Sickle Cell Disease Implementation Study Protocol

Sickle Cell Disease Implementation Consortium (SCDIC)

Implementing an Individualized Pain Plan (IPP) with Patient and Provider Electronic Health Record Access, for Adult Emergency Department Treatment of Vaso-occlusive Episodes in Sickle Cell Disease: A Pre-post Study Design

Sponsors and Partners

National Heart, Lung, and Blood Institute
National Institute for Minority Health and Health Disparities

June 22, 1010
Version 1.3

Principal Investigators
Paula Tanabe, PhD (PI)
Alison King, MD, PhD, MPH (co-PI)

Co-Investigators
Ana Baumann, PhD
Chris Carpenter, MD, MSc
Joe Colla, MD
Yvonne Carroll, RN, JD
Lisa Cox, MS
Robert Gibson, PhD
Greg Hall, MD
Lisa Klesges, PhD
Richard Lottenberg, MD
Mathew Lyon, MD
Lingzi Luo, MSW, MPH
Cathy Melvin, PhD
Sarah Norell, MDes, MFA
Martina Mueller, PhD
Michael Potter, MD
Rachel Richesson PhD, MPH
Lynne Richardson, MD
Gery Ryan, PhD
Lauren Siewny, MD
Marsha J. Treadwell, PhD
Leslie Zun, MD, MBA
Janelle Armstrong-Brown, PhD, MPH

Version 1.3 June 22, 2020

Table of Contents

Tables

Figures

Instruments

Abstract

The Sickle Cell Disease Implementation Consortium (SCDIC) was established in 2016 to improve the health and well-being of adolescents and young adults with sickle cell disease (SCD). It is a cooperative research program of eight clinical centers, a data coordinating center, and the National Heart, Lung, and Blood Institute (NHLBI) that uses implementation science methods to identify and address barriers and facilitators to guideline-based care in SCD and promote quality of care for patients with SCD between ages 15 and 45. The SCDIC conducted a systematic literature review and a comprehensive needs assessment among the eight participating centers, and results suggested that establishing standardized treatment in adult emergency departments (EDs) is key to improved clinical outcomes and care-seeking experiences for patients with SCD.

The overall purpose of this proposed study is to improve management of vaso-occlusive episodes (VOEs) in adult EDs. We aim to implement NHLBI recommendations for VOE treatment by embedding Individualized Pain Plans (IPPs) in the electronic health record (EHR). The EHR-embedded IPP will serve as a record of patients' SCD genotype and will include analgesic medication recommendations developed by the SCD provider. In this project, we will provide access to the IPP for both adult patients with SCD and ED providers. The proposed multisite study will use a pre-post study design, with a core set of mandatory intervention components and strategies for each participating site and optional components and strategies to allow for intervention adaptation to local needs and resources. The EHR-embedded IPP will be available for all adult ED providers to use as their routine practice, and patients will be invited to participate and enroll in the study. We will use a simplified Technology Acceptance Model to explain the use of the IPP and the RE-AIM framework to assess the Reach, Effectiveness, Adoption, Implementation, and Maintenance of the intervention.

The study aims are as follows:

Aim 1: Assess the overall effectiveness of EHR-embedded IPPs on improving patient and provider outcomes associated with pain treatment in the adult ED setting. We will evaluate the effectiveness of the intervention on both patients and providers using a pre-post study design.

> **Sub-aim 1.a. To examine effectiveness of the EHR-embedded IPP on improving patients' perceived quality of ED pain treatment.** We hypothesize that among enrolled patients with at least one ED VOE visit during the intervention period, the perceived quality of ED pain treatment will increase by 0.5 standard deviation (primary outcome) after an ED VOE visit when compared with the last ED VOE visits made by these patients within 90 days before enrollment. We will measure change pre- and post-intervention in secondary patient outcomes, including hospital admission rate within 12 months, ED VOE revisit rate, ED VOE readmission rate, and time to first dosage of pain medication provided in the ED.
>
> **Sub-aim 1.b. To examine the effectiveness of the EHR-embedded IPP on improving providers' self-efficacy in treating pain for patients with SCD and perceived quality of ED pain treatment.** We hypothesize that the intervention will increase providers' self-efficacy in treating VOEs and managing pain for patients with SCD when compared with self-efficacy before the intervention. We will also explore the effect of the intervention on ED providers' perceived quality of ED pain treatment.

Aim 2: Assess the reach, adoption, implementation, and maintenance of the EHR-embedded IPP components and implementation strategies at each participating site. We will use the RE-AIM framework to evaluate intervention outcomes in addition to intervention effectiveness.

> **Sub-aim 2.a. To assess the reach of the EHR-embedded IPP.** We will assess the reach of the intervention at the patient level by examining the proportion of patients enrolled in the study among all patients the team has reached out to recruit, and at the clinic level by examining the proportion of clinics participating in the intervention.

Sub-aim 2.b. To assess the adoption and implementation of the EHR-embedded IPP and track implementation strategies adopted by each site. We will assess the adoption of the intervention by examining characteristics of individual EDs that participate relative to the number of individual EDs affiliated with each study site who could have been recruited. We will assess implementation fidelity and outcomes, such as the proportion of eligible hematologists and nurse practitioners who receive IPP training, number of IPPs written and included in the EHR, required and optional intervention elements that are implemented as planned, IPP use by patients and providers, provider IPP adherence, and patients' and providers' perceived ease of use of the IPPs. We will track and report strategies used by participating sites through both quantitative data collection and qualitative interviews.

Sub-aim 2.c. To assess the intent to continue using the IPP from a multi-stakeholder perspective. We will assess patients' and providers' intent to continue using the IPP during the implementation period. At the end of the intervention, we will assess ED administrators' intent to continue using the IPP.

Aim 3: Assess organizational readiness at the beginning of the implementation and barriers and facilitators to the use of EHR-embedded IPPs. We will perform a Readiness Assessment to measure organization- and staff-level readiness at the beginning of the intervention to inform the selection and adaptation of implementation strategies. We will assess facilitators and barriers in adopting and implementing the IPPs from multiple stakeholder perspectives: patients, providers, and ED administrators.

Embedding IPPs in the EHR that are accessible to both ED providers and patients is a promising intervention to support the NHLBI evidence-based recommendations to guide treatment of VOE in the ED setting and improve quality of pain treatment in the ED and better patient outcomes. If EHR-embedded IPPs implemented and evaluated in this study show preliminary effectiveness, they could be scaled up within SCDIC Centers and expanded to other institutions outside the SCDIC. The results of this proposed study will accelerate the uptake of the NHLBI recommendation and establish standardized treatment in EDs for patients with SCD.

List of Acronyms

DCC	data coordinating center
DMS	data management system
ED	emergency department
EDC	electronic data capture
EHR	electronic health record
GLMM	generalized linear mixed model
HIPPA	Health Insurance Portability and Accountability Act
IPP	individualized pain plan
IRB	Institutional Review Board
LMM	linear mixed model
MOO	manual of operations
NHLBI	National Heart, Lung, and Blood Institute
PI	Principal Investigator
RE-AIM	Reach, Efficacy, Adoption, Implementation, and Maintenance Model
SCD	sickle cell disease
SCDIC	Sickle Cell Disease Implementation Consortium
SD	standard deviation
TAM	Technology Acceptance Model
VOC	vaso-occlusive crisis
VOE	vaso-occlusive episode

1. Administrative Information

Overview: For preparing the study protocol, we followed the Standards for Reporting Implementation Studies and the Standard Protocol Items for Clinical Trials, where applicable.

1.1 **Title—**Implementing an Individualized Pain Plan (IPP) with Patient and Provider Electronic Health Record Access, for Emergency Department Treatment of Vaso-occlusive Episodes in Sickle Cell Disease: A Pre-post Study Design

1.2 **Trial Registration—**Submission to follow OSMB approval

1.3 **Funding—**National Heart, Lung, and Blood Institute

2. Introduction

2.1 Background and Rationale

Sickle Cell Disease and the Emergency Department Experience

Sickle cell disease (SCD) is an inherited red blood cell disorder affecting about 100,000 Americans in the United States, predominantly African Americans.[1] In the past few decades, clinical interventions have facilitated significant improvement in patient outcomes. The survival rate to adulthood in SCD improved to nearly 95% in 2010, and the median age at death of patients with SCD increased from 28 years in 1979 to 43 years in 2014.[2,3] However, individuals with SCD often experience acute painful events previously referred to as vaso-occlusive crisis (VOC), now referred to as vaso-occlusive episodes (VOEs). During a VOE, the transfer of oxygen and nutrients to tissues is decreased because of blood vessel blockage from polymerization.[4] There is a growing demand to improve the treatment of VOE in adults with SCD, especially in emergency departments (ED) where patients with SCD often require immediate pain treatment.

Results from our Sickle Cell Disease Implementation Consortium (SCDIC) needs assessment show having a pain episode is the most common reason for patients with SCD to visit an ED. Across sites, 62.5% of the patients surveyed had four or more pain episodes in the last 6 months, and 37.8% reported they visited an ED for painful events and then were discharged home three or more times in the past 12 months.

During these ED visits, individuals with SCD often had negative experiences. Across SCDIC sites, patients and providers reported that patients are often subjected to long wait times, stigmatization or disrespect in the ED, which can result in poor VOE management and pain control. These data support findings from the literature showing that individuals with SCD and ED providers are often frustrated with care.[5] One of the reasons for frustration is the widespread perception that individuals with SCD are addicted to pain medications and that individuals with SCD who come to the ED are "drug-seeking." Additionally, several studies have measured provider attitudes toward patients with SCD and found negative attitudes are common.[6,7] Qualitative SCDIC needs assessment results show these negative experiences may, in turn, result in avoidance of health care use.

An educational effort using a video to improve attitudes of providers has been found to be effective in a sample of nurses.[8] Although educational programs can be helpful, they are difficult to sustain in an environment with rapid staff turnover, and they may be insufficient to ensure every patient with SCD receives the ED care they deserve.

The systematic development and use of electronic health record (EHR) embedded Individualized Pain Plans (IPPs), which include a record of patients' SCD genotype, recommended pain medication, and dosing plan developed by the patients' SCD providers, and are accessible to both the patient and provider may facilitate sustainable changes in ED care processes. The presence of an IPP written into the EHR by the patient's hematologist can increase ED providers' confidence in how to treat the pain. IPPs can improve patients' and providers' perceived quality of ED pain treatment and providers' self-efficacy and delivery of adequate pain control.

The Need of Standardized Practice to Treat Pain in the Adult ED

In response to the clear need to improve SCD treatment broadly, in 2014, the National Heart, Lung, and Blood Institute (NHLBI) published evidence-based recommendations for SCD management.[9] The report, *Evidence-based Management of Sickle Cell Disease: Expert Panel Report,* synthesized available scientific evidence on SCD and proposed recommendations based on best available evidence and on senior expert panel expertise and experience treating VOE for decades. It made 17 specific evidence-based recommendations for treating VOE—one of which was the use of "an individualized prescribing and monitoring protocol or an SCD-specific protocol whenever possible to promote rapid, effective, and safe analgesic management and resolution of the

VOC" for all settings.[9] At the time of the publication, most recommendations were based on expert panel expertise.

After publication, a randomized controlled trial was conducted in two EDs to strengthen the evidence.[10] Patients were randomized to receive either a patient-specific or weight-based opioid pain plan for VOE treatment. These pain plans were developed by the patient's hematologist before any ED visit, and were made available in the EHR to the ED physician when ordering pain medication. Over the course of 1 year, 52 patients had a total of 106 ED visits. Both the patient-specific pain plan and weight-based pain plan included NHLBI-recommended opioids, doses, routes, monitoring, and repeat doses. The primary difference between these two types of pain plans was individualized opioid doses were based upon their current chronic opioid therapy and previously known effective VOE management, whereas a weight-based pain plan's initial opioid dose was based on patient weight. Patients *randomized to the patient-specific dosing strategy experienced a significantly greater reduction in pain scores from arrival to ED discharge* (43.0 ± 18.6 mm vs. 26.4 ± 10.6 mm reduction, 0–100 mm on a Visual Analogue pain scale) and a lower rate of hospital admission rate (25% vs. 37%).[10] For analgesic adherence, 88.7% of ED providers followed the pain plan–suggested medication in first dose, and 95.3% of ED providers followed the weight-based pain plan but found no statistical significance in the difference.[10] This trial provides evidence that (1) hematologists can write individualized pain plans, 2) ED providers will follow them, and 3) IPPs result in a greater reduction in pain score and use of IPPs for the treatment of VOE is supported.

Prior studies with a less rigorous design also support the use of individualized dosing for the treatment of VOE in the ED. In one pediatric ED, children with a VOE who were treated with the aid of an IPP had fewer hospital admissions and readmissions and showed improvement in pain score during ED management compared with those who did not have an IPP in comparable hospitals.[11] Providers perceived that having an IPP improved efficiency and quality of pain management.[11,12] In another study of children at a different ED, researchers demonstrated a decline in admission rate for the highest care users after an IPP document in a unique folder was created for these patents.[13] In summary, the evidence to support the use of IPPs as an intervention for VOE treatment is strong and supported not only by the NHLBI recommendations but by subsequent research.

Despite NHLBI guideline recommendation and research evidence, 5 years after the NHLBI recommendation, most adult EDs do not have—or do not have easy access to—IPPs for VOE treatment. Findings from the SCDIC local needs assessment confirm a continued lack of IPPs. Providers described the lack of access to IPPs as a barrier to care and a facilitator of more effective pain management when they were present. Among 234 ED providers surveyed during the SCDIC needs assessment, 35.8% reported their ED does not have a protocol (either generic or individualized) to treat SCD pain, and 8% of the providers were unaware if such protocols exist in their ED. Additionally, 31.6% of the ED providers reported that their ED does not use an individualized dosing protocol to treat SCD pain, and 12.8% of providers did not know if such protocols exist.

An additional barrier to effective pain management identified during the SCDIC needs assessment was ED providers' low self-efficacy regarding SCD pain management, reflected by reported lack of comfort with analgesic medication doses requested by or indicated for treatment of individuals with SCD. Thirty percent of providers that responded to the SCDIC survey identified this as a barrier to treating patients with SCD in the ED. Thus, having an IPP quickly available to ED providers and patients with SCD, as suggested by the NHLBI recommendations, is very likely necessary to improve ED management of VOE. The proposed protocol will include IPP availability in the EHR to all ED providers and patients. Provider self-efficacy will be evaluated pre- and post- implementation. We hypothesize self-efficacy will improve because hematologists will be responsible for determining the individual pain plan before ED visits and ensuring the plan is available in the EHR. A plan written by a hematologist should increase the ED provider self-efficacy, because they will not need to determine an opioid dose.

Evidence Supporting the Use of Electronic Health Record Embedded Interventions to Improve ED Care

To facilitate rapid access to the IPP, and maintain "believability" of the plan, the *location* of the plan is critical. Past efforts have attempted to present the IPP to ED providers by providing a letter from the SCD provider containing the IPP or putting the letter on a flash drive. Both of these strategies necessitate that the patient must be in possession of the letter or flash drive and the patient must remember to bring it to the ED and share it with the ED providers. Anecdotal experience demonstrates these strategies have not been successful, primarily because of ED providers' continued lack of trust in SCD patients.

EHRs provide what is likely the most systematically accessible and credible location for IPPs. EHRs are now increasingly available globally and have great potential to improve the quality and efficiency of clinical practice.[14-16] With the implementation of the Patient Protection and Affordable Care Act and requirement for health systems to use an EHR, hospitals in the United States have rapidly adopted EHRs. From 2008 to 2015 EHR use in nonfederal acute care hospitals has increased from 9.4% to 83.8%.[17] Taking advantage of this expansion, EHR-embedded IPPs will be generalizable across the country and can potentially become part of standard care for all patients with SCD. In the previously discussed randomized controlled trial comparing individualized with weight-based pain plans, all plans were made available to the ED provider, and adherence to the protocol was very good.[10]

To enhance *accessibility* of the EHR-embedded IPP, individuals with SCD and ED providers should be aware of where the plan is located and how to access it. Thus, easy patