**PROTOCOL TITLE:**

**South Carolina Sickle Cell Disease Access to Care Pilot Program (SC)2: Data Collection Protocol***.*

**PRINCIPAL INVESTIGATOR:**

**Shannon Phillips, PhD, RN**

Objectives / Specific Aims

Aim 1: Longitudinal biologic data collection including demographics, radiologic assessments, anthropomorphic and laboratory values to improve the understanding of sickle cell disease and the relationship of the environment on patient health and well-being.

Aim 2: Acute care information and prescription refill history will be collected in order to improve individual patients’ disease management and provide population health information for patients with sickle cell disease in South Carolina. This data will also be utilized for quality assessment of the (SC)² program and for quality improvement activities.

Aim 3: We will collect patient reported outcomes including previously validated pain reporting and quality of life tools to ensure patient satisfaction and input in the (SC)² program.

Aim 4: Utilize the ECHO model (explained below\*) to improve the quality and quantity of knowledge of providers in providing care for individuals with sickle cell disease.

Aim 5: Each patient will receive a customized individual care plan including pain medication plan available to all treating providers to enhance patient-specific treatment.

\*ECHO is a lifelong learning and guided practice model that revolutionizes medical education and exponentially increases workforce capacity to provide best-practice specialty care and reduce health disparities. The heart of the ECHO model™ is its hub-and-spoke knowledge-sharing networks, led by expert teams who use multi-point videoconferencing to conduct virtual clinics with community providers. In this way, primary care doctors, nurses, and other clinicians learn to provide excellent specialty care to patients in their own communities.

Long term objectives/goals:

* **Enhanced access to disease modifying medication:**  Hydroxyurea (HU) is currently the only FDA-approved disease-modifying drug for SCD. Appropriate use of HU results in decreased hospital utilization, cost savings, and reduced mortality. Currently, despite improvements on hospital admissions, quality of life, and overall reduction in pain, only 10% of eligible patients are currently

prescribed HU. Thus, with enhanced education and care transformation, there will be significant improvement in HU utilization. Recent data demonstrates that we can expect an annual decrease in cost of $6,000/patient who takes the medication.

* **Improving transfusion utilization:** Stroke is one of the biggest complications of SCD. Blood transfusions are indicated for stroke prevention in those at-risk with SCD or for acute treatment of severe organ dysfunction, or symptomatic acute anemia. Transfusion therapy remains a cost effective method of stroke prevention in identified “at-risk” persons with SCD. However, providers without SCD training/knowledge often transfuse affected individuals for treatment of uncomplicated pain. This practice contributes to complications and unnecessary expense. Through disease specific educational conferences, we can increase the understanding of the disease and reduce the unnecessary procedure, saving up to $500 per event and decreasing the risk of unnecessary blood transfusions.
* **Increased evidence based screening and preventative care:**  The NHLBI guidelines clearly state the importance of screening of persons with SCD for end organ damage. This project will link affected patients with both a SCD provider and a primary care provider to help insure appropriate assessments are completed (e.g. eye exams). Additionally, the (SC)² program manager will provide statewide patient navigation to assist in directing patients to screening and ensuring follow-up.
* **Acute care utilization:**  Through increased access to disease-specific care, the (SC)² program will decrease the rate of unnecessary acute care utilization (including emergency room and hospital admission visits). While some of these visits are unavoidable, research has shown that SCD-specific care can greatly decrease the number of these encounters.

# Background

Sickle Cell Disease (SCD) is the most common inherited blood disorder in the United States. Despite improvements in childhood care, it remains a life-limiting disease with multi-organ complications that reduces the quality of life. The majority of affected patients in the United States are of African descent and the question of race has been linked with SCD since its recognition. According to the Center for Disease Control, health disparities between African Americans and other populations are apparent in life expectancy, death rates, and other measures of health status. It is clear that the severity of SCD make the impact of these health disparities both more pronounced and more disparate. Added to these concerns are

a significant lack of medical knowledge about SCD and a paucity of providers trained to treat affected adults. The majority of primary care and emergency department physicians have not received education in

SCD management. Thus, primary care providers are often uncomfortable with SCD patients and many patients in South Carolina do not have access to academic medical centers where disease specific care is available. Thus, adult patients are highly underserved and are forced to rely on urgent care treatment, which is not disease or patient-focused.

The current geographic, socioeconomic and disease-specific barriers are resulting in poor quality, high cost-high utilization of the affected population and subsequent increase in mortality in young adulthood. The South Carolina Sickle Cell Disease Access to Care Pilot Program (SC)² will increase access to both primary and specialty care for all persons with SCD in South Carolina through a hub and spokes care delivery and education model using a collective impact approach. This approach will harness the

resources of the state to approach SCD and also use a technologic based approach to increase education of providers.

