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TITLE: A Comparative Effectiveness Study of Peer Mentoring [PM] versus Structured Transition Education Based Intervention [STE] for the Management of Care Transitions in Emerging Adults with Sickle Cell Disease (SCD)

The Sickle Cell Trevor Thompson Transition Project (ST3P-UP Trial)

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The study will be conducted in compliance with the protocol, ICH/GCP and any applicable regulatory requirements.

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PROTOCOL SIGNATURE PAGE

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The signature below constitutes the approval of this protocol and the attachments, and provides the necessary assurances that this trial will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable U.S. federal regulations and ICH guidelines.

_____ _____

Signature of Sponsor-Investigator Date

PAYAL DESAI, MD
Sponsor-Investigator Name (printed)

SYNOPSIS

TITLE	A Comparative Effectiveness Study of Peer Mentoring [PM] versus Structured Transition Education Based Intervention [STE] for the Management of Care Transitions in Emerging Adults with Sickle Cell Disease (SCD)
STUDY POPULATION	Emerging Adults with Sickle Cell Disease aged 16 – 25 years
SUMMARY OF STUDY RATIONALE	Emerging adults with sickle cell disease (EA-SCD) experience significant difficulties with transition from pediatrics to adult care despite the impressive gains in childhood survival. Acute care utilization dramatically increases, and quality of life drops along with an increased mortality. There is currently no clinical practice standard for transition programming for EA-SCD. Recently *Got Transition* Center for Healthcare Transition Improvement recommended an approach that involves incorporating the *Six Core Elements of Transition* into clinical practices that provide care for children with special healthcare needs (CSHCN) as noted in www.gottransition.org. The American Academy of Pediatrics (AAP) in partnership with the American Academy of Family Physicians (AAFP) and the American College of Physicians (ACP) proposed these Six Core Elements in 2011 in a consensus statement that provided clear guidance and a supportive decision algorithm that describes six practice-based recommendations (Fig 4); **1: transition policy, 2: transition youth registry, 3: transition preparation, 4: transition planning, 5: transition and transfer of care, and 6: transition completion** that should be a part of ANY planned health care transition program for all CSHCN. They based these recommendations on the premise that *optimal health care is achieved when individuals of all ages receive "medically and developmentally appropriate care" in a process that includes ensuring that high- quality, developmentally appropriate health care services are available uninterrupted as the person moves from adolescence to adulthood."*[28] This project seeks to establish the comparative effectiveness of adding peer mentoring to a structured education-based transition program to improve self-care skills among EA- SCD. The peer mentoring comparator was chosen based on existing evidence of its utility in improving transition outcomes in other chronic diseases of childhood such as juvenile diabetes and solid organ transplant. We will test the hypothesis that the addition of peer mentoring to a structured education-based transition program will improve acute care reliance, quality of life and satisfaction with transition outcomes for EA-SCD using a cluster randomized study approach. The qualitative research portion of the study is aimed at gathering substantive qualitative information to evaluate the ST3P-UP Study's

	process outcomes, quality improvement, and impact through eliciting descriptions of participant experiences with one-to-one peer mentoring since we are unable to quantitatively assess the Standard Education + Peer Mentoring comparator as originally planned within the ST3P-UP Study.
STUDY DESIGN	This is a cluster randomized study comparing the effectiveness of adding virtual peer mentoring to a structured education-based transition program based on the Six Core Elements of transition in improving acute care reliance, quality of life and satisfaction with transition process in EA-SCD. The study will involve 14 clinical sites with a 1:1 randomization at the site level. A total of 537 EA-SCD between the ages of 16 and 25 years who are currently receiving care in a pediatric SCD program will be enrolled and followed prospectively for at least 6 months in pediatrics and at least 24 months in adult care. We will use rapid cycle PDSA improvement methods to implement the structured education-based program in adherence to the 6 core elements and measure adherence to these practice guidelines over time.
OBJECTIVES	<u>Primary Objective:</u> • Compare the effectiveness of STE+PM versus STE at decreasing the number of acute care visits per year over a 24-month period among EA-SCD. <u>Secondary Objectives:</u> • To compare the effectiveness of STE+PM versus STE at improving patient- reported outcomes (PROs) among EA-SCD. • To compare the effectiveness of STE+PM versus STE at reducing healthcare utilization among EA-SCD. <u>Qualitative Objectives:</u> • Identify the facilitators and barriers to enrollment of EA-SCD and mentors from multi stakeholder perspectives • Assess mentor-mentee experiences with one-to-one peer mentoring • Assess site experiences with the implementation of Quality Improvement methods within their clinical practices • Determine the effect of engagement activities on communication within the site triad (adult/pediatric physicians, CBOs, patients) • Develop a definition of transition success across the triad (adult/pediatric physicians, CBOs, and patients)
KEY INCLUSION CRITERIA	• Any Sickle Cell Disease genotype • Age 16 – 25 years receiving care in a pediatric sickle cell program • Able to complete all study procedures with reasonable accommodations

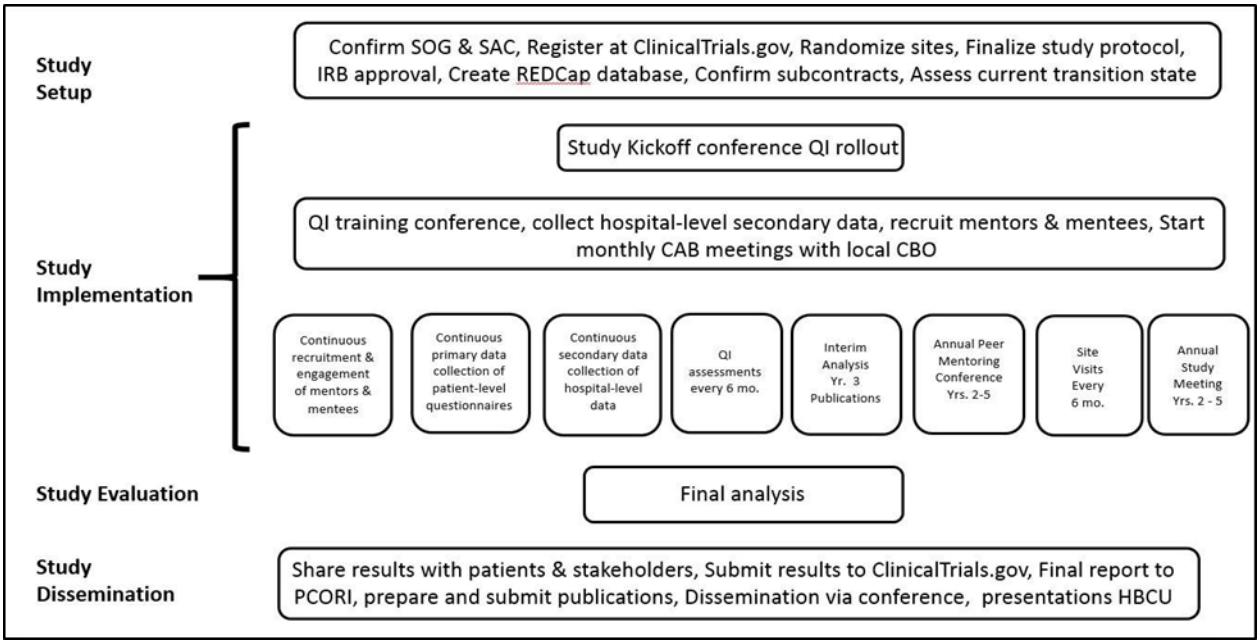
STATISTICAL CONSIDERATIONS	Estimated average acute care utilization rate for EA-SCD is 6 visits / year. This study is designed to detect a 20% reduction in the number of acute care encounters per year which is considered clinically significant to our patient stakeholders. Based on a two- sided alpha = 0.05 significance level, 67 subjects per arm would provide approximately 85% power to detect a 20% reduction in the number of acute care utilizations under individual randomization, assuming the number of encounters follows a Poisson distribution for rare events. Sample size was inflated based on the cluster size coefficient of variation among our 14 participating clinical sites (55%) and the intra-class correlation (ICC) assumed to be 0.05. Based on these parameters, 183 subjects per arm (366 total subjects) will retain approximately 85% power. The sample size was increased to 537 total EA-SCD subjects to account for potential missing data and allow for robust evaluation of secondary endpoints. It is estimated that this can be accomplished with an enrollment rate of 35% of the EA-SCD patient population.
NUMBER OF EA-SCD PARTICIPANTS	537 total participants will be enrolled Each arm will enroll approximately 269 EA-SCD aged 16 – 25 years
NUMBER OF CLUSTERS	There will be 14 cluster sites, each cluster site comprised of a pediatric SCD clinic, an adult SCD clinic and a SCD CBO. There are 8 large cluster sites with ≥40 EA-SCD currently in pediatrics and 6 small cluster sites with <40 EA-SCD currently in pediatric care. Based on self-reported enrollment targets from each site, 80% of participants will come from large clusters.

SCHEMA

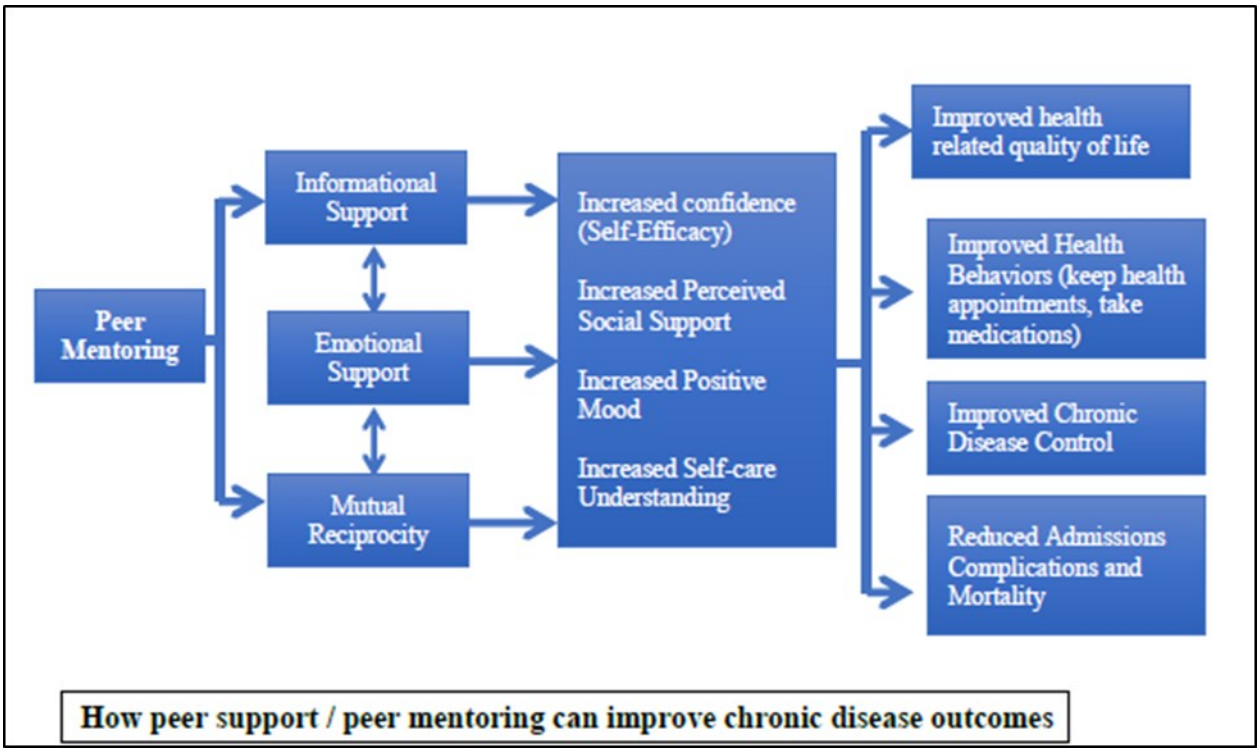
Study Schema Figure 1: Overview of Study Design

Study Schema			
Practices with Emerging Adults with SCD (EA-SCD) aged 16 - 25y Randomized at the Practice Level			
Small Sized Program [≤ 40 EA-SCD]		Large Sized Program [> 40 EA-SCD]	
Arm 1- A	Arm 1- B	Arm 2-A	Arm 2-B
Structured Education Based Transition Program [STE]	Structured Education Based Transition Program [STE] + Peer Mentoring [STE + PM]	Structured Education Based Transition Program [STE]	Structured Education Based Transition Program [STE] + Peer Mentoring [STE + PM]
Outcome Measures at 24 Months			
Primary Outcome: Change in number of acute care visits [ED visits, Admissions, Readmissions at 14d, 30d, Total Hospital Days]			
Secondary Outcome: Change in patient reported outcomes (MOS-SS, TIP-RFT, PedsQL-SCD, ASCQ-Me QOC], Satisfaction with Transition Process, Change in Ambulatory Care visits			
Process Outcome: Change in Adherence to Standard Transition process, Transition Feedback survey			

Study Schema Figure 2: Overview of Study Implementation Outline



Study Schema Figure 3: Peer Mentoring Impact on Clinical Outcomes



GLOSSARY OF TERMS

ACR	Acute Care Reliance
ASCQ-ME	Adults Sickle Cell Quality of Life Measure
CAB	Community Advisory Board
CBO	Community-Based Organization
CHW	Community Health Workers
CSHCN	Children with Special Healthcare Needs
DCC	Data Coordinating Center
DSMC	Data Safety Monitoring Council
EA	Emerging Adult
EA-SCD	Emerging Adult with Sickle Cell Disease
ED	Emergency Department
HBCU	Historically Black Colleges and Universities
HCT	Healthcare Transition
Hgb	Hemoglobin
IRB	Institutional Review Board
MOS-SSS	Medical Outcomes Study Social Support Survey
PDSA	Plan – Do – Study – Act
PedsQL™	Pediatric Quality of Life
PM	Peer Mentoring
PRO	Patient Reported Outcomes
QI	Quality Improvement
QI Coordinator	Quality Improvement Coordinator
QOL	Quality of Life
SAC	Study Advisory Committee
SCD	Sickle Cell Disease
FSCDQ	"How Much Do I Know about SCD" Quiz
SE US	Southeastern United States
SOG	Study Oversight Group
STE	Structured Education-Based Transition Program

