | |
|---|---|---|---|---|---|
| how often did it take you a very long time to get out of bed because of stiffness? | ○ | ○ | ○ | ○ | ○ |

Page Break

Q46 **In the <u>past 30 days</u>,...**

| | Never | Rarely | Sometimes | Often | Always |
|---|---|---|---|---|---|
| how much did you rely on others to take care of you because of your health? | ○ | ○ | ○ | ○ | ○ |
| how often did your health slow you down? | ○ | ○ | ○ | ○ | ○ |
| how often did your health make it hard for you to do things? | ○ | ○ | ○ | ○ | ○ |
| how often did your health keep you from going out? | ○ | ○ | ○ | ○ | ○ |
| how much did your health make it hard for you to do things with your friends? | ○ | ○ | ○ | ○ | ○ |

Page Break

End of Block: Section I Part C: Information about you and your well being

Start of Block: Section I Part E: Information about your social support

Q49 **INSTRUCTIONS**: This section asks questions about the social support you receive. People sometimes look to others for companionship, assistance, or other types of support. **How often is each of the following kinds of support available to you if you need it?** Choose one number from each line. Please answer all questions.

Q50 How often is each of the following kinds of support available to you if you need it?

| | None of the time | A little of the time | Some of the time | Most of the time | All of the time |
|---|---|---|---|---|---|
| Someone you can count on to listen to you when you need to talk | ○ | ○ | ○ | ○ | ○ |
| Someone to give you information to help you understand a situation | ○ | ○ | ○ | ○ | ○ |
| Someone to give you good advice about a crisis | ○ | ○ | ○ | ○ | ○ |
| Someone to confide in or talk to about yourself or your problems | ○ | ○ | ○ | ○ | ○ |
| Someone whose advice you really want | ○ | ○ | ○ | ○ | ○ |
| Someone to share your most private worries and fears with | ○ | ○ | ○ | ○ | ○ |
| Someone to turn to for suggestions about how to deal with a personal problem | ○ | ○ | ○ | ○ | ○ |
| Someone who understands your problems | ○ | ○ | ○ | ○ | ○ |
| Someone to help you if you were confined to bed | ○ | ○ | ○ | ○ | ○ |

| | | | | | |
|---|---|---|---|---|---|
| Someone to take you to the doctor if you needed it | ○ | ○ | ○ | ○ | ○ |

Page Break

Q51 How often is each of the following kinds of support available to you if you need it?

| | None of the time | A little of the time | Some of the time | Most of the time | All of the time |
|---|---|---|---|---|---|
| Someone to prepare your meals if you were unable to do it yourself | ○ | ○ | ○ | ○ | ○ |
| Someone to help with daily chores if you were sick | ○ | ○ | ○ | ○ | ○ |
| Someone who shows you love and affection | ○ | ○ | ○ | ○ | ○ |
| Someone to love and make you feel wanted | ○ | ○ | ○ | ○ | ○ |
| Someone who hugs you | ○ | ○ | ○ | ○ | ○ |
| Someone to have a good time with | ○ | ○ | ○ | ○ | ○ |
| Someone to do something enjoyable with | ○ | ○ | ○ | ○ | ○ |
| Someone to get together with for relaxation | ○ | ○ | ○ | ○ | ○ |
| Someone to do things with to help you get your mind off things | ○ | ○ | ○ | ○ | ○ |

End of Block: Section I Part E: Information about your social support

Start of Block: Section I Part D: Information about your self-efficacy

Q47 **INSTRUCTIONS**: This section asks questions ask about how sure you are in dealing day-to-day with sickle cell disease. There are no right or wrong answers; we just want to know what you think. So for each question, tell us how sure you are by circling the response that best tells how you feel. Please answer every question.

---

Q48 **How sure are you that...**

| | Not at all sure | Not sure | Neither | Sure | Very sure |
|---|---|---|---|---|---|
| you can do something to cut down on most of the pain? | ○ | ○ | ○ | ○ | ○ |
| you can keep doing most of the things you do day-to-day? | ○ | ○ | ○ | ○ | ○ |
| you can keep sickle cell disease pain from interfering with your sleep? | ○ | ○ | ○ | ○ | ○ |
| you can reduce your sickle cell disease pain by using methods other than taking extra medication? | ○ | ○ | ○ | ○ | ○ |
| you can control how often or when you get tired? | ○ | ○ | ○ | ○ | ○ |
| you can do something to help yourself feel better if you are feeling sad or blue? | ○ | ○ | ○ | ○ | ○ |
| you can manage your life from day-to-day as compared with other people? | ○ | ○ | ○ | ○ | ○ |
| you can manage your sickle cell symptoms so that you can do the things you enjoy doing? | ○ | ○ | ○ | ○ | ○ |

| | | | | | |
|---|---|---|---|---|---|
| you can deal with the frustration of having sickle cell disease? | ○ | ○ | ○ | ○ | ○ |

Page Break

End of Block: Section I Part D: Information about your self-efficacy

Start of Block: Section I Part A: Demographics

Q4 **INSTRUCTIONS:** This next section asks about your sociodemographic and clinical information. Please answer the following questions to help us better understand your responses.

