Protocol for: **Understanding and Addressing the Social Determinants of Health for Families of Children with Sickle Cell Anemia within Pediatric Hematology (SCA WE CARE)**

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Understanding and Addressing the Social Determinants of Health for Families of Children with Sickle Cell Anemia within Pediatric Hematology (SCA WE CARE)

Table of Contents

Specific Aims/Objectives

Although pediatric professional guidelines are now recommending medical providers screen for social determinants of health (SDoH), there is no evidence to date that SDoH screening improves the health of pediatric patients and studies have fallen short of exploring its impact on the health of children with medical complexity, including children with sickle cell anemia (SCA). The proposed mixed-methods study aims to understand the implementation of a previously tested, efficacious SDOH screening and referral intervention in the outpatient pediatric hematology setting; qualitatively assess possible mechanisms for such interventions on improving child health; and obtain population-specific empirical estimates to plan a large-scale clinical trial.

Our **specific aims** are to: **(1)** Implement WE CARE in two pediatric hematology clinics in order to field test key study logistics and understand the facilitators and barriers to implementation and accelerate its adoption; **(2)** Obtain population-specific empirical estimates of study parameters to plan a large-scale multi-site cluster RCT of WE CARE that will definitely assess its impact on improving health outcomes for children with SCA; and **(3)** Qualitatively assess possible mechanisms linking social determinants of health interventions to improved health outcomes.

Background and Significance

Social determinants of health are key drivers of health and health disparities, beginning in childhood. The social determinants of health (SDoH) – the social circumstances in which people are born, work, live, and age – affect disparities in risk and health outcomes through a myriad of physiological and behavioral pathways.[2,23-25] Some[26] have estimated that up to 70% of variation in health outcomes is attributable to SDoH.[27] SDoH such as unmet material needs (e.g., food insecurity), has been linked to detrimental health and healthcare utilization outcomes, including higher rates of hospitalizations.[28-30] The correlation between poverty and SDoH is well established,[31,32] with those living in impoverished conditions more likely to have unmet material needs. Unfortunately, children constitute the poorest segment of the population in the United States (US) with racial/ethnic minority children disproportionately affected.[33] Childhood is a particularly vulnerable period for the imprinting of harmful environmental exposures associated with poverty and its related adverse social determinants (e.g., food insecurity, housing instability, parental unemployment, and lack of high-quality childcare)[24,31,32] and has been shown to affect health across the lifespan.[28-30,34,35] *Children with medical complexity are especially at-risk and have been designated as a priority population for health care policy given their high healthcare need and utilization[4,36] compared to healthy children.* Overall, approximately one in five children in the US has a medically complex condition.[5]

The medical system is increasingly recommending routine SDoH screening at healthcare visits. Although addressing SDoH has long been a goal of the US public health system, it was not a key priority in the delivery of medical care until recently when the World Health Organization (WHO) and National Academy of Medicine (NAM) emphasized the need for clinicians and health systems to address SDoH within the context of healthcare visits.[37-39] In 2016, the American Academy of Pediatrics (AAP) became the first medical organization to recommend screening for SDoH at pediatric visits,[2] and listed Dr. Garg's (study PI) WE CARE instrument as an example of an evidence-based screening tool. In addition, the Centers for Medicare & Medicaid Services invested $157 million in their Accountable Health Communities initiative,[40,41] which is implementing SDoH screening and referral in 32 sites across the US and assessing its impact on reducing unnecessary healthcare utilization, primarily in adults. Finally, some Medicaid programs, such as the one in Massachusetts, have developed value-based payment models that provide additional payments for patients identified as having unmet social needs, such as housing,[42] thereby incentivizing SDoH screening.

The Problem: There is no evidence that SDoH screening improves child health, and the underlying mechanisms for how SDoH screening may improve health remains unexamined. Although there is strong epidemiological evidence linking adverse SDoH and detrimental health and healthcare utilization outcomes,[28-30] *there is no evidence, to date, demonstrating the success of SDoH screening and referral interventions on improving child health.* Two recent studies offer promising preliminary results: one demonstrating increased parental report of excellent/very good child health in primarily healthy children; the other demonstrating improvement in blood pressure and cholesterol levels in adults.[14,43]

In addition, *the underlying mechanisms by which SDoH screening and referral interventions can improve*

child health are also currently unknown. Understanding the processes linking SDoH interventions and health outcomes has the dual benefit of contributing to our scientific knowledge of SDoH and informing treatment targets in future intervention studies. Since SDoH burden falls disproportionately on those with lower socioeconomic status and on racial/ethnic minority families, it will be critical to examine these processes within diverse samples. Given the significance of this emerging field, the NIH is convening a workshop on SDoH screening and referral interventions and its future research directions in May 2018.[3]

Children with sickle cell anemia are the ideal population in which to study how SDoH interventions may improve health. Sickle cell disease affects approximately 100,000 people in the US, primarily those of African and Hispanic descent.[15,44] Sickle cell anemia (SCA) is the most severe form and represents approximately 60% of the sickle cell population.[1] Manifestations of SCA, including sepsis and painful vaso-occlusive episodes, begin in infancy and expected survival is approximately 45 years, nearly 30 years less than for African Americans overall.[15] Use of daily antibiotic prophylaxis in children with SCA until age 5 years reduces mortality, especially in early infancy.[18,19] Guidelines also recommend that hydroxyurea (HU) be offered to children with SCA beginning at 9 months of age.[45] [46] *However, adherence to therapies proven effective for SCA is low*.[47] One study of >2,800 eligible children with SCA found that only 18% had prescriptions filled for antibiotic prophylaxis for ≥300 days, far short of the recommended daily intake.[48] In addition, a study of a state Medicaid program showed that only 41% of children prescribed HU were adherent, defined as supplied (from pharmacy records) to cover at least 80% of days in a year.[49] A recent meta-analysis found mixed findings regarding the possible mechanisms underlying low rates of medication adherence among children with sickle cell disease, with medication barriers (e.g., competing demands) having the strongest effect size.[50]

In addition to the high morbidity and low adherence, most children with SCA live in impoverished households. A multicenter clinical trial found that children with SCA live in households with a median income of $6,250.[16] Another study also demonstrated that over 90% of families of children with sickle cell disease have at least one unmet material need.[17] Although not yet examined empirically, per *Maslow's Hierarchy of Needs model* (see C1)[51] it is very likely that difficulties related to adverse SDoH, such as food or housing insecurity, likely impede parents' ability to adhere to treatment plans[52] by limiting the degree to which parents can focus on SCA as opposed to more basic tasks of living.[50] *In sum, SCA is an ideal medically complex condition in which to test the impact of an evidence-informed SDoH screening and referral intervention on improving child health outcomes due to its significant morbidity; most children with SCA live in impoverished households;[16] and the known association between poverty and SDoH that likely impacts parental disease management.*