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1. BACKGROUND AND RATIONALE

1.1 Background

Nearly 100,000 individuals are living with sickle cell disease (SCD) in the United States (US), 60% are adults (≥18y) and a third are emerging adults (16-25y; EA-SCD).[1-4] The disease predominantly affects minorities with over 30% residing in the region planned for this intervention (southeastern [SE] US).[2] SCD is characterized by a spectrum of symptoms and complications, including periods of unpredictable acute pain, debilitating chronic pain, multi-organ injury, reduced quality of life (QOL), and shortened lifespan.[2,5] Over 95% of children with SCD will survive into adulthood, due to early diagnosis, innovative preventative therapies, and improved comprehensive care.[6] Unfortunately, mortality rates continue to rise for adults with SCD, in part due to a dire lack of access to high-quality care for the influx of EA-SCD who are surviving into adulthood.[7] Healthcare systems have not adjusted to the shifting epidemiology of SCD in adults that need complex care coordination and support to optimally manage the medical and psychosocial comorbidities that increase with age.[8] While the mortality rates among children with SCD have declined ~3% per year between 1979 to 2005, there has been a steady 1% per year increase in adult mortality rates.[7] Median life expectancy for individuals with SCD in the US in the 1990s ranged between 42-48 years for hemoglobin SS (Hgb SS) and 60-68 years for hemoglobin SC (Hgb SC).[9] A more recent population-based SCD surveillance report from CA and GA cites tripling of all-cause mortality rates amongst 15-24 year olds (y) compared to those under age 14.[10] All-cause mortality rates remain higher for SCD compared to all African Americans (AA) and the general US population.[10]

Transition from pediatrics to adult care is a critical time for EA-SCD. The emergency department (ED) becomes a primary source for care, with ED visits and admissions per year doubling, and avoidable acute care visits rising to account for two-thirds of all SCD hospitalizations.[8,11,12] Data from the Healthcare Cost and Utilization Project State Inpatient Databases and State Emergency Department Databases from eight states showed that EA-SCD (18–30y) had the highest acute care utilization rates compared to children 10-17y (3.61 vs 2.04 visits/patient/year).[13] The 30-day readmission rate doubled from 27.4% to 48.9% respectively.[13] Data from the Registry and Surveillance for Hemoglobinopathies (RuSH) Project cite an increase in acute care utilization rates among EA-SCD (Fig 1). In GA, utilization rose from 0.8 to 3.0/person/year among individuals 10-19y of age compared to those 20 - 49y.[14] In NC, the average annual acute care visits per person increased from 5 in those <18 years to 12 among 18-35y.[4] Disparities also exist with school absenteeism, and EA-SCD miss an average of 20-40 school days/year due to illness, have worse standardized test scores, higher rates of repeat grades and lower overall school attainment compared to controls.[15] There is limited research to support evidence-based interventions that effectively reduce the high mortality, morbidity, and poor QOL during transition.

Barriers to Transition:

Several identified patient, provider and health system factors contribute to the poor health outcomes of EA-SCD during transition.[16-18] EA-SCD struggle emotionally with adjusting from a more paternalistic pediatric model to the adult "individualistic" model of care. Adherence to disease modifying treatment drops significantly as they struggle with the developmental maturation process.[19] Changes or lapses in insurance lead to gaps in comprehensive care -

specialized and primary - during transition, amplifying existing barriers to accessing crucial services as disease burden is increasing.[20,21] A retrospective study showed that patients who are transitioning received 46% fewer transfusions by age 22y compared to children and were 4.7 times less likely to receive iron chelation by age 25y.[21] At Atrium Health (formerly known as Carolinas Healthcare System), a large healthcare system in the SE US that provides care for 1300 adults and 400 children with SCD, only 8-14% of EA-SCD accessed a scheduled visit with their primary care/SCD provider in 2015 with mean acute care reliance (ACR; number of acute care visits per year/ [all acute care visits + all ambulatory care visits]) rates of 42% (Fig 2). Mean acute care visits/year rose significantly from 2.1 ± 2.9 among 16- 18y to 4.2 ± 6.8 among 19 - 21y and was highest among 21 - 25y at 5.3 ± 8.5 ($p<0.01$). ACR (≥0.33) is an indicator of inadequate access to primary and preventative care.[22] EA-SCD report having inadequate information about adult care and a poor understanding of their disease and how it becomes more complex with age.[14, 16] There are significant knowledge gaps and poor communication between pediatric and adult providers that worsen the problem created by a lack of standardized EA-SCD patient education curriculum.

Limited evidence on effective transition programming:

A population-based approach to care coordination provided through effective and culturally acceptable delivery models during and after the transition is essential to reduce the unacceptable morbidity and mortality of EA-SCD. Healthcare transition refers to "the purposeful and planned movement of adolescents and young adults with chronic physical and medical conditions from child- centered to adult-oriented health care systems".[23] A planned and structured transition process will maximize lifelong functioning and well-being, optimize health and assist EA-SCDs in reaching their full potential by providing support in acquiring independent health care and life skills, preparing for the differences in an adult model of care, and transferring successfully to new adult providers without disruptions in care. Transition planning that involves engagement between EAs, their caregivers and providers has been shown to lead to improvements in adherence to, continuity with, and overall satisfaction with healthcare.[11,24] When transition education is targeted and structured there is increased probability of achieving independent self-care among EA-SCD.[25] A recent report on the state of transition practices for children with special health care needs (CSHCN) revealed a lack of established best practices for EA transition, with only 25 programs nationwide that evaluated transition care in juvenile diabetes, SCD, solid organ transplant and other chronic childhood conditions.[26] Education-based interventions, use of a multidisciplinary team and a transition coordinator were common themes. Most programs evaluated disease status, adherence to adult appointments or medical regimen and patient satisfaction. A study by Maslow et al included a structured mentoring program showing improved self-efficacy and transition readiness among participants.[27] Only two studies were randomized trials, and none had a concurrent comparison group. The review highlighted the need for further prospective studies with concurrent comparison groups utilizing well-defined transition outcomes to measure the entire transition process. Additional evidence gaps identified include the need to involve health systems in the transition process, have longer follow up (> 1y), increase use of Quality Improvement (QI) initiatives to help identify best practices and overcome the challenges with patient level randomization, and use of validated tools to assess patient reported outcomes (PROs). Patient education was common to all 25 identified transition programs; therefore, our choice for a standard comparative transition model for this proposal will evaluate an education-based, structured transition program that utilizes a QI approach to standardize the transition process across clinical sites and integrate this into routine care for all EA-SCD.

1.2 Study Rationale and Study Design

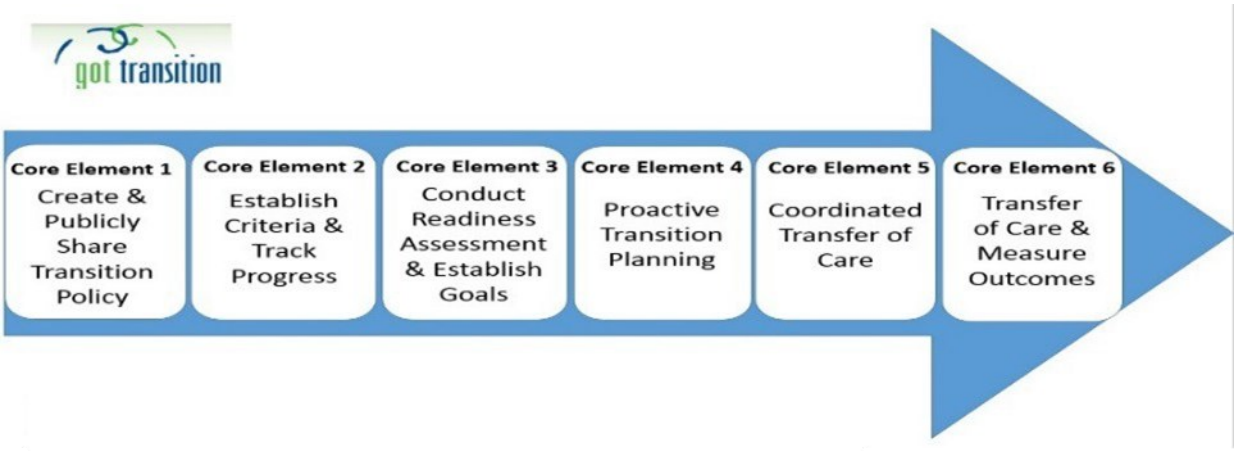

Figure 4: Core Elements of Transition

The disparities in health outcomes during transition for EA-SCD result from a complex interplay of factors related to the patients, their families and social networks, communities, healthcare providers and systems, practice settings, and government policies. There is currently no community standard for EA-SCD transition; however, there has been a resounding request from the SCD community and stakeholders (providers, healthcare systems, insurance payors, community-based organizations (CBO's), and patients, etc.) for a standardized transition process to be established. The high ACR rates for EA-SCD have garnered significant attention, as SCD is a leading reason for readmission and increased length of stay in most hospital systems. The topic of pediatric to adult transition has been featured in regional and national forums repeatedly with increasing urgency over the past 6 years. In 2011, the American Academy of Pediatrics (AAP) in partnership with the American Academy of Family Physicians (AAFP) and the American College of Physicians (ACP) co-authored a consensus statement that provided clear guidance and a supportive decision algorithm that describes practice- based recommendations and Six Core Elements (**Fig 4**; 1: transition policy, 2: transition youth registry, 3: transition preparation, 4: transition planning, 5: transition and transfer of care, and 6: transition completion) that should be a part of ANY planned health care transition program for all CSHCN based on the premise that "optimal health care is achieved when individuals of all ages receive medically and developmentally appropriate care in a process that includes ensuring that high-quality, developmentally appropriate health care services are available uninterrupted as the person moves from adolescence to adulthood."[28] Further expansions of the Six Core Elements of optimal transition was refined by the Got Transition/Center for Health Care Transition Improvement, which resulted in an open access comprehensive toolkit **(www.gottransition.com).**

A QI time-series comparative study of change was done in five large pediatric and adult academic primary care practices in the District of Columbia by the Got Transition team. Using the Health Care Transition Process Measurement Tools (pediatric and adult versions) to examine improvements in the six specific core indicators of transition performance, they found measurable improvements in all quality indicators over a 2 year QI learning collaborative that resulted in the development of a systematic clinical transition process.[29] Another pediatric-to-adult managed care transition pilot project for EA with chronic mental health challenges used the QI process to incorporate the "Six Core Elements of Health Care Transition (2.0)" into routine care showing significant improvement in the Transition Index and all six core elements over an 18-month

period.[30] In the southeast USA, twenty- one clinical sites participated in a needs assessment reporting a formal SCD transition program (60%); process for tracking and monitoring EA-SCD through transition (62%); readiness assessment protocol (48%); transition planning process (71%); established referral network of adult providers with a protocol for transfer (52%) with only 38% having a formal process of contacting the EA-SCD three to six months after transfer and only 10% having a formal process for ongoing communication with the receiving adult provider. The Health Care Transition Process Measurement Tools (pediatric and adult versions) will be used to examine the adherence to and adoption of the Six Core Elements of Transition practice performance at 14 pediatric and adult clinical sites. The rapid Plan–Do–Study– Act (PDSA) cycles will be utilized to implement the QI process to prospectively evaluate both the process and outcome of implementing the 6 core elements.

Study Design and Outcomes:

This will be a cluster-randomized study involving 14 clinical sites with randomization occurring at the site level. All clinical sites will implement a structured education-based transition program (STE) that will be implemented across all sites using quality improvement methodology. Implementation of this STE program will be monitored for adherence to QI process and for improvement in clinical outcomes over the 5 years of the study with the goal to fully implement the standard process within the first 18-24 months and allow for 24 months of ongoing follow up. EA-SCD participants will be enrolled while still in pediatrics and must spend a minimum of 6 months and maximum of 12 months in pediatrics to allow them to benefit from the STE intervention prior to transfer to adult care where this intervention will continue. Sites will be randomized 1:1 to receive peer mentoring or no peer mentoring [PM]. Mentoring will occur through a virtual platform and include structured frequent contacts between mentor and mentee for a minimum of 30 months. Primary outcome measures include acute care reliance (reductions in acute care visits and admissions and increase in ambulatory preventative care). Secondary outcomes include improvements in transition readiness, quality of life measures including social support, dexterity with self-care, satisfaction with transition experience for EA-SCD participants and providers, and improvements in quality of care experienced.

Rationale for Structured Education Based Transition Program [STE]:

Increase in disease knowledge, independence with self-care skills, and improved pediatric and adult provider EA-SCD transition support and knowledge is a critical goal of transition readiness. Structured patient education increases disease knowledge, provides self-management skills and is effective at increasing autonomy, self-efficacy and disease self-management that reduces acute complications in juvenile diabetes.[16] An education-based intervention tested for feasibility revealed twice as many EA-SCD in the intervention arm completing their first adult healthcare visit within 3 months of leaving pediatric care.[25] Patient education to achieve optimal transition readiness will use a standardized module entitled the “Who, What, Where, When, Sickle Cell Transition Education Module” or other site standard SCD education.[31-34] Each site will be given a QI change package that includes details of the Six Core Elements, the QI process training, the standard education module, and supplemental resources on QI and Transition. An EA-SCD will be identified to become a member of the transition team at each clinical site to provide the patient’s perspective during the QI process.

Rationale for Peer Mentoring [PM] as Comparator:

This project will compare the effectiveness of **STE+PM** over **STE** alone in improving health outcomes in EA-SCD. While most transition coordination models utilize specific education to address patient-level barriers to care (medication adherence, disease knowledge, transition readiness), they neglect the more complex societal environment within which the EA-SCD must navigate independently in adulthood.[35] Challenges remain with how to establish, sustain, and measure optimal support within and outside the adult medical setting to keep EA-SCD engaged in comprehensive care through the trajectory of transition. Health system-based interventions alone are inadequate to address all the needs of EA-SCD during transition, particularly with establishing social networks outside of healthcare. EA-SCD have also identified isolation as a key challenge as they navigate transition and learning from someone who has been through the process is a desirable component of a transition program.[17, 35] PM targets the social aspects of transitioning and helps model better self-management skills. The importance of PM, where an older peer with experience provides support and guidance, emerged as a desired approach repeatedly over the past year during our dialogue with patient partners. Various studies have confirmed that without sustained support, outcomes, e.g., costly hospitalizations and increased complications worsen.[36] PM can effectively sustain support for EA-SCD by reducing isolation and improving community engagement and self-efficacy, while modeling independent life skills without the high-cost of professional support systems.[37] A peer with lived experience that provides support and mentoring was considered a desired part of transition coordination by patient partners as it reduces social isolation and increases community engagement, while teaching independent life skills. PM provides the opportunity for a reciprocal relationship between two individuals with a shared experience where the more experienced "mentor" encourages and assists the less experienced "mentee" to develop his or her full potential while offering both individuals an opportunity for development and growth.[37] There is robust literature to support PM in assisting youth in acquiring the optimal skills, knowledge and attitudes to be more successful.[38] While there is little comparative evidence on the efficacy of PM for EA-SCD, previous studies have demonstrated improved EA outcomes using PM for juvenile idiopathic arthritis (JIA) and other chronic disease groups.[39-42] A waitlist pilot randomized control study of EA with JIA "iPeer2Peer Program" deployed trained mentors to provide support and self-management education over 8 weeks using Skype video calls.[39]. Fifty percent of pairings completed the intervention, average time on calls was twice the required duration (44.72+/- 15.76 min) and participant engagement level was robust 8.53/10 (range 7-10). The Adolescent Leadership Council (ALC) mentoring program designed by Maslow et al used a group mentoring and leadership framework to promote the psychosocial development of EA with chronic physical illness focusing heavily on structured mentoring and leadership skills.[27] Additional studies of PM have been described and support PM as a reasonable intervention during transition.[41- 45]

Patient stakeholders chose a PM program that draws from the "Chronic Disease Self-Management (CDSM) Program" in combination with mentoring techniques that focus on the African American population.[46] The conceptual models considered relied on the need for a deliberate focus that points youth toward a more positive and productive future rather than just a buddy system.[47-49] Our patient stakeholders also requested that mentors be paired with "advisors" who can provide the mentors with additional support to reduce burnout in what they referred to as the "village".

Rationale for Use of Supplemental Qualitative Methods:

The qualitative portion of the research plan is designed to supplement the original ST3P-UP study aims and will be approved as a separate protocol through Georgia Southern University. The supplemental qualitative aims will provide a viable and robust approach that will allow for evaluation of the study's processes, quality improvement, impact, and outcomes including: 1) the identification of the facilitators and barriers to enrollment of EA-SCD and mentors from multi stakeholder perspectives; 2) an assessment of mentor-mentee experiences with one-to-one peer mentoring; 3) an assessment of site experiences with the implementation of Quality Improvement methods within their clinical practices; 4) a determination of the effect of engagement activities on communication within the site triad (adult/pediatric physicians, CBOs, and patients); and 5) the development of a definition of transition success across the triad (adult/pediatric physicians, CBOs, and patients).

A deeper dive into the lessons learned related to the peer mentoring comparator within the ST3P-UP study will be gleaned from these supplemental qualitative aims.

Conceptual Model:

Based on the review of the literature on SCD Transition, *the bio-psychosocial ecological model* was identified as the best theoretical framework to address the comparative multi-level interventions that are needed to optimize transition outcomes in this population.[10,22,38] This model proposes that it is necessary to examine an individual's health by considering the interactions of biology, psychology and social factors within the individual's environment to produce a more effective, multi-dimensional approach to chronic disease management. The model removes the focus from "microscopic" individual level factors (e.g. adherence, individual conduct) and broadens the view of the individual to understand "macroscopic" (communities, health care systems, etc.) influences on illness and behavior and allows practitioners to view the individual in constant interaction with their environment. Thus, we chose a health system approach to improving transition processes within the clinical setting that included individual level education. Our hypothesis is that the addition of a PM intervention that influences social interactions and the microsystem that touches the EA-SCD will be more effective than a STE-based transition program alone in improving acute care utilization.

2. STUDY OBJECTIVES

2.1 Primary Objective

The primary objective of this study is to compare the effectiveness of STE+PM versus STE at decreasing the number of acute care visits per year over a 24-month period among EA-SCD.

2.2 Secondary Objectives

2.2.1 Patient-Reported Outcomes

To compare the effectiveness of STE+PM versus STE at improving patient-reported outcomes (PROs) among EA-SCD (Appendix A). Surveys used to evaluate PROs will include:

- Adults Sickle Cell QOC Measure (ASCQ-ME QOC) for health-related quality of life
- PedsQLTM-SCD module for health-related quality of life
- Medical Outcomes Study Social Support Survey (MOS-SSS)
- Transition Readiness Score as measured by the TIP-RFT scale
- Health Care Transition Feedback Survey for Youth and Young Adults

2.2.2 Healthcare Utilization

To compare the effectiveness of STE+PM versus STE at reducing healthcare utilization among EA- SCD.

Measures to assess healthcare utilization will include:

- The number of acute care visits per year over the entire study period
- The number of ambulatory visits per year over the entire study period
- The number of visits with adult providers over the entire study period
- The number of hospitalization days over the entire study period
- 14-day and 30-day readmissions over the entire study period

2.2.3 Intervention Fidelity (PM Intervention Feasibility)

- Number of consented mentor candidates that complete each step of eligibility and training activities
- Timelines for major milestones for mentors
- Time from consent to enrollment for EA-SCDs
- Frequency of mentor-EA-SCD contacts via the platform

2.2.4 ST3P-UP Application Usage

- Frequency of contacts between study subjects (EA-SCD, Mentor, or Advisor) and transition coordinator
- Frequency of contacts between investigators and transition coordinators
- Frequency of contacts between investigators
- Frequency of education resource views from application

2.3 Exploratory Objectives

- Evaluate the adoption of and adherence to the Six Core Elements of transition practice performance at each site.
- Identify through a modified Delphi process and other qualitative research methods the patient and stakeholder determined optimal outcome(s) of transition and compare to predetermined outcome of acute care reliance.

2.4 Qualitative Research Objectives

- Determine the facilitators and barriers to enrollment of EASCDs and mentors from multi stakeholder perspectives.
- Describe mentor-mentee experiences with one-to-one peer mentoring.

- Assess site triad experiences with implementing quality improvement within their clinical practices.
- Determine the effect of engagement activities on communication within the site triad (adult/pediatric physicians, CBOs, patients).
- Develop a multi-stakeholder, ecologically focused definition of transition success.

3. SUBJECT SELECTION

3.1 Subject Identification and Recruitment

EA-SCD Subject Recruitment

EA-SCD subjects will be recruited at Atrium Health and other participating institutions. Recruitment will include patients with SCD 16 to 25 years of age who are currently receiving care in a pediatric SCD program. Recruitment will include both males and females, and all race and ethnicity classifications.

Mentor Subject Recruitment

Mentor subjects will be recruited at Atrium Health and other participating institutions. Recruitment will include individuals with SCD age 26 years or older receiving care from an adult SCD provider. Recruitment will include both males and females, and all race and ethnicity classifications.

Advisor Subject Recruitment

Advisor subjects will be recruited at Atrium Health and other participating institutions. Recruitment will include individuals with SCD age 36 years or older receiving care from an adult SCD provider. Recruitment will include both males and females, and all race and ethnicity classifications.

Qualitative Participant Recruitment

Sites will be provided the IRB approved Qualitative Participant Recruitment script to ask participants for permission to share their names with Georgia Southern University faculty. Participant names will be entered into REDCap (Atrium Health's Secure Electronic Data Capture System). Sites will document a yes/no response from the participant in REDCap.

3.2 EA-SCD Eligibility

3.2.1 Inclusion Criteria

Subject must meet all the following applicable inclusion criteria to participate in this study:

1. Informed consent signed by subject or parent/ guardian (where applicable) and HIPAA authorization for release of personal health information. NOTE: HIPAA authorization may be included in the informed consent or obtained separately.

2. Assent will be obtained in appropriately aged subjects per IRB or institutional guidelines.

3. Age ≥ 16 and ≤ 25 years at the time of consent AND being cared for in a PEDIATRIC SICKLE CELL PROGRAM

4. Any sickle cell genotype

5. Not known to be currently pregnant

6. Readily available access to a computer with internet and phone

7. Ability to read and understand the English language

8. Subject is planned to be transferred to an adult sickle cell program within 6 -12 months of consent. If an EASCD subject, at a peer mentor site, is reconsented due to a delay in matching the EASCD subject must continue to meet eligibility from the date of reconsent.

3.2.2 Exclusion Criteria

Subjects meeting any of the criteria below may not participate in the study:

1. Already receiving one on one peer mentoring as part of a transition program
2. As determined by the Investigator, uncontrolled undercurrent medical, psychiatric, or cognitive condition, or social situation that would limit compliance with study requirements:
    - pregnant, incarcerated, or otherwise unable to attend all study related visits
    - lack of easy access to the technology required to complete study surveys (e.g., internet in home setting, public area or at local CBO) or to conduct mentoring sessions
    - other factors that would cause harm or increase risk to the participant or close contacts, or preclude the participant's adherence with or completion of the study

3.3 Mentor Eligibility

To be eligible to serve as a mentor, individual must meet all the following applicable inclusion criteria to participate in this study:

1. Informed consent signed by subject and HIPAA authorization for release of personal health information. NOTE: HIPAA authorization may be included in the informed consent or obtained separately.

2. Be an adult living with SCD who has successfully transitioned to adult care (defined as having had at least 3 clinical visits with an adult SCD provider/clinic within the past 24 months).

3. Age ≥ 26 years old

4. Readily available access to a computer with internet and phone

5. Have completed and passed a background check that reflects no prior convictions with the exception of minor traffic violations, parking tickets, and/or any dismissals

6. Ability to read and understand the English language

7. Endorsed by their healthcare provider as reliable and able to meet the physical, psychological and cognitive requirements for serving as a mentor

8. Have successfully completed Peer Mentoring University training

There are no exclusion criteria to list.

3.4 Advisor Eligibility

To be eligible to serve as an advisor, individual must meet all the following applicable inclusion criteria to participate in this study:

1. Informed consent signed by subject and HIPAA authorization for release of personal health information. NOTE: HIPAA authorization may be included in the informed consent or obtained separately.

2. Be an adult living with SCD who has successfully transitioned to adult care (defined as having had at least 3 documented visits of continuous care with a SCD provider/clinic within 24 months.

3. Age ≥ 36 years old

4. Readily available access to a computer with internet and phone

5. Ability to read and understand the English language

6. Endorsed by their healthcare provider as reliable and able to meet the physical, psychological and cognitive requirements for serving as an advisor

7. Have successfully completed Peer Mentor University training

There are no exclusion criteria to list.

3.5 Qualitative Research Eligibility

Participants who have been an active member of one of the site triads (adult/pediatric providers, community based organization, patient), a mentor or EA-SCD who enrolled in the study, or a patient or patient caregiver who interacted with the triad will be eligible to be contacted for future qualitative research.

3.6 Screen Failures

A consented subject who, for any reason (e.g., failure to satisfy the eligibility criteria or withdraws consent for study participation), terminates his/her study participation before enrollment (as defined in section 10.1) is regarded as a "screen failure." All screen failures will be recorded in the ST3P-UP Study REDCap database.

The Sponsor Investigator requests sites to also record pre-screen failures through REDCap. Pre-screen failure is defined as a subject that did not sign informed consent but was considered for potential study participation.

4. REGISTRATION AND RANDOMIZATION

4.1 Study ID Number Assignment

Following informed consent, subjects will be assigned a study ID number as determined by the Data Coordinating Center. This number will be used to register the participant into the study database (REDCap). Sites should complete all screening and baseline study assessments accordingly. Subject study assignment numbers will be issued by the DCC once the registration form has been uploaded and reviewed for completeness. This process may take up to 72 hours therefore sites should continue all study related assessments regardless of study number assignment.

4.2 Randomization Method and Stratification Factors

Sites will be randomized in a 1:1 fashion to either the STE+PM arm or the STE arm. To avoid cross- contamination, the randomization will be constrained so that the Novant and Atrium Health (formerly known as Carolinas Healthcare System) sites will be randomized to the same treatment arm. Prior to study activation, the LCI Department of Cancer Biostatistics will perform randomization. A stratified block randomization will be utilized, stratifying on site size (large [≥ 40 subjects] versus small [< 40 subjects]) to reduce confounding of comparisons between the treatment arms. Sites must have subcontracts executed and subjects must be registered and consented prior to starting study intervention. The study intervention is not blinded to the subject or the investigator.

5. STUDY PLAN

See Schema (page IV).

This multi-site, cluster randomized trial is designed to compare the effectiveness of transition programs that comprise of structured education-based transition program plus peer mentoring to structured education-based transition program alone in improving acute care reliance among EA-SCD. Using rapid cycle PDSA we will implement standardized transition processes within clinical practices in adherence to the Six Core Elements of transition as positioned by the Got Transition / Center for Healthcare Transition Improvement over 18 - 24 months.

The combination [STE+PM] intervention will be evaluated to determine if it results in a reduction of acute care reliance among EA-SCD and improves patient reported outcomes as measured by validated tools specific to the SCD population.

This study will last 5 years and includes at least 24 months of QI work to implement the Six Core Elements of transition within pediatric and adult SCD practices. Enrolled subjects will be tracked longitudinally for a minimum of 6 months in pediatrics to a minimum of 24 months in adult care to determine the impact of adding PM to standard education-based transition programming on clinical outcomes.

Enrollment in this study is voluntary and will not impact clinical care. ALL subjects seen at study sites may benefit from the QI work that will be offered, regardless of enrollment status on this study.

5.1 Study Intervention

5.1.1 Implementing a Structured Education Based Health Care Transition Quality Improvement Process [STE] within pediatric and adult SCD clinics

This intervention will involve incorporating the Six Core Elements of Health Care Transition into the pediatric and adult SCD clinics at each clinical site using quality improvement strategies. There will be 14 clinical sites enrolled in this trial. Each site is comprised of a pediatric SCD clinic, and adult SCD clinic and their partner CBO. Buy-in from both the adult and pediatric clinical leadership and the community has been obtained.

A study kick-off meeting will be held to orient all investigators, patient partners and research team to study procedures and to begin training on the QI process. Each of the 14 clinical sites and their corresponding CBOs will be provided funds to purchase a HIPAA compliant electronic tablet to facilitate education and training of site staff, stakeholders and study participants.

5.1.2 Transition QI Objective

The implementation of the Six Core Elements of health care transition into the clinical process will be evaluated every six months to assess the level of adherence to a standard process for transition for EA- SCD in both the pediatric and adult SCD clinics. This will be measured using a Health Care Transition (HCT) Process Measurement Tool. Specifically, sites with higher adherence are considered those with a higher than average score by the end of 24 months.

5.1.3 Starting a Transition Quality Improvement Process Using the Six Core Elements of Health Care Transition

Experience has offered some basic lessons to help start or improve a transition process for youth transitioning to adult care. Below are suggested initial steps that are applicable whether youth are moving from a pediatric practice and/or pediatric approach to care to an adult practice and/or adult approach to care. These are intended for use in pediatric, family medicine, medicine-pediatrics, and internal medicine practices (both primary care and specialty practices), and health systems. The outlined steps are interrelated and often occur at the same time, and the tips for success have been learned from transition improvement

projects across the United States. Transition tools and measurement resources to accompany these suggestions are available at: www.gottransition.org and in the study QI Binder. A compendium of resources and open access tools will be provided to each site in the form of a Transition QI "Change Package" to support the QI work that sites will be doing.

5.1.4 ST3P-UP Application

This mobile app based on both Android and iOS platforms will be deployed to all site investigators and their clinical team, as well as all mentors, advisors and transition coordinators. This app will provide access to decision support tools to enhance the transition experience of all patients as they see their provider. It will provide ready access to the 2014 National Heart, Lung, And Blood Institute [NHLBI] SCD clinical guidelines and ambulatory care clinical pathway for management of SCD according to genotype and age/gender. This app will also house the "Who, What, Where, When, Sickle Cell Transition Education Module" that can be deployed during clinic visits and other patient encounters to ensure that the appropriate educational content is made available to the EASCD patient. An important feature of this app is the "Reach Out" feature that allows the ST3P UP site PIs the ability to communicate amongst themselves within the protocol network to address specific clinical dilemmas and questions in close to real time. In addition, the ST3P UP app allows the Transition Coordinators the ability to communicate with ST3P-UP study participants to address questions that will facilitate adherence to study procedures and clinical appointments.

Table for Structured Transition Program [STE] Collaborative Change Package

A. Initiating a Transition QI Project ° Raise staff awareness of need for the Structured Transition Program ✓ Introduction to Six Core Elements ° Establish a Transition team with identified roles ° Introduction to Quality Improvement Process ✓ Develop an Aim statement ✓ Understand the PDSA process ° Complete practice assessment or organizational assessment
B. Professional Education ° Webinar 1 – Care Coordination: Starting a Transition Process ° Webinar 2 – Care Coordination: Transition Preparation ° Webinar 3 – Care Coordination: Transfer to Adult Care ° Webinar 4 – Care Coordination: Integration into Adult Care ° Webinar 5 – Care Coordination: Youth/Young Adult and Parent Engagement
C. Transition Policy ° Process developed for review of Transition Policy by patient/parent with transition team ° Process developed for sharing Transition Policy with all patients ° Communication with patients and family
D. Patient Tracking and Monitoring ° Process developed for tracking patients of transition age ° Options (paper checklist, excel, Redcap, EMR) ° What is tracked – demographic, diagnostic data, date received each core element
E. Readiness Assessment ° Process for administering TIP-RFT ° Review TIP-RFT

F. Transition Planning ° Goal setting based on TIP-RFT readiness assessment tool ° Start updating the Transition Summary ° Prepare youth for adult approach to care – should start at age 18y ° Transition Checklist ° Provide links and resources for insurance, emergency care plan, legal documents, etc.
G. Transfer of Care ° Confirm date for first adult provider appointment ° Complete Transfer package ° Confirm appointment was made
H. Transfer Completion ° Ensure ongoing adult follow up every 3 months for up to 24 months ° Contact young adult regularly to confirm transfer occurred and remains in adult care ° Communicate with adult practice confirming completion of transfer process and help as needed ° Build ongoing collaborative relationship with adult practice

5.1.5 Implementation of a Virtual Peer Mentoring Program for EA-SCD at sites randomized to Peer Mentoring

The PM Arm of the study will be supported using technology via the InquisitHealth™ Mentor 1to1TM platform. InquisitHealth™ Mentor 1to1TM is a full-service virtual mentoring platform vendor focused on improving clinical outcomes of high risk, high cost patients by connecting them to peer mentoring support that is standardized and structured without burdening resources. Mentor 1to1™ will be used to connect mentors to mentees and will be the sole method for conducting the secure mentor-mentee communication required for the study.

The Peer Mentoring program is a telephone-based health coaching intervention. The program pairs emerging adults transitioning from pediatric to adult care with mentors who themselves have successfully navigated their own transitions in the context of SCD. Through Mentor 1to1TM, the mentee and mentor arrange a time to speak via the platform on a regular basis and can also securely communicate via text messages within the platform. During the phone calls, trained and supervised mentors guide mentees through adaptive behavioral changes specific to SCD transition.

Peer Mentoring Platform Structure: We will utilize a virtual mentoring platform called Mentor1to1TM. The Mentor1to1TM platform creates the foundation for effective, scalable delivery of 1-on-1 peer mentoring. It is a HIPAA-compliant 1-to-1 Mentoring Platform that provides a variety of tools that allow mentors to communicate with their mentees (via phone/SMS) while they also effectively manage mentee-mentor relationships and track their mentee's progress. The platform was built with two purposes in mind: bring maximum efficiency to mentors while using insights and data to tailor the mentoring journey for each mentee - all in a secure shell. Mentor1to1TM provides two platforms that facilitate the mentoring process:

- Administrator Platform: The administrator platform will be used by the study project manager or designee to track advisor-mentor chat messages and mentor-mentee phone calls for quality assurance and ongoing training purposes. The study project

manager or designee will monitor advisor-mentor and mentor-mentee assignment ratio to ensure it remains consistent with protocol requirements. Individual sites will not be allowed to access the administrator platform.

- Mentor Platform: The mentor platform will be used by advisors, mentors, and mentees for all advisor-mentor and mentor-mentee communication. Advisors will use the platform to accept mentor assignments and send messages via the chat feature to the mentors. Mentors will use the platform to accept mentee assignments, initiate phone calls with mentees, and to access a list of suggested talking points geared to improve disease self-management. The mentor platform also allows advisors and mentors to complete escalation forms for issues that go beyond their scope or comfort (e.g. medication supply/cost, gaps in/loss of insurance coverage, stress/mental health, etc.). The DCC will be notified by InquisitHealth™ and will have 72 business hours from this time to inform the appropriate clinical site. For urgent needs, the mentor is advised to instruct the mentee to call their provider or 911. Individual sites will not be allowed to access the mentoring platform.

5.1.6 Peer Support for Mentors from dedicated "Advisors"

At the request of the community, we have incorporated the concept of "Advisors" into this PM program. An Advisor is an older individual living with SCD who has also successfully navigated the transition into adult care and who provides support to the Mentors enrolled in this project.

The Advisor Arm of the study will be supported using technology via the InquisitHealth™ Mentor 1to1™ platform to enroll and train advisors (similar to the mentor training but without practice calls). Mentor 1to1™ will be used to connect advisors to mentors and will be the sole method for conducting the secure 1:1 advisor-mentor communication required for the study. Through Mentor 1to1™, the advisor can send secure messages to their assigned mentor using the chat feature within the platform on, at least, a monthly basis. The purpose of this communication is to offer additional support and encouragement for the mentor as they proceed along their mentoring journey.

5.2 Procedures for Standardizing PM Implementation at Each Site

Peers are individuals who share some common characteristics, attributes or circumstances. These may relate to age, ability, interests, etc. Peer mentors are individuals who have more experience within a common area along with additional training in how to assist another in acquiring skills, knowledge and attitudes to be more successful. Peer mentoring is a process through which a more experienced individual encourages and assists a less experienced individual to develop his or her potential within a shared area of interest.

5.2.1 Mentor / Advisor Recruitment Strategies

Recruitment strategies used in this project will include:

- Direct contact by site transition coordinator
- Promotion of the project within CBOs, adult clinics, etc. using recruitment flyers including using social media.
- Distribution of IRB-approved recruitment material provided by the Sponsor by direct email, via US mail, or in-person at community events.
- Contacting hematology colleagues to explain the project and seek referrals

- Giving presentations to student or community groups, conferences and other venues
- Contacting individuals with SCD with prior interest in peer support projects

5.2.2 Identifying Mentors/Advisors

Clinical sites will identify mentors and advisors via a collaborative effort between the site's pediatric and adult SCD clinics and the affiliated community-based organization (CBO) during the enrollment phase of the study. Clinical and CBO staff will determine if identified mentors/advisors are interested in participating in the project and the potential mentor/advisor will be referred to their partner adult SCD Clinic for consenting, eligibility verification and enrollment onto study (if their partner clinic is randomized to be a peer mentoring site). If their partner adult SCD clinic is not randomized to peer mentoring, the potential mentor/advisor will be referred to the DCC, who will then refer them to an appropriate peer mentoring site for completion of consent and eligibility verification. CBOs and pediatric clinics will not be consenting mentors/advisors. Once a potential mentor/advisor has been consented, eligibility will be confirmed (including a background check for mentors). Checkr™ is a company that provides modern and compliant background checks for InquisitHealth™, and, once cleared and deemed eligible, potential mentor/advisor will be enrolled and scheduled for formal orientation and training. Cleared and deemed eligible is defined as having no prior convictions with the exception of minor traffic violations, parking tickets, and/or any dismissals. The DCC will communicate the pass/fail result of the background check to the appropriate peer-mentoring site. Training for mentors and advisors will include orientation to the Mentor1to1™ Platform.

5.2.3 Mentor/Mentee and Advisor/Mentor Matching

A mentor's experience with managing their disease supported by a written endorsement recommendation by an adult sickle cell provider will be a consideration in being selected to participate in this project as a mentor. Similarly, an advisor's experience with managing their disease supported by a written endorsement recommendation by an adult sickle cell provider will be a consideration in being selected to participate in this project as an advisor.

Matching of mentors to mentees will be facilitated via the Mentor1to1™ platform, with matching based on age (at least 5-year age difference between mentor/mentee), availability for scheduling mentoring phone calls, and mentee's gender preference as indicated in the informed consent form (ICF).

Matching of advisors to mentors will be facilitated via the study EDC (REDCap) platform, with matching based on age (at least 5-year age difference between advisor/mentor, unless the mentor is greater than 40 years of age) and availability for taking on an additional mentor as indicated in the ICF. Matching of advisors to mentors will not be facilitated via the Mentor1to1™ platform with oversight from the DCC, however all contact between advisors and mentors will be only through the Mentor1to1™ platform.

To reduce the potential for mentor / mentee or advisor/ mentor communication outside of the platform, mentees will be matched to mentors outside of their local site and mentors will be matched to advisors also outside of their local site.

•Mentors will be assigned mentees based on a mentor:mentee ratio of up to 1:3 at any point in time, and mentorship will continue until the end of study. The Mentor1to1™ platform and study EDC platform will track the number of assigned mentees to each mentor and only add an additional mentee when review of mentoring progress shows that mentor is comfortable and successful in working with current mentee(s) with capacity to add another.

- Should a mentee go off study prior to end of study, the mentor will have availability to be assigned a new mentee.
- Should a mentor go off study prior to end of study, the mentees assigned to that mentor will be reassigned to another mentor.
- If a mentor is unable to continue with their study related activities, an alternate mentor will be recruited.
- Should a mentor be consented, but not initiate training within 30 days and/or complete training within 60 days of consent, he/she will be deemed a screen fail.
- Should a mentor consent to study but fail to be enrolled within 90 days consent or reconsent he/she will be deemed a screen fail.
- Reconsent will be obtained according to Advarra IRB's policy.

•Advisors will be assigned mentors based on an advisor:mentor ratio of up to 1:5 at any point in time, and mentorship will continue until the end of study. Advisors will communicate with their mentors at least once monthly through the platform. The study EDC platform will track the number of assigned mentors to each advisor and only add an additional mentor when review of advisor ratio is under the maximum allowed of 1:5.

- Should a mentor go off study prior to end of study, the advisor will have availability to be assigned a new mentor.
- Should an advisor go off study prior to end of study, the mentors assigned to that advisor will be reassigned to another advisor.
- If an advisor is unable to continue with their study related activities, an alternate advisor will be recruited.
- Should an advisor be consented to study, but not initiate training within 30 days and/or complete training within 60 days of consent, he/she will be deemed a screen fail.
- Should an advisor consent to study but fail to be enrolled within 90 days of consent or reconsent, he/she will be deemed a screen fail.
- Reconsent will be obtained according to Advarra IRB's policy.

5.2.4 Mentor/Advisor Training

Once mentors /advisors are recruited and deemed eligible they will be scheduled to receive 8- 10 hours of structured virtual training that will be conducted via the Peer Mentor University platform. The virtual training is expected to be completed in no more than 3 weeks (+/- 1 week) from enrollment. Once this virtual training is complete, the mentor / advisor will then be trained on how to access and use the Mentor1to1™ platform to make the required mentoring contacts via telephone (mentors to mentees only) and contacts via SMS messaging (required for all advisor and mentor contacts). SMS messaging can be used as a supplementary resource for mentor to mentee contacts). Mentors will receive an automated

email from InquisitHealth™ to establish an account which prompts them to proceed with platform training.

Mentor/advisor education material specific to SCD have been created for use with the Mentor1to1TM platform and was prepared in line with evidence-based "Elements of Effective Practice for Mentoring" prepared by the National Mentoring Partnership (Elements for Effective Practice for Mentoring, 2015) following the guidelines provided in Chronic Disease Self-Management (CDSM) program.

Mentor contact via telephone calls (and supplemental SMS messaging) will be monitored and evaluated through the Mentor1to1™ Administrator Platform. Calls between mentors and mentees will be recorded and monitored periodically for quality assurance. All transcripts of mentor–mentee supplemental communication via SMS messaging through the platform will also be available for review for quality assurance by platform administrator.

Mentors will initially be assigned 1 mentee and will complete 1-2 calls with their mentee. These initial calls will be monitored retrospectively by the platform administrators or designee to determine adherence to talking points, quality of mentorship, and to determine any areas of improvement for the mentor. Based on completion of at least four Mentor-Mentee calls, Mentors will be evaluated and assigned additional mentees (up to a maximum of 3) or a plan for improvement in mentoring skills.

- Mentors are expected to have at least 4 calls within a calendar month with mentees during the first 3 months after enrollment.
- Once a total of 12 calls have been completed AND at least 3 months have elapsed since enrollment, mentors are expected to have at least 2 calls per calendar month with mentees until the completion of the study.
- This call frequency will be used for both prospective evaluation and retrospective data to help define potential deviations.

In rare cases, it may be determined that the individual is not a good fit for the role of a mentor. In these cases, the individual will be provided with feedback and will be disenrolled from the platform by the administrator.