Q5 **What is your sex?**

- ○ Male
- ○ Female
- ○ Prefer not to answer

Q6 **What is your current age?**

_____

Q7 **Which of the following best describes your race or ethnicity?**

- ○ African American/Black
- ○ American Indian/Alaska Native
- ○ Asian
- ○ Hispanic
- ○ Native Hawaiian/Other Pacific Islander
- ○ White/Caucasian
- ○ Other (please specify) _____

Q8 **Which of the following describes your current living situation?**

- ○ Living alone
- ○ Living with family/partner
- ○ Living with friends
- ○ Other (please specify) _____

Q9 **What is the highest level of education you have completed?**

- ○ Less than high school
- ○ High school/GED
- ○ Some college
- ○ 2 year college degree
- ○ 4 year college degree
- ○ Professional degree (e.g. J.D., M.D.)
- ○ Masters' degree
- ○ Doctoral degree

---

Q10 **Which of the following describes your main occupation?**

- ○ Employed/Self-employed full time
- ○ Employed part-time
- ○ Retired
- ○ Home-maker
- ○ Student
- ○ Seeking work
- ○ Other (please specify) _____

---

Q11 **Please indicate the region of the country in which you reside.**

- ○ Northeast
- ○ Midwest
- ○ South
- ○ West

---

Q12 **Do you currently have health insurance?**

- ○ Yes
- ○ No

*Skip To: Q28 If Do you currently have health insurance? = No*

---

Q13 **What type of health insurance do you currently have?**

- ☐ Public insurance (e.g. Medicare, Medicaid, VA)
- ☐ Private insurance (e.g. Blue Cross Blue Shield, Aetna, Humana)
- ☐ Other (please specify) _____

---

Q62

How often have you had issues getting your opioid prescription for your pain because of any of the following reasons:

- pharmacy did not have the particular opioid in stock
- doctor did not prescribe an opioid for your pain
- your insurance would not cover it
- you had to pay a high copay (more than $50) for your opioid prescription

