PROTOCOL TITLE: SMYLS: A Self-Management Program for Youth Living with Sickle Cell Disease

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1.0 Objectives / Specific Aims

Primary Aims:
Aim 1: *Assess feasibility of implementation processes among adolescents/caregivers, young adults, and providers including reach, enrollment, fidelity, adoption, acceptability, and satisfaction using the RE-AIM framework.*
Aim 2: *Monitor health care activities that occur via adolescent/caregiver- or young adult-provider health communication and explore relationships between health care activities, such as provider screening, supporting, informing, and referring, and adolescent self-management behaviors, such as monitoring and tracking symptoms, attending clinic appointments, and administering home medications and treatments, and symptom outcomes.*
Secondary Aim: *Obtain estimates of variability for measures of transition readiness, physical and psychological symptoms, healthcare utilization, and quality of life among adolescents, caregivers, and young adults.*

2.0 Background

Risk of comorbidities and early death increase as adolescents with SCD transition to adulthood.
Approximately 100,000 individuals in the US have SCD, a hereditary hemoglobinopathy characterized by an altering in the shape of red blood cells. Over 90% of these individuals are African American (1). One of the most immediate, complex, and bothersome symptoms of SCD is pain, but long-term complications can occur in nearly every body system (2-4). Pain and other symptoms of SCD such as fever, fatigue and sleep disturbance begin in childhood, contributing to poorer physical, psychological, and social well-being than children in general. As children with SCD become older and develop disease-related complications including end-organ damage and stroke, quality of life continues to decline (5, 6). Early mortality was expected for children with SCD, but survival rates for individuals with SCD have improved remarkably in the past few decades; nearly all children with SCD now survive into adulthood. Despite this success, during the period of transition from adolescence to adulthood, increases occur in rates of complications, risk of death and symptom burden (7-9).
The prevention of complications and reduction of bothersome symptoms is challenging because adolescents with SCD face unique barriers to successful transition from pediatric to adult care. Early, ongoing care delivered by a multidisciplinary team that includes the adolescent and parent/caregiver is necessary to prevent or minimize SCD complications (2, 4). Unfortunately, adolescents with SCD have difficulty accessing and maintaining adult-based SCD healthcare. Transition from pediatric to adult care is challenging for all populations of children with chronic conditions; however, studies show adolescents with SCD also have higher rates of public health insurance, greater risk of stroke (which may negatively impact cognition), excessive symptom burden, and higher risk of comorbid disease, all of which can further complicate transition from pediatric to adult care (10). An essential barrier to receiving ongoing care is access to adult providers, which includes difficulty with navigating the health care system, transportation barriers, and lack of adult SCD providers (11, 12). As a consequence of barriers to obtaining adult-based SCD care, many young adults with SCD lack primary and preventive care, and they have the highest rates of hospitalization, ED visits, and rehospitalization, and are more likely to visit multiple EDs (13, 14). Early self-management becomes important to promote transition readiness and improve symptoms outcomes. Interventions that enhance reach, such as those delivered via smartphones (mHealth), are essential for development of self-management behaviors in the out-of-clinic setting.
Effective self-management and support from providers is critical to promoting transition readiness, managing symptoms, minimizing long-term complications,

and reducing ED visits and hospitalizations. Given the complex nature of SCD and the fact that pain management frequently begins at home, effective self-management strategies to promote transition readiness are critical in this population. Transition is a dynamic process that includes transition readiness, or the decisions and actions of the adolescent, family, and healthcare providers to prepare for and complete transition (15). Self-management is a critical component of transition and transition readiness, since transition not only includes moving from pediatric to adult-centered healthcare, but also includes day-to-day health management (15, 16). Parents of adolescents with SCD are often involved in all of the adolescent's healthcare activities, particularly among younger adolescents (17). Approaches guided by Modi et al.'s (18) framework for developing self-management behaviors, which include taking medications, self-monitoring symptoms, and attending clinic appointments through processes such as seeking disease information have excellent potential to positively impact self-management behavior development, adherence, and symptom and utilization outcomes. Approaches should include communication with the medical team that involves the adolescent, family, and healthcare provider, all of whom are essential members of the transition process (10). Specifically, adolescents need avenues for communicating with providers to establish themselves as partners in care decisions, and to facilitate development of self-efficacy and self-advocacy, which can contribute to improved self-management and health outcomes (19-21).

Interventions that facilitate development of effective self-management behaviors in adolescents with SCD are critically needed and should incorporate elements to support transition from parent-managed to self-managed care. Transitioning from adolescence to adulthood is a developmental milestone that includes negotiating with parents/caregivers and gaining independence. This transition is particularly complicated for adolescents with chronic conditions who are also required learn to manage complex health needs. In fact, adolescents with SCD have been found to have low levels of transition readiness (22), and adolescents with SCD and their parents/caregivers perceive particular challenges to transitioning care from parent-managed to adolescent self-managed. Adolescents with SCD reported challenges with mastery of self-management and complex symptoms, communicating symptoms, and maintaining control of self-care (23). Among the needs reported by adolescents are tailored self-management support, and mechanisms to visualize self-management progress (24). Further, adolescents with SCD perceived that responsibility for medication, attending appointments, communicating with medical staff were among the behaviors most important for assuming responsibility of their own care and transferring from pediatric to adult providers (17). Parent-reported challenges include surrendering care to the adolescent, communicating management of care with the adolescent, and finding balance between protecting the adolescent and promoting independence (23). This K23 research plan is based on the **scientific premise** that facilitating self-management behaviors will improve symptom outcomes, quality of life, and utilization outcomes, and improve transition readiness and successful transition from parent-managed to adolescent self-managed care. Findings from this study have potential for translation to other populations of adolescents with chronic conditions transitioning to adulthood.

3.0 Intervention to be studied

The web-based SMYLS app consists of three major components: patient-centered educational materials; symptom monitoring and tracking; and young adult (YA) and A/CG-provider communication. Educational materials on SCD pathophysiology, home management strategies, and symptom prevention are derived from patient-facing, guideline-based information endorsed by authoritative sources. Educational materials have been translated to an app-friendly format and are subdivided by age (up to 12 years, 12 – 17 years, adult), role (parent), or "hot" topics (hydroxyurea, research participation, hematopoietic stem cell transplantation). For symptom monitoring, pain is the predominant symptom YA and A/CG track via the app. YA and A/CG record pain scores and location via an avatar, then proceed through a series of screens to record

additional information pertaining to the pain, and additional symptoms that may co-occur. A graph is available by which YA and A/CG can observe trends in recorded pain, including specifics such as the numeric pain rating, the site of the pain, description of the pain, and actions taken to relieve pain. YA-provider or A/CG-provider communication is facilitated by a health history page intended for YA or A/CG to complete with their provider. In addition to this static option, the app also includes a link that takes the user to MyChart to complete a message to the provider via the EHR portal. Ideally, YA or A/CG will use the app daily to record and track symptoms, and as needed to access educational materials and message providers, and providers will communicate via messaging with YA or A/CG. However, a primary aim of this study is to assess participant engagement with the app. User activity and records are recorded in a secure database housed at TACHL for analysis.