# Utilizing the “Extension for Community Healthcare Outcomes” (ECHO) model, the South Carolina Sickle Cell Disease Access to Care initiative will work to deliver specialty medical care to this specific underserved population though education and an interdisciplinary team-based outreach approach. The goal will be to both enhance access to care for affected individuals and help local providers to develop knowledge and self-efficacy in treating and managing Sickle Cell Disease.

# Inclusion and Exclusion Criteria/ Study Population

* + Potential subjects will be identified either from patients already seen at MUSC or who are referred to MUSC Pediatric Hematology/Oncology for treatment of sickle cell disease.
  + Patients included will be those of all ages with a diagnosis of sickle cell disease. No patients will be excluded due to co-morbidities. Only patients unable to consent who do not have a designated care-giver will be excluded.
  + The majority of individuals living with sickle cell disease in South Carolina are African-American with limited exceptions which are why the targeted enrollment is almost entirely black/African-American. Children (<12 years of age) will be included since they also have sickle cell disease (parental consent will be required for children <18 with assent from the patients >12 years of age.

# Number of Subjects

The anticipated number of subjects to be enrolled locally is 1500. The anticipated number of subjects to be enrolled at all sites is 3000.

# Setting

All study visits will take place either in single patient rooms in the clinic or inpatient unit. Only essential personnel will take part in the visits. The principle investigator will conduct this study at these collaborating sites as part of the protocol:

Tidelands Health

Beaufort Memorial Hospital

Palmetto Health\*

\*Dr. Carla Roberts will join the study team as a sub-investigator of (SC)2 and will consent patients to join the statewide network at Palmetto Health to encourage enhanced continuation of care.

# Recruitment Methods

Potential subjects will be identified either from patients already seen at MUSC or who are referred to MUSC Pediatric Hematology/Oncology for treatment of sickle cell disease. All patients with sickle cell disease in South Carolina will have access to the (SC)² network. Patients can be referred to centers associated with the network by primary care providers, SCD foundations (who see and council individual patients with sickle cell disease), emergency rooms or other care providers including insurance companies. All patients referred to (SC)² network will be invited to participate in the data collection protocol for quality improvement. If patients opt out of the data collection protocol, they can still continue their care (standard of care) through the (SC)² network.

A tri-fold brochure designed for patients and physicians will be made available to the public via printed copy and on the (SC)² website. The brochure will contain information about the (SC)² network, clinical partners, and clinical care provided.

The (SC)² website was created and is maintained by the Digital Team Program at the Medical University of South Carolina specifically for the South Carolina Sickle Cell Disease Access to Care Pilot Program. The website will offer information about the (SC)² network, clinical partners, and clinical care provided.

# Consent Process

Upon determination that a patient might be eligible for this data collection protocol, the subject and parents or legal guardian will be approached by the PI or co-investigators with information about the pilot program.

While in a clinic or the inpatient unit, a copy of the consent form will be given to the parents/legal guardian to read and it will be reviewed with them by the consenting investigator. Information will be presented in developmentally appropriate language.

This information will include purpose of the research, study requirements, length of participation, subject rights, and safeguards of protected health information. Opportunities for questions will be provided. Once the parents/legal guardians indicate understanding of the research study and consent form, signatures will

be obtained on the consent document. Children capable of providing assent will be asked if they understand the information prior to obtaining signature for assent.

Copies of the signed, original consent form will be made. One copy will be given to the subject/family. The original consent is maintained in the research record.

All staff has been trained in research methods and protection of human subjects.

# Study Design / Methods

All treatment will be provided to each patient per standard of care for sickle cell disease. The only risk of the associated investigation is the data collection and risk of loss of confidentiality.

To prevent this risk, all data will be stored on MUSC servers in password protected documents. All statistical evaluations will be performed on de-identified data. Patients will consent to the acquisition of

data for statistical assessment and for permission to share individualized treatment protocols with outside providers for continuity of care.

The patient will be asked to provide permission to have the following information sent from their treating facilities to the South Carolina Sickle Cell Disease Access to Care Pilot Program (SC)² database:

* Patient name
* Patient birth date
* Patient postal/zip code
* Type and characteristics of SCD
* Patient race and ethnicity
* Patient medication and refill history
* Patient past history of hospital visits
* Patient transfusion history
* Patient future medication and refills
* Patient future hospital visits

The patient will be asked to fill out surveys annually about their treatment, their clinic experience, their pain, and quality of life to help us improve the program.

The patient will be asked if they are willing to be contacted in the future to consider participating in sickle cell research studies that may involve them. They will only be contacted by the study team after research studies have undergone scientific review and were found to be important.

**(SC)2 Optional Bio-Repository**

The patients will be asked if they are willing to participate in an optional Bio-Repository.