Significance*: *Our proposal has significant potential to inform the burgeoning SDoH interventional research field, transform current clinical practice and improve health outcomes for medically complex children. Although medical organizations and payers are increasingly recommending routine SDoH screening in medical practices,[1,37-39] there is an absence of clinical trials on SDoH screening and referral interventions that assess health outcomes. This study addresses this clinically- and policy-relevant research gap by determining how to exert transformational practice change to implement an intervention that systematically addresses SDoH into the care for medically complex children (such as those with SCA), and exploring its impact on healthcare utilization and outcomes. Studies and practice guidelines for SCA, to date, primarily focus on pharmacologic interventions, as opposed to modifying social and environmental contributors to disease. While the contribution of social adversity and socioeconomic factors to the morbidity and mortality of SCA has been demonstrated,[55] no one has yet developed an intervention that modifies these factors as a part of routine clinical care, nor have they carefully considered the processes through which SDoH impacts child health outcomes. Our mixed-

methods findings will inform whether, and how, to provide SDoH screening on a larger scale in the future. It will also add significantly to the sickle cell disease implementation science field since there is a great need for this type of research given the paucity of prior dissemination and implementation studies in children with SCA.[56] More broadly, the knowledge gained from this proposal is likely to be directly translatable and applicable not only to SCA but also to other medically complex conditions. From a societal perspective, this proposal has great significance, as approximately one in five children in the US has a medically complex condition such as SCA,[5] and these children are a priority population for healthcare policy given their high healthcare need and utilization.[4,36] Given the near universal reach of child healthcare,[57] this proposal has significant public health implications.

Preliminary Studies

Family-centered approach for addressing SDoH for low-income children utilizing existing clinical infrastructure: the WE CARE Model. Our extensive groundwork[13,53] has demonstrated that a family-centered screening and referral intervention that relies on parental desire for assistance administered during pediatric preventive care visits led to increased provider referrals for, and parental receipt of, community resources. WE CARE (Well-Child care visit, Evaluation, Community Resources, Advocacy, Referral, Education) was efficacious in connecting families to community resources and resulted in higher parental employment, receipt of fuel assistance and childcare, and lower odds of living in a homeless shelter,[13] thereby reducing material need when tested in pediatric primary care clinics. Ongoing work is providing a better understanding for the barriers (e.g., staff burden, lack of time and/or resources) and facilitators (e.g., clinic culture and leadership) for implementing this relatively simple intervention in general pediatric practice. This is necessary given the well-known challenge of incorporating efficacious innovations into routine medical practice.[54] *Our WE CARE studies so far have focused on children without medically complex conditions and have been implemented only in primary care pediatric practices. Our studies to date have not been designed to measure the impact of WE CARE on child health outcomes, since they have targeted parents with healthy children.*

> ***Our team has conducted extensive groundwork to develop and implement a family-centered system for SDoH screening and referral in safety-net pediatric primary care clinics.***[16,30,39] We have crafted and validated a screening tool for six material needs and tested it among parents at general pediatric clinics. Given its reliance on existing clinical processes and infrastructure (i.e. no additional staff), we have purposefully measured implementation metrics in our recent studies. We have developed a system and feasible workflow (with documented acceptability for providers, staff, and parents) for administering the tool in the primary care setting. This work documented that use of the tool results in identification of unmet SDoH needs for which parents desire help, elicits referrals by the clinical team to community resources, and leads to actual receipt of services by parents. We have also developed simple, easy-to-use community resource sheets to address each type of social need.

Design and Methods

Study Design

Study 1 (Aim 1): The implementation of a practice-based social determinants of health screening and referral intervention in two pediatric hematology clinics to field test key study logistics and understand the facilitators and barriers to implementation and accelerate its adoption

Two of our four proposed pediatric hematology clinical sites will be randomized to implement WE CARE as standard of care for SCA patients. At baseline and every six months throughout the study period, the Boston Medical Center-based team (hereafter termed the core research team) will conduct focus

groups with stakeholders (e.g., clinical and administrative staff) at each of the four pediatric hematology clinic sites to better understand the barriers and facilitators to implementation of WE CARE. The site PI at each institution will help us identify staff members. Before beginning each focus group, the Boston Medical Center PIs and members of their research team will meet with clinic stakeholders at their staff meetings and provide an overview of the study. The Boston Medical Center-based team will conduct focus groups with pediatric hematology clinic staff every six months throughout the study period.

Study 2 (Aim 2): Obtaining population-specific empirical estimates of study parameters to plan a future large-scale cluster RCT of WE CARE for children with SCA

For this study, we will be conducting a pilot cluster RCT. Two of our four proposed pediatric hematology clinical sites (Boston Children's Hospital, Connecticut Children's Medical Center, Hasbro Children's Hospital (HCH) and Yale-New Haven Children's Hospital) will be randomized to implement WE CARE as standard of care for SCA patients. To assign the sites to either the control or the intervention group, we will first fix the number of sites to each group (i.e. 2 sites per group) and then assign sites to group using the random function for the uniform distribution in SAS 9.4.

Study 3 (Aim 3): Qualitatively assess possible mechanisms linking SDoH interventions to improved health outcomes, such as increasing a parent's ability to manage their child's disease through medication adherence

The Boston Medical Center-based team will conduct individual in-depth, semi-structured interviews with English- and Spanish-speaking parents of children aged ≤12 years who receive medical care for SCA at the two control sites (i.e., those in which the WE CARE intervention is not implemented).

Inclusion/Exclusion Criteria

Inclusion Criteria

- Staff (e.g., physicians, nurses, front desk) at the outpatient hematology sites who are able to converse in English or Spanish, and are 18 years of age or older.
- English- or Spanish-speaking parents and caregivers of children with SCA aged 0-12 who receive care at one of the four study sites and take daily penicillin or hydroxyurea.

Exclusion Criteria

- Staff at the four sites who are unable to converse in English or Spanish or are under 18 years of age.
- Parents < 18 years of age, parents with children with SCA who are 13 years of age or older, parents whose child does not take daily penicillin or hydroxyurea, foster parents, caregivers who speak neither English nor Spanish, and caregivers previously enrolled in the study.