4.0 Study Endpoints

We will obtain outcomes data on feasibility, self-management behaviors, and healthcare activities (primary aim), and transition readiness, symptoms, quality of life, and healthcare utilization (secondary aim).

5.0 Inclusion and Exclusion Criteria/ Study Population

The participants in this project will be young adults (YA) with sickle cell disease (SCD), adolescents (A) with SCD, their primary caregivers (CG), and healthcare providers. All participants will be recruited through the Medical University of South Carolina (MUSC) Pediatric Sickle Cell Clinic.

Young adult, adolescent and caregiver participants will be identified by healthcare providers at the MUSC Pediatric Sickle Cell Clinic. The PI will communicate the inclusion and exclusion criteria with the providers and will ask them to preliminarily identify potentially eligible participants. Providers involved with the prospective participants' clinical care will first inform them about the research study. Once the potential participants agree to speak with IRB-approved study personnel (to the provider), the study personnel will approach the potential participants and conduct eligibility screening by which participants will confirm by self-report or parent/caregiver report whether eligibility criteria are met.

After healthcare providers volunteer interest in participation, IRB-approved study personnel will determine eligibility by provider self-report of meeting criteria.

Inclusion Criteria:

- Young Adults:
  - Age 18 – 25 years
  - Diagnosis of sickle cell disease, as reported by clinician at the MUSC Lifespan Sickle Cell Clinic
  - Self-reported history of pain (acute or chronic) at least once per month
  - Owns a smartphone
- Adolescents:
  - Age 11 - 17 years
  - Diagnosis of sickle cell disease, as reported by clinician at the MUSC Lifespan Sickle Cell Clinic

- Self-reported history of pain (acute or chronic) at least once per month
- Caregiver willingness to participate
- Owns a smartphone

- Caregivers:
  - The parent or primary caregiver of the adolescent
  - Owns a smartphone
- Healthcare Providers
  - At least 6 months' experience caring for individuals with SCD
  - Provides healthcare for adolescents with SCD

Exclusion Criteria:

- Adolescent or young adult not under the care of a provider participant
- Cognitive disability or delay that precludes ability to participate
  - Defined as: classified severe neurocognitive deficits as documented by neuropsychological evaluation in the medical record
- Lack of Wi-Fi access

Inclusion of Children
Individuals included in the proposed study will include adolescents ages 11- 17 years, adult caregivers of the adolescent participants, and adult healthcare providers. A key purpose of the study is to determine the feasibility of an intervention designed to aid transition from parent/caregiver-managed to adolescent self-managed care. Therefore, adolescents with SCD and without cognitive delay that precludes ability to participate ages between the ages of 11-17 years will be included in the study.

6.0 Number of Subjects

A total of 30 A/CG dyads (60 individuals), 15 young adults, and up to 5 healthcare provider participants will be consented into this study.

7.0 Setting

We will recruit 30 adolescents ages 11 – 17 and the parent/primary caregiver to participate as an A/CG dyad (n = 60) and 15 young adults ages 18 – 25 (total n = 75) from the MUSC Pediatric Sickle Cell Clinic, which serves over 500 children with SCD, approximately 150 of whom are adolescents ages 11 – 17 years. The Pediatric Sickle Cell Clinic continues to care for young adults with SCD up to 25 years of age prior to transitioning to an adult provider. Healthcare providers will also be recruited from the MUSC Pediatric Sickle Cell Clinic. However, as the purpose of the study is to test the feasibility of an intervention for improving self-management, young adult and adolescent/caregiver participants will use the interventions in their homes or in the settings of their everyday life.

8.0 Recruitment Methods

Our first method for recruiting young adults and children/adolescents and caregivers will be to identify participants who have indicated they would like to be contacted for future research opportunities on the informed consent documents of our prior studies. We will

contact these individuals by phone to ask if they are interested in participating. If yes, we will proceed with eligibility screening.

Our second method for recruiting young adults and children/adolescents and caregivers will be facilitated by providers at the MUSC Pediatric Sickle Cell Clinic. Providers will be given the inclusion and exclusion criteria to preliminarily assess potential participants for eligibility. The MUSC Pediatric Sickle Cell clinic has an embedded psychologist who conducts developmental screening, developmental evaluations, and neuropsychological evaluations on all patients from birth to 21 years. Therefore, the preliminary assessment will include providers checking the medical record for classification of severe neurocognitive defects. Treating providers will approach potential participants by phone or during clinic visits to determine interest in the study, and with permission, study personnel will then approach potential participants, conduct eligibility screening, obtain informed consent, and enroll interested participants. Study personnel will either approach potential participants in person during the clinic visit, or, providers will obtain permission to share contact information with study personnel for contact by phone after the clinic visit.

Study personnel will present the inclusion and exclusion criteria to healthcare providers in the clinic in person and/or by email. Healthcare providers will be asked to volunteer for the study. After the providers volunteer, study personnel will confirm eligibility, obtain informed consent, and enroll the providers.

In addition to these methods of recruitment, IRB-approved flyers will be posted in public areas at the MUSC Pediatric Sickle Cell Clinic. Study postings on the internet will be viewable through public access such as SCResearch.org. MUSC Pediatric Sickle Cell providers will also be given a handout to share with potentially eligible adolescents/caregivers who enter the healthcare delivery system.

9.0 Consent Process

The informed consent interview will be conducted by the PI or IRB-approved study personnel. For research conducted with adolescents ages 12 – 17 years, consent will be obtained from the caregiver and written assent from the adolescent. Consent will be obtained from caregivers for research conducted with adolescents who are 11 years, consent will be obtained from young adults ages 18 – 25, and consent will be obtained from participating healthcare providers. Informed consent will occur in the comfort and safety of a private clinic room at the MUSC Pediatric Sickle Cell Clinic prior to data collection. Potential participants will be given the informed consent document to read and review, and/or may have it read to them by the researchers if they prefer. After reviewing the Consent document, the healthcare provider, young adult, adolescent, and/or caregiver will be given the opportunity to ask any questions about the study that they may have and will be requested to demonstrate what is expected from them should they enroll in the study through a questioning of their understanding of study procedures and risks. Prior to consenting, all questions will be resolved to the provider, young adult, adolescent, and/or caregiver's satisfaction. If a participant does not appear to understand the information contained within the Consent document, the PI or IRB-approved study personnel will review the consent document again with the participant. If after this second review, the subject does not demonstrate an understanding, they will not be enrolled in the study. Only participants with no classified cognitive impairment will be consented and enrolled into the study, as outlined in the inclusion/exclusion criteria. No wait time is scheduled between informing participants and obtaining consent; however, potential participants will be given the option to consider whether or not they wish to participate for as long as needed prior to providing consent.