- ○ Always
- ○ Often
- ○ Sometimes
- ○ Rarely
- ○ Never

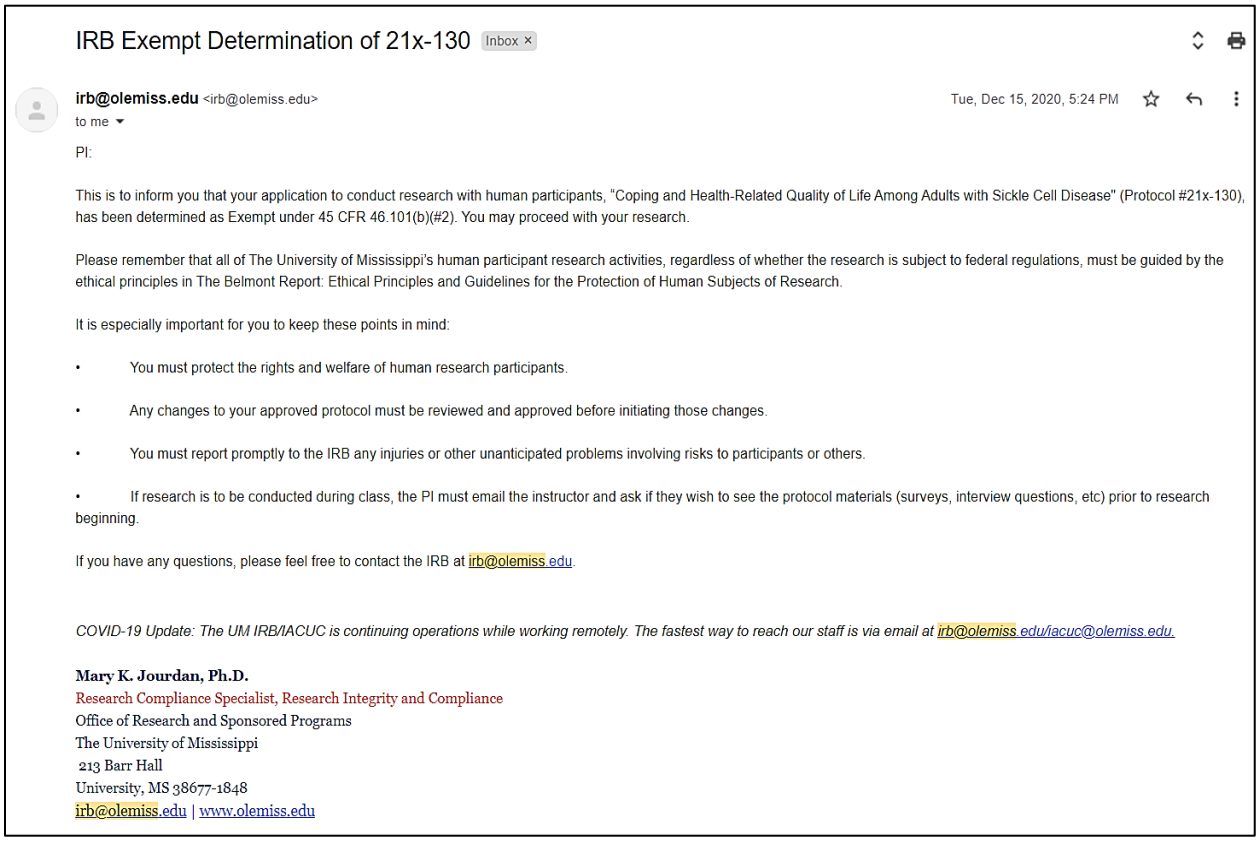
---

Q28 **Please complete the following sentence: As a result of the COVID-19 pandemic, my quality of life has _____ .**

- ○ Worsened
- ○ Remained the same
- ○ Improved

**End of Block: Section I Part A: Demographics**

# APPENDIX C: IRB APPROVAL



IRB Exempt Determination of 21x-130 Inbox ×

**irb@olemiss.edu** <irb@olemiss.edu> Tue, Dec 15, 2020, 5:24 PM

to me

PI:

This is to inform you that your application to conduct research with human participants, "Coping and Health-Related Quality of Life Among Adults with Sickle Cell Disease" (Protocol #21x-130), has been determined as Exempt under 45 CFR 46.101(b)(#2). You may proceed with your research.

Please remember that all of The University of Mississippi's human participant research activities, regardless of whether the research is subject to federal regulations, must be guided by the ethical principles in The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research.

It is especially important for you to keep these points in mind:

- You must protect the rights and welfare of human research participants.
- Any changes to your approved protocol must be reviewed and approved before initiating those changes.
- You must report promptly to the IRB any injuries or other unanticipated problems involving risks to participants or others.
- If research is to be conducted during class, the PI must email the instructor and ask if they wish to see the protocol materials (surveys, interview questions, etc) prior to research beginning.

If you have any questions, please feel free to contact the IRB at irb@olemiss.edu.

*COVID-19 Update: The UM IRB/IACUC is continuing operations while working remotely. The fastest way to reach our staff is via email at irb@olemiss.edu/iacuc@olemiss.edu.*

**Mary K. Jourdan, Ph.D.**
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# VITA

## Monika Salkar, MS

### Professional Summary

Monika Salkar is a strategic and independent HEOR professional with research experience in large database analyses, statistical programming, patient reported outcomes, and pharmacoeconomic analyses. She has skill in designing, directing, and conducting independent research in collaboration with academic partners across several disease areas including hematology, dermatology, inflammatory and metabolic diseases. Monika is experienced in disseminating HEOR evidence through a variety of avenues such as presentations, posters, and manuscripts. In addition, she has excellent communication skills, is very detail oriented, and can convey complex topics in a succinct manner.