Patient Selection

Study 1 (Aim 1): The implementation of a practice-based social determinants of health screening and referral intervention in two pediatric hematology clinics to field test key study logistics and understand the facilitators and barriers to implementation and accelerate its adoption

The site PI at each institution will help us identify staff members. The BMC-based team will provide an information sheet about Aim 1 of the study in advance so that practitioners and staff have time to consider the consent and come to the focus groups ready with questions regarding the consent. Before beginning the focus groups, the study PIs (Garg and Kavanagh) and members of the research team will meet with clinic stakeholders at their staff meetings and provide an overview of the study. All eligible participants will be told that taking part in the research is voluntary and that the decision to not take part will not result in any loss of benefits to which they are entitled to or effect their employment. We

will schedule the focus groups at convenient times for the staff such as prior to beginning of a clinic session or during staff meetings. The Boston Medical Center-based team will conduct focus groups with pediatric hematology clinic staff every six months throughout the study period. We expect that there will be staff turnover during the study and we will be in regular communication with the medical director to monitor and make sure the research team is aware of this.

Study 2 (Aim 2): Obtaining population-specific empirical estimates of study parameters to plan a future large-scale cluster RCT of WE CARE for children with SCA

Eligible study participants will be identified by the research staff by reviewing the clinic schedule in advance. We will also ask front desk personnel to assist us in identifying potential subjects, if they are willing, and, in some sites, to assist in handing out informational flyers. If a family is identified as likely to meet eligibility criteria, a member of the study team will approach potentially eligible parents in a private location at the practice, such as an exam room. If the parent is eligible for the study, a study team member will review the study with him/her..

Study 3 (Aim 3): Qualitatively assess possible mechanisms linking SDoH interventions to improved health outcomes, such as increasing a parent's ability to manage their child's disease through medication adherence

Families will be enrolled from the two control sites (i.e., those in which the WE CARE intervention is not implemented). A research assistant at the two control sites will coordinate recruitment efforts, which will include telling potentially-eligible families about the study and conducting initial eligibility screening. Families who are both eligible and interested in participating will be scheduled for an interview, which will occur in the hematology clinic on the same day as a future routine medical visit to decrease participant burden. Study participants will be engaged in the interview only once; therefore, we will not need to retain participants in this study.

Description of Study Treatments or Exposures/Predictors

WE CARE SDoH Screening and Referral intervention: WE CARE is a relatively simple intervention that has two key components: (1) the WE CARE SDoH Screening Survey and (2) SDoH Community Resource sheets. The intervention will be fully implemented at two of four study sites, after which subjects will be enrolled to collect the outcomes described on pages 7-8, *Definition of Primary and Secondary Outcomes/Endpoints.*

Table 1. Summary of the WE CARE Components.

Key Components:	Description
WE CARE SDoH Screening Survey (see attachments)	Administered at all visits Identifies 6 unmet material needs and parent desire for assistance with: *childcare, employment, food security, utilities (heating/cooling, water, electricity), housing, inadequate education* 3rd grade reading level; 0.92 test-rest reliability of original survey[69]
SDoH Community Resources	One-page information sheets listing available resources 5th grade reading level

Component 1: WE CARE SDoH Screening Survey. The survey consists of 12 questions designed to: (1) briefly identify 6 unmet material needs (e.g., childcare, employment, food security, household heat,

housing inadequate education) by self-report (e.g., "Are you employed?") and (2) using a family-centered approach, determine whether parents would like assistance with each problem (i.e. "If no, do you want help?"). Parents wanting help will receive a resource referral (see below). The survey has been translated into Spanish. Because it is a component of the practice-wide implementation of the WE CARE SDoH screening and referral program, the survey will be given at all visits by the front desk staff to all parents of SCA patients who present to the pediatric hematology clinic—not solely to caregivers who enroll in the study. The front desk staff and/or research staff will instruct parents to complete the screener. Clinic staff will be trained to review the WE CARE SDoH survey at visits and to provide community resource information sheets to parents with needs (see below). The completed surveys will be scanned into the EHR.

Component 2: Family Resource Book. The Family Resource book will contain one-page information sheets listing community resources (e.g., food pantries) and their contact information (e.g., telephone number) for each specific material need (e.g., food insecurity). Information sheets will be specific to each site and written at, or below, the 8th grade level.[69] The book will contain six separate tabs, one for each unmet need, and will contain multiple copies of the information sheets. The Family Resource Book will be made available in each exam room. We will work with each practice to create a Family Resource Book prior to study initiation. For parents with an identified need, providers will be instructed to give an information sheet and document this in the electronic health record (EHR), as done in previous studies.

Definition of Primary and Secondary Outcomes/Endpoints

Because qualitative research is by nature exploratory, we have not defined outcomes for the focus group discussions with practice staff (***Aim 1);*** however, we will use the Promoting Action on Research Implementation in Health Services (PARIHS) framework to guide these discussions about facilitators and barriers to WE CARE implementation. Key areas of exploration will be (1) evidence: attitudes and beliefs about evidence of the WE CARE system; (2) context: organizational, systemic, and sociopolitical features that promote or hinder implementation of WE CARE; and (3) facilitation: attributes of the facilitation that supported or impeded the implementation, and needed adaptations.

Primary outcomes for ***Aim 2*** include the following:

- *Identification of unmet needs and provision of referrals*. Previously utilized forms will be used during baseline and follow-up questionnaires to measure whether practitioners provided families resource handouts.
- *Parental enrollment in community-based resources*. Baseline and follow-up questionnaires to measure enrollment in community resources.
- *Process measures*. Data will be collected on adherence to clinic visits (appointments kept, cancelled, and no-show). We will collect data on medications adherence in two ways. First, we will collect laboratory markers that are commonly affected by HU, including hemoglobin and hemoglobin F levels, white blood cell and absolute neutrophil counts, and MCV. We will also collect data on prescriptions written and filled for HU and penicillin through EHR review and parent report.
- *Health outcomes*: Data on vaso-occlusive episodes, acute chest syndrome and sepsis will be collected from the EHR at 6-month- and 12-month follow-up. Quality of life will also be assessed through both the PedsQL, which has been validated in children with sickle cell disease and is responsive to change, and the PedsQL Sickle Cell Disease Module.
- *Healthcare utilization outcomes*: Data on emergency department visits, hospitalizations, and clinic visits will be collected from the EHR at baseline and 12-month follow-up. We have chosen

emergency department visits as our primary outcome because it has been extensively, and commonly, used as a measure of lack of outpatient care and non-adherence to treatment regimens in this population. We will also calculate ED reliance (clinic visits kept / clinic visits kept + ED visits), as it has been used to discriminate frequent emergency department users.

Because qualitative research is by nature exploratory, we have not defined outcomes for the qualitative interviews with parents of children with SCA ***(Aim 3)***. Qualitative interviews will aim to examine parents' perceptions of factors that promote or hinder effective management of their child's SCA.

Data Collection Methods, Assessments, Interventions and Schedule

Study 1 (Aim 1): The implementation of a practice-based social determinants of health screening and referral intervention in two pediatric hematology clinics to field test key study logistics and understand the facilitators and barriers to implementation and accelerate its adoption

Study Procedures. At baseline and every six months throughout the study period, the Boston Medical Center-based team will conduct focus groups with stakeholders (e.g., clinical and administrative staff) at each of the four pediatric hematology clinic sites to better understand the barriers and facilitators to implementation of WE CARE. The site PI at each institution will help us identify staff members. The BMC-based team will provide an information sheet about Aim 1 of the study in advance so that practitioners and staff have time to consider the consent and come to the focus groups ready with questions regarding the consent. Before beginning the focus groups, the study PIs and members of their research team will meet with clinic stakeholders at their staff meetings and provide an overview of the study. We will conduct focus groups with pediatric hematology clinic staff every six months throughout the study period. At baseline, the Boston Medical Center-based team will conduct focus groups (6-8 individuals per group) with key stakeholders identified by the site PI at the two WE CARE pediatric hematology clinics to better understand the barriers and facilitators to implementation. They will include both clinic leadership and individuals known within the clinic to be thought leaders. The composition of these groups may vary at each time point, but the structure, discussion topics, and goals of the later focus groups will be the same as the earlier focus groups. Individuals participating in multiple focus groups will be re-consented at each time point.

Quality improvement methodology will be used to both gather key information and optimize the implementation of WE CARE. We will employ the Model for Improvement's Plan-Do-Study-Act (PDSA) methodology to assess the implementation of WE CARE in an iterative fashion for one year in each clinic. Best practices regarding key elements of the intervention will be continually assessed throughout the QI phase. Drs. Garg and Kavanagh will initially meet weekly with clinic stakeholders via video conferencing to review the WE CARE process data and identify areas for improvement. We expect, based on our prior experience that we will gradually scale back to monthly meetings. This phase of the study will not involve human subjects.

Intervention Fidelity Data: Study staff, as we have previously done, will collect data on the implementation of WE CARE from the electronic health record (EHR). Specifically, to determine whether WE CARE *screeners were given and whether referrals were made at clinic visits*, and to assess for drift during the study period, we will measure the scanned surveys in the EHR for SCA visits. Of note, the WE CARE survey has a referral checkbox that providers mark if a referral is made. Clinical staff will be instructed to check off the box if she/he provides an information sheet from the Family Resource Book

for an unmet need. Every six months, we will randomly select 10 patients who had a visit and review their EHR for distribution of surveys and referrals. This study phase will not involve human subjects.

Materials. The research data will include audio-recordings of focus groups. Only study PIs Drs. Garg and Kavanagh, Drainoni (co-I), and trained study staff at each of the study sites will have access to participants' identifying information. The site PIs and RAs from the two control sites will not have access to the identifiable qualitative data. We will use excel spread sheets to document our descriptive QI and fidelity data (e.g., distribution of WE CARE surveys, unmet needs, referrals); no HIPAA identifiers will be collected.

Study 2 (Aim 2): Obtaining population-specific empirical estimates of study parameters to plan a future large-scale cluster RCT of WE CARE for children with SCA

Study Procedures. Parents will be asked to complete a baseline and 12-month follow-up questionnaire at their child's medical visit and complete a brief telephone interview 3, 6, and 9 months post-enrollment.

Eligible study participants will be identified by the front desk staff and research staff at each clinic. Prior to each clinic session, the research staff will identify potentially eligible study subjects by reviewing the daily appointment list. We will also ask front desk personnel to assist us in identifying potential subjects, if they are willing, and, in some sites, to assist in handing out informational flyers If a family is identified as likely to meet eligibility criteria, a member of the study team will approach potentially eligible parents in a private location at the practice, such as an exam room. If the parent is eligible for the study, a study team member will review the study with him/her. Informed consent will be obtained via written consent. The original hard copies of the ICFs will be stored in a locked file in a locked room in the hematology research space at that site. Each clinical site will maintain a tracker linking each patient to a unique subject ID number, which does not contain any combination of information that allows the identification of a subject; this tracker will not be shared outside that clinical site. Participants will be provided with a copy of their signed informed consent form.

Data will be collected from parents primarily from parent-administered surveys at enrollment and at follow-up which will occur one year post-index visit. These surveys will be completed using a study tablet (e.g., iPad) and backed up on to a HIPAA-compliant Boston Medical Center installation of REDCap, which is backed up on the secure, password-protected Boston University Medical Campus server. To complete these surveys, subjects will enter their unique ID number. A brief telephone interview will be conducted 3, 6, and 9 months post-enrollment to ascertain unmet needs, contact and enrollment in community-based resources, and parent report of prescription refills for penicillin or hydroxyurea. A hair cortisol sample will also be collected from the parent at enrollment and 1-year follow-up. Finally, site research staff will collect data from the electronic health record (EHR) on child health outcomes (i.e., adherence to clinic visits, medication adherence, ED visits, hospitalizations, vaso-occlusive episodes, acute chest syndrome, and infections). Data from the EHR will be collected three times (baseline, 6-months post-enrollment, and 12-months post-enrollment).

**Research Electronic Data Capture (REDCap) is a research focused, electronic web-based data capture system. REDCap is a data collection tool and allows for storage and management of both surveys and databases. REDCap is a secure storage system and meets HIPAA compliance standards. REDCap software will be used to facilitate parent consents, questionnaires, and forms.*

Materials. The research data will include questionnaires completed by parents/caregivers both in-person and via telephone, parent hair cortisol samples, and medical chart review. Only trained project staff at each clinical site will have access to participants' identifying information.

For the hair cortisol samples, we will be following the hair collection protocol developed by Dr. Jerrold Meyer from the University of Massachusetts (UMASS). Hair will be cut at the level of the scalp from 2-3 locations and cut to 3cm at the distal end. Hair samples will be placed directly into a plastic vial; each vial will be labeled by an ID number uniquely linked to each study subject (see below). Hair cortisol is stable at room temperature indefinitely, thus vials will be stored in a locked file cabinet.

For the *medical chart review*, existing trained research staff members at each study site, will collect the data. We decided to use existing research staff for the data collection component of the study since getting chart review credentialing is difficult at each of the study sites. At baseline and 12-month follow-up, medical charts will be reviewed in order to determine the number of appointments kept versus cancelled or no-show, the number of days covered by prescription refills for penicillin and hydroxyurea, and blood tests for monitoring hydroxyurea (including WBC, HB F%, and MCV). At 6-month and 12-month follow-up, medical charts will be reviewed in order to determine the frequency of vaso-occulsive episodes, acute chest syndrome, and sepsis diagnoses.

All enrolled parent-child dyad study participants will be assigned ID numbers which do not contain personal identifiers. All data will be tracked using these ID numbers. The data will be stored in computer files that are protected by a series of passwords known only to study staff and will be stored separately from participant identifiers (i.e., child's name, medical record number). Only the PIs and the research staff at each clinical site will have access to subjects' identities. The master code for each site will be stored in computer files on each site's HIPAA compliant server; they will be protected by a series of passwords known only to the research staff. The database will be stored in computer files on the Boston University Medical Campus HIPAA compliant server; it will also be protected by a series of passwords known only to the Boston Medical Center-based research team (hereafter termed core research team).

Study 3 (Aim 3): Qualitatively assess possible mechanisms linking SDoH interventions to improved health outcomes, such as increasing a parent's ability to manage their child's disease through medication adherence

Study Procedures. The Boston Medical Center-based team will conduct individual in-depth, semi-structured interviews (~60 minutes) with English- and Spanish-speaking parents of children aged ≤12 years who receive medical care for SCA at the two control sites (i.e., those in which the WE CARE intervention is not implemented). The interviews will be conducted in a designated private area (e.g., exam room) in the outpatient hematology clinic. A research assistant at the two control sites will coordinate recruitment efforts, which will include telling potentially-eligible families about the study and conducting initial eligibility screening. Specifically, eligibility will be determined by study staff. Eligible children's medical charts will be flagged. We will also ask front desk personnel to assist us in identifying potential subjects, if they are willing, and, in some sites, to assist in handing out informational flyers. The flyer will give a brief description of the project. If a family is identified as likely to meet eligibility criteria, a member of the study team will approach the parent about the study during their child's visit (in a private location at the practice, such as an exam room) and explain to them the purpose of the study and the expectations for the participant. Families who are both eligible and interested in

participating will be scheduled for an interview, which will occur in the hematology clinic on the same day as a future routine medical visit to decrease participant burden. If participants are willing to participate and express a desire to consent during this initial encounter, the site RA will obtain written informed consent from participants at this time; however, participants will not be required to consent during this initial encounter, as they will be given the opportunity to consent on the day of their interview. The RA will work with the site PIs to schedule study participants, and the Boston Medical Center-based research team (Dr. Long and a RA trained in qualitative methodology) will conduct interviews at the control sites. A maximum of 3 interviews will be conducted per day, in order to allow the research team to incorporate interim findings into the interview guide. In this way, data collection and analysis will be iterative.

At the time of the interview, if informed consent has not previously been conducted by the site RA, Dr. Long and the Boston Medical Center-based RA will take responsibility for performing informed consent procedures and collecting qualitative data (both of which will occur at the control sites), as well as managing and analyzing qualitative data. Informed consent will be obtained via written consent. The original hard copies of the ICFs will be stored in a locked file in a locked room in the hematology research space at that site. Each clinical site will maintain a tracker linking each patient to a unique subject ID number, which does not contain any combination of information that allows the identification of a subject; this tracker will not be shared outside that clinical site. Participants will be provided with a copy of their signed informed consent form.

Enrollment will continue until saturation is reached (i.e., more interviews will not generate additional information) in primary research questions. Qualitative interviews will examine parents' perceptions of factors that promote or hinder effective management of their child's SCA. Dr. Long's team will conduct interviews in pairs, and therefore will always have a member of the research team available for childcare, if necessary.

Materials. The research data will include audio-recordings and transcripts of qualitative interviews with parents. Only study PIs (Drs. Garg and Kavanagh), co-I (Long), and trained project staff who are deployed to each of the study sites (hereafter termed core research team) will have access to participants' identifying information. The site PIs and RAs from the two control sites will not have access to the identifiable qualitative data. However, the PIs and RAs from the control sites will be responsible for storing informed consent forms securely at their site.

Study Timeline

	Pre-Award	**Year 1**				**Year 2**				**Year 3**				**Year 4**			
Quarter		**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**
Obtain IRB approval	X																
Hire and train research staff	X	X															
Finalize procedure materials	X	X															
Pre-implementation data collection from key clinic stakeholders (Aim 1)			X	X													
Assessing the implementation of WE CARE (Aim 1)				X	X	X	X	X	X	X	X	X	X	X	X		
Accrue study sample to measure empiric estimates (Aim 2)					X	X	X	X	X	X							
Data collection (Aim 2)					X	X	X	X	X	X	X	X	X	X			
Qualitative work assessing possible			X	X	X	X	X	X									

mechanisms (Aim 3)																	
Final quantitative data analysis (Aim 3)													X	X	X		
Writing and publication of manuscripts							X	X	X	X	X	X	X	X	X	X	X

Adverse Event Criteria and Reporting Procedures

The study PIs, Drs. Garg and Kavanagh, will meet weekly with the core research team to review study data, compliance with data collection and security procedures, data storage processes, any actual breaches of confidentiality, along with any other issues of subject safety. We believe that there is only minimal risk involved with the participants, primarily concerning breach of confidentiality. Each week, the study PIs will review with the research team whether any breaches of confidentiality have occurred along with any instances of non-compliance with the study's protocol. Research staff will be in monthly contact with the study site PI at each clinic to review data and study compliance, and to identify any issues with data or emerging patterns of concern. Adverse events (AEs) will be recorded and assessed by the study team and study PIs, both on an individual basis and in aggregate (to discover any trends which could mean additional risks to subjects). Any AE or group of AEs that together meet the definition of Unanticipated Problem (UP) will be reported as soon as possible and within 2 business days to the BUMC IRB, and 7 business days to the NHLBI. An Unanticipated Problem is defined as any event that meets all three of the following criteria: unexpected, possibly related to the research, and suggests that the research places subjects or others at a greater risk of harm than was previously known or recognized. OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events; OHRP, HHS; January 15, 2007). Throughout the course of the study, the data and adherence to the processes in place to protect the data and prevent any breach of confidentiality will also be monitored monthly by Drs. Garg and Kavanagh (study PIs) in consultation with Dr. Tripodis (biostatistician). The study PIs are ultimately responsible for the ethical conduct of the study, data integrity, and overall safety of this study.

Data Management Methods

Aim 1. Implement WE CARE in the outpatient pediatric hematology setting. Focus groups with stakeholders from each clinical site will be conducted at baseline to identify perceived facilitators and barriers to implementation. Once WE CARE is implemented in the two experimental sites, we will gather implementation data from stakeholders every six months. Recordings of the focus groups will be audiotaped and transcribed for analysis as word processing text files suitable for manipulation using the qualitative software program, N-VIVO11. The audio-tapes will be transcribed verbatim; each transcript will then be reviewed by a research assistant for accuracy. Recordings will be destroyed after seven years.

Aim 2. Obtain population-specific empirical estimates of study parameters to plan a pragmatic large-scale cluster RCT. Data will be collected from parents primarily from parent-administered surveys at enrollment and at follow-up which will occur one year post-index visit. These surveys will be completed in REDCap* using a study tablet (e.g., iPad). REDCap (Research Electronic Data Capture) is a research focused, electronic web-based data capture system. REDCap is a data collection tool and allows for storage and management of both surveys and databases. REDCap is a secure storage system and meets HIPAA compliance standards. REDCap software will be used to facilitate parent consent, questionnaires, and forms.

A brief telephone interview will be conducted 3, 6, and 9 months post-enrollment to ascertain unmet needs, and contact and enrollment in community-based resources, and parent report of prescription

refills for penicillin or hydroxyurea. A hair cortisol sample will also be collected from the parent at enrollment and 1-year follow-up. Finally, site research staff will collect data from the electronic health record (EHR) on child health outcomes (i.e., adherence to clinic visits, ED visits, hospitalizations, vaso-occlusive episodes, acute chest syndrome, and infections). Data from the EHR will be collected three times (baseline, 6-months post-enrollment, and 12-months post-enrollment). Recordings will be destroyed after seven years.

Aim 3. Qualitatively assess possible mechanisms linking SDoH interventions to improved health outcomes. The in-depth interviews with parents will be recorded, transcribed verbatim, and checked for accuracy. Spanish transcripts will be translated into English to facilitate interpretation by the research team. Transcripts will be entered into NVIVO11, to facilitate coding and analysis.

Quality Control Method

For the *medical chart review*, each research assistant will periodically (every six months) review at least five randomly selected visits at his or her own site. Inter-rater reliability will be determined using the kappa statistic. Any discrepancies will be reviewed with the co-PIs present and resolved. For the qualitative interviews and focus groups, one quarter of transcripts will be independently double-coded and compared to ensure comprehensiveness and accuracy of coding. Inter-coder concordance will be calculated.[129] The REDCap database used for parent questionnaires will use branching logic and validation rules in order to diminish opportunities for error. There will be no opportunity for errors transcribing parent questionnaires into the study database, because parents will independently enter questionnaire responses directly into REDCap.

Data Analysis Plan

Aim 1. Implement WE CARE in the outpatient pediatric hematology setting. To code the data, we will analyze each interview initially according to PARIHS's three core components: (1) evidence: attitudes and beliefs about evidence of the WE CARE system; (2) context: organizational, systemic, and sociopolitical features that promote or hinder implementation of WE CARE; (3) facilitation: attributes of the facilitation that supported or impeded the implementation, and needed adaptations. In general, we will follow the general procedures of grounded theory to identify themes that are unexpected. We will first create an initial set of conceptual categories using the Constant Comparative Method developed by Glaser and Strauss. According to this method, the initial conceptual categories are then applied to new data, and the categories are revised to reflect the addition of the new data. Upon completion of this process and review of all transcripts, we will have then identified a series of categories that reflect participants' experiences with the implementation of WE CARE. Passages referring to the different conceptual categories of the PARIHS model and other areas will be marked and identified by terms that reflect the conceptual category. Marked passages will be compared to enable the identification of similarities and differences across study sites. Issues of reliability and validity will be handled in the following way. First, two members of the study team will jointly examine each transcript to develop a common set of content codes, formulate coding rules and develop the codebook. They will independently code additional transcripts using the codebook; they will then meet after each transcript has been coded to compare their findings and assess the reliability of the coding rules. Discrepancies will be resolved and coding rules modified via discussion among the team. This process will be repeated with all coded transcripts. The goal of this qualitative analysis is to establish a shared, coherent set of codes and coding rules through a process of critical review and consensus building.

Run charts will be used to observe changes in specific measures over weeks or months, due to iterative PDSA cycles. Run charts will observe changes in frequency of distribution of screeners by clinic staff, recorded SDoH assessments within the EHR, and resource sheet dissemination by providers for positive screens.

Aim 2. Obtain population-specific empirical estimates of study parameters to plan a pragmatic large-scale cluster RCT. We will summarize the number of parents contacted, lost to follow-up, refusing participation, and enrolled. We will examine this by gender (e.g., father vs. mother). We will note reasons for refusals. We will determine parents' recruitment and attrition rates and receipt of WE CARE using descriptive statistics. We will also determine the data collection completion rate, including hair cortisol, for each data time point (baseline, 3-, 6-, 9-, and 12-month follow-up) via descriptive statistics. Each outcome and process variable described above will be first transformed into its final composite value/score. We will calculate within-group mean and standard deviation of our SDoH, process, mediator and health utilization and health outcome variables. We will also break down the intervention group into two subgroups differentiated by whether parents enrolled in resources at follow-up, and explore any differences. An intention-to-treat approach will be used to explore differences between the intervention and control groups. We will also report all data disaggregated by gender. Two independent sample t-test and chi-square tests will be used to determine bivariate differences. Mixed effects regression models will be used to estimate the effect size of the intervention on SCA outcomes accounting for baseline differences in sociodemographics, types of SDoH, cumulative needs, receipt of services, and *a priori* determined covariates (i.e. sociodemographic characteristics). To explore potential moderators for the intervention effect at the parent, child and family levels (e.g., gender, race, ethnicity, age, language, household income), we will use Rothman's methodology; specifically, we will conduct stratified analyses for each potential moderator followed by using standard interaction terms in our models. We will also explore mediation of our hypothesized potential mediators between SDoH and the intervention with each SCA health outcome using the approach recommended by MacKinnon, Lockwood, and Williams.[128] We will account for the clustering by study site by calculating the intraclass correlation.[92]

Aim 3. Qualitatively assess possible mechanisms linking SDoH interventions to improved health outcomes. Qualitative interviews will be analyzed using applied thematic analysis methodology, including: 1) increasing familiarity with the data and generating preliminary codes; 2) generating initial codes and coding structures, including data reduction and complication; 3) combining codes into higher-level themes; and 4) refining and defining themes and identifying ways in which themes fit together. *A priori* research questions and probes will serve as the initial draft of the coding structure.