As an alternative to in-person consent, if an in-person meeting is inconvenient, not possible, or poses undue burden on the potential participant, the potential participants will be offered the option to provide e-consent via the MUSC e-consent REDCap template. In the case of obtaining e-consent, potential participants will have already spoken with IRB-approved study personnel by phone, will have been introduced to the study and its demands, and had initial questions answered. Young adults, adolescents/caregivers or providers who are further interested will be allowed as much time as needed to read and review the consent document in the privacy of their own home or at a place of their choosing. They will be provided with the telephone and email contact details in the survey instruction header for study personnel, should they have any questions before providing their consent by adding their respective signatures to the form and submitting it. Prior to providing their physical e-consent, IRB-approved study personnel will coordinate with these families and providers so as to be on the telephone and be available to further answer any questions that they may have during the e-consent process. Should a participant have any questions or concerns about the study, study personnel will address these issues to the best of their abilities and knowledge. Upon submitting the e-consent, a REDCap trigger will immediately notify the study personnel, who will then provide their countersignature to the document.

All consented subjects will be given a copy of their executed and countersigned Consent form. If a child participant should reach an age of majority while enrolled in the study, they will be asked to provide written consent.

10.0 Study Design / Methods

This single-group study will assess feasibility to test reach, efficacy, adoption, implementation, and maintenance of SMYLS using the RE-AIM framework (25) (Table 1) with 30 adolescents (A)/caregivers (CG), 15 young adults, and 5 healthcare providers involved with their care. YA and A/CG will be enrolled for a total of 6 months (12-week intervention with 3-month follow-up). Providers will be enrolled for as long as an adolescent under their care is currently enrolled ($\geq$6 months). We will obtain outcomes data on feasibility, self-management behaviors, and healthcare activities (primary aim), and transition readiness, symptoms, quality of life, and healthcare utilization (secondary aim). Measures include patient report via surveys, data recorded via the app, such as symptoms and app use, communication content from MyChart messaging, and in-depth data via key informant interviews.

Table 1 outlines the data to be collected and survey instruments to be administered at each of four data collection points: baseline, 6-weeks (mid intervention), 12-weeks (end of intervention), and 3-months post-intervention. Participants will be given the option of completing surveys in one of three ways: in person in a private room at the MUSC Pediatric Sickle Cell Clinic, by phone, or electronically through a link to REDCap. Estimated time for completion of surveys at each of the 4 visits is approximately 45 minutes. For in-person and phone data collection methods, all data will be recorded in REDCap by the PI or IRB-approved study personnel. Reimbursement to young adult and adolescent/caregiver dyads will be $50 in the form of a gift card presented at each of the 4 data collection points. For A/CG participants, payments will be given to the caregiver; in the case of phone or electronic data collection, participants will be mailed the gift card by certified mail or will receive an electronic gift card via email.

Healthcare providers will complete a demographic survey in person or electronically at baseline. Subsequently, no surveys will be administered to healthcare providers.

Healthcare providers' study activities involve communicating with the young adults and adolescents/caregivers via MyChart.

Data on young adult-provider or dyad-provider communication and healthcare activities will be collected via MyChart messaging. All messages between young adults and providers or dyads and providers will be retrieved as transcripts for analysis. Patients and families at the MUSC Pediatric Sickle Cell clinic do not frequently use MyChart messaging to communicate with providers and instead send text messages. To encourage use of the more secure EHR portal (MyChart) – which has the added benefit of improved provider workflow – participants will be compensated for sending messages via MyChart. Participants will be compensated with $2 for each message with a maximum possible compensation of $20. The number of messages sent will be tallied at the end-of-intervention (12 weeks) and provided in the form of a gift card at that time.

Data on self-management behaviors, including monitoring and tracking symptoms and administering home medications and treatments will be collected via the app and stored in the secure app database. Specifically, we will collect data on the frequency symptoms are recorded (pain, fatigue, fever, etc.) and the frequency of accessing the pain graph component of the app. We will also collect data via the app on medication adherence and recorded treatments for symptoms (drinking water, heating pad, etc.). Data on clinic appointment attendance, ED visits, and details of appointments to assess acceptability of the intervention will be obtained during weekly phone checks. Also during weekly phone checks, adolescent participants will be asked 2 – 3 questions on functioning from the PedsQL Sickle Cell Disease Module and young adult participants will be asked 2 – 3 questions on functioning from the Adult Sickle Cell Quality of Life Measurement Information System (ASCQ-Me).

Post-intervention interviews: Post-intervention interviews will be conducted by phone or in person (according to participant preference) with up to 15 adolescent/caregiver dyads and with up to 15 young adult participants to obtain more in-depth data on accessibility, usability, adherence to the intervention, and to explore how self-management behavior development influenced healthcare decision-making, such as actions taken to prevent pain. Participants who have completed the 12-week intervention period will be asked if they are interested in participating in an interview. We will use a purposeful sampling strategy to identify up to 15 dyads for interviews and will ask all young adult participants if they are interested in participating in an interview. Semi-structured interviews will be conducted using a qualitative descriptive approach, will last approximately 45 – 60 minutes, and will be conducted according to an interview guide with open-ended questions and prompts. The interviews will be audio recorded and transcribed by an outside agency with which MUSC has established a BAA for subsequent review and analysis. Dyads participating in key informant interviews will be compensated with a $50 gift card.

In addition to conducting interviews with young adults and dyads, we will also conduct key informant interviews with up to 5 healthcare providers in person or by phone. Similarly to interviews with young adults and dyads, interviews with providers will be conducted to obtain more in-depth data on accessibility, usability, and adherence to the intervention. Semi-structured interviews will be conducted using a qualitative descriptive approach, will last approximately 45- 60 minutes, and will be conducted according to an interview guide with open-ended questions and prompts. Interviews will be audio recorded and transcribed by an outside agency with which MUSC has established a BAA

for subsequent review and analysis. Providers participating in key informant interviews will be compensated with a $50 gift card.

