Community Health Workers and Mobile Health for Improving Transition to Adult Sickle Cell Disease Care: The COMETS Trial Protocol

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Table of Contents

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Tanisha Danielle Belton[1*] DrPH, MPH; Caren M Steinway[2, 3*] LMSW, MPH; Olivia Teng[2] MPH; Justine Shults[4, 5] PhD, MS; Lamia P. Barakat[6] PhD; Banu Aygun[7] MD; Abena Appiah Kubi[7] MD, MPH; Lori E. Crosby[8, 9] PsyD; Omar Niss[10] MD; Biree Andemariam[11] MD; Lisa A. Schwartz[6] PhD; Samantha Luma[5]; Kyle A. Smith[5]; Tracey B. Johnson[5]; David Rubin[1] MD, MSCE; Kim M. Smith-Whitley[12] MD; Sophia Jan[2, 3] MD, MSHP

[1]PolicyLab Division of General Pediatrics Children's Hospital of Philadelphia Philadelphia US
[2]Department of Pediatrics Northwell Health New Hyde Park US
[3]Department of Pediatrics Donald & Barbara Zucker School of Medicine at Hofstra/Northwell Hempstead US
[4]Department of Biostatistics, Epidemiology, and Informatics Perelman School of Medicine at the University of Pennsylvania Philadelphia US
[5]Department of Pediatrics Children's Hospital of Philadelphia Philadelphia US
[6]Division of Oncology Children's Hospital of Philadelphia Philadelphia US
[7]Pediatric Hematology Oncology and Stem Cell Transplantation Cohen Children's Medical Center New Hyde Park US
[8]Behavioral Medicine and Clinical Psychology Cincinnati Children's Hospital Medical Center Cincinnati US
[9]Department of Pediatrics Cincinnati Children's Hospital Medical Center Cincinnati US
[10]Division of Hematology Cincinnati Children's Hospital Medical Center Cincinnati US
[11]New England Sickle Cell Institute University of Connecticut Health Farmington US
[12]Division of General Pediatrics Children's Hospital of Philadelphia Philadelphia US
[*]these authors contributed equally

Corresponding Author:
Tanisha Danielle Belton DrPH, MPH
PolicyLab
Division of General Pediatrics
Children's Hospital of Philadelphia
2716 South Street
11th Floor
Philadelphia
US

Abstract

Background: Transitioning from pediatric to adult sickle cell disease (SCD) care is challenging for emerging adults (17-25 years old). This period is marked by a seven-fold increase in mortality rates, and has the highest rates of hospitalizations, emergency room visits, and hospital readmissions compared to children living with SCD. These challenges are exacerbated by fragmented care coordination, difficulty navigating adult healthcare systems, and increased self-management responsibilities.

Objective: This study aims to compare the effectiveness of two interventions designed to support emerging adults living with SCD during this transition: a mobile health (mHealth) application and community health worker (CHW) support to standard care.

Methods: The Community Health Workers and Mobile Health for Emerging Adults Transitioning Sickle Cell Disease Care (COMETS Trial) is an ongoing multicenter, three-arm, open-label randomized controlled trial (RCT); 375 emerging adults (17 to 25 years old) are being enrolled and randomized 1:1:1 to (1) a 6-month CHW intervention focused on self-management skills, symptom tracking, care coordination, and transition planning, (2) a 6-month mHealth self-management program (enhanced iManage application) with tailored SMS texting (THRIVE 2.0), or (3) enhanced usual care (control). Participants are followed for 18 months. The primary outcome is the change in self- reported health-related quality of life (HRQOL) assessed using the PedsQL Sickle Cell Disease Module. Secondary outcomes include acute care utilization (hospitalizations, ED visits), patient activation, self-management behavior, and successful transfer to adult hematology care.

Results: The Institutional Review Board (IRB) at Children's Hospital of Philadelphia approved this study in June 2018. We have enrolled a total of 405 participants.

Conclusions: This trial addresses a critical gap in transition intervention research for young adults with SCD. It will provide evidence on the comparative effectiveness of two promising interventions (CHW and mHealth) and inform the development of scalable and sustainable transition support programs. Findings will have implications for improving HRQOL, reducing acute care utilization, and promoting successful transition to adult-centered SCD care for this vulnerable population. Clinical Trial: ClinicalTrials.gov NCT03648710: https://clinicaltrials.gov/study/NCT034648710

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Trial Registration: ClinicalTrials.gov NCT03648710: https://clinicaltrials.gov/study/NCT034648710

Keywords: sickle cell disease; pediatrics; health care transition; adolescents and young adults; self-management; quality of life; mHealth; community health worker

Introduction

Emerging adults with sickle cell disease (SCD) face a seven-fold increase in mortality rates during the transition from pediatric care to adult care [1]. Additionally, this sub-population (17 to 25 years old), experiences the highest rates of hospitalizations, emergency room visits, and hospital readmissions compared to children living with SCD [2]. This alarming increase in mortality and acute care use stems partly from the cumulative effects of SCD leading to organ dysfunction, with the risk of comorbidities like stroke and silent infarcts worsening as individuals age [3,4]. In addition, during this transition process, emerging adults with SCD experience fragmented care coordination which increases their vulnerability.

Emerging adults with SCD face shifts in insurance, inconsistent transfer processes, and a lack of comprehensive adult-focused programs [4–6]. For instance, while adherence to chronic transfusion therapy and hydroxyurea therapy can substantially mitigate the risk of neurologic complications and

other adverse outcomes, inadequate care coordination during the transition to adult care, coupled with suboptimal patient engagement and SCD self-management skills, markedly heighten the risk of neurologic complications[6–9]. These complications can exert enduring and profound impacts on physical function, educational attainment, employment, income, and overall health-related quality of life (QOL).

Beyond health system challenges, emerging adults face additional psychosocial challenges, including the struggle for financial independence and insurability, which can be complicated by job instability and the loss of dependent coverage on parents' insurance plans [10]. Transportation barriers may also limit access to necessary medical appointments or therapies, especially for those living in areas with limited adult healthcare resources [8]. Additionally, many emerging adults with SCD experience limited access to mental health care, which can exacerbate issues like depression, anxiety, and the psychological burden of managing a chronic illness [11]. Social determinants of health (SDOH), including poverty, housing instability, food insecurity, and lack of educational opportunities, also further complicate the ability of emerging adults with SCD to manage their condition effectively as well as navigate the healthcare system [11]. Furthermore, the absence of adequate social support and educational resources compounds these challenges, leaving emerging adults with SCD underprepared and less equipped to navigate their transition effectively [6,12].

Disruption in continuity of care, combined with socioeconomic factors, can lead to worse health outcomes and an increased risk of complications show the need for effective interventions [11,12]. Community health worker (CHW) programs and mobile health (mHealth) platforms have shown promise in addressing these challenges and improving in health outcomes for chronic diseases transition patients [13,14] . Research shows that CHW programs enhance chronic disease management and healthcare navigation, improving outcomes in low-resource settings for conditions

such as asthma, hypertension, and diabetes [15,16]. For instance, the IMPaCT CHW Program demonstrated that participants in the intervention arm received more timely post-hospital care, better discharge communication, and experienced fewer readmissions [13].