- Advisor contact with a mentor via SMS messaging through the platform will be expected to occur at least monthly but may occur more often based on the relationship built between advisor and mentor. All advisor to mentor communication transcripts will be available for review for quality assurance by platform administrator.
- Supplemental mentor / advisor training will be provided virtually and facilitated by the partner CBO and/or will occur during the annual PM conference. Supplemental mentor / advisor training will occur within 6 mo (+/- 1 mo) of initiation of mentoring role (defined as first mentor-mentee or advisor-mentor call).

Annual refresher training will be provided at the PM conferences (either in-person or virtually) to all mentors and advisors.

Virtual supplemental training will also be available if mentors and advisors are not able to attend the annual PM conferences.

5.2.5 Mentor – Mentee and Advisor – Mentor Communication

Participants will ONLY communicate using the Mentor1to1™ application via a laptop or desktop computer. Each participant will be asked to create a unique password to access the application.

The Mentor1to1™ web-based application software uses two-way line-bridging technology and text messaging to facilitate peer mentoring relationships. The system uses a generic phone number to call the mentor and mentee separately then bridges the line together. Phone numbers are not exchanged between the mentee and mentor, and thus calls are not possible during non-scheduled times. Mentees can respond to phone calls from their mentor through the system generated phone number; they will be prompted to leave a voice message that is delivered to the mentor.

- Mentors are expected to have at least 4 calls within a calendar month with mentees during the first 3 months after enrollment.
- Once a total of 12 calls have been completed AND at least 3 months have elapsed since enrollment, mentors are expected to have at least 2 calls per calendar month with mentees until the completion of the study.
- This call frequency will be used for both prospective evaluation and retrospective data to help define potential deviations.
- Advisors should have contact with mentors monthly.
- Automated phone calls may be generated by Mentor1to1TM platform to the mentees if they become hard to reach. Similar alerts are sent to the mentors if they have not made their required mentoring contacts and/or have incomplete mentoring workbooks after a mentoring call. Structured responses, as appropriate will be sent with specific instructions (best time to call, etc.).

5.2.6 Mentor/Advisor Retention

CBOs will be responsible for engaging mentors/advisors in activities such as Community Advisory Board Meetings, community engagement activities and support groups.

- Mentors will be assigned advisors to provide ongoing support and to help reduce mentor burnout.
- Mentors and advisors will be invited to attend an annual mentor conference to provide ongoing education and training, improve the mentoring experience, and enhance mentor and advisor retention. The annual mentor conference will occur every year until the end of the study

5.2.7 Mentor/Advisor Compensation

If permitted under applicable regional laws or regulatory guidelines, mentor/advisors may be reimbursed for time and effort directly related to their role and responsibilities as outlined in the ICF.

5.3 Study Outcome Measures

Study-related surveys will be completed on paper, administered via study-supplied iPad or tablet either within a healthcare setting or sent electronically to the EA-SCD participants via a link

through REDCap by email. EA-SCD participants will be encouraged to access their ongoing study assessments online, or on paper either at home or during a scheduled study-related clinic visit to optimize study data capture.

5.3.1 PedsQL™ Sickle Cell Disease Module

The **PedsQL™** Sickle Cell Disease Module 3.0 comprises 6 domains and was derived from qualitative methods involving patient/parent interviews and expert opinion across multiple sites and has been validated for use in the evaluation of SCD specific health related quality of life in research and clinical practice.[50] This 43-item scale measured on a 5-point Likert-type scale shows excellent feasibility, excellent reliability for the Total Scale Scores (patient self-report $\alpha = 0.95$; parent proxy- report $\alpha = 0.97$), and good reliability for the nine individual scales (patient self-report $\alpha = 0.69–0.90$; parent proxy-report $\alpha = 0.83–0.97$).

5.3.2 ASCQ-Me QOC

Adult sickle cell disease care poses significant challenges resulting from poor access to knowledgeable providers and suboptimal treatment in the Emergency departments. The ASCQ-Me quality of care measure was developed to assess the quality of ambulatory and emergency department care experienced by persons living with SCD. The SCD quality of care survey questions were developed and pilot tested in 557 patients using methodology consistent with the Consumer Assessment of Healthcare Providers and Systems survey. This measure is useful in documenting and tracking disparities in quality of care for SCD. [51]

5.3.3 Sickle Cell Transition Intervention Program – Readiness for Transition (TIP-RFT) Assessment

The Sickle Cell **TIP-RFT** instrument was developed to provide a validated SCD specific readiness for transition assessment tool with established reliability for routine use in the clinical domain.[17] The current TIP-RFT has 4 subscales and 54 items that quantifies knowledge, skills and attitudes necessary for a successful transition from pediatric to adult care.[16,52] The domains assessed include knowledge and skills in medical self-care, social support, health benefits, independent living and educational/vocational skills. The TIP-RFT assessment will be used to guide interventions to improve transition readiness and can provide a foundation for future research on other variables that might be associated with transition readiness.

5.3.4 Medical Outcomes Study – Social Support Scale (MOS-SSS)

The Medical Outcomes Study - Social Support Survey (MOS-SSS) was developed as a brief multidimensional social support survey for persons living with chronic illness.[53] MOS-SSS assesses support ranked on a 5-point Likert-type scale along four dimensions, emotional /informational, tangible, affectionate, and positive social interaction, to give an overall functional social support index.[53]

5.3.5 Healthcare Transition Feedback Survey for Youth/Young Adult

This survey will provide feedback information on the experiences of youth and young adults with the transition process. This 13-question survey solicits EA-SCD subject-reported feedback on their clinical experiences while in the process of transition from a pediatric SCD clinic to an adult SCD clinic.

5.3.6 Health Care Transition (HCT) Process Measurement Tool

To determine the level of improvement in a practice with adherence to the Six Core Elements, each pediatric and adult practice will be scored according to whether some or all of the implementation steps have been completed using the HCT Process Measurement Tool developed by GotTransition.org. Scores for each step will vary depending on complexity or importance. Each practice will be scored every six months to determine the degree to which they move closer to adherence to the desired standardized clinical practice pattern.

6. STUDY CALENDAR

6.1 Site Level Quality Improvement Calendar

Site Level Quality Improvement																					
Study Month	**Baseline**	**3**	**6**	**9**	**12**	**15**	**18**	**21**	**24**	**27**	**30**	**33**	**36**	**39**	**42**	**45**	**48**	**51**	**54**	**57**	**60**
Health Care Transition Process Measurement Tools (Pediatric Clinic)	●	Every 6 months																			
Health Care Transition Process Measurement Tools (Adult Clinic)	●	Every 6 months																			
Satisfaction with Transition Services (Provider)	●	Annually																			

6.2 Site Level Advisor/Mentor Calendar

Site Level Peer Mentoring																						
Study Month	**Screening**	**Baseline**	**1**	**2**	**3**	**6**	**9**	**12**	**15**	**18**	**21**	**24**	**27**	**30**	**33**	**36**	**39**	**42**	**45**	**48**	**51**	**54**	**57**	**60**
Informed Consent	•																							
Determine Eligibility	•																							
Demographics/Disease Characteristics	•																							
Mentor Role Training	•																							
Advisor/Mentor sign W-8 or W-9 Form	•																							
Distribution of Greenphire Clincard to Advisor/Mentor	•																							
Train on Mentor 1to1 Platform[a]	•																							
Test Mentor-Mentee call(s)[b]	•																							

Assign Mentee[c]		•				
Supplemental mentor/advisor in person training[d]						
Mentor- Mentee Contacts 4 times a month for first 3 months[c]			•	•	•	
Mentor- Mentee Contacts 2 times per month[c]						Mentor contacts Mentee 2 times per month starting in month 4
Advisor- Mentor contacts monthly			Advisor contacts Mentor monthly throughout study			
Attend CBO Engagement Activity[a]			Attend bi-annual CBO engagement activities and CAB meetings			
Annual Refresher Training[e]		PM Sites Only				Annual beginning in year 2

a - Mentor training must be initiated within 30 days of consent and training must be complete within 60 days of consent.
b - Test or "mock" Mentor -Mentee call(s) will be done through the platform with a DCC designee as part of initial Mentor/Advisor Training.
c - Additional mentees may be added, as appropriate up to a maximum of 3 per mentor at any given time, after completion of at least four Mentor-Mentee calls or DCC approval of additional mentee. Mentors are expected to have at least 4 calls within a calendar month with mentees during the first 3 months after enrollment. Once a total of 12 calls have been completed AND at least 3 months have elapsed since enrollment, mentors are expected to have at least 2 calls per calendar month with mentees until the completion of the study.
d - Supplemental mentor / advisor training at the partner CBO /PM conference will occur within 3 mo +/- 1 mo after mentoring has started. This can also be provided via 1:1 virtual training by the DCC consultant
e - Mentors and advisors will be invited to participate in an annual mentor/advisor conference, but attendance is optional; for those unable to attend, and virtual training will be available.

6.3 EA-SCD Participant Level Assessment Calendar

EA-SCD Participant Level Assessment Calendar																								
Study Month	**Screening**		**Baseline**	**3**	**6**	**9**	**12**	**15**	**18**	**21**	**24**	**27**	**30**	**33**	**36**	**39**	**42**	**45**	**48**	**51**	**54**	**57**	**60**	**Off Study**
	All Sites	**Peer Mentor Sites Only**																						
Eligibility Screening	●																							
Informed Consent / Assent	●																							
Demographics/Disease Characteristics[a]	●																							●
Mentor Matching[b]		●[g]																						
Acute and Ambulatory Care Visit Data Collection[c]			●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Transition Education Intervention Q3			●[h]	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
PedsQL-SCD Module			●[h]		●		●		●		●		●		●		●		●		●		●	●
MOS-SSS			●[h]		●		●		●		●		●		●		●		●		●		●	●
TIP-RFT			●[h]		●		●		●		●		●		●		●		●		●		●	●
ASCQ-ME QOC			●[h]		●		●		●		●		●		●		●		●		●		●	●
Health Care Transition Feedback Survey for Youth/Young			●[h]				●				●				●				●				●	●
ST3P-Up App	Download[e]		Download[f]	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●

a - Demographic information collected at baseline will be re-assessed at end of study for updates and/or changes
b - During screening, EA-SCD subjects are required to provide their day/time availability for peer mentoring calls to facilitate mentor matching. These subjects MUST be matched to a mentor prior to administering baseline surveys
c - Ambulatory and acute care visits will be collected for the preceding 12 months (a month is defined, numerically, as 30.4375 days, and visit windows are based on the date of enrollment). Ambulatory visits will include visits within the healthcare setting, primary care visits, and virtual visits via telephone ONLY. Acute care visits may include, but are not limited to ED, urgent care, day hospitals, infusion centers, and hospital admissions.
d - Study visits will occur with a +/- 4 weeks window for q3mo visits. EA-SCD subject must be seen by their SCD provider during these visits. However, these visits may occur in other locations within the healthcare setting where SCD care is provided or virtually as long as required structured and targeted transition education is provided

e - ST3P-UP App contains "Who, What, Where, When" Sickle Cell Transition Education Modules that are required for 3-month visits. If app is not available, the education modules are provided to the sites in the QI Change Package and via PowerPoint from the DCC. Alternatively, sites can utilize any standard SCD education module.

f - Patients are encouraged but not required to download the ST3P-UP App. Directions to access the ST3P-UP app and instructions for use will be provided to participants by local site Transition Coordinators. Transition Coordinators are encouraged to use study- provided tablets and/or iPads to facilitate follow- up visit adherence communication and for structured transition education.

g - For PM sites, mentee availability should be captured in the REDCap database at the time of consent. For subjects with delayed enrollment, confirmation of availability should be revisited at the time of Mentor-Mentee matching.

h - Every effort should be made to complete the baseline survey within a healthcare setting but if administration occurs via survey link, this must be provided to the participant within 72 hours from the date of consent (for the STE arm) or from the date of match (for the PM arm). The survey link will expire within 2 weeks of receipt. If the survey remains incomplete after two weeks, please discontinue efforts to contact the participant for completion of the baseline survey.

6.4 Schedule of Assessments

6.4.1 Screening

Subjects who consent for participation and meet the eligibility criteria for enrollment into this study will undergo the following screening assessments (See Section 3.2 for additional details on assessments):

- Collection of baseline demographic and disease characteristics:
  - Date of birth
  - Age
  - Race
  - Ethnicity
  - Gender
  - Sickle cell genotype
  - Zip code of residence (for urban vs rural residency status)
  - Presence of a sibling, parent, or child (first degree relative) with SCD
  - Academic achievement
  - Disability status
  - Marital status
  - Employment status
  - Living arrangement
  - Household income

- Mentor matching (Peer Mentoring sites only)
  - Mentee day/time availability information capture
  - Match facilitated through the Mentor1to1™ platform

6.4.2 Baseline

Subjects who are enrolled into this study will undergo the following baseline assessments (See Section 3.3 for additional details on assessments):

- SCD Provider Clinic Visit
- Historical Healthcare Utilization Data Collection: acute care utilization history (ED/ urgent
- care visits and hospital admissions) and ambulatory visits (SCD provider and Primary Care provider) in the preceding 12 months from the date of enrollment
- TIP-RFT
- MOS-SSS
- ASCQ-Me QOC
- PedsQL-SCD Module
- Health Care Transition Feedback Survey for Youth/Young Adults

6.4.3 Every 3 months after enrollment

- SCD Provider Clinic Visit

A Study Visit will be defined as a touch point with the healthcare team (either in person or virtually) during which the participant receives the structured transition education intervention. The education can be shared with a participant during the virtual visit and providing review or sharing the educational tools via email and requesting a response in review of the information.

- Healthcare Utilization Data Collection: acute care utilization history (ED/urgent care visits and hospital admissions) and ambulatory visits (SCD provider and Primary Care provider) in the preceding 3 months

- "**Who, What, Where, When, Sickle Cell Transition Education Module"** and/or other sickle cell structured transition education will be shared with the patient either during a SCD clinic visit, at other locations where care is received within the healthcare system or virtually every 3 months to ensure ongoing structured transition education support.

6.4.4 Every 6 months after enrollment

- TIP-RFT
- MOS-SSS
- ASCQ-Me QOC
- PedsQL-SCD Module

6.4.5 Every 12 months after enrollment

- Health Care Transition Feedback Survey for Youth/Young Adults

6.4.6 End of Study

- Demographic update: any change in participant's demographics (e.g. zip code of residence, presence of a sibling, parent or child with SCD, academic achievement, disability status, marital status, employment status, living arrangement, and household income)
- Healthcare Utilization Data Collection: acute care utilization history (ED/ urgent care visits and hospital admissions) and ambulatory care visits (SCD provider and primary care provider) in the preceding 3 months
- TIP-RFT
- MOS-SSS
- ASCQ-Me QOC
- PedsQL-SCD Module
- Health Care Transition Feedback Survey for Youth/Young Adults

6.5 Schedule of Assessments (Mentors/Advisors)

6.5.1 Screening

Subjects who consent for participation and meet the eligibility criteria for enrollment into this study as mentors or advisors will undergo the following screening assessments (See Section 3.4 for additional details on assessments):

- Date of birth
- Race
- Ethnicity
- Gender
- Sickle cell genotype
- Zip code of residence (to determine urban or rural residency status)
- Presence of a sibling, parent, or child (first degree relative) with SCD
- Academic achievement
- Disability status
- Marital status
- Employment status
- Living arrangement
- Household income
- Age at transfer to adult care
- Type of SCD adult provider (primary care versus specialty)
- Mentor matching (Peer Mentoring sites only)
- Advisor matching (Peer Mentoring sites only)

6.5.2 Study Completion

- Demographic update: any change in participant's demographics (e.g. zip code of residence, presence of a sibling, parent, or child with SCD, academic achievement, disability status, marital status, employment status, living arrangement, and household income).

6.6 Schedule of Assessments – Quality Improvement (All Clinical Sites)

6.6.1 Baseline QI Assessment

- Health Care Transition Process Measurement Tools:
  - For Transitioning Youth to Adult Healthcare Providers (pediatric clinics)
  - For Integrating Young Adults to Adult Healthcare Providers (adult clinics)

- Provider Satisfaction with Transition Programming Feedback survey

6.6.2 Monthly QI Activities After Baseline Assessment

- Site Transition Team will meet monthly to work on implementing the Six Core Elements of transition
- Sites will attend monthly coaching calls hosted by the study QI team

- Sites will be directed to submit their progress on QI initiatives (specifically monthly chart audits on the number of completed readiness basement and emergency care plans) once they have completed the training on QI data collection
- Sites will participate in ongoing Community Advisory Board meetings with local Community-Based Organization per CBO required calendar.

6.6.3 Every 6 months QI Assessment

- Health Care Transition Process Measurement Tools
  - For Transitioning Youth to Adult Healthcare Providers (pediatric clinics)
  - For Integrating Young Adults to Adult Healthcare Providers (adult clinics)

- A formal ST3P-UP study site visit by the coordinating center's QI team will be done with each site to review progress and support QI initiatives in addition to reviewing overall study progress as the site. This may be either in person or virtually.

6.6.4 Every 12 months QI Assessment

- Provider Satisfaction with Transition Programming Feedback survey is administered annually

7. REMOVAL OF SUBJECTS FROM STUDY

7.1 Off Study

Subjects may stop their participation in this study at any time if they no longer wish to participate, or if the investigator believes this to be in the best interest of the subject. When subjects are removed from the study, the reason for study removal and date the subject was removed should be documented in the ST3P UP REDCap database. Reasons a subject may be removed from study include, but are not limited to:

- Subject non-compliance with study participation, in the opinion of the investigator
- The subject or legal representative (such as a parent or legal guardian) withdraws study consent
- The subject is lost to follow-up
- Study completion
- Investigator's decision to withdraw the subject
- Subject death

Subjects who have been lost to follow-up for a period without three documented follow up attempts, should be transitioned off study due to lack of compliance with the study required visits per protocol. The off-study date should be documented in the EDC as the day the PI deems the subject as coming off study. This date must correlate with the end of available utilization data after every effort has been made to collect and enter available utilization and survey data. In the event of discrepancy between the documented consecutive attempts to reach the patient and utilization data, please review the data with the DCC PIs to ensure the most appropriate date for

lost to follow up is documented. HIPAA guidelines must be followed. A copy of all communication sent to the subject will be maintained in the research chart.

Subjects that are off study will not participate in future or additional study-related procedures, including data collection.

Subjects who remain enrolled at the completion of the funded project will be off study on the date of study completion.

Subjects that are consented (but not enrolled on study) and withdraw participation will not be required to complete the end of study CRF. Documentation of study withdrawal should be maintained in the research chart.

7.2 Special Considerations

- Pregnancy: If pregnancy should occur post enrollment, the site PI should consult with the Sponsor to determine if the subject should continue to participate in the study.
- Subject Relocation: If subjects relocate away from a study site, the site PI should consult with the sponsor to determine the impact this will have on the subject's continued study participation.
- Other Forms of Mentoring: As part of this project, clinical sites cannot implement concurrent 1:1 mentoring program for patients in their practice regardless of site randomization status. Partner CBOs also cannot implement 1:1 mentoring for their clients with SCD. Many sites offer group mentoring activities such as support groups, girl/guy talks, etc. This is acceptable regardless of sites' randomization status.
- The use of Community Health Workers (CHW) is also common practice among CBO partners and is commonly used in clinical care. Therefore, with the exclusion on 1:1 mentoring, CHW can serve as a source of support for SCD clients regardless of randomization status.

8. DATA AND SAFETY

8.1 Safety Monitoring

This protocol will be monitored according to the processes in effect for all LCI investigator-initiated studies and the protocol-specific monitoring plan and will abide by standard operating procedures (SOPs) set forth by both Atrium Health (formerly known as Carolinas Healthcare System) Office of Clinical and Translational Research and LCI (and/or other participating institutional SOPs). It is the responsibility of the Sponsor-Investigator to monitor any safety data (i.e., unanticipated problems/potential risks, as per Section 9, regularly to monitor subject consents, enrollment and retention, safety data, and validity/integrity of the data. Documentation of these meetings will be kept with the study records. The LCI Data and Safety Monitoring Committee will provide central monitoring oversight for this study. This will be performed under the auspices of the LCI Data Safety Monitoring Plan. The Sponsor-Investigator will submit data to the LCI Data and Safety Monitoring Committee as required.

8.2 Data Monitoring

This study will be organized, performed, and reported in compliance with the study protocol, SOPs of the LCI and Atrium Health (formerly known as Carolinas Healthcare System) Offices of Clinical and Translational Research (and/or other participating institutional SOPs), and other applicable regulations and guidelines (e.g. ICH GCP).

Subjects will be monitored by each participating institution, as per their guidelines and policies. The LCI Research QA Department and the DCC will maintain central oversight. Data from this study will be collected on paper and/or electronic case report forms (eCRFs) and from study-specific applications. Monitoring will be done by comparing source documentation to the eCRFs. Any variation between the two data sets will be discussed with the Investigator and/or other study team members as appropriate. Investigators and their relevant personnel must be available during the monitoring visits and must allocate enough time to be devoted to the monitoring process.

Levine Cancer Institute (of Atrium Health, formerly known as Carolinas Healthcare System) will be the central data coordination and monitoring center for this study and will provide monthly progress reports to the Scientific Oversight Group. This will include monitoring of enrollment, derivation of study endpoints, data logic checks, assessment of data missingness, attrition, and safety. Importantly, ongoing estimation and monitoring of the coefficient of variation of site enrollment size will be conducted. This will allow risk-mitigating adjustments to the study enrollment strategy in the event it becomes apparent that the cluster size coefficient of variation markedly deviates from initial assumptions. Similarly, ongoing estimates and monitoring of the intra-class correlation [ICC] for acute care utilizations will be conducted. The cadence of the central monitoring will be monthly. Comprehensive monitoring reports will be provided to the Sponsor-Investigator, while reports focusing on enrollment, subject disposition, and safety will be provided to the Scientific Oversight Group. The goals of the data coordination and monitoring function include assurance of subject safety, and risk mitigation regarding enrollment targets, key design assumptions, and data quality.

9. POTENTIAL RISKS/UNANTICIPATED PROBLEMS

9.1 Potential Risks

In general, involving clinical practices in QI processes to standardize care delivery is widespread and accepted as posing no additional risk to the patient.

9.1.1 Subject Confidentiality

All data and records generated during this study will be kept confidential in accordance with Institutional policies on subject privacy and HIPAA; the investigators and other site personnel will not use such data and records for any purpose other than conducting the study. No breach of confidentiality is anticipated as no records will be shared with any personnel outside the research team. All medical information including assessments and other medical records will be recorded and stored in a database. The database will exist on password protected secured servers. All records will be kept confidential.

Calls between mentors and mentees will be recorded and may be monitored for safety purposes. Contacts between advisors and mentors via SMS messaging will be saved and may be monitored for safety purposes.

To minimize risks to confidentiality, data will only be monitored by the Principal Investigators and trained research staff. At a minimum, research staff will have completed basic human subject protection research training that includes content on vulnerable subjects (children).

Study platform vendor (InquisitHealth™) will utilize a 3rd party vendor (Checkr™) to conduct background checks for mentors and advisors and will make every effort to ensure confidentiality and protection of participants' information. Mentors and advisors will be asked to complete a W9 to facilitate participant reimbursement (if applicable). SickleSoft, Inc LLC, the ST3P UP Application developer, will provide oversight and manage access for sites roles within the application. They will make every effort to ensure confidentiality and protection of participants' information.

9.1.2 Emotional Distress

Some study activities can make participants feel uncomfortable, anxious, and/or emotionally fatigued which are symptoms of emotional distress. If an EA-SCD, mentor, or advisor experiences and reports emotional distress, study activities will be paused until the issue is resolved (see reporting in Section 9.2.2).

9.2 Unanticipated Problems (UAP)

9.2.1 Definition

A UAP is any incidence, experience or outcome that is unexpected (e.g., a lost or stolen laptop computer that contains sensitive study information) given the information provided in research- related documentation (e.g., informed consent) and the study population characteristics, that is related or possibly related to participation in the research study and places the participant at an increased risk.

9.2.2 Reporting

All EA-SCD UAPs related to study activities will be reported to the site study team by the participant. It is the responsibility of the site to report the event in the study REDCap UAP form within 5 business days of event awareness and to the central IRB within 10 business days of event awareness.

All mentor and advisor UAPs related to study activities will be reported through the InquisitHealth™ escalation form located within the platform. The DCC will be notified by InquisitHealth™ and will have 72 business hours from this time to inform the appropriate site. It is the responsibility of the site to report it in the study REDCap UAP form within 5 business days of event awareness, and to the central IRB within 10 business days of event awareness.

10. STASTICIAL CONSIDERATIONS

10.1 Milestones

10.1.1 Registration Date

For all Participants:

The date the subject signs the informed consent.

10.1.2 Enrollment Date

EA-SCD Participants:

The date the baseline survey is administered to a subject (either within a healthcare setting or via survey link).

For participants on the PM arm, administration of the baseline survey and completion of the enrollment CRF occurs after confirmation of mentor matching from the DCC (see study calendar 6.3).

Mentor and Advisor Participants:

The date the participant completes all training activities. For mentors, this is the date the participant completes practice call 2. For advisors, this is the date the participant completes Peer Mentor University training.

10.1.3 Off Study Date

For All Participants:

The date the subject terminates participation on the study or is removed from the study per the criteria in Section 7.1.

10.2 Sample Size and Accrual

Sample size calculations are based on the primary endpoint of acute care utilization visits per year (at the EA-SCD participant level). Utilizing a randomized cluster design, seven clinical sites will be randomized per arm. The sample size calculation strategy is to calculate the required minimum sample size based on an individual patient randomized design, and then inflate the sample size based on cluster randomized considerations.[54] A conservative estimate of the average acute care utilization rate for EA-SCD is 6 acute care visits per year based on data for North Carolina reported by the RuSH population surveillance project.[4] In South Carolina, the acute care utilization rates among 18-30 y with SCD was reported as 7.17 (95% CI 6.34-7.99).55 At Atrium Health (formerly known as Carolinas Healthcare System), 295 EA-SCD had 1972 emergency department visits and 221 hospital admissions in 2015 with an average acute care

utilization rate of 6.82 visits per year. This study is designed to detect a 20% reduction in the number of acute care encounters per year (assuming a base case of 6 encounters). A 20% reduction in acute care utilization is considered clinically significant based on patient partners reporting that 1 less acute care visit a year is meaningful. Based on a two- sided alpha = 0.05 significance level, 67 EA-SCD participants per arm would provide approximately 85% power to detect a 20% reduction in the number of acute care utilizations under individual randomization, assuming the number of encounters follows a Poisson distribution for rare events. The sample size will be inflated based on two parameters: the cluster size coefficient of variation and the intra-class correlation (ICC).[54] The cluster size coefficient of variation observed among the 14 participating clinical sites is 55%. Therefore, the coefficient of variation is assumed to be 60% and the ICC is assumed to be 0.05.[56] Based on these parameters, a minimum of 183 EA-SCD participants per arm (366 total EA-SCD participants) will retain approximately 85% power. To account for potential missing data and allow for robust evaluation of secondary endpoints the sample size will be increased to a total of 537 EA-SCD participants. It is estimated that this enrollment can be accomplished with an enrollment rate of 35% of the EA-SCD patient population.

10.3 Endpoints

10.3.1 Definition of Primary Endpoint

Acute care visits will be calculated for each EA-SCD participant as the average number of acute care visits over a24-month period. Acute care visits will also be calculated for each EA-SCD participant as the average number of acute care visits per year over the entire study as a secondary endpoint. Acute care visits may include, but are not limited to hospital admissions, ED, urgent care, day hospital, or infusion center visits. The calculations for these endpoints are below:

$$Months\ on\ study = \frac{(Off\ Study\ Date - Enrollment\ Date)}{30.4375}$$

$$Acute\ care\ visits\ per\ 24\ months = \frac{Total\ \#\ acute\ care\ visits\ reported\ on\ study}{Months\ on\ study} * 24\ months$$

$$Acute\ care\ visits\ per\ 12\ months = \frac{Total\ \#\ acute\ care\ visits\ reported\ on\ study}{Months\ on\ study} * 12\ months$$

10.3.2 Definition of Secondary Endpoint

Quantitative EA-SCD participant-reported outcome scores will be captured longitudinally for each subject. Data will be collected for each subject using the following scales:

- Adults Sickle Cell QOC Measure (ASCQ-ME QOC) for health-related quality of life
- PedsQLTM-SCD module for health-related quality of life
- Medical Outcomes Study Social Support Survey (MOS-SSS)
- Transition Readiness Score as measured by the TIP-RFT scale
- Health Care Transition Feedback Survey

Count variables capturing healthcare utilization will be calculated for each EA-SCD participant for the following variables. These will be annualized to 12-month and 24-month periods as described above.

- The number of ambulatory visits
- The number of visits with adult providers
- The number of hospitalization days
- 14-day and 30-day readmission rates

10.3.3 Definition of Intervention Fidelity (PM Intervention Feasibility) Endpoint

- The number of consented mentor candidates that complete each step of eligibility and training activities (i.e., background check, practice call 1, PMU training, practice call 2, match with EA-SCD)
- Timelines for major milestones for Mentors
    - Time from consent to background check result
    - Time from background check result to practice call 1
    - Time from practice call 1 to completion of PMU training
    - Time from completion of PMU training to practice call 2 (enrollment/completion of training activities)
    - Time from practice call 2 to first match with EA-SCD (post-enrollment)
- Time from first consent date to enrollment for EA-SCDs on the PM arm
- Frequency of mentor-mentee contacts via the platform

10.3.4 Definition of ST3P UP Application Usage

- Usage will be documented in two ways for each study subject (EA-SCD, mentor, and advisor):
    - Frequency of contacts between subjects and transition coordinator
    - Frequency of educational resource views
- Usage will also be documented on the investigator and transition coordinator level, as frequency of contacts between investigator and transition coordinator and contacts between investigators across sites within the project.

10.3.5 Definition of Site-Level Endpoints

Health Care Transition Feedback Survey for providers:

- Provider satisfaction with transition services will be collected using a standard 5-point Likert scale.

Health Care Transition Process Measurement Tools:

- For Transitioning Youth to Adult Healthcare Providers (pediatric clinics)
- For Integrating Young Adults to Adult Healthcare Providers (adult clinics)

These elements of healthcare transition will be captured longitudinally for each site and will consist of the Core Elements of Health Care Transition. Scores will be self-reported by sites and then confirmed by the QI Coordinator. All Core Elements scores will be a

weighted sum of the individual items, and the overall HCT score will be a sum of the Six Core Element scores.

10.4 Analysis Populations

All EA-SCD participant-level analyses will be conducted on the population of all enrolled EA-SCD participants (consented EA-SCD participants who are enrolled per section 10.1.2), regardless of how long the EA-SCD participant was on study or regardless of the extent of data missingness.

10.5 Analysis Methods

10.5.1 Timing of Analysis

Study outcomes will be evaluated on an ongoing basis to monitor enrollment, derivation of study endpoints, assessment of missingness, and attrition. Additionally, the cluster size coefficient of variation and ICC will be evaluated on an ongoing basis to assess design assumptions.

A planned interim analysis will be performed as described in Section 10.5.8. A final analysis will be conducted after all EA-SCD participants are off study.

10.5.2 Subject Disposition

EA-SCD participant disposition will be provided in terms of a CONSORT diagram with an extension to cluster randomized trials. This will include all EA-SCDs consented, those initiating transition, and EA-SCD withdrawals. Reasons for EA-SCD withdrawals will be provided as well as a summary of the number of and reasons for missing data for key outcome measures.

10.5.3 Baseline Subject Characteristics

A summary of EA-SCD participant demographics, disease characteristics, and acute/ambulatory care utilization in the 12 months prior to enrollment will be assessed.

A summary of mentor/advisor demographics and disease characteristics will also be completed.

10.5.4 Primary Analysis

To evaluate the impact of PM, the acute care utilization rate per year will be compared between the PM+STE and STE arms. This will be accomplished using generalized linear mixed model with a Poisson distribution-log link construct. The model will include fixed effects for baseline acute care visits per year, the stratification factor (large sites vs small sites) and treatment arm, and a random effect for clinical site. Corresponding 95% confidence intervals will be calculated for the estimated ACU rate in each treatment arm.

Supportive and sensitivity analyses will be conducted to include potential confounding factors such as urban versus rural sites, education level, older first degree relative with SCD, genotype, age at transfer to adult care, and type of receiving provider (primary versus specialty). Univariate models will be fit for each factor, and those identified to be individually prognostic will be included in a multivariable model, and backward elimination followed by forward selection will be used to identify factors that are independently prognostic and to establish a final base model. Finally, treatment arm will be added to the base model to evaluate the impact of the intervention adjusting for significant baseline factors.

Two analyses will be conducted to estimate the impact of differential accrual between arms over time: (1) An additional term of year of enrollment will be added to the GLMM as a categorical variable; (2) We will subset the analyses to EA-SCD who were contemporaneously enrolled. Comparison of the PM+STE and STE ACU estimates from this subset to those results including all enrolled with and without controlling for year of enrollment will provide a comprehensive assessment of the potential bias due to differential accrual between arms over time. ACU rate in the STE only arm will be compared to historical ACU rates which were used for the original power calculations. Although these are comparisons to historical controls, this will provide preliminary evidence using a robust sample size of the potential impact of the structure transition education.

An additional sensitivity analysis will be conducted to assess the impact of the cluster of mentees/patients within mentors for the intervention arm. We will analyze the data using the recommended heteroscedastic partially nested mixed effects model (Candlish et al BMC Medical Research Methodology 2018 18:105) and compare the results to the primary analysis which only adjusts for the clustering within site.

Additionally, the number of ambulatory visits, the number of visits with adult providers, hospitalizations, and readmissions will be analyzed in a similar fashion as described above. An acute care reliance measure will be estimated based on the model-based estimates of **Acute Care Visits / [Acute Care Visits + Ambulatory visits].**

10.5.5 Secondary Analysis

EA-SCD PRO's will be analyzed quantitatively using linear mixed models for repeated measures. The models will include fixed factors for baseline scales, the site size stratification factor, treatment arm, assessment time point, and the treatment arm by time point interaction. Random factors will include investigational site and subject within site to account for correlation in responses within individual sites and within the same subject. Model-based estimates of PRO scores will be used to estimate percentage change between the treatment arms. Additionally, PRO will be analyzed using survival analysis techniques. For each EA-SCD participant, the time from baseline to a 10% worsening (TTW) in the scale will be calculated. For EA-SCD participants not experiencing a 10% worsening, TTW will be censored at the last patient reported outcome assessment. TTW will be analyzed using Kaplan-Meier techniques and Cox proportional hazards models. The

proportional hazards models will include the same factors as described for the primary analysis. Planned sensitivity analysis will be conducted to evaluate time to worsening for worsening thresholds ranging from 10% to 30%. The repeated measures and survival analyses of the EA-SCD PRO's will also include supportive and sensitivity analyses to account for potential baseline confounders as previously described in the primary analysis. EA-SCD satisfaction with transition services will be summarized descriptively.

Intervention fidelity will be analyzed descriptively. A CONSORT-type diagram will be provided, including a summary of all mentors who consented, had a background check, passed the background check, completed practice call 1, completed Peer Mentor University online training, completed practice call 2, and were matched with at least one EA-SCD. Timelines for mentors and EA-SCDs on the PM arm will be summarized descriptively. Frequency of mentor contacts will be analyzed descriptively in terms expected contacts per protocol versus actual. This will include calls placed (mentor to EA-SCD), calls answered (EA-SCD to mentor), messages sent (mentor to EA-SCD), and messages received (EA-SCD to mentor).

ST3P UP application usage will be analyzed descriptively in terms of number of contacts between study subjects and transition coordinators, transition coordinators and PIs, and between PIs. Additionally, the use of education resources in the application will be summarized descriptively for the study subjects. Associations between EA-SCD outcomes (particularly acute care utilizations) and contact frequency, will be analyzed similarly to the methods described above for the primary analysis, with treating the app usage as a continuous covariate. Additionally, application usage will be correlated with EA-SCD PROs (specifically TIP-RFT assessments) similarly to the methods described above, treating the app usage as a continuous covariate. For the analysis described about regarding application usage, this will be done in two ways: (1) including all subjects and, for subjects who did not use the application, usage would be equal to zero; (2) only including the subset of subjects who used the application and looking at the impact of amount of usage on outcomes.

Composite QI-validated scores of the Six Core Elements provided by the sites in 6-month intervals will be analyzed using linear mixed models for repeated measures. One goal of the QI analyses is to assess the convergence in scores between pediatric and adult practices. This will be accomplished with a model that includes baseline QI score, clinic (pediatric versus adult), time, and the provider by time interaction as fixed factors. Site will be included as a random factor to account for repeated observations over time. Importantly, the type of provider will also be evaluated. This will be accomplished using a similar model as described above but will use provider type: Pediatrician to Pediatrician; Pediatrician to Internist; Pediatrician to Med/Peds Specialist, Med/Peds specialist to Med Peds specialist as the treatment factor. Additionally, composite QI-validated scores will be compared with site self-reported scores for concordance over time. Provider satisfaction with transition services will be summarized descriptively.

10.5.6 Missing Data

The impact of missingness in the covariates will be evaluated in several ways. Multivariable models will be based on complete case analyses. The robustness of the complete case analyses will be evaluated by comparing key baseline characteristics between the full dataset and the complete case dataset. Additionally, unadjusted outcome results will be compared between the two datasets. Multiple imputation methods will be utilized to complete baseline missingness, and these baseline-adjusted results will be compared to the complete case adjusted results. The proposed mixed models for repeated measures are valid under the missing at random mechanism (MAR) to address missingness in the PRO. The pattern of missingness in PRO will be assessed to evaluate the MAR assumption.

If data from questionnaires are missing, when possible, the reason for the missing data will be categorized and documented as follows:

- subject felt too ill
- clinician or nurse felt the subject was too ill
- subject felt it was inconvenient or took too much time
- subject felt it was a violation of privacy
- subject didn't understand the actual language or was illiterate
- administrative failure to distribute the questionnaire
- not required at this time point
- other, specify
- unknown

10.5.7 Exploratory Analysis

Heterogeneity of Treatment Effects: We will evaluate the consistency of the intervention across site and patient level characteristics. The heterogeneity of treatment effects (HTE) will be evaluated using potential treatment effect modifiers measured prior to randomization. Site level factors will include cluster size (large vs small) and urban vs rural sites, while subject level factors are those previously listed in the multivariable modeling description. For each factor, subgroup analysis will be conducted on each of the mutually exclusive factor levels. Evaluation of the HTE will be performed qualitatively by comparing the treatment group differences across the factor levels. More formally, each subject- level factor will be evaluated using models to include treatment arm, the baseline factor, and the treatment by factor interaction.

10.5.8 Qualitative Methods

Participants will be asked for permission to contact them for future qualitative research related to the ST3P-UP Study. Future research will be approved separately through Georgia Southern University. Participant information will be kept confidential and will only be provided to authorized personnel.

10.5.9 Interim Analysis

A planned interim analysis of primary and secondary endpoints, as well as QI data will take place in year 3. The study is designed with no formal stopping rules and no alpha spend

will occur. The interim analysis will be in support of the interim progress report. We estimate that the interim analysis will include 60% of the total enrollment and the median follow up time for subjects included in the interim analysis is estimated to be approximately 11 months.

11. STUDY COMPLETION OR TERMINATION

11.1 Completion

The study will be considered complete when one or more of the following conditions is met:

- All subjects have withdrawn from the study
- All subjects have discontinued from the study
- The IRB, LCI DSMC, or Sponsor-Investigator discontinues the study because of safety considerations
- The Sponsor-Investigator defines an administrative or clinical cut-off date

11.2 Termination

The study will be terminated when one or more of the following conditions occur:

- If risk-benefit ratio becomes unacceptable owing to, for example,
    - Safety findings from this study (e.g., UAPs)
    - Results of parallel clinical studies
    - If the study conduct (e.g., recruitment rate, drop-out rate, data quality, protocol compliance) does not suggest a proper completion of the trial within a reasonable time frame
- The Sponsor-Investigator has decided to withdraw funding support at any time before trial completion
- Study participation will be terminated at study sites if study conduct does not achieve expected agreed upon milestones, there is concern for violation of study procedures or other impropriety, for recurrent failure to adhere to study procedures including submission of required data, or failure to achieve expected subject recruitment.

For any of the above closures, the following applies:

- Closures should occur only after consultation between involved parties.
- All affected institutions must be informed as applicable according to local law.
- In case of a partial study closure, ongoing subjects, including those in follow-up, must be taken care of in an ethical manner.

12. STUDY MANAGEMENT

12.1 IRB Approval

This study requires reliance on Advarra IRB as the Central IRB.

The site must submit site- and investigator-specific information to the central IRB to obtain approval for participation in the study. This includes the Sponsor informed consent document with any site- required language included. The Sponsor will obtain electronic copies of approval documents within the central IRB portal on behalf of the site.

For sites using a local IRB in addition to the central IRB:
If the local IRB requires/requests changes to the site documents, the site must submit the changes to the Sponsor for review and approval. Once changes are approved by the Sponsor, the site will submit a modification to the central IRB for approval prior to implementing changes.

12.2 Informed Consent

Before recruitment and enrollment onto this study, the subject and/or his/her parent/guardian will be given a full explanation of the study and will be given the opportunity to review the subject consent form. Prior to a subject's participation in the trial, the informed consent process shall be administered (by each participating site) in accordance with applicable laws, federal regulations, and institutional and IRB policies. The informed consent form should be signed and dated by the subject (and/or parent/guardian, as applicable) and by the person who conducted the informed consent discussion. Assent will be obtained in appropriately aged subjects per institutional guidelines. If reconsent is required and the subject is out of visit window, reconsenting may be done according to Advarra's consent policy.

Informed consent will also be obtained from all mentors and advisors prior to their participation in the study.

12.3 Protocol Adherence

Except for an emergency in which proper care for the protection, safety, and well-being of the study subject requires alternative treatment, the study shall be conducted exactly as described in the approved protocol.

12.4 Changes to Study Documents

If it is necessary for the study protocol, the informed consent/assent, or other study documents to be revised, the revised documents must be approved by the Sponsor-Investigator and the Sponsor IRB in advance of implementation.

If a site requires additional revisions to its site-specific consent(s), the site must provide the tracked amended site consents/assents to the Sponsor for review and approval prior to IRB submission.

12.5 Other Protocol Deviations

If an unexpected deviation occurs, the event should be reported via REDCap to the Sponsor as soon as possible, but within no more than 5 business days of becoming aware of the event. Any IRB reportable event that occurs must be reported to the central IRB per IRB policies.

NOTE: Protocol deviations that, in the Investigator's judgment, potentially caused harm to participants or others or indicates that the participants or others are at an increased risk of harm or has adversely impacted data integrity will be reported promptly to the IRB per IRB reporting requirements.

The local Investigator is responsible for informing the Sponsor of any planned deviation from the protocol prior to implementation and in accordance with local requirements.

12.6 Retention of Records

Essential documentation (e.g., informed consents), including all IRB correspondence, will be retained for at least 2 years after the investigation is completed. Documentation will be readily available upon request.

12.7 Ethical and Legal Conduct of the Study

The procedures set out in this protocol pertaining to the conduct, evaluation, and documentation of this study, are designed to ensure that the Investigator abide by GCP guidelines. The study will also be carried out in full conformity with the ICH E6 and in keeping with applicable local law(s) and regulation(s).

Documented approval from appropriate agencies (e.g., IRB) will be obtained at participating centers before any subject enrollment can occur at these sites, according to GCP, local laws, regulations and organizations.

Strict adherence to all specifications laid down in this protocol is required for all aspects of study conduct; the investigators may not modify or alter the procedures described in this protocol.

The Sponsor-Investigator is responsible for the conduct of the trial at the sites in accordance with the Declaration of Helsinki. The Sponsor-Investigator is responsible for overseeing all study subjects. The Sponsor-Investigator must assure that all study site personnel, including sub-investigators and other study staff members, adhere to the study protocol and all applicable regulations and guidelines regarding clinical trials both during and after study completion.

The Investigator will be responsible for assuring that all the required data will be collected and properly documented.

12.8 Confidentiality of Records

All records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available.

12.9 Compliance with ClinicalTrials.gov

The Sponsor-Investigator is solely responsible for determining whether the trial and its results are subject to the requirements for submission to ClinicalTrials.gov (http://www.clinicaltrials.gov).

13. REFERENCES

1. U.S. Department of Health and Human Services; National Institutes of Health; National Heart Lung and Blood institute. Evidence –Based Management of Sickle Cell Disease: Expert Panel report, 2014.
2. Brousseau DC, Panepinto JA, Nimmer M, et al. The number of people with sickle-cell disease in the United States: national and state estimates. Am J Hematol. 2010; 85:77–78.
3. Hassell KL. Am J Prev Med. 2010 Apr;38(4 Suppl): S512-21. doi: 10.1016/j.amepre.2009.12.022. Population estimates of sickle cell disease in the U.S.
4. https://www.cdc.gov/ncbddd/sicklecell/documents/scd_in_nc_providers.pdf.
5. Schnog JB, Duits AJ, Muskiet FA, ten Cate H, Rojer RA, Brandjes DP. Sickle cell disease; a general overview. *Neth J Med.* 2004;62(10):364-374.
6. Quinn CT, Rogers ZR, McCavit TL, Buchanan GR. Improved survival of children and adolescents with sickle cell disease. *Blood.* 2010;115(17):3447-3452.
7. Lanzkron S, Carroll CP, Haywood C. Mortality rates and age at death from sickle cell disease: U.S., 1979-2005. *Public Health Rep.* 2013;128(2):110-116.
8. Adams-Graves P, Bronte-Jordan L. Recent treatment guidelines for managing adult patients with sickle cell disease: challenges in access to care, social issues, and adherence. Expert Rev Hematol. 2016 Jun;9(6):541-52. doi: 10.1080/17474086.2016.1180242
9. Platt OS, Brambilla DJ, Rosse WF, et al. Mortality in sickle cell disease. Life expectancy and risk factors for early death. N Engl J Med. 1994; 330:1639–1644.
10. Paulukonis ST, Eckman JR, Snyder AB, et al. Defining sickle cell disease mortality using a population-based surveillance system, 2004 through 2008. Public Health Rep. 2016; 131:367–375.
11. Treadwell M, Telfair J, Gibson RW, Johnson S, Osunkwo I. Transition from pediatric to adult care in sickle cell disease: establishing evidence-based practice and directions for research. Am J Hematol. 2011 Jan;86(1):116-20.
12. Steiner CA, Miller JL. Sickle Cell Disease Patients in U.S. Hospitals, 2004. HCUP Statistical Brief #21. December 2006. Agency for Healthcare Research and Quality, Rockville, MD. [cited 2015 Sep 29].
13. Brousseau DC, Owens PL, Mosso AL, et al. Acute care utilization and re-hospitalizations for sickle cell disease. JAMA. 2010; 303:1288–1294.
14. https://www.cdc.gov/ncbddd/sicklecell/documents/scd_in_ga.pdf].
15. Schwartz LA, Radcliffe J and Barakat LP. Associates of School Absenteeism in Adolescents with Sickle Cell Disease. Pediatr Blood Cancer. 2009 Jan; 52(1): 92–96.
16. Treadwell M, Johnson S, Sisler I, Bitsko M, Gildengorin G, Medina R, Barreda F, Major K, Telfair J, Smith WR. Self-efficacy and readiness for transition from pediatric to adult care in sickle cell disease. Int J Adolesc Med Health. 2016 Nov 1;28(4):381-388. doi: 10.1515/ijamh- 2015-0014.
17. Sobota AE, Umeh E, Mack JW. Young Adult Perspectives on a Successful Transition from Pediatric to Adult Care in Sickle Cell Disease. J Hematol Res. 2015 Dec;2(1):17-24.
18. Bemrich-Stolz CJ, Halanych JH, Howard TH, Hilliard LM, Lebensburger JD. Exploring Adult Care Experiences and Barriers to Transition in Adult Patients with Sickle Cell

Disease. Int J Hematol Ther. 2015; 1(1): 10.15436/2381-1404.15.003.

19. Sturman DA, Moghaddam B. The neurobiology of adolescence: changes in brain architecture, functional dynamics, and behavioral tendencies. Neurosci Biobehav Rev. 2011 Aug; 35(8):1704-12.
20. Kanter J, Kruse-Jarres R. Blood Rev. 2013 Nov;27(6):279-87. doi: 10.1016/j.blre.2013.09.001. Epub 2013 Sep 19. Management of sickle cell disease from childhood through adulthood.
21. Blinder MA, Vekeman F, Sasane M, et al. Age-related treatment patterns in sickle cell disease patients and the associated sickle cell complications.
22. Kroner EL, Hoffmann RG, Brousseau DC. Emergency department reliance: a discriminatory measure of frequent emergency department users. Pediatrics. 2010 Jan;125(1):133-8. doi: 10.1542/peds.2009-0960. Epub 2009 Dec 14.
23. Blum R, Garell D, Hodgman C, *et al.* (1993) Transition from child-centered to adult health- care systems for adolescents with chronic conditions. A position paper of the Society for Adolescent Medicine. J Adolesc Health 14:570–576.
24. Crowley R, Wolfe I, Lock K, McKee M. Improving the transition between paediatric and adult healthcare: a systematic review. Arch Dis Child. 2011 Jun;96(6):548-53.
25. Hankins JS, Osarogiagbon R, Adams-Graves P et al. A transition pilot program for adolescents with sickle cell disease. J Pediatr Health Care. 2012 Nov-Dec;26(6): e45-9.
26. Davis AM, Brown RF, Taylor JL, Epstein RA, McPheeters ML. Transition care for children with special health care needs. Pediatrics. 2014 Nov;134(5):900-8. doi: 10.1542/peds.2014- 1909.
27. Maslow G, Adams C, Willis M, et al. An evaluation of a positive youth development program for adolescents with chronic illness. *J Adolesc Health*. 2013;52(2):179–185.
28. Cooley WC, Sagerman PJ, Sagerman PJ White PH et al. Supporting the health care transition from adolescence to adulthood in the medical home. 2011 Jun 27. American Academy of Pediatrics; American Academy of Family Physicians; American College of Physicians; Transitions Clinical Report Authoring Group, Cooley WC, Sagerman PJ. Collaborators (13) Pediatrics. 2011 Jul;128(1):182-200. doi: 10.1542/peds.2011-0969.
29. McManus M, White P, Barbour A, et al. Pediatric to adult transition: a quality improvement model for primary care. J Adolesc Health. 2015 Jan;56(1):73-8. doi: 10.1016/j.jadohealth.2014.08.006.
30. McManus M, White P, Pirtle R, Hancock C, Ablan M, Corona-Parra R.. Incorporating the Six Core Elements of Health Care Transition into a Medicaid Managed Care Plan: Lessons Learned from a Pilot Project. J Pediatr Nurs. 2015 Sep-Oct;30(5):700-13. doi: 10.1016/j.pedn.2015.05.029.
31. Smith GM, Lewis VR, Whitworth E, Gold DT, Thornburg CD. Growing Up With Sickle Cell Disease: A Pilot Study of a Transition Program for Adolescents With Sickle Cell Disease.
32. Kinney TR, Ware RE. The adolescent with sickle cell anemia. Hematol Oncol Clin North Am.1996; 10:1255–1264.
33. Butler DJ, Beltran LR. Functions of an adult sickle cell group: education, task orientation, and support. Health Soc Work. 1993; 18:49–56.

34. Baskin ML, Collins MH, Brown F, et al. Psychosocial considerations in sickle cell disease (SCD): the Transition from Adolescence to Young Adulthood. J Clin Psychol Med Setting. 1998; 5:315–341.
35. Griffin A; Gilleland J; Johnson A; Cummings L; New T; Brailey T; Eckman J; Osunkwo I. Applying a developmental–ecological framework to sickle cell disease transition. Clinical Practice in Pediatric Psychology, Vol 1(3), Sep 2013, 250-263. http://dx.doi.org/10.1037/cpp000002.
36. DiMatteo MR, Giordani PJ, Lepper HS, Croghan TW. Patient adherence and medical treatment outcomes: a meta-analysis. Med Care 2002 Sep;40(9):794-811.
37. Dennis C-L. Peer support within a health care context: a concept analysis. Int J Nurs Stud. 2003;40(3):321–32.
38. Ahola Kohut S, Stinson JN, Giosa L, Luca S, van Wyk M. Systematic review of peer support interventions for adolescents with chronic illness: a narrative analysis. Int J Child Adoles Health. 2014;7(3):183–97.
39. Stinson J, Ahola Kohut S, Forgeron P et al. The iPeer2Peer Program: a pilot randomized controlled trial in adolescents with Juvenile Idiopathic Arthritis. Pediatr Rheumatol Online J. 2016 Sep 2;14(1):48.
40. Sandhu S, Veinot P, Embuldeniya G et al. Peer-to-peer mentoring for individuals with early inflammatory arthritis: feasibility pilot BMJ Open. 2013 Mar 1;3(3). pii: e002267. doi: 10.1136/bmjopen-2012-002267.
41. Daley BJ Sponsorship for adolescents with diabetes. Health Soc Work. 1992 Aug;17(3):173- 82.
42. Powers, L. E., Turner, A., Westwood, D., Matuszewski, J., Wilson, R., & Phillips, A. (2001). TAKE CHARGE for the future: A controlled field-test of a model to promote student involvement in transition planning. *Career Development for Exceptional Individuals*, *24*(1), 89-104.
43. Olsson, Craig A., Boyce, Mark F., Toumbourou, John and Sawyer, Susan M. 2005, The role of peer support in facilitating psychosocial adjustment to chronic illness in adolescence*, Clinical child psychology and psychiatry*, vol. 10, no. 1, pp. 78-87
44. Blake, J. E. (1997). A mentoring program for adolescents with diabetes. Diabetes Educ, 23(6),681-684.
45. Smith-Jentsch KA, Scielzo SA, Yarbrough CS, Rosopa PJ. A comparison of face-to-face and electronic peer-mentoring: Interactions with mentor gender Journal of Vocational Behavior Volume 72, Issue 2, April 2008, Pages 193–206.
46. Corbie-Smith G, Thomas SB, Williams MV, et al. Attitudes and beliefs of African Americans toward participation in medical research. J Gen Intern Med. 1999; 14:537–546.
47. Haywood C, Lanzkron S, Diener-West M, Haythornthwaite, Strouse J, Bediako S, Onojobi G, MD, Beach MC for the IMPORT Investigators. Attitudes Towards Clinical Trials Among Patients with Sickle Cell Disease. Clin Trials. 2014 Jun; 11(3): 275–283.
48. Sequeira PA, Pyatak EA, Weigensberg MJ, et al. Let's Empower and Prepare (LEAP): Evaluation of a Structured Transition Program for Young Adults with Type 1 Diabetes. Diabetes Care. 2015 Aug;38(8):1412-9.

49. Treadwell MJ, 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. doi: 10.1097/AJP.0000000000000054.
50. Panepinto, J. A., Torres, S., & Varni, J. W. (2012). Development of the PedsQLTM sickle cell disease module items: qualitative methods. Quality of Life Research, 21(2), 341–357. http://doi.org/10.1007/s11136-011-9941-4.
51. Evensen, C. T., Treadwell, M. J., Keller, S., Levine, R., Hassell, K. L., Werner, E. M., & Smith, W. R. (2016). Quality of care in sickle cell disease: Cross-sectional study and development of a measure for adults reporting on ambulatory and emergency department care. Medicine, 95(35), e4528. http://doi.org/10.1097/MD.0000000000004528.
52. Treadwell M, Johnson S, Sisler I, Bitsko M, Gildengorin G, Medina R, Barreda F, Major K,Telfair J, Smith WR. Development of a sickle cell disease readiness for transition assessment Int J Adolesc Med Health. 2016 May 1;28(2):193-201. doi: 10.1515/ijamh-2015- 0010.
53. Hays, RD (1994). The Medical Outcomes Study (MOS) Social Support Survey. Retrieved May 21, 2018 from the RAND Corporation web site: https://www.rand.org/health/surveys_tools/mos/social-support/survey-instrument.html
54. Hemming K, Girling AJ, Sitch AJ, Marsh J, Lilford RJ. Sample size calculations for cluster randomised controlled trials with a fixed number of clusters. BMC Med Res Methodol. 2011 Jun;11:102. doi: 10.1186/1471-2288-11-102.
55. Schlenz AM, Boan AD, Lackland DT, Adams RJ, Kanter J. Needs Assessment for Patients with Sickle Cell Disease in South Carolina, 2012. Public Health Rep. 2016 Jan- Feb;131(1):108-16.
56. Campbell MK, Fayers PM, Grimshaw JM: Determinants of the intracluster correlation coefficient in cluster randomized trials: the case of implementation research. Clinical Trials. 2005 2:99-107. doi: 10.1191/1740774505cn071oa.

14. APPENDICES

Appendix A: Peds QL-SCD QOLs (Adult, Teen, Young Adult)

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