Table 1: Measurement Framework

*A = adolescents, CG = caregivers, HCP = healthcare providers

	Measures/instruments (number of items; Cronbach's alpha)	**Sources**	**Time points**
Demographic and clinical characteristics	Demographic survey	YA, A/CG report HCP report	Baseline
RE-AIM			
Reach: (primary aim) Sample Recruitment	Electronic log of sample characteristics; recruitment and enrollment activities	Recruitment tracking tools	Ongoing
Efficacy: *Self-management outcomes (primary aim):* Monitoring and tracking symptoms Attending clinic appointments Administering home medications and treatments *Symptoms and health-related outcomes (secondary aim):* Healthcare utilization (A only) Transition Readiness (A only) Pain (A only) Fatigue (A/CG) Depression (A/CG) Anxiety (A/CG) Sleep Interference (A/CG) Self-Efficacy (A/CG) Quality of Life (A/CG)	Pain and other symptom recording; treatments recorded; utilization reports • PROMIS Pain Interference : *Adult/Peds/parent proxy* (8;0.87) (26) • PROMIS Fatigue SF : *Adult* (4; >0.9)(27); *Peds/parent proxy* (10 ; 0.87)(28) • PROMIS Emotional Distress: Depressive Symptoms SF : *Adult* (4; 0.97) (29); *Peds/parent proxy* (8; 0.94)(30) • PROMIS Emotional Distress: Anxiety SF *Adult* (4;0.97) (31); *Peds/parent proxy* (8; 0.83) (26) • PROMIS Self-Efficacy including general, manage daily activities, manage meds/treatment, manage symptoms: *Adult* (16; 0.97) (32) • Sickle Cell Self Efficacy Scale (9) • PROMIS Sleep Disturbance: *Adult* (4; 0.88)(33) • Adolescent Sleep Wake Scale (28; 0.86) (34) • Peds QL with Sickle Cell Disease Module (43; 0.95) (35) • Adult Sickle Cell Quality of Life Measurement Information System (30) • PROMIS Global Health *Adult* (10) • STARx (18; 0.8) (36) • Youth and Parent Sickle Cell Responsibility Scale	YA, A/CG report Web-based application data capture Semi-structured interview Quality checks	Baseline, 6 weeks, 12 weeks, 3-months post intervention Ongoing Weekly
Adoption: (primary aim) Adherence (A/CG, HCP) Acceptability (A/CG, HCP) Education (A/CG) Symptom monitoring and tracking (A/CG) Communication (A/CG, HCP)	App overall use data; app component use data; satisfaction; reported problems; YA, A/CG-provider message content; MAUQ_SPA	Web-based application data capture Semi-structured interview Quality checks	Post intervention Ongoing Weekly
Implementation: (primary aim) Technology (A/CG, HCP) Consistency of intervention (A/CG, HCP)	Reported problems; fidelity to protocol; assistance/instructions required	Quality checks Semi-structured interview	Weekly Post intervention
Maintenance: (primary aim) Projection of future adoption (A/CG, HCP)	Perceptions of intervention; perceptions of feasibility; interest in continuing intervention	Semi-structured interview	Post intervention

Minimizing Research-Associated Risk:

Diligent study safety monitoring will be conducted by the PI, Program Coordinator (PC), and the study's Safety Monitoring Committee (SMC) throughout the conduct of this study in compliance with the following required elements of MUSC IRB's continuing review process:

1. Tracking and follow-up of participant accrual (inc. withdrawn consents) will minimize risk by identifying, disclosing, and mitigating any potentially unknown risk(s) of harm to study participants. These risks are minimal.
2. Timely and appropriate reporting of informed consent process deficiencies, protocol deviations, privacy breaches, conflicts of interest, and/or changes in personnel.
3. Ongoing soliciting, monitoring and appropriate reporting of adverse event activities.
4. Timely and appropriate IRB submission of safety-related documents such as audit reports, sponsor progress reports, SMC reports, and other materials or communications that might impact the safe conduct of this study.
5. Active cooperation with the IRB, ACO, sponsor, and other applicable entities in the event of a random or for-cause internal or external audit.

11.0 Data Management

Sex as a biological variable. We recruit equal numbers of male and female adolescents and preliminarily explore for differences by sex in outcomes, such as acceptability, satisfaction, communication content, symptoms, quality of life, transition readiness, and utilization by conducting preliminary subgroup analyses in preparation for the subsequent larger trial.
Feasibility processes. Variables will include those pertaining to study procedures as well as participant variables. Specifically, 95% confidence intervals for proportions will be used to estimate dichotomous outcomes including the proportion of YA, A/CG who agree to participate out of the number approached, the proportion adherent to the intervention protocol, i.e., providing daily symptom monitoring/tracking, using the education component, responding to messaging, lost to follow up, etc. For the continuous feasibility measures (length of time spent in app components), frequency distributions and the median and mean responses with 95% confidence intervals will be obtained. Benchmarks for feasibility success are recruitment rate of at least 2 YA or A/CG per week, retention rates of 70%, use of at least one component of the app $\geq$ 2 days per week (adherence), and expressed satisfaction in key informant interviews (37).
Outcome measures and estimates of variability. Secondary aim outcomes variables will include measures of symptoms (pain, fatigue, depression, anxiety, sleep interference), quality of life, transition readiness, and utilization (number of appointments kept, number of ED visits). Demographic and clinical variables obtained at baseline will be described via measures of central tendency (mean, median), variability and frequency distributions as appropriate. Additionally, demographic and clinical characteristics for those who adhered to the study protocol versus those who did not adhere (non-adherers and drop outs) will be compared to better describe the study population. For continuous quality of life measures, the difference between pre-and post-intervention measurements will be estimated via 95% confidence intervals. To assess preliminary intervention effects, we will conduct repeated measures ANCOVA with variables in individual models adjusting for "dose" defined as number of times each portion of the app was accessed, total time spent in each portion of the app, number of days symptoms were recorded, and number of A/CG-provider messages.
Content of patient-provider communication. Our methods of analysis are modeled after the work of Goldsmith and colleagues, who created a framework of caregiver communication types from qualitative data, and subsequently used the framework as a coding structure (38, 39). We will analyze the messages between YA and providers and A/CG and providers using directed content analysis (40) and nVivo 11 (41). We will build on the work of Goldsmith (39) and of Jacob et al. (42), who applied an inductive approach to analyze text messages and developed a framework of healthcare activities that occur via text communications. According to Jacob's framework, the two main healthcare categories are collaborating and coaching, and the four subcategories are screening, referring, informing and supporting. Jacob's framework will serve as the initial coding framework for our analysis. Data that do not fit in any of the framework codes will be analyzed separately to identify new, additional codes. We will then conduct frequency

counts to identify the number of YA and A/CG with each type of code and the number and types of codes for each YA and A/CG. Also modeled after the work of Goldsmith and colleagues (38), we will conduct preliminary analyses to explore relationships between number and types of healthcare activities and self-management and symptom outcomes in A/CG.