Similarly, mHealth platforms have been effective in promoting self-management and adherence among both adults [17,18] and emerging adults with chronic conditions, including diabetes and post-liver transplant care [14,19,20]. A randomized controlled trial of MD2Me, an internet and mobile phone-delivered disease management intervention utilizing automated SMS algorithms, showed that emerging adults with Type 1 diabetes, inflammatory bowel disease, and cystic fibrosis in the intervention arm significantly improved disease self-management and health-related self-efficacy [14]. This technology holds great promise for adolescents with chronic diseases due to the widespread use of smartphones [21]. Integrating CHW and mHealth initiatives can substantially alleviate healthcare transition challenges and address psychosocial factors, thus improving care continuity and outcomes for patients with chronic diseases.

Gaps in evidence highlighted by Viola et al., 2021 [6], demonstrate the need for multi-site randomized controlled trials (RCTs) focusing on long-term care outcomes. Current research, while promising, offers inconclusive results due to limited sample sizes and methodological constraints. Recognizing these limitations, our study aims to bridge this gap by conducting comprehensive multi-site RCTs that evaluate both clinical and psychosocial outcomes, ultimately aiming to enhance chronic disease management and overall health during this critical period. We hypothesize that emerging adults in the CHW or mHealth arm will have increased health-related quality of life (HRQOL) compared to those in the enhanced usual care arm.

Methods

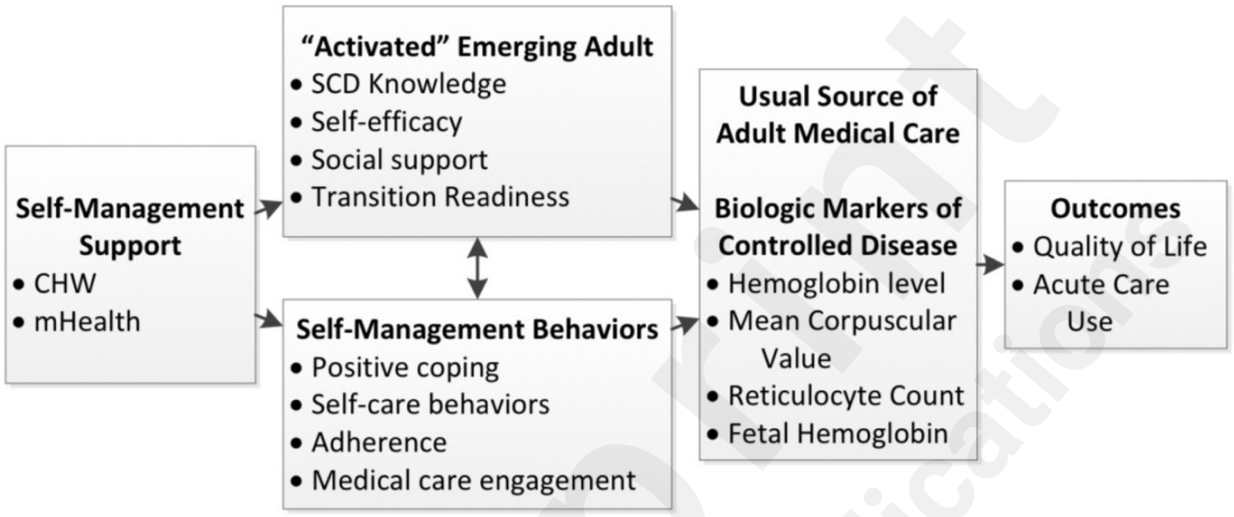
Theoretical Framework

Our intervention leverages two key frameworks: the SMART Model (Social-Ecological Model for Adolescents and Young Adults Readiness to Transition) and the Chronic Care Model. Effective transition care, as emphasized by the SMART model requires integrating both pre-existing and modifiable factors among patients, parents, and healthcare providers that influence transition readiness. Modifiable factors—such as knowledge, self-management skills, confidence (or self-efficacy), and social support—are critical targets for enhancing transition readiness, especially for individuals managing chronic conditions. The SMART Model has been validated across various populations and has been updated for health equity after this trial was designed, including childhood cancer survivors, parents, and healthcare providers [22–24].

For individuals with SCD, as well as their parents and healthcare providers, the ability to independently manage their sickle cell disease is recognized as a crucial goal during the transition to adult care [6,25–27]. Self-management behaviors—defined as the daily, self-motivated, and collaborative activities required to manage symptoms—are essential for successful disease management. In the context of SCD, these behaviors include self-awareness, seeking emotional support, managing diet and hydration, avoiding alcohol, tobacco, and drugs, and adhering to prescribed treatments such as daily hydroxyurea or regular transfusion and chelation therapy.

Self-management support is a foundational element of the Chronic Care Model [28], which is widely regarded as an effective framework for improving chronic illness care. According to this model, improved health outcomes—including better disease control, a smoother transition to adult care, and enhanced QOL—are achieved through the activation and engagement of patients in self-management behaviors, supported by proactive healthcare teams. In this context, individuals who are more 'activated' tend to exhibit higher levels of the modifiable factors outlined by the SMART Model, such

as increased knowledge, self-efficacy, and social support, all of which are crucial for successful self-care and transition. We chose to target these modifiable factors because SCD patients, parents and clinicians agree that it is critical to engage in disease self-management to optimize health during the transition period [29].



(Figure 1: Key Clinical Question and Conceptual Model)

Study design

The COMETS study is an ongoing pragmatic, multicenter, three-arm, open-label randomized controlled trial (RCT). Five pediatric SCD centers located in four states (Connecticut, New York, Ohio, and Pennsylvania) are participating in this study. Eligible participants are randomized 1:1:1 across sites to a 6-month community health worker program, 6-month mobile health self-management program with tailored SMS texting, or to enhanced usual care (control).

Specific Aims

The overall goal of this study aims to answer the question "How can community health workers and mobile applications help me to improve my ability to take care of myself (activated patient, self-management), stay connected with my doctors (usual source of care), avoid visits to the ER and hospital (acute care use), and ultimately maximize my quality of life while I am transitioning from

my pediatric to adult doctors?"

Aim 1: Compare the effectiveness of two self-management support interventions versus enhanced usual care to improve health-related quality of life and acute care use for transitioning youth with SCD. This aim will test the following hypothesis:

- Emerging adults in the CHW arm or mHealth arm will have higher quality of care and lower acute care use than those in the usual care arm at 6, 12, and 18 months.

Aim 2: Identify and quantify whether patient activation, self-management behaviors, biologic markers, and transfer to adult care are mediators of intervention treatment effects. This aim will test the following hypotheses:

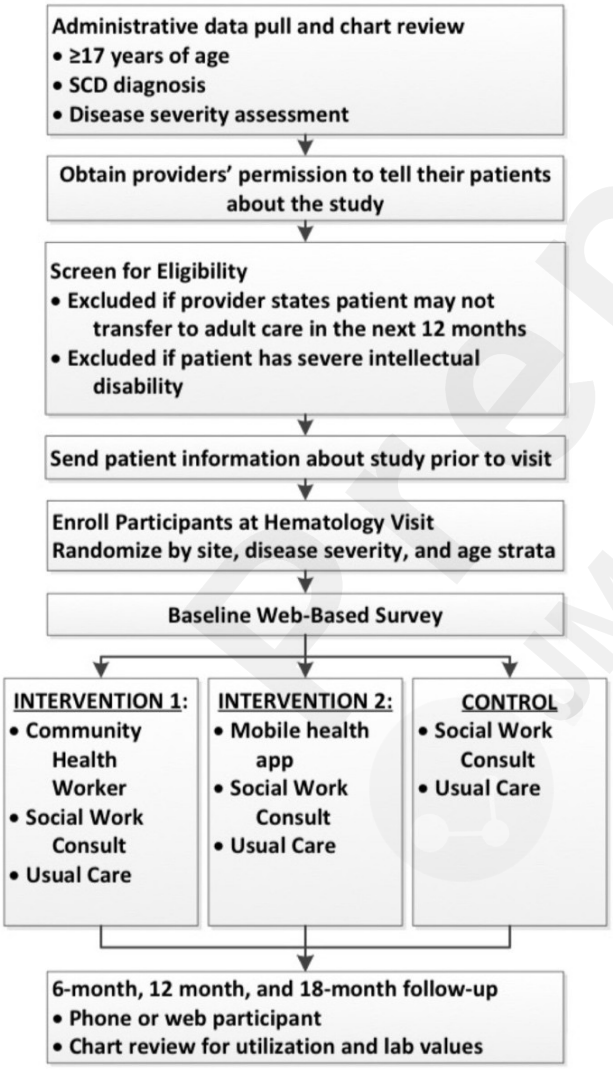
- Patients in the CHW arm and M health arm will have greater patient activation and self-management behaviors compared to those in the usual care as six months.
- Patients with greater patient activation and self-management behaviors will have better treatment outcomes compared to those in usual care at 6, 12, and 18 months.
- Patients in the CHW arm and mHealth arm will affect the total number of adult hematology visits and magnitude of biologic markers compared to those in usual care 18 months.
- Patients with greater adult hematology visits or higher biologic markers will have better outcomes compared to those in usual care at 18 months.

Aim 3: Identify individual and family factors that moderate intervention treatment effects. We will test the following hypotheses:

- Emerging adults with SCD and high disease severity in the CHW arm or mHealth arm will have higher HRQOL and lower quality of life or lower acute care use than those in the usual care arm at 6, 12, and 18 months.
- Older adults (≥22 years) with SCD in the CHW arm or mHealth arm will have higher quality of life or lower acute care use than those in the usual care arm at 6, 12, and 18 months.
- We will also explore whether patient demographics (gender, education or employment, health

literacy, insurance type, zip code), family demographics (living with parent or caregiver, maternal education), and recruitment method moderate outcomes in the CHW arm or mHealth arm compared to similar patients in the usual care.

Exploratory Aim: Explore the association of enhancements to usual care on pediatric and adult care utilization. We will test the hypothesis that enhancements to usual care will decrease pediatric acute utilization and increase adult acute utilization.



(Figure 2: COMETS Study Flowchart Among Emerging Adults with Sickle Cell Disease)

Study population, recruitment, and enrollment

Eligible participants are young adults ages 17 to 25 with SCD diagnosis of all genotypes who plan to transition to an adult hematologist within 12 months, have access to a mobile device tablet or computer, and can interact with a mobile or web-based program. Eligible participants are identified by reviewing each recruitment site's daily hospitalized patients, weekly hematology appointments, and hematology practice registries. Across the five pediatric SCD centers, we estimate that there will be 745 eligible patients over the recruitment period, with an equal distribution between males and females.

Recruitment strategies include in-person enrollment during appointments or admissions and mailed/emailed communications with a recruitment letter, study flyer, and a recruitment video. During the COVID-19 pandemic telephone recruitment and electronic consent were added to maintain recruitment goals. Retention strategies include completion of enrollment and follow-up procedures in-person, telephone, or an email/text, automatic reminders, and incentives for effort.

IRB approval

The COMETS study was funded in September 2017, IRB approval was received in June 2018 (IRB #18-015106) at the prime institution, The Children's Hospital of Philadelphia and submitted to each participating site for site-level approach. This study was registered in August 2018 (NCT03648710). The study is being conducted in accordance with the IRB-approved protocol (December 15, 2020).

Randomization

Random assignment takes place after enrollment and the completion of the baseline survey. Enrolled participants will be randomly assigned to a treatment arm after being stratified by recruitment site, age (≤21 years, ≥22 years), and disease severity (moderate and severe), resulting in 12 different randomization strata [30,31]. Severe SCD disease will be determined by chart review and defined by the following: (1) Any history of stroke, acute chest syndrome, or ≥3 emergency room visits within

the 3 years prior to enrollment, which are all indications for disease modifying therapy such as daily hydroxyurea or monthly exchange transfusion therapy[32–34]; (2) receipt of monthly exchange transfusion therapy, defined by 2 or more exchange transfusions in an outpatient setting within 6 month period [34]. Severe disease will be defined as any history of acute chest syndrome, stroke, or ≥3 hospitalizations in the last 3 years [32,35].

Control Arm: Enhanced Usual Care

Enhanced usual care, standardized across all sites through transition/transfer of care checklist and is administered by the social work team at each recruitment site. During the intervention development phase, all recruitment site investigators reviewed and decided on the elements to be included in this checklist based on transition elements at their institution. The checklist is reviewed at the 12-month timepoint in the trial with the participant during a scheduled hematology visit. Elements of the checklist include (1) patient seen by the pediatric provider with the parent outside the examination room at least once, (2) a social work consult to screen and address sociodemographic risk factors, (3) information on health insurance availability provided to patient, (4) adult hematologist identified, (5) adult primary care provider identified, (6) medical release signed, and (7) medical record viewable or sent to adult provider. Elements of the checklists are based on existing checklists by organizations such as the Transfer of Care Checklist developed by Got Transition/Center for Health Care Transition Improvement [36] and those developed by the National Institute for Child Health Quality [37]. All study participants received standardized enhanced usual care.

Enhanced Usual Care + Peer Community Health Worker

The CHW program is modeled after the IMPaCT Program developed by IMPaCT Care, Inc [13,38,39]. Components of the CHW program include (1) development of patient-centered goals and individualized action plan around self-care, symptom tracking, and transition to adult care; (2) provision of information, skills, and tips; and (3) tailored peer support using telephone calls and/or

visits.

To identify the components of the CHW intervention, virtual workgroup meetings were held to define the role and training components [40]. Training topics included local hospital and community knowledge; SCD and transition to adulthood education; basic clinical research training; foundational CHW skills and concepts; and trial-specific aims and resources.

Additionally, CHWs attended IMPaCT's two-week training course, completed onboarding and orientation at their respective sites, and Collaborative Institutional Training Initiative for clinical research. With an emphasis on ongoing support and education, CHWs meet weekly with a trial supervisor and their site supervisor to review caseloads and address any concerns. Monthly group huddles are held to support peer-to-peer learning for both CHWs and their supervisors. CHWs are expected to contact participants weekly during the 6-month intervention period to remain consistent with other successful protocols [41,42].

Enhanced Usual Care + Mobile Health

Participants randomized to the mHealth arm will download an enhanced version of iManage [43] called iManage SCD, developed by Crosby and colleagues in collaboration with adolescents and young adult patients with SCD [29,40]. Key components of iManage SCD include (1) development of patient-centered goals around self-care, symptom tracking, and the transition to adult care; (2) provision of information, skills, and tips to support these goals; (3) virtual peer support, where users can encourage others, form teams, and interact with fellow youth with SCD; (4) daily symptom tracking and visual monitoring of goal completion. IManage SCD is an mHealth application accessible via smartphone, tablet, or web, and has been shown to be highly feasible and beneficial for emerging adults with SCD.

Enhancements to the iManage application were identified through the convening of a multi-

stakeholder group, including an application development firm, clinicians, researchers, and young adults with SCD across the five identified recruitment sites. The development process of the enhanced application has been described [29]. Interviews with stakeholders explored eight topics including 1) social behaviors and entertainment; 2) treatment; 3) pain impact; 4) pain management; 5) SCD knowledge; 6) lifestyle & goals; 7) communication & support; 8) envisioning the future. Final components of the application include health behavior challenges, tracking of medications and symptoms, an educational material library, discussion boards, and medical summary. User engagement was tracked through analytic tools integrated within the mHealth app [29].

Additionally, daily tailored texting (THRIVE2.0, Texting Health-related Resources to Inform, motiVate, and engage) [44], based on patient-defined goals were delivered to participants randomized to the mHealth arm of the study. Preliminary studies have found that THRIVE2.0 improves health-promoting behaviors, such as sunscreen use among adolescent and young adult cancer survivors. These text messages were tailored around modifiable factors and delivered twice a week. Two types of messages were delivered, educational and interactive. Messages focused on SCD knowledge, skills and efficacy, relationships, self-management, school/work, and coping.

Participants will receive training on how to use and customize iManage SCD during enrollment and have access to a helpdesk for support. The content on iManage SCD was continuously monitored by research staff. Participants were able to access the application after the 6-month active intervention period.

Data Collection

Participants are followed with measures related to health-related quality of life, acute care use, patient activation, self-management behaviors, and experiences with the COVID-19 pandemic collected through web-based survey, phone, or in-person at baseline, 6, 12, and 18-months. Disease severity, healthcare utilization, and biologic markers will be measured from the electronic medical

record at baseline, 6, 12, and 18 months. Study data is stored and managed using the Research Electronic Data Capture (REDCap) online system, overseen by the Children's Hospital of Philadelphia. Site study coordinators are responsible for data entry at their respective sites.

Baseline clinical and demographic information: Baseline data will be gathered from electronic medical records and includes age, SCD genotype, history of intellectual disability, depression, anxiety, stroke, acute chest syndrome, emergency room visits, and prescribed disease-modifying therapies (hydroxyurea or exchange transfusions).

Intervention Adherence Process Measures: For the mHealth intervention, adherence will be tracked using app usage metrics (e.g., days and frequency of access, responses to SMS messages, goal progress) through REDCap. CHW intervention adherence includes contact frequency (in-person, phone, email, SMS), and goal attainment. Usual care measures include social work consults and chart review transition checklists, tracking key actions like insurance review and provider identification.

Health-Related Quality of Life (Primary Outcome): HRQOL will be measured using the PedsQL Sickle Cell Disease Module [32,43], a validated 43-item tool that assesses pain, emotional health, treatment experience, and communication.

Healthcare Utilization: Healthcare utilization data, including acute care (emergency department visits, hospital admissions) and ambulatory care, will be collected from patient reports, electronic medical records (EMRs), and Medicaid billing data.

Validation of Healthcare Utilization Data: Patient-reported data on healthcare utilization was validated with EMR data, calculating annualized acute care utilization and ambulatory care use for both pediatric and adult hematology.

Measures of Self-Management Behavior: Self-management will be measured through several tools: the Brief COPE for coping strategies [45], the Jenerette Self-Care Assessment Tool for self-care actions [46], the Medical Adherence Measure for medication adherence [47,48], medical chart reviews for appointment no-shows, and chronic transfusion adherence (based on patient report and chart review).

Measures of Patient Activation (Mediator): Patient activation will be assessed using the Sickle Cell Disease Knowledge Questionnaire (SCDKQ) [49], the Transition Readiness Assessment Questionnaire (TRAQ) [50], and the Medical Outcomes Study Social Support Survey (MOS-SSS) [51].

Experience with the COVID-19 Pandemic: A 33-question survey will be utilized to assess COVID-19 symptoms, mental health impacts, trauma, social distancing effectiveness, care access issues, and telehealth satisfaction, adapted from the Johns Hopkins COVID-19 Community Response Survey [52] and US Census Household Pulse Survey [53]. These questions were chosen with input from young adult stakeholders and site PIs.

Biologic Marker of Disease Control (Mediator): Biologic markers, including hemoglobin levels, mean corpuscular volume, reticulocyte count, and fetal hemoglobin percentage, will be obtained from chart review. These markers reflect anemia, hydroxyurea adherence, stroke risk, and disease severity.

Measure	# of Items	Source
Primary Outcome Measures		
PedsQL SCD	43	Panepinto et al., (2013)
Activated Emerging Adult Patient Measures (Mediators)		
SCDKQ	23	Original scale: Armstrong et al, (1993) used in Barakat et al., (2010), Logan et al (2002)
PAM-13	13	Hibbard et al (2004), Hibbard et al, (2005)
TRAQ	20	Sawicki et al (2011), Wood, et al (2014)
MOS-SSS	19	Sherbourne & Stewart, (1991)
Self-Management Behavior Measures (Mediator)		
Brief COPE	28	
MAM	17	Zelikovsky & Schast, (2008)
COVID-19 Pandemic Measures		
COVID19 symptoms and testing experience: Symptoms; Diagnosis	4	Mehta (2020)
COVID19 and Mental health impacts: Mental Health	10	Mehta (2020)
COVID19 and Violence and trauma: Violence; Fear of Violence	3	Mehta (2020)
COVID19 and Social distancing: Social Distancing; Social Impact	10	Mehta (2020)
Reduced Access to Care	2	US Census Bureau (2020)
Satisfaction with Telehealth Services	4	Parmanto, et al (2016)

(Table 1: Patient-Reported Scales, Characteristics, and Source)

Outcomes

The primary outcome of the COMETS Study will be the change in HRQOL. The secondary outcomes are acute care utilization (hospitalizations, ED visits), patient activation, self-management behaviors, and successful transfer to adult hematology care.

Statistical Methods

This study is ongoing; therefore, the statistical analyses have not been performed.

Sample Size

Sample size calculations are based on our primary endpoint of change in HRQOL and healthcare utilization for each subject over their study participation[54]. Details of the sample size calculations are presented in Online Appendix A.

Primary Analysis

Analyses will be conducted in Stata 18.0, with two-sided tests of hypothesis and a p-value < 0.05 as the criterion for statistical significance.

To compare the effectiveness of two self-management support interventions (community health workers and mobile health) versus enhanced usual care on the primary outcomes (HRQOL and acute care use), we will first compare groups at baseline, using chi-square tests for categorical variables and one-way analysis of variance (ANOVA) or Kruskall-Wallis, as appropriate, for continuous variables. We will use descriptive summaries and graphical displays to evaluate the distribution of and relationship between variables. When required, transformations to achieve normality will be considered.

The initial analysis will use one-way ANOVA to test the hypothesis that the three treatment groups showed no change from the end of the intervention to the baseline in the primary and secondary outcomes. If the hypothesis of equal group means is rejected (there was a change detected), 3 post-hoc tests will be applied (with Bonferroni adjustment for multiple testing) to identify pairwise differences between treatment groups. We postulate that a difference in change of 10 points in PedsQL SCD total between groups will be clinically meaningful.

Next, we will construct longitudinal models that include baseline, 6-month, 12-month, and 18-month measurements as outcomes. Longitudinal models account for correlation of measures within emerging adult over time; use all data collected; allow for and can be used to adjust for dropout or non-adherence to assigned treatment; can adjust for differences in patient characteristics not balanced by randomization; can include indicator variables for clinical site; and permit continuous, count, and binary outcomes. We will build models using generalized estimating equations (GEE) or quasi-least squares (QLS)[55]; QLS is based on GEE but allows for implementation of the Markov correlation

structure that is appropriate if participants intermittently miss appointments. Mixed effects models may also be considered. For example, mixed models can be used to relax the assumption of constant variance that is required for QLS and GEE; they will therefore be useful if residual diagnostics for GEE/QLS suggest an increase in the variance of outcomes over time.

The longitudinal models will include indicator variables for visit, group, and time by visit group interaction terms. (If appropriate, time will be included as a continuous variable.) If the time by group interaction terms differ significantly from zero, this will indicate that the change over time in outcomes differs significantly between the treatment groups. In sensitivity analysis to examine the impact of treatment intensity (IR-5), we will also evaluate the effects of the intervention stratified by intervention dosage (frequency of interaction with the community health worker or mHealth / texting program.

Secondary Analysis

Next, we will assess whether patient activation, self-management behaviors, biologic markers, and transfer to adult care are mediators of intervention treatment effects. This analysis focuses on the role of patient activation and self-management behaviors at 6 or 12 months as mediators of the effect of the intervention on the study outcomes. We will perform the mediation analysis using structural equation modeling; this will allow us to estimate the total effect of the treatment on outcomes as a sum of direct effects and indirect effects that are mediated by patient activation, self-management behaviors, biologic markers, or transfer to adult care. To evaluate the role of each potential mediating variable, we will calculate the proportion of the total effect that is mediated; the ratio of the indirect effect to the direct effect; and the ratio of the total effect to the direct effect. We also evaluate percentile and bias-corrected bootstrapped standard errors and confidence intervals for the effects.

We will next perform an exploratory analysis to identify individual and family factors that moderate

intervention treatment effects. To test the hypothesis that adults with SCD and high disease severity will moderate the effect of intervention on outcome measures at 6, 12, and 18 months, we will first evaluate whether the impact of the intervention on overall changes (six month minus baseline) differs between the high versus low severity groups. This will be tested by building a regression model with changes (end of intervention minus baseline) as the outcome variable, and that includes indicator variables for treatment groups, severity group (high versus low), and group by severity interaction terms. If the interaction term for a particular treatment group differs significantly from zero, this will indicate that the impact of that intervention differs according to (is moderated by) severity of disease. Next, to evaluate moderation in longitudinal models, we will fit models with change since baseline at 6, 12, and 18 months as the outcomes; these models will also include indicator variables for treatment groups, indicator variables for severity group, and time by severity interaction terms. If the interaction terms differ significantly from zero, then this will indicate that the change since baseline depends on both treatment group and severity status (i.e., that the impact of treatment is moderated by severity of disease). We anticipate that this model will be adequate to evaluate interactions; however, it may be necessary to consider more complex models, by modifying the longitudinal models for analysis of our primary outcome variable to include time by severity group, severity group by intervention, and severity by time by treatment group (three-way interaction) models. Finally, to explore the moderating effects of individual and family demographic characteristics on treatment effects, we will convert all patient and family demographic variables into dichotomous variables and evaluate potential moderation using the approach just described for severity status.

Results

The COMETS study was funded in September 2017, received IRB approval in June 2018 (IRB #18-015106), and was registered in August 2018 (NCT03648710). The study is being conducted in accordance with the IRB-approved protocol (December 15, 2020). Participant recruitment began in

January 2019 and ended December 2022. Data collection will be completed in November 2024, with results expected to be submitted for publication in 2025.

Discussion

This research aims to compare the effectiveness of two interventions, a CHW intervention and a mHealth intervention, to enhanced usual care alone. Our study seeks to address the significant gap in research focused on transition to adult care, while examining the impact of such interventions on chronic disease management, healthcare utilization, or health outcomes. The COMETS trial is one of the first multi-site, randomized controlled trials to assess the effectiveness of these interventions specifically for young adults with SCD.

Despite the understudied effectiveness of mHealth and CHW programs in improving the transition to adult care for emerging adults with SCD, this research hypothesizes that incorporating either a CHW or an mHealth application will improve HRQOL and reduce acute care utilization. This trial aims to identify effective interventions to support young adults with SCD as they navigate the complexities of adult care, addressing gaps in current research. Positive results could translate into significant cost savings for payers and healthcare systems by reducing avoidable emergency department visits and hospitalizations, informing funding agencies like HRSA and State Title V Programs dedicated to improving care for children with special healthcare needs. Integrating these interventions into standard care models could lead to more personalized, accessible, and efficient care. CHW and mHealth interventions were chosen for their potential cost-effectiveness and scalability. Ultimately, demonstrating measurable improvements in health outcomes and cost savings will be key to integrating these personalized and accessible interventions into standard transition care models, leading to more efficient care and sustained improvements in health outcomes for young adults with SCD.

Strengths and Limitations

The study employs several key strengths to enhance its effectiveness and scalability. Firstly, the involvement of stakeholders, particularly young adult co-investigators, during the development phase ensures that research is aligned with their real-world experiences. This provides a comprehensive understanding that can inform implementation. Additionally, building upon the established IMPACT program [42], the study leverages past research and implementation insights for further refinement and enhancement. In response to the limitations posed by COVID-19, such as reduced in-person recruitment opportunities, the study incorporates diverse communication methods to increase accessibility and engagement. Lastly, the use of robust patient registries allows for real-time monitoring and identification of SCD patients who meet study criteria, facilitating a streamlined recruitment process even with pandemic-related constraints.

SCD interventions have anticipated limitations that must be acknowledged, particularly when engaging young adults. Emerging adults are often at pivotal time in their lives where they might be transitioning into college or the workforce. This stage of life is inherently demanding and can make it challenging for young adults to adhere to treatment plans and prioritize participation in SCD programs. Additionally, there is a widespread distrust of the healthcare system among this demographic, often rooted in historical and systemic inequities, which can be exacerbated by experiences of discrimination and stigma in both healthcare settings and broader society [56]. These factors together can lead to feelings of alienation and reluctance to engage with and adhere to SCD treatment plans or seek necessary care [56]. Addressing these challenges requires targeted strategies that build trust through culturally competent care, increase accessibility by aligning program delivery with young adults' schedules, and provide support systems that acknowledge and alleviate the unique pressures faced during this life transition.

In conclusion, the results of this study will contribute significantly to filling the gap in transition care research for emerging adults with SCD, guiding future intervention strategies, and providing valuable evidence for healthcare systems, payers, and policymakers. The potential impacts of these interventions extend beyond clinical outcomes, offering the possibility of improved psychosocial well-being, enhanced patient self-efficacy, and a more successful transition to adult care for individuals with sickle cell disease.

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SJ, KSW, CS, LC, LS, LB, BAy, BAn, AAK, KS, SL and DR designed this study; JS designed the statistical analysis plan; TB, CS, SJ, KSW, LC, LS, LB, BAy, BAn, AAK, and DR carried out this trial, TB and OT drafted this manuscript, and all authors read, carefully reviewed, edited, and approved the final manuscript.

Conflicts of Interest

Kim Smith-Whitley initiated this project as a full-time Perelman School of Medicine University of Pennsylvania employee and Director of the Comprehensive Sickle Cell Center at Children's Hospital of Philadelphia. She transitioned to Professor Emeritus and Physician Affiliate at CHOP in May 2021 with Global Blood Therapeutics and in September 2022 with employer Pfizer. All other authors declare that they have no conflict of interest, including affiliations with or involvement in any organization or entity with any financial interest or nonfinancial interest in the subject matter or materials discussed in this manuscript.

Abbreviations:

CHW: community health worker

GEE: generalized estimating equations

HRQOL: health-related quality of life

RCT: randomized controlled trial

REDCap: Research Electronic Data Capture

SMART Model: Social-Ecological Model for Adolescents and Young Adult Readiness to Transition

SCD: sickle cell disease

QLS: quasi-least squares

REFERENCES

1. 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(2):367-375.

2. Brousseau DC, Owens PL, Mosso AL, Panepinto JA, Steiner CA. Acute care utilization and rehospitalizations for sickle cell disease. JAMA. 2010;303(13):1288-1294. doi:10.1001/jama.2010.378

3. Ohene-Frempong K, Weiner SJ, Sleeper LA, et al. Cerebrovascular accidents in sickle cell

disease: rates and risk factors. Blood. 1998;91(1):288-294.

4. DeBaun MR, Armstrong FD, McKinstry RC, Ware RE, Vichinsky E, Kirkham FJ. Silent cerebral infarcts: a review on a prevalent and progressive cause of neurologic injury in sickle cell anemia. Blood. 2012;119(20):4587-4596. doi:10.1182/blood-2011-02-272682

5. Jordan L, Swerdlow P, Coates T. Systematic Review of Transition From Adolescent to Adult Care in Patients With Sickle Cell Disease. J Pediatr Hematol Oncol. 2013;35(3):165-169.

6. Viola A, Porter J, Shipman J, Brooks E, Valrie C. A scoping review of transition interventions for young adults with sickle cell disease. Pediatric Blood & Cancer. 2021;68(9):e29135. doi:10.1002/pbc.29135

7. Jones AP, Davies SC, Olujohungbe A. Hydroxyurea for sickle cell disease. In: The Cochrane Library. John Wiley & Sons, Ltd; 2001. Accessed December 10, 2016. http://proxy.library.upenn.edu:2154/doi/10.1002/14651858.CD002202/full

8. Saulsberry AC, Porter JS, Hankins JS. A program of transition to adult care for sickle cell disease. Hematology. 2019;2019(1):496-504. doi:10.1182/hematology.2019000054

9. Inusa BPD, Stewart CE, Mathurin-Charles S, et al. Paediatric to adult transition care for patients with sickle cell disease: a global perspective. Lancet Haematol. 2020;7(4):e329-e341. doi:10.1016/S2352-3026(20)30036-3

10. Calhoun C, Luo L, Baumann AA, et al. Transition for Adolescents and Young Adults With Sickle Cell Disease in a US Midwest Urban Center: A Multilevel Perspective on Barriers, Facilitators, and Future Directions. Journal of Pediatric Hematology/Oncology. 2022;44(5):e872-e880. doi:10.1097/MPH.0000000000002322

11. Prussien KV, Crosby LE, Faust HL, et al. An Updated Equitable Model of Readiness for Transition to Adult Care: Content Validation in Young People With Sickle Cell Disease. JAMA Pediatr. 2024;178(3):274-282. doi:10.1001/jamapediatrics.2023.5914

12. Crosby LE, Quinn CT, Kalinyak KA. A Biopsychosocial Model for the Management of Patients With Sickle-Cell Disease Transitioning to Adult Medical Care. Adv Ther. 2015;32(4):293-305. doi:10.1007/s12325-015-0197-1

13. Kangovi S, Grande D, Carter T, et al. The use of participatory action research to design a patient-centered community health worker care transitions intervention. Healthcare. 2014;2(2):136-144. doi:10.1016/j.hjdsi.2014.02.001

14. Huang JS, Terrones L, Tompane T, et al. Preparing Adolescents With Chronic Disease for Transition to Adult Care: A Technology Program. PEDIATRICS. 2014;133(6):e1639-e1646. doi:10.1542/peds.2013-2830

15. Krieger J, Takaro TK, Song L, Beaudet N, Edwards K. A Randomized Controlled Trial of Asthma Self-management Support Comparing Clinic-Based Nurses and In-Home Community Health Workers: The Seattle–King County Healthy Homes II Project. Arch Pediatr Adolesc Med. 2009;163(2):141-149. doi:10.1001/archpediatrics.2008.532

16. Palmas W, March D, Darakjy S, et al. Community Health Worker Interventions to Improve

Glycemic Control in People with Diabetes: A Systematic Review and Meta-Analysis. J GEN INTERN MED. 2015;30(7):1004-1012. doi:10.1007/s11606-015-3247-0

17. Free C, Phillips G, Galli L, et al. The Effectiveness of Mobile-Health Technology-Based Health Behaviour Change or Disease Management Interventions for Health Care Consumers: A Systematic Review. PLOS Medicine. 2013;10(1):e1001362. doi:10.1371/journal.pmed.1001362

18. Holtz B, Lauckner C. Diabetes Management via Mobile Phones: A Systematic Review. Telemedicine and e-Health. 2012;18(3):175-184. doi:10.1089/tmj.2011.0119

19. Militello LK, Kelly SA, Melnyk BM. Systematic Review of Text-Messaging Interventions to Promote Healthy Behaviors in Pediatric and Adolescent Populations: Implications for Clinical Practice and Research. Worldviews Ev Based Nurs. 2012;9(2):66-77. doi:10.1111/j.1741-6787.2011.00239.x

20. Miloh T, Annunziato R, Arnon R, et al. Improved Adherence and Outcomes for Pediatric Liver Transplant Recipients by Using Text Messaging. Pediatrics. 2009;124(5):e844-e850. doi:10.1542/peds.2009-0415

21. Amanda Lenhart. Teens, Social Media & Technology Overview 2015. Pew Research Center: Internet, Science & Tech. April 9, 2015. Accessed December 15, 2016. http://www.pewinternet.org/2015/04/09/teens-social-media-technology-2015/

22. Schwartz LA, Tuchman LK, Hobbie WL, Ginsberg JP. A social-ecological model of readiness for transition to adult-oriented care for adolescents and young adults with chronic health conditions. Child. 2011;37(6):883-895. doi:10.1111/j.1365-2214.2011.01282.x

23. Schwartz LA, Brumley LD, Tuchman LK, et al. Stakeholder Validation of a Model of Readiness for Transition to Adult Care. JAMA Pediatr. 2013;167(10):939-946. doi:10.1001/jamapediatrics.2013.2223

24. Prussien KV, Crosby LE, Faust HL, et al. An Updated Equitable Model of Readiness for Transition to Adult Care: Content Validation in Young People With Sickle Cell Disease. JAMA Pediatrics. 2024;178(3):274-282. doi:10.1001/jamapediatrics.2023.5914

25. Andemariam B, Owarish-Gross J, Grady J, Boruchov D, Thrall RS, Hagstrom JN. Identification of risk factors for an unsuccessful transition from pediatric to adult sickle cell disease care. Pediatr Blood Cancer. 2014;61:697-701.

26. Sobota AE, Umeh E, Mack JW. Young Adult Perspectives on a Successful Transition from Pediatric to Adult Care in Sickle Cell Disease. Journal of hematology research. 2015;2(1):17. doi:10.12974/2312-5411.2015.02.01.3

27. Aronson PL, Nolan SA, Schaeffer P, Hieftje KD, Ponce KA, Calhoun CL. Perspectives of Adolescents and Young Adults With Sickle Cell Disease and Clinicians on Improving Transition Readiness With a Video Game Intervention. Journal of Pediatric Hematology/Oncology. 2024;46(2):e147-e155. doi:10.1097/MPH.0000000000002810

28. Bodenheimer T, Wagner EH, Grumbach K. Improving Primary Care for Patients With Chronic Illness: The Chronic Care Model, Part 2. JAMA. 2002;288(15):1909-1914. doi:10.1001/jama.288.15.1909

29. Steinway C, Shilly S, Belton T, et al. Development of the iManage SCD mobile health application for transition. Health Care Transitions. 2024;2:100074. doi:10.1016/j.hctj.2024.100074

30. Zelen M. The randomization and stratification of patients to clinical trials. Journal of Chronic Diseases. 1974;27(7):365-375. doi:10.1016/0021-9681(74)90015-0

31. Kernan WN, Viscoli CM, Makuch RW, Brass LM, Horwitz RI. Stratified Randomization for Clinical Trials. Journal of Clinical Epidemiology. 1999;52(1):19-26. doi:10.1016/S0895-4356(98)00138-3

32. Panepinto JA, Torres S, Bendo CB, et al. PedsQL™ Sickle Cell Disease Module: Feasibility, Reliability and Validity. Pediatr Blood Cancer. 2013;60(8):1338-1344. doi:10.1002/pbc.24491

33. Beverung LM, Varni JW, Panepinto JA. Clinically meaningful interpretation of pediatric health-related quality of life in sickle cell disease. J Pediatr Hematol Oncol. 2015;37(2):128-133. doi:10.1097/MPH.0000000000000177

34. Evidence-Based Management of Sickle Cell Disease: Expert Panel Report. U.S. Department of Health and Human Services; National Institutes of Health; National Heart, Lung, and Blood Institute.; 2014.

35. Beverung LM, Varni JW, Panepinto JA. Clinically Meaningful Interpretation of Pediatric Health-related Quality of Life in Sickle Cell Disease. Journal of Pediatric Hematology/Oncology. 2015;37(2):128-133. doi:10.1097/MPH.0000000000000177

36. GotTransition.org. GotTransition.org - Health Care Transition Resources. GotTransition.org. May 10, 2017. Accessed May 9, 2017. http://www.gottransition.org/resources/index.cfm#paymentandtransition

37. Improving Sickle Cell Transitions of Care Through Health Information Technology. The National Institute for Children's Health Quality. Accessed November 21, 2024. https://nichq.org/publication/improving-sickle-cell-transitions-of-care-through-health-information-technology/

38. Szalda D, Steinway C, Greenberg A, et al. Developing a Hospital-Wide Transition Program for Young Adults With Medical Complexity. Journal of Adolescent Health. 2019;65(4):476-482. doi:10.1016/j.jadohealth.2019.04.008

39. Wu K, Szalda D, Trachtenberg S, Jan S. Transitioning From "Sick Kid" to Community Health Worker: Building Better Bridges to Adult Care. Pediatrics. 2018;142(2):e20180962. doi:10.1542/peds.2018-0962

40. Belton TD, Wu K, Steinway CM, et al. Training young adults as community health workers specializing in pediatric to adult health care transition to support emerging adults with sickle cell disease. Health Care Transitions. 2024;2:100050. doi:10.1016/j.hctj.2024.100050

41. Kangovi S, Mitra N, Grande D, et al. Patient-Centered Community Health Worker Intervention to Improve Posthospital Outcomes: A Randomized Clinical Trial. JAMA Intern Med. 2014;174(4):535. doi:10.1001/jamainternmed.2013.14327

42. Kangovi S, Carter T, Charles D, et al. Toward A Scalable, Patient-Centered Community Health Worker Model: Adapting the IMPaCT Intervention for Use in the Outpatient Setting. Population Health Management. 2016;19(6):380-388. doi:10.1089/pop.2015.0157

43. Crosby LE, Ware RE, Goldstein A, et al. Development and evaluation of iManage: A self-management app co-designed by adolescents with sickle cell disease. Pediatric Blood & Cancer. 2017;64(1):139-145. doi:10.1002/pbc.26177

44. Schwartz LA, Daniel LC, Butler E, et al. A Pilot Text Messaging Intervention for Adolescents and Young Adults Recently Off Treatment for Cancer. Journal of Adolescent Health. 2016;58(2):S30. doi:10.1016/j.jadohealth.2015.10.073

45. Gil KM, Williams DA, Thompson RJ, Kinney TR. Sickle Cell Disease in Children and Adolescents: The Relation of Child and Parent Pain Coping Strategies to Adjustment. J Pediatr Psychol. 1991;16(5):643-663. doi:10.1093/jpepsy/16.5.643

46. Jenerette CM, Murdaugh C. Testing the theory of self-care management for sickle cell disease. Research in Nursing & Health. 2008;31(4):355-369. doi:10.1002/nur.20261

47. Zelikovsky N, Schast AP, Palmer J, Meyers KEC. Perceived barriers to adherence among adolescent renal transplant candidates. Pediatr Transplant. 2008;12(3):300-308. doi:10.1111/j.1399-3046.2007.00886.x

48. Zelikovsky N, Schast AP. Eliciting accurate reports of adherence in a clinical interview: development of the Medical Adherence Measure. Pediatr Nurs. 2008;34(2):141-146.

49. Treadwell MJ, Hassell K, Levine R, Keller S. Adult Sickle Cell Quality-of-Life Measurement Information System (ASCQ-Me). Clin J Pain. 2014;30(10):902-914. doi:10.1097/AJP.0000000000000054

50. Moser A, Stuck AE, Silliman RA, Ganz PA, Clough-Gorr KM. The eight-item modified Medical Outcomes Study Social Support Survey: psychometric evaluation showed excellent performance. Journal of Clinical Epidemiology. 2012;65(10):1107-1116. doi:10.1016/j.jclinepi.2012.04.007

51. Sherbourne CD, Stewart AL. The MOS social support survey. Social Science & Medicine. 1991;32(6):705-714. doi:10.1016/0277-9536(91)90150-B

52. JHU COVID-19 Community Response Survey-Disaster Research Response (DR2) Resources Portal. National Institute of Environmental Health Sciences. Accessed November 29, 2024. https://tools.niehs.nih.gov/dr2/index.cfm/resource/22096

53. Bureau UC. Household Pulse Survey: Measuring Emergent Social and Economic Matters Facing U.S. Households. Census.gov. Accessed November 29, 2024. https://www.census.gov/householdpulsedata

54. Fritz MS, MacKinnon DP. Required Sample Size to Detect the Mediated Effect. Psychol Sci. 2007;18(3):233-239. doi:10.1111/j.1467-9280.2007.01882.x

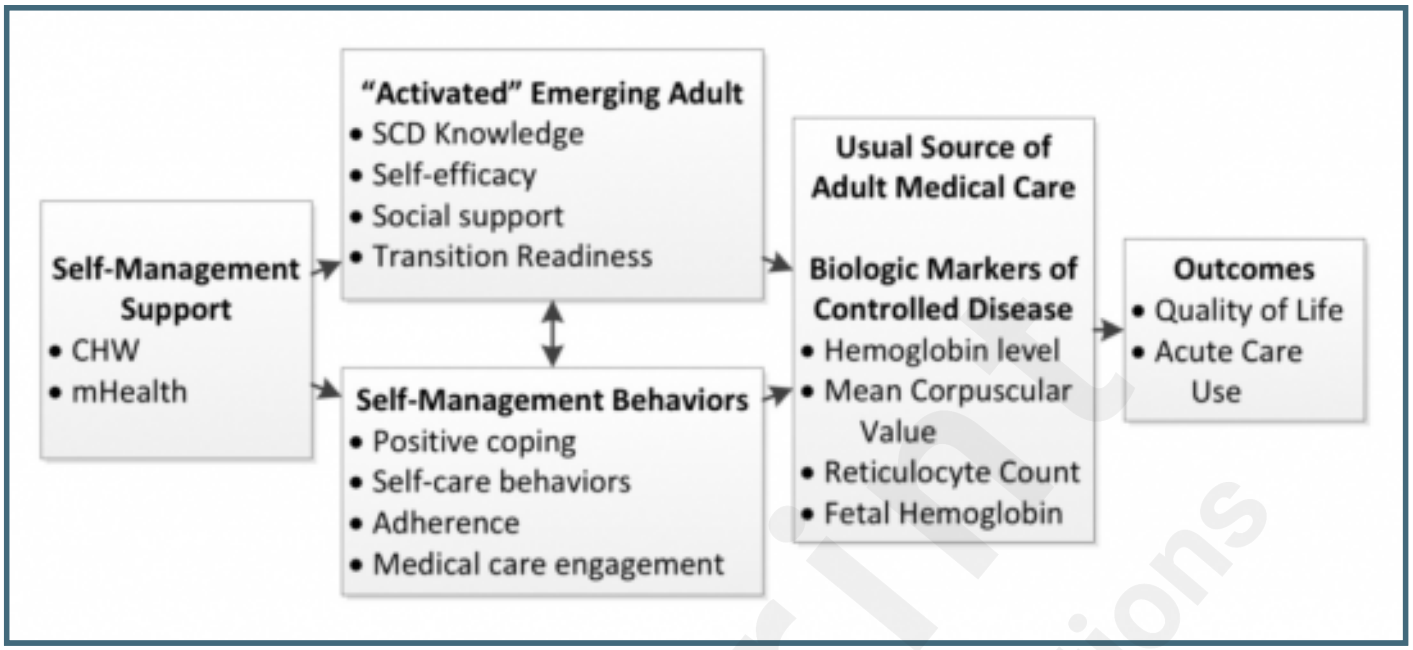
55. Shults J, Hilbe JM. Quasi-Least Squares Regression. 0 ed. Chapman and Hall/CRC; 2014. doi:10.1201/b16446

56. Smith WR, Valrie C, Sisler I. Structural Racism and Impact on Sickle Cell Disease. Hematology/Oncology Clinics of North America. 2022;36(6):1063-1076. doi:10.1016/j.hoc.2022.08.008

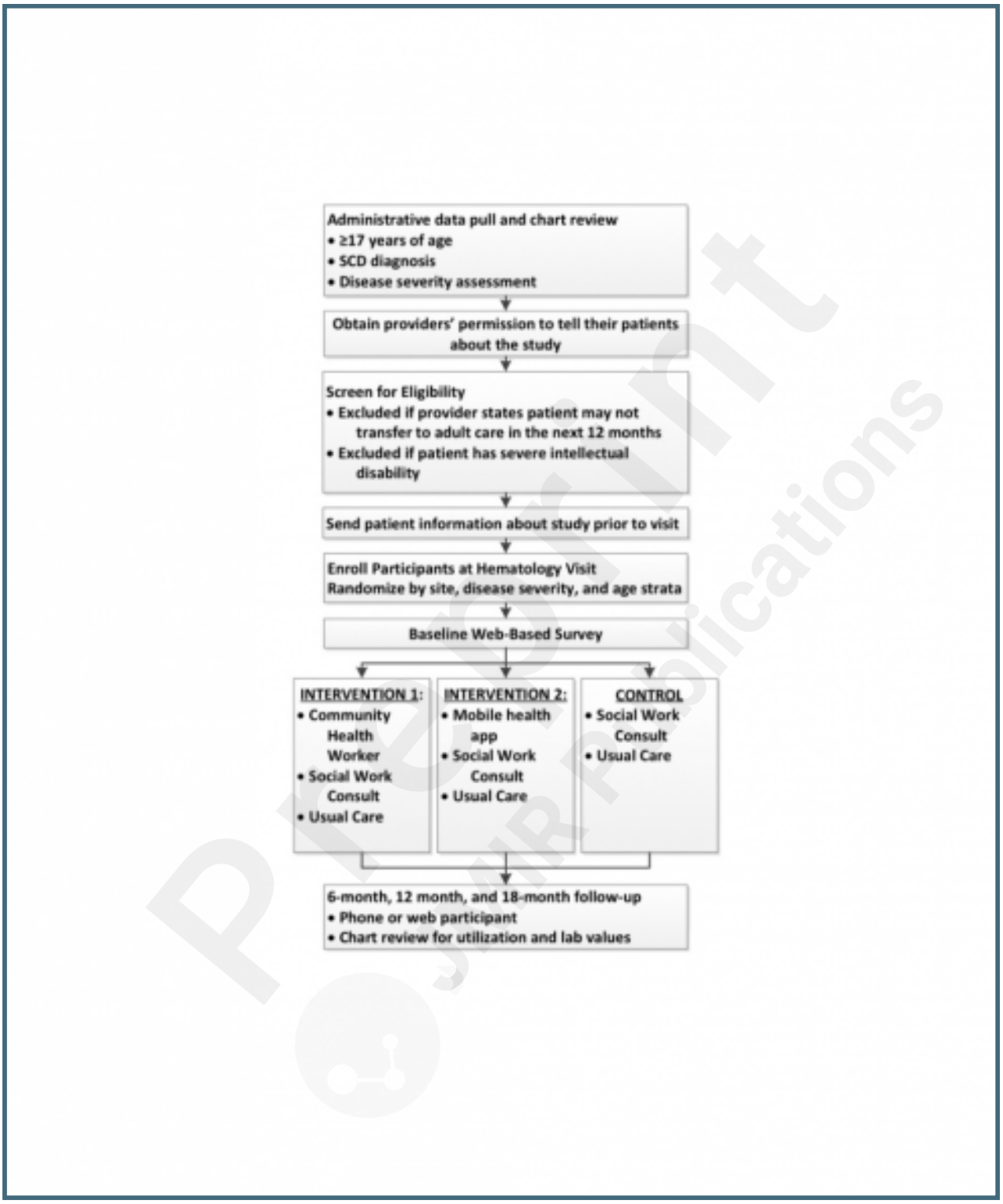
Supplementary Files

Figures

Key clinical question and conceptual model.



COMETS study flowchart among emerging adults with sickle cell disease.



Multimedia Appendixes

Online appendix: sample size calculations.
URL: http://asset.jmir.pub/assets/229d7dedce265c3d617885580b696e08.docx

Existing Peer-Review Reports from Funding Agencies (for protocols/proposals only)s

Peer review report from PCORI.
URL: http://asset.jmir.pub/assets/fe653d2ca4afc0150da7ff4e0f6785c2.pdf