Several blood-based biomarkers have been used to reflect the individual organ and systemic dysfunction in SCD including measures of inflammation, coagulation, oxidative stress, apoptosis, hemolysis, and endothelial function. Additional evaluation of genomic and proteomic predictors of outcomes will help better define phenotypes in sickle cell disease. Evaluation of the underlying pathophysiological processes relevant to vaso-occlusive crisis (inflammation and coagulopathy) will be done in patients with frequent vaso-occlusive events using biomarkers that have been shown to correlate to risk for vaso-occlusive events in SCD.

There is no maximal amount of time in which samples can be stored but individuals consenting for the biorepository can opt for withdrawal at any time.

All samples will be drawn during a routine blood draw so that no additional needle stick is requited. The actual dates and times of the blood collections will be recorded in the source and in the (SC)2 database.

Biorepository will include:

• Proteomics

• RNA assay

• Genomics

• Inflammatory markers

• Red cell aggregation

• Coagulation markers

• Whole blood viscosity

# Data Management

To measure the success of the (SC)² program and utilize a collective impact approach it is necessary to identify and use mutually agreeable outcome measures that support both the affected individuals (patients), local providers, and health care systems. Due in part to the recent publication of the NHLBI

SCD guidelines, there are specific goals that SCD stakeholders have agreed to. These are listed below. To assess the data, (SC)² will partner with the Care Coordination Institute (CCI). The CCI is a non-profit organization that is committed to partnering with physicians, hospitals and other healthcare providers to transform the health of communities. CCI utilizes complex data analysis to provide monthly reports that indicate how their outcomes compare to other providers who are treating patients with the same diagnoses. CCI can assess frequency of patient visits, use of specific medication, transfusion utilization,

and screening tests. They are recognized for their ability to produce data to support meaningful use and patient-centered medical homes. These data intend to demonstrate the success of (SC)² as well as the cost improvements for affiliated managed care organizations.

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| **Goal** | **Projected Results over 3 years** | **How will efforts be incorporated & support sustainability of (SC)²** |
| Increase in Hydroxyurea utilization in SCD | Increase Hydroxyurea prescribing by 50% with 80% adherence | Increased numbers of patients taking HU will decrease hospital utilization and SCD complications |
| Reduction in UNNECESSARY transfusion utilization | Decrease in unnecessary utilization by 60% | Decreased unnecessary transfusions will decrease expenses as well as transfusion‐related complications |
| Improvement in NECESSARY transfusion therapy | Increase in necessary transfusion therapy in patients with neurologic risk by 30% | Improved transfusion therapy in at-risk patients for stroke prevention |
| Comprehensive care | Increase number of patients who see both a specialist and PCP by 50% (CCI data) | Improved comprehensive care will decrease avoidable utilization to increase patient engagement |
| Decrease overall number of hospital days per patient | Patients with > 3 hospital visits per year will have a 50% decrease in days hospitalized | Improved cost of care and enhanced repayment |
| **Secondary Goals:** | | |
| Quality of Life Assessment  \*The Adult Sickle Cell Quality of Life Measurement Information System (ASCQ-Me) | 60% of patients will demonstrate a quantitative improvement in quality of life using standardized measure | A measure of physical, social and environmental quality of life specific to SCD which will lead to improved patient-environment interaction |
| Pain burden assessment | 60% of patients will demonstrate a quantitative improvement in pain burden | Improved pain burden will lead to decreased unnecessary utilization and decreased per patient cost |
| Individualized pain medication treatment plans | 75% of patients will have individualized care plans in place by year 3 | Individualized pain regimens will decrease admissions and repeat ER visits by affected patients |

All results will be assessed using appropriate statistical technique (logistic regression, 2 sided t-test) and descriptive analysis based on the individual data element to be measured.

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# Risks to Subjects

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assessment and for permission to share individualized treatment protocols with outside providers for continuity of care.

There are no associated biomedical or behavioral research interventions.

There is no “clinical trial” in this protocol. Subjects will not receive any novel biomedical or behavioral intervention.

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# Potential Benefits to Subjects or Others

This research study is not expected to directly benefit individual subjects, but is likely to yield generalizable knowledge which contributes to the field.

Individuals who opt to enroll in the data collection protocol for (SC)² network may benefit from additional quality assessment of their individual care and specific quality improvement activities related to their care. It is hoped that individuals with SCD in South Carolina as a whole will benefit from improvement in care accessibility and delivery due to the network.

Currently, many articles have cited the need for improved care delivery and care coordination for individuals living with sickle cell disease. However, there have been no attempts on using a statewide network to improve care for individuals. This project has the potential to dramatically improve care delivery for individuals with SCD in South Carolina and the ability to be replicated in other states to enhance care delivery and access to care.

# References

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