Key informant interview analyses. Data will be analyzed using content analysis (43) and nVivo 11 (41). Analysis will be conducted in three phases. First, during preparation, the unit of analysis will be selected based on meaning, and may include a word, sentence, phrase, or paragraph. We will also immerse ourselves in the data to make sense of the whole by listening to audio recordings and reading transcripts multiple times. Second, we will organize the data using a deductive approach and the RE-AIM framework as an unconstrained coding matrix. To use an unconstrained matrix, we will apply the principles of inductive analysis to identify categories within the RE-AIM framework (43). Data will be reviewed and coded within the identified categories. Third, results will be described through the meaning of categories and subcategories. Emergent categories and subcategories will provide essential information on overall perceptions of the intervention, satisfaction, acceptability, and anticipated future use.

Integration of adolescent, caregiver, and provider findings. A matrix using the RE-AIM framework will be developed to assimilate results obtained from analysis of app use, surveys, YA-provider and A/CG-provider messages, and key informant interviews and determine convergence and divergence of findings. In addition to determining implementation feasibility, integration of findings will lead to development of a model of healthcare activities occurring via YA – provider and A/CG – provider communication associated with the development of self-management behaviors.

To secure data and maintain confidentiality, the following steps will be taken:

Participant Screening and Enrollment. All data from participants screened for the study will be entered into an electronic REDCap study database. Designated IRB-approved research staff will collect, gather, and enter required data (written informed consent, HIPAA Authorization, and demographics) onto study data forms. Screened patients who do not meet study eligibility will have specific screening data entered into the study database. The collected data will be helpful in examining the patient population and feasibility of enrollment criteria and will include reason for exclusion. All dates will be shifted and other Personal Health Information (PHI) will be removed from the study database upon study completion. All data obtained from this study will be used for research purposes only and will comply with Federal HIPAA regulations. Master Screening and Enrollment Logs will be maintained by the PI or PC and will be used by the PI or PC to prepare reports on accrual and attrition for the SMC.

Case Report Forms. All proposed study specific case report forms (source documents) for data collection will be designed by the PI or PC and, when possible, transferred by the PI or PC into electronic Case Report Forms (eCRFs) for use in the study's REDCap database. These study specific eCRFs source documents (study logs for correspondence, compensation and other forms such as pre-eligibility screens) will be coded by the participant's unique study ID# for all data collected including study instruments and will be maintained in the participant research record. Completed instruments that require signature on a paper CRF will be scanned and uploaded into the study database to all for remote electronic safety monitoring as well as maintained on file in accordance with MUSC policies and applicable Federal Regulations for the Conduct of Human Participant Research.

Binders. The PI or PC will prepare and maintain a participant-specific binder for each participant containing all non-eCRFs records. A regulatory file will also be maintained to include the IRB-approved Protocol, original Informed Consent documents, HIPAA forms and other study-related regulatory documents. All paper research records and CRFs will be maintained in a locked file cabinet, stored in a room for research files that is accessible only via a password protected entry system that features security cameras, within the MUSC College of Nursing. Access to the research

records, study database and PHI's will be restricted to study personnel as approved by the PI and MUSC IRB. As with all studies conducted at MUSC, this study is also eligible for a random audit by MUSC Office of Compliance.

Data Processing. This study will use Research Electronic Data Capture (REDCap) for data capture and management. REDCap is a software toolset and workflow methodology for the electronic collection and management of research and clinical trials data. REDCap provides secure, web-based, flexible applications, including real-time validation rules with automated data type and range checks at the time of data entry. Exports are made available for several statistical packages including SPSS, SAS, SATA, R and Microsoft Excel. The study-specific REDCap electronic database will be designed and developed by the PI or PC in concert with the BS. The provision of REDCap is made available through the South Carolina Clinical & Translational Research (SCTR) Institute at MUSC with NIH Grant awards UL1RR029882 and UL1TR000062.

Data Security. Ensuring data security, compliance with 45 CFR 46 and maintaining the integrity of PHI is a top priority. MUSC has Standard Operating Procedures (SOP) to ensure a high level of data security while coordinating electronic and paper data management activities for clinical research trials. The REDCap study database will be hosted in the Biomedical Informatics secure data center at MUSC, a secure environment for data systems and servers on campus, and includes firewall, redundancy, failover capability, backups and extensive security checks. The secure data center has strict access control; only authorized core personnel may access the facility un-escorted. Only authorized users are allowed to connect to the network, and the security of the network is actively monitored. Power and environmental controls have several layers of backups, from interruptible power supplies to alternate and redundant feeds to the local utility company. The REDCap system administrator contributes to the maintenance of institutional disaster recovery and business continuity plans. Load balancers and a highly fault tolerant SAN infrastructure contribute to high availability.

The REDCap system itself has several additional layers of protection including password protection. Access to the data and its security is managed institutionally by sponsored login IDs through a Shibboleth login with an MUSC issued NetID and features a user account management filter that controls who can access the data and to what degree. All personnel must pass an employment background check before being issued an ID. Password complexity, history and expiration standards are implemented at the institutional level. Access to individual REDCap projects and their data is managed by the owner of the project. All transactions are securely delivered to the application using Secure Sockets Layer (SSL – SHA-1 with RSA Encryption; 2048-bits). It is then transmitted internally (behind the firewall) to the database server. All transactions are logged at the server layer (httpd logging), application layers (REDCap logs activity to a database table), and the database layer, using both query and binary logging. This feature provides audit trails for all changes, queries, data exports and reports. MUSC Information security policies are available at: https://mainweb-v.musc.edu/security/policy/

Data Entry. Only MUSC IRB approved study personnel that are authorized to have access to the REDCap study database will be granted password access. Study personnel using computers that are connected to the Internet will directly enter data into the remotely housed database. As such, no electronic study data will be stored on hard drives and/or any portable electronic devices. Additionally, all personnel with access to the database will have current University of Miami CITI training in the Conduct of Human Subject Protections, and HIPAA and Information Security trainings that are completed annually. Each participant will be assigned a unique study identifier, all PHIs will be masked, and data exports will be limited to the PI, the mentor, the PC, or the BS for generating reports and the conduct of statistical data analysis.