### Education

- **PhD Candidate:** Department of Pharmacy Administration, University of Mississippi — Aug 2017-Nov 2021
  - **Major:** Health Economics and Outcomes Research
  - **Minor:** Applied Biostatistics
- **MS**, Health Outcomes and Socioeconomic Sciences, University of Toledo — Aug 2015-May 2017
- **BS**, Pharmacy, Bombay College of Pharmacy, India — June 2011-May 2015

### Relevant Coursework

Biostatistics | Patient Reported Outcomes and Psychometrics| Secondary Data Techniques| Pharmacoepidemiology |Theoretical Foundations in Marketing | Marketing Systems | Pharmacy & Healthcare Administration | Pharmacoeconomics & Outcomes Research | Research Methods in Pharmacy Practice | Public Health Epidemiology

### Work Experience

- Summer Internship, AbbVie — Jun 2020-Aug 2020
  - Developed and executed study protocol for retrospective claims analyses (Optum Clinformatics, Truven MarketScan) using Instant Health Data (IHD) platform to examine treatment switch patterns in psoriasis patients

- Partnered with PRO team to understand and explore the PRO/ClinRO's landscape in follicular lymphoma through clinical trials, approved label claims and published literature
- Successfully defended study protocol in the protocol review committee meeting
- Collaborated cross-functionally and with internal biostatistician to execute HEOR study
- Presented HEOR study to cross-functional partners, TA lead, KOLs and HEOR colleagues
- Explored and summarized literature using PubMed, EBSCO, Medline, and Cochrane to examine the psoriasis treatment patterns
- Engaged in discussions with vendors and provided input on a prospective patient reported outcomes study in psoriasis

▪ Summer Internship, GlaxoSmithKline (GSK) Jun 2018-Aug 2018
- Assisted in study protocol development and retrospective claims analyses (Truven MarketScan) using IHD platform and SAS software to determine healthcare utilization and expenditure for patients with sickle cell disease resulting in 1 poster presentation
- Reviewed and summarized literature using PubMed, EBSCO, Medline, and Cochrane to determine the patient reported outcome instruments for sickle cell disease population
- Collaborated with internal VEO team and external vendors to drive projects under supervision

▪ Summer Internship, Scientific Pharmacy, India May 2015-July 2015
- Transformed and managed experimental data utilizing Excel. Responsible for verifying and interpreting client reports to better understand the quality and level of care delivered

**Academic Experience**

**Graduate Research Assistant**, University of Mississippi Aug 2017-May 2021

▪ Dissertation
- Evaluating Patient Reported Outcomes in Adults with Sickle Cell Disease

▪ Primary data analyst for R15 NIH grant project to study the safety of long-term opioid use among older adults with chronic non-cancer pain using 5% National Medicare Data
▪ Collaborated with a team of 6 researchers in conducting a scoping review on interventions focusing on diabetes prevention
▪ Collaborated with a team of 2 researchers in determining the association of polypharmacy and health-related quality of life (HRQOL) among elderly cancer patients using Medical Expenditure Panel Survey Data (MEPS)
▪ Built a decision tree model to assess cost-effectiveness of Venlafaxine versus Duloxetine for Painful Diabetic Neuropathy using TreeAge software

**Graduate Teaching Assistant,** University of Mississippi Aug 2017-May 2018

- Assisted 4 faculties in preparing class syllabus, exams, quizzes, and grading for a class of 100 PharmD students
- Conducted doubt solving sessions for PharmD students on topics related to research methods

**Graduate Research Assistant**, University of Toledo Aug 2016-May 2017

Assisted a team of 3 researchers in conducting a cost-effectiveness study of Pregabalin and Venlafaxine for Painful Diabetic Neuropathy

- Systematically reviewed literature using PubMed, EBSCO, Medline, and Cochrane to acquire information related to varied Hepatitis C treatment options leading to 1 poster presentation
- Consistently led a team of 4 researchers in assessing and analyzing CORRONA registry data, culminating in determination of cost-effectiveness of Tofactinib prescribed for Rheumatoid Arthritis

**Graduate Teaching Assistant,** University of Toledo Aug 2015-May 2016

- Lectured on different US health care settings to a class of 100 Pharm D students
- Mentored and taught a group of 6 students on conducting systematic reviews, using statistical software's such as SAS, R, SPSS, various research topics (e.g. Medication Therapy Management, Pharmacoeconomics)
- Liaised with faculties in preparing and grading 20 exams and 50 assignments and rendering Blackboard technical support

**Software Skills**

- Statistical Software: SAS, R, SPSS, TreeAge, Instant Health Data (IHD)
- Other software: MS Office, Endnote, Zotero