Statistical Power and Sample Considerations

We will enroll up to 235 subjects in this study, including up to 60 practice staff and 175 parents of children with SCA.

Because the goal for ***Aim 1*** is to examine the implementation of WE CARE in the outpatient pediatric hematology clinical setting our sampling will be purposeful. Based on our previous experience, we anticipate up to 15 practice staff per site will participate in focus group discussions.

For ***Aim 2***, we are proposing to enroll 35 families from each of the four study sites (2 experimental, 2 control) to field test study logistics, including collecting empiric estimates of study parameters for a larger pragmatic trial. To demonstrate the feasibility of our study design, we use ED visits (primary

outcome) and penicillin adherence as examples. Assuming a 5% error rate, and based on our R00 WE CARE study, we expect a cluster coefficient no larger than 0.01. Based on recent data, we expect at least 80% of children in our control group to have at least one ED visit within our study observation period. We expect that our intervention group will have a much lower proportion, with ≤40% having with one or more ED visits. Our proposed study sample has >90% power to detect differences of at least 25% in the proportion of children with ED visits. In addition, based on estimates from the literature we expect a 9-month medication adherence of 40% and 10% in the intervention and control groups, respectively. Our study will have 90% power to detect differences of at least 20% in penicillin adherence, which is considered clinically significant. Consistent with CONSORT guidelines for pilot studies, we will not use results from this study to determine efficacy, since effects sizes from pilot studies likely overestimate or underestimate the true effect size; rather we will determine empiric estimates from the control group as the basis for power calculations for a future multi-site trial.

For ***Aim 3***, in order to explore an array of beliefs and practices regarding family contextual factors that promote or prevent effective SCA management, enrollment will continue until saturation is reached (i.e. more interviews will not generate additional information) in primary research questions. Based on our previous experience, we expect 25-35 parents will be sufficient to reach saturation.

Study Organization

Multiple Principal Investigator Leadership Plan

This proposal brings together two well-established research investigators with complementary areas of expertise in health disparities and social determinants of health research and Sickle Cell Anemia. Drs. Garg and Kavanagh together have over 20 years of experience as health services researchers. Dr. Garg's intimate knowledge of WE CARE and Dr. Kavanagh's extensive expertise in treating children with Sickle Cell Disease make them the perfect team for this proposal. Their partnership ensures that the leaders of this study have the insight and know-how in both the content and target population to achieve the aims set forth in this proposal. ***Drs. Garg and Kavanagh are well-equipped to serve as study PIs and will utilize their varied but complementary and synergistic expertise in the conduct of the proposed project.***

Professional Relationship: The study PIs have been colleagues for eight years with a shared interest in and commitment to improving care to reduce disparities in outcomes for vulnerable children. In addition to their routine professional interactions within the Pediatrics department, Drs. Garg and Kavanagh have successfully collaborated on implementing Dr. Garg's approach to screening and referral for social determinants of health (SDoH) in the Pediatric Primary Care Clinic at Boston Medical Center (BMC) via quality improvement methods; have submitted an abstract on this work to the Pediatric Academic Societies' (PAS) Meeting; and are currently preparing a manuscript to submit to a peer-reviewed journal.

Expertise of the study PIs:

Arvin Garg, MD, MPH, is an Associate Professor of Pediatrics and Assistant Dean for Student Affairs at Boston University School of Medicine (BUSM) as well as a practicing general pediatrician at BMC with extensive research experience. Dr. Garg has been Principal Investigator on numerous grants funded by NIH and foundation sources. He is the creator of the WE CARE screening and referral system aimed at mitigating social determinants of health, which forms the basis for the proposed implementation of screening and referral for social determinants in the outpatient Pediatric Hematology setting. His previous K99 NICHD examined the efficacy of WE CARE in pediatric clinics treating underserved populations. His current NIMHD R01 award is primarily designed to test the implementation and effectiveness of WE CARE in urban general

pediatric clinics for *healthy* young children who present for well-child care on improving healthcare utilization outcomes. His current NICHD R01 award focuses on the implementation of WE CARE using in-person or webinar training strategies in 18 diverse general pediatric practices in the United States. A robust evaluation of WE CARE has demonstrated its efficacy in the pediatric primary care setting; however, his prior and current studies were conducted in **healthy children** and were not primarily designed to assess the impact of WE CARE on *health outcomes*. The current application addresses a clinically- and policy-relevant research gap in the healthcare delivery for children, particularly children with medically complex conditions. This proposal also aims to identify the contextual factors at the family and health system levels that may impact the widespread adoption of SDoH interventions for medically complex children. Dr. Garg's expertise in implementing WE CARE into general pediatric practices and conducting clinical trials will be vital to ensuring the success of the project.

Patricia Kavanagh, MD, is an Associate Professor of Pediatrics at BMC. She has spent the past ten years devoted to health disparities research through the lens of Sickle Cell Anemia. She was the recipient of a K23 from NHLBI and recently completed a study of a home pain plan with children with Sickle Cell Anemia and their parents, as little is known about the current patterns of pain and medication use in the home setting. In addition, she has improved the quality of care for children and young adults with Sickle Cell Anemia by employing quality improvement techniques and health information systems tools to improve care delivery in the outpatient and emergency department settings. Given her knowledge of Sickle Cell Anemia and her previous work with this patient population, her expertise will be vital to optimizing the intervention for the target population.

Rationale for Choice of Team Members: The study PIs have assembled an expert research team that is well-positioned to complete the work proposed in this application. The team includes: an implementation expert (Dr. Drainoni), a biostatistician (Dr. Tripodis), a Clinical and Biological-Health Psychologist (Dr. Long), a Pediatric Psychologist who specializes in Sickle Cell Disease (Dr. Barakat), and a child health policy expert (Dr. Raphael), all of whom have published broadly on child health disparities. In addition, the team includes four pediatric hematologists with significant expertise in Hemoglobinopathies, including Sickle Cell Anemia (Dr. Esrick, Dr. Sprinz, Dr. Boruchov, and Dr. Pashankar).

Scientific Responsibilities of the study PIs: The study PIs will be jointly responsible for scientific issues and developing and evaluating methods for communicating results, with input from research team members. Dr. Garg will oversee *Aims 1 and 2* given his experience and expertise in conducing cluster RCTs and prior collaborations with Dr. Drainoni on related WE CARE implementation studies. Additionally, Dr. Garg will oversee the grounding of the study in the child health policy landscape regarding SDoH given his strong relationship with Dr. Raphael (a national leader in child health policy) and his national reputation in incorporating SDoH screening and referral interventions into the delivery of medical care. Dr. Kavanagh will be the liaison to participating sites given her longstanding relationship with the medical directors at each sites, leadership role in sickle cell disease treatment, and involvement in the New England Sickle Cell Consortium. She will also oversee *Aim 3* given her expertise and clinical experience in the care of children with Sickle Cell Anemia.

Administrative Responsibilities of the study PIs: The study PIs will be jointly responsible for administrative management. Dr. Garg will serve as contact PI and submit all necessary forms and reports to the NIH. Dr. Garg will also be responsible for supervising the Research Coordinator and other staff. Dr. Kavanagh will serve as the liaison to the participating clinical sites and will be actively involved in monitoring study recruitment and attrition. The study PIs will share responsibility for fiscal and regulatory activities of the project.

Communication: The study PIs' offices are located on the same floor of the Vose Hall Building on the Boston University Medical Campus, therefore it will be easy for the study PIs to communicate regularly. They will hold weekly meetings in person, and will communicate as needed in between scheduled meetings. Research team members will participate in these meetings as needed.

Resolving disputes: In the unlikely event that a conflict develops, the study PIs will meet in person and attempt to resolve the dispute. If they fail to resolve the dispute, the disagreement will be referred to an arbitration committee consisting of one impartial senior executive from BMC and two impartial senior executives mutually agreed upon by both study PIs. No members of the arbitration committee will be directly involved in the research grant or disagreement.

Publication and Data Access: The study PIs will develop procedures for authorship of publications and presentations, as well as access to the de-identified data. Authorship will be based on the relative scientific contributions of the study PIs and other collaborators. Procedures will be subject to modification based on input from the research team. Given the extent to which many members of this project have collaborated successfully in previous research studies, the study PIs do not anticipate problems in this area.

Responsibilities of the Site PIs: Site PIs will be responsible for overseeing the day-to-day research operations at their respective sites. They will be responsible for meeting regulatory obligations, such as obtaining informed consent, overseeing the implementation of the approved protocol, and reporting unanticipated problems and study progress to the single IRB (sIRB). Site investigators will communicate relevant information necessary for the sIRB to consider local context issues and state/local regulatory requirements during its deliberations. Participating sites will rely on the sIRB to satisfy the regulatory requirements relevant to the ethical review.

The sIRB will be hosted at Boston Children's Hospital, for which Dr. Erica Esrick is the site PI. She is a pediatric hematologist dedicated to clinical care and advancing clinical research for patients with hemoglobinopathies, including sickle cell disease (SCD) and thalassemia. During her fellowship, she conducted research in the laboratory of Dr. Benjamin Ebert in the Department of Hematology at Brigham and Women's Hospital, with a focus on fetal hemoglobin induction for SCD treatment. Her lab-based research projects were translational in scope and supported her long-standing goal of performing clinical research in hemoglobinopathy populations. After fellowship, she sought to transition away from the lab, and has gained experience in a variety of clinical research studies. As the co-PI of an upcoming BCH-sponsored trial of gene therapy for patients with SCD, she is the primary protocol author, and has worked with a multidisciplinary clinical research team to successfully complete several pre-IND regulatory approvals. As the co PI for an active pilot clinical trial studying the use of plerixafor as a stem cell mobilizing agent in patients with sickle cell disease, she successfully applied to the FDA for an IND and to the BCH IRB for approval, developed the case report forms, led the subject recruitment process, and is currently completing subject participation. She is currently the site PI for a phase 3 therapeutic trial for patients with thalassemia. In this trial she has worked very closely with a research nurse and clinical research assistant to lead all aspects of subject enrollment, communication with industry sponsor and medical monitors, IRB communication, and other aspects of trial management. During her training and career at BCH and DFCI, she has had the opportunity to work with many leaders in non-malignant hematology. Along with a dedicated team of social workers and nurses, she is a regular participant in outreach and education projects for our SCD patients and families. Her clinical research experience, leadership role in the hemoglobinopathy program at BCH, active SCD patient panel, and access to superb clinical research support staff will allow her to successfully serve as the Boston Children's Hospital Site PI for SCA WE CARE.

Overall structure of the study team, by study aim

Study 1 (Aim 1): The implementation of a practice-based social determinants of health screening and referral intervention in two pediatric hematology clinics to field test key study logistics and understand the facilitators and barriers to implementation and accelerate its adoption

The study team will include the study PIs (Drs. Garg and Kavanagh); Dr. Drainoni (implementation expert); site PI of each participating institution (Dr. Esrick, Dr. Sprinz, Dr. Boruchov, Dr. Pashankar); and the research staff. Dr. Garg will oversee the study given his experience and prior collaborations with Dr. Drainoni on related WE CARE implementation studies.

Study 2 (Aim 2): Obtaining population-specific empirical estimates of study parameters to plan a future large-scale cluster RCT of WE CARE for children with SCA

The study team will include the study PIs (Drs. Garg and Kavanagh); Dr. Tripodis (Biostatistician); site PI of each participating institution (Dr. Esrick, Dr. Sprinz, Dr. Boruchov, Dr. Pashankar); and the research staff. Dr. Garg will oversee the study given his experience and expertise in conducing cluster RCTs and history of successful collaborations with Dr. Tripodis.

Study 3 (Aim 3): Qualitatively assess possible mechanisms linking SDoH interventions to improved health outcomes, such as increasing a parent's ability to manage their child's disease through medication adherence

The study team will include the study PIs (Drs. Garg and Kavanagh); Dr. Long (clinical and biological-health psychology expert); site PI of each participating institution (Dr. Esrick, Dr. Sprinz, Dr. Boruchov, Dr. Pashankar); and the research staff. Dr. Kavanagh will oversee the study given her expertise, prior qualitative research work and clinical experience in the care of children with Sickle Cell Anemia.

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