Data Monitoring. Ongoing quality control procedures will be implemented for data collection, storage and processing. The PI or PC will conduct monthly monitoring of the study database and generate a report for review at team meetings. Standing agenda items for these meetings will include participant recruitment and retention, AE's, protocol deviations, data integrity and overall study conduct. The PI and PC will work to resolve and validate discrepant data. Discrepancies that warrant clarification will be sent to appropriate parties for review and resolution. All data entry and changes made in the study database by authorized study personnel will be automatically logged by REDCap, and provide a transparent visible audit trail for reviewers.

12.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

Data Safety Monitoring Plan
K23NR017899-01A1
PI Dr. Shannon M. Phillips
Study Title: SMYLS: A Self-Management Program for Youth Living with Sickle Cell Disease

SECTION A. Monitoring Entity.
Considering the study rationale, population, procedures, and the risk: benefit profile as outlined, the overall risk level for participation in this study is classified as: **Minimum Risk.**

1) Data Safety Study Monitoring Committee (SMC)
The following members of the study's SMC will perform data safety monitoring of the study:

- Dr. Cristina Lopez (Independent SMC Chair)
- Mr. Madisetti, MS (Independent Committee member)
- Margaret Prentice, MBA (Program Coordinator)

2) Individual Roles and Responsibilities
Principal Investigator, (PI). As PI, **Dr. Phillips** will overall be responsible for the immediate protection of all human participant study participants.

Primary Mentor. **Dr. Teresa Kelechi**, as Dr. Phillips' primary mentor on this K23 application, will serve as the senior individual responsible for providing oversight and guidance on Dr. Phillips' function as PI. Drs. Kelechi and Phillips will discuss human subjects' participation and protections during mentoring meetings and as needed. Dr. Kelechi will provide guidance to Dr. Phillips trial oversight and reviewing AE, as well as providing guidance on organizing SMC meetings and reports.

Dr. Lopez is an independent investigator and an is Associate Professor at Medical University of South Carolina. She has a PhD and a background as a clinical psychologist with expertise in adolescent behavioral research. Dr. Lopez has no real or apparent conflict of interest that would affect her performance in this role on the study. Dr. Lopez will correspond semi-annually as part of the SMC to review de-identified cumulative AE study data to assess any impact on the safety of participants or on the ethics of the study. She will be responsible for reviewing all cumulative reported SAE related to study treatment. She will also review data safety monitoring reports generated by the biostatistician (BS) to provide study recommendations to the PI, MUSC's IRB and NINR. Dr. Lopez will be notified within 24 hours of the occurrence of any SAE by the PI or project coordinator and will be provided with the necessary study information to provide an informed recommendation in real-time regarding the protocol and human participant safety.

Ms. Prentice will be responsible for the classification of all reported adverse events (AE) and ensuring that all serious adverse events (SAE) are forwarded to the PI, her mentor, and the other members of the SMC within 24 hours and in compliance with MUSC IRB and NINR's reporting requirements. In addition, and in conjunction with the PI, the PC will be responsible for amending the protocol in accordance with SMC recommendations, submitting reportable SAEs to the IRB; and, submitting annual Progress Reports to the NIH/NINR through MUSC's OSRP. The PC will also be responsible for ensuring data management validation and verification of the electronic study research database, and the accurate reporting and timely notification of all AEs to the PI, and the other members of the SMC. As part of the SMC, the PC will be responsible for: conducting monthly internal quality control audits on all participant records and notifying the PI of any deficiencies; participating in data safety monitoring study management meetings; assisting in the generation of ad hoc participant data safety reports as requested; and, the forwarding of reportable SAEs to the NIH/NINR Program Official through MUSC's Office of Research and Special Programs (OSRP) within 72hrs of IRB review and acknowledgement.

Mr. Madisetti is the Director of Research at College of Nursing and a member of MUSC Institute of Human Values with Fellowship certification in Research Ethics. Mr. Madisetti has served and is currently serving as a member of numerous NIH/NINR R01/R21/P20 DSM Boards and Committees, and FDA Industry Sponsored Clinical Trials. Additionally, he also has over 6 years of experience working on HRSA and PCORI funded demonstration program s and studies among patients with Sickle Cell Disease. With no study involvement, Mr. Madisetti has no apparent conflict of interest to serve in this capacity. Mr. Madisetti will be responsible for conducting semi-annual interim analyses, generating semi-annual AE safety reports from the electronic study research database and disseminating de-identified information to the other members of the SMC. The interim data analyses will only include safety related results; analyses in regard to study outcome will not be performed. The interim AE reports will provide typology, frequency data and outcomes of all reported and documented AE in the electronic study database. As part of the SMC, Mr. Madisetti will also participate in safety monitoring study management meetings.

SECTION B. Procedures for Safety, Risk and Confidentiality

1) Monitoring Study Safety

From the initial screening of the participant by inclusion and exclusion criteria to the informed consent process to the provision of participant study instruction to staff training in Good Clinical Practices (GCP) and regulations pertaining to the Conduct of Human Participant Research to weekly contact with participants to internal monthly quality control audits and protocol fidelity monitoring to the real-time review of AE by the SMC to the oversight of MUSC's IRB, procedures for monitoring study safety are consistently carried out throughout the study. Specific procedures include:

- Participants will be screened for inclusion and exclusion per the protocol; the PI or PC shall verify 100% of participants' eligibility prior to study enrollment through review of inclusion and exclusion criteria with potential participants.
- Participants will be fully informed as to all know risks and the possibility of risk from study participation in the informed consent process. These risks are minimal.
- Participants will be instructed to notify the researchers of any/all suspected or experienced adverse events whether they believe them to be related or not to the intervention.
- The PI or PC will track all reported participant AEs through to resolution. Please see Section C. 1 – 4.
- All investigators and research staff will maintain active CITI training.
- The PI or PC will maintain weekly contact with all participants to elicit information about AEs and to monitor participant study progress, compliance and safety.
- The PI or PC will review participants study logs for fidelity compliance with the intervention.