**Publications**

- **Salkar**, M., Rosenthal, M., Thakur, T., & Arnold, A. (2019). Patient Centered Studies Focusing on Diabetes Self-Management: A Scoping Review. *Current Diabetes Reviews*.
- **Salkar**, M., Gangan, N., & Yang, Y. (2020). Association Between Work Absence and Health Services Utilization and Costs Among Employed Individuals with Arthritis. *Journal of Occupational and Environmental Medicine*, 62(6), e240-e244.
- Ramachandran S, **Salkar M**, Bentley JP, Eriator I, Yang Y. Pattern of use and geographic variation in long-term prescription opioid use among older adults in the United States: A study of Medicare administrative claims data [in press]. *Pain Physician*.
- **Salkar M**, Ramachandran S, Bentley P, Eriator I, McGwin G, Twyner C, Yang Y. Do Formulation and Dose of Long-term Opioid Therapy Contribute to the Risk of Adverse Events Among Older Adults with Chronic Pain? (under review in *Journal of General Internal Medicine*)
- Prevalence of long-term opioid use in older adults with chronic non-cancer pain: A systematic review (manuscript under works)
- Gender disparity in childhood immunizations in India (under review in Indian Journal of Public Health)

**Poster Presentations**

- **Salkar M,** Ramachandran S, Bentley JP, Eriator I, Yang Y. Pattern of use and geographic variation in long-term prescription opioid use among older adults in the United States: A study of Medicare administrative claims data. International Society for Pharmacoeconomics and Outcomes Research (ISPOR) 25th Virtual Annual Conference; 2020 May 18- 20.
- **Salkar M**, Thakur T, Arnold A, Rosenthal M. Patient Centered Interventions Focusing on Diabetes Self-Management: A Scoping Review. American Pharmacists Association (APhA) Annual Meeting & Exposition; 2019 March 22-25, Seattle, WA
- Ray M, Shen Q, **Salkar M**, Pokras S. All-Cause Healthcare Resource Utilization and Costs Among Us Adult Sickle Cell Patients. International Society for Pharmacoeconomics and Outcomes Research (ISPOR) 24th Annual Conference; 2019 May 18- 22, New Orleans, LA
- **Salkar M**, Gangan N, Yang Y. The Effect of Work Absences on Health Services Utilization and Costs Among Employed Individuals with Rheumatoid Arthritis. International Society for Pharmacoeconomics and Outcomes Research (ISPOR) 24th Annual Conference; 2019 May 18- 22, New Orleans, LA
- **Salkar M**, Banahan III B, Noble S. Racial Disparity in the Use of First-Line Psychosocial Care for Children and Adolescents Initiating Therapy on Antipsychotics. International Society for Pharmacoeconomics and Outcomes Research (ISPOR) 23rd Annual Conference; 2018 May 19- 23, Baltimore, MD
- **Salkar M**, Zhang Y, Ramachandran S. Is Medication Adherence A Mediator of the Relationship Between Race/Ethnicity and Healthcare Cost in Patients with Rheumatoid Arthritis. International Society for Pharmacoeconomics and Outcomes Research (ISPOR) 23rd Annual Conference; 2018 May 19- 23, Baltimore, MD
- **Salkar M**, Sah J, Pinto S, Vaidya V. Patient-Related Barriers to Medication Adherence in Type 2 Diabetic Patients: A Systematic Review. International Society for Pharmacoeconomics and Outcomes Research (ISPOR) 21st Annual Conference; 2016 May 21- 25, Washington DC
- Le D, Osundina F, **Salkar M**, et al. Determining patient preferences of community pharmacy attributes: a systematic review. American Pharmacists Association (APhA) Annual Meeting & Exposition; 2016 March 4-7, Baltimore, MD
- Le D, **Salkar M**, Vaidya V, et al. Inflammatory bowel disease: impact of cost-sharing on health resource utilization and medication adherence. 17th Midwest Social and Administrative Conference; 2016 Aug 9-12, Ann Arbor, MI
- Bhattacharya DS, **Salkar M**, Majumdar A. Encumbrance to the Treatment of Osteoporosis: Physicians and Patient Perception. International Society for Pharmacoeconomics and Outcomes Research (ISPOR) 6th Asia Pacific Conference; Sept 6-9, 2016; Beijing, China

**Leadership Experience**

- President of University of Mississippi International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Student Chapter 2019-2020

- Vice-President of University of Mississippi ISPOR Student Chapter 2018-2019
- Senator of Graduate Student Council (GSC) University of Mississippi 2018-2020
- Member of ISPOR Meeting Planning Committee 2019-2020
- Member of Rho Chi, the Academic Honor Society in Pharmacy 2018-2020Secretary of University of Toledo International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Student Chapter 2016-2017

**Grants and Awards**

- Graduate Student Research Grant (2020)
- Terrence Downer Scholarship (2020)
- ISPOR Travel Grant (2019)
- Graduate School Conference Travel Grant (2019)