- The PI or PC will conduct a monthly internal quality control audit of all participant records to ensure compliance with MUSC IRB regulations; the PI and PC will work together to correct any errors.
- The PI and/or designee will observe and evaluate ten (10%) percent of eligibility screening visits, informed consents and study instructions performed by IRB approved study personnel and provide feedback and/or retraining of study personnel if fidelity to both applicable federal regulations and the protocol is not observed.
- The BS shall generate semi-annual AE reports for the PI, mentor, and the SMC to review.
- The SMC will have access to data on SAE within 24 hours and will be able to provide immediate recommendations to the PI, her mentor, and the PC.
- Investigator performance and compliance will be provided for through adherence to the MUSC IRB and Office of Research Integrity (ORI) Statement of Assurance and Policy 5.3: Education and Training Requirements for Individuals Involved in Human Research (https://research.musc.edu/resources/ori/irb/policies)

2) Minimizing Research-Associated Risk

Diligent study data and safety monitoring will be conducted by the PI, mentor, PC, and the study's SMC throughout the conduct of this study in compliance with the following required elements of MUSC IRB's continuing review process:

1. Tracking and follow-up of participant accrual (including withdrawn consents) will minimize risk by identifying, disclosing, and mitigating any potentially unknown risk(s) of harm to study participants. These risks are minimal.
2. Timely and appropriate reporting of informed consent process deficiencies, protocol deviations, privacy breaches, conflicts of interest, and/or changes in personnel.
3. Ongoing soliciting, monitoring and appropriate reporting of adverse event activities.
4. Timely and appropriate IRB submission of safety-related documents such as audit reports, sponsor progress reports, SMC reports, and other materials or communications that might impact the safe conduct of this study.
5. Active cooperation with the IRB, sponsor, and other applicable entities in the event of a random or for-cause internal or external audit.

Institution-Wide Assurances

This protocol will be conducted fully in keeping with the signed MUSC IRB Principal Investigator Statement of Assurance and Department Chair's Statement of Assurance, when submitted to the IRB as a required component of the MUSC IRB Human Research Review Application. Assurances include the following safety-related considerations:

3) Protecting Confidentiality of Participant data

Participant Screening and Enrollment. All data from participants screened for the study will be entered into an electronic study database. Designated research staff will collect, gather, and enter required data (written informed consent, HIPAA Authorization, and demographics) onto study data forms. Screened patients who do not meet study eligibility will have specific screening data entered into the study database. The collected data will be helpful in examining the patient population and feasibility of enrollment criteria and will include reason for exclusion. All dates will be shifted and other Personal Health Information (PHI) will be removed from the study database upon study completion. All data obtained from this study will be used for research purposes only and will comply with Federal HIPAA regulations. Master Screening and Enrollment Logs will be maintained by the PI or PC and will be used by the PI or PC to prepare reports on accrual and attrition for the SMC.

Case Report Forms. All proposed study specific case report forms (source documents) for data collection will be designed by the PI or PC and, when possible, transferred by the PI or PC into electronic Case Report Forms (eCRFs) for use in the study's REDCap database. These study specific eCRFs source documents (study logs for correspondence, compensation and other forms such as pre-eligibility screens) will be coded by the participant's unique study ID# for all data collected including study instruments and will be maintained in the participant research record. Completed instruments that require signature on a paper CRF will be scanned and uploaded into the study database for remote electronic safety monitoring as well as maintained on file in accordance with MUSC policies and applicable Federal Regulations for the Conduct of Human Participant Research.

Binders. The PI or PC will prepare and maintain a participant-specific binder for each participant containing all non-eCRFs records. A regulatory file will also be maintained to include the IRB-approved Protocol, original Informed Consent documents, HIPAA forms and other study-related regulatory documents. All paper research records and CRFs will be maintained in a locked file cabinet, stored in a room for research files that is accessible only via a password protected entry system that features security cameras, within the MUSC College of Nursing. Access to the research records, study database and PHI will be restricted to study personnel as approved by the PI and MUSC IRB. As with all studies conducted at MUSC, this study is also eligible for a random audit by MUSC Office of Compliance.

Data Processing. This study will use Research Electronic Data Capture (REDCap) for data capture and management. REDCap is a software toolset and workflow methodology for the electronic collection and management of research and clinical trials data. REDCap provides secure, web-based, flexible applications, including real-time validation rules with automated data type and range checks at the time of data entry. Exports are made available for several statistical packages including SPSS, SAS, SATA, R and Microsoft Excel. The study-specific REDCap electronic database will be designed and developed by the PI or PC in concert with the BS. The provision of REDCap is made available through the South Carolina Clinical & Translational Research (SCTR) Institute at MUSC with NIH Grant awards UL1RR029882 and UL1TR000062.

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SECTION C. Procedures for Identifying, Reviewing and Reporting Adverse Events

1) Identifying. Potential minimum risks identified for participants are outlined in the Protection of Human Subjects section of the K23 grant application and are also outlined in the IRB-approved protocol and informed consent document. Additional unknown risks may occur and, if so, will be identified through diligent monitoring by the PI, mentor, or PC throughout the conduct of this study. During the informed consent process, participants will be advised of the potential risks of participation as identified in the IRB-approved informed consent document and reminded throughout the study that the researchers should be promptly informed about any concerns regarding potential side effects, adverse events, or clinical deterioration. Participants will also be instructed to notify the PI, PC, and/or designee of any suspected adverse events immediately if possible. All participants will be recruited via the MUSC Pediatric Sickle Cell clinic and will be current patients of the clinic. Therefore, if a participant notifies the PI or PC of an acute medical event, the participant will be advised to follow the usual processes of care as directed by his/her regular provider at the Pediatric Sickle Cell clinic. This may include calling the Pediatric Sickle Cell clinic during regular hours, calling the on-call provider after hours, or going to the emergency department if recommended by the regular provider. Throughout the course of study enrollment, the researchers will maintain weekly telephone and/or face-to-face contact with the all study participants to elicit information about experienced AE and to monitor participant progress. The PI or PC will maintain an electronic record of all reported adverse events and notify the SMC of all reportable events as they occur. The SMC will have real-time access to the study database to review and monitor all reported SAE that were reported as related to the intervention. The PI (with the mentor) or PC will generate and provide de-identified monthly administrative human subject safety reports for the SMC to review participant progress, accrual and attrition rates, and monitor the frequency of all reported side effects and AE. Additionally, the BS will generate and provide de-identified cumulative administrative human participant semi-annual safety reports for the SMC to review.

2) Reviewing. Adverse events will be assessed and graded by the members of the SMC according to the MUSC IRB Unanticipated Problems and Adverse Events Policies and Procedures, located at section 4.7 on the following webpage: https://research.musc.edu/resources/ori/irb/policies, and described below.

- **Expected/Anticipated**—Identified in nature, severity, or frequency in the current protocol, informed consent, investigator brochure, or with other current risk information.
- **Unexpected/Unanticipated**—Not identified in nature, severity, or frequency in the current protocol, informed consent, investigator brochure, or with other current risk information.
- **More Prevalent**—Occurs more frequently than anticipated or at a higher prevalence than expected.
- **Serious**—Results in death, is life threatening, requires inpatient hospitalization or prolongs existing hospitalization, results in persistent or significant disability/incapacity, cancer, overdose, or causes a congenital anomaly/birth defect.

The relationship of adverse events to study participation will be determined by the SMC according to the MUSC IRB Adverse Event Reporting Policy:

- **Unrelated**—There is not a reasonable possibility that the adverse event may have been caused by the drug, device or intervention.
- **Possibly Related**—The adverse event may have been caused by the drug, device, or intervention, however there is insufficient information to determine the likelihood of this possibility.
- **Related**—There is a reasonable possibility that the adverse event may have been caused by the drug, device or intervention.

3) Reporting. All reportable AE, SAE and unanticipated problems experienced by participants will be reported to the NIH/NINR and MUSC IRB in compliance with their Adverse Event Reporting Policy requirements, using the IRB's password protected on-line secure server adverse event reporting system. Within 24 hours after a reportable AE, SAE or unanticipated problem has been reported by the participant, it will be graded by the PI, her mentor, or PC, forwarded to the study's SMC for review, and then will be submitted by the PI to MUSC IRB. The Institutional Official(s) will review the event and discuss the report with the IRB Chair and the Director of the Office of Research Integrity. After IRB review and acknowledgement, the PI will further review, and the PI, her mentor, or PC will forward a copy of the reportable AE, SAE or unanticipated problem and IRB acknowledgement letter to the NIH/NINR Program Officer through MUSC's OSRP. The activities will be reported to the NIH/NINR within 72 hrs. In addition, all cumulative reportable AE, SAE and unanticipated problems included in the SMC reports will be submitted to the NIH/NINR in the PI's Annual Progress Reports.

4) Examples of Potential Reportable Adverse Events. In accordance with MUSC IRB Adverse Event Reporting Policy, an AE is reportable if it meets all of the following criteria: 1) is unexpected 2) is related and/or possibly related, and 3) is serious and/or suggests that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized. Additionally, per MUSC's policy all participant deaths, protocol deviations, complaints about the research, and breaches of confidentiality are reportable events. An example of an AE would be new onset of chest tightness and discomfort (symptom) that could potentially be associated with an acute exacerbation of the child's comorbid asthma. The participant's parent reported he/she recently ran out of his/her medication. The steps to be taken include withdrawing the subject from the study and inviting him or her to restart the study after symptoms subside. An example of an SAE would be the death of a participant from acute chest syndrome or stroke, which although would be viewed as unexpected and unrelated to the intervention is nonetheless a reportable serious event. No further steps would be taken except to review, grade and report the event. An example of an unanticipated problem would be the participant trips and falls while retrieving his/her phone to read a message from the provider. The steps in this case would be to report the event as per the IRB and NINR policy, and to discuss appropriate actions regarding whether the participant should remain in the study with the SMC. These events and problems will be reported in accordance with the IRB and NIH/NINR policy as noted in Section C.3.

SECTION D. Multi-site Monitoring and Compliance

This is not a multi-site study.

SECTION E. Assessment of External Factors

The PI will conduct a semiannual assessment of external factors through a review of literature related to new developments in the areas of self-management, symptom management (including pain and fatigue), symptom reporting and other approaches that may have an impact on the safety of participants or on the ethics of the study. To determine whether any changes are necessitated to the study protocol, the PI, the mentor, and the members of the SMC will review any identified literature or product safety data that may pose as a potential impact to the risk benefit ratio study and/or safety of study participants.

SECTION F. Interim Analysis

This study aims to test the feasibility of a multi-component, technology-based intervention to promote self-management and symptom management among adolescents with sickle cell disease during the transition process from pediatric to adult care and parent-managed to adolescent self-managed care. To our knowledge, there are no similar interventions specifically designed for this patient population and purpose. As such, the BS will generate semi-annual qualitative interim analysis reports on a) adverse events; and b) data obtained during phone call and returned end-of-study surveys to understand issues related to the uptake, usability, and adoption of this platform among this population. We will evaluate the screening and enrollment procedures, barriers to participation and retention, including, safety, adherence, acceptability, technology problems encountered, if any, and user feedback from the participants and providers. This information gained from this structured process will be used to both guide the refinement of the current protocol and to inform the design of a larger efficacy trial. Interim analysis of outcome variables (transition readiness, adolescent pain, adolescent and caregiver fatigue and other symptoms, and quality of life) was not considered to avoid inexact inferences and increased chance of error due to few data points, as well as potential for bias if interim results were known to the investigators. Therefore, there are no planned stopping rules for this study.

13.0 Withdrawal of Subjects

The PI may withdraw a participant from the study at any time if they decide it is in their best interest, if they do not follow the investigator's instructions, or if they fail to keep study visits. This may also occur if there is a protocol violation or early closure of the study.

14.0 Risks to Subjects

We do not anticipate any significant risks related to the completion of this study. However, as with any research study there is a risk of disclosure of information that can lead to a loss of confidentiality. As well as having a comprehensive plan that details data safety, handling, monitoring, storage and security procedures, we will further minimize the potential for loss of confidentiality through the physical separation of participant names from their research record.

Additionally, it is possible that a participant might experience some emotional distress while responding to the survey questions or participating in key informant interviews. If this were to occur, the participant would be referred to a psychologist or psychiatrist for counseling. Reactions will be monitored by the PI (who will be conducting the key informant interviews) and signs of significant distress will be followed-up to identify any serious psychological problems. In the rare and unexpected event of serious or life threatening level of distress, a psychologist or psychiatrist will be contacted as well as the participant's primary care provider of record.

The PROMIS Emotional Distress: Depressive Symptoms Instrument will be administered to young adult, adolescent and caregiver participants at baseline, 6-weeks, 12-weeks, and 3-months

post-intervention. The REDCap database will be developed with scoring to allow study personnel to immediately view scores, including a raw score, t-score, and response pattern scoring. If any of the following criteria are met, the participant will be asked if they would like assistance with obtaining mental health resources:

- t-score for depression is one standard deviation above the mean (60) for the general population (44), or above
- t-score demonstrates a minimally important difference (3.0 – 4.5) from previous assessment (45)

15.0 Potential Benefits to Subjects or Others

If a participant agrees to take part in this study, there will be no direct medical benefit to them. We hope the information learned from this study will aid patients and clinicians in the future. The data collected from this study will not directly affect the treatment being given to the patients. The risks associated with the proposed study are minimal and include psychological and physical strains that might be encountered in everyday life. The benefits of the study outweigh the risks. We anticipate this study will lead to improved self-management of SCD through the use of mobile health technology. As such, the resulting information would be used to develop self-management strategies among young adults and adolescents with SCD and their families moving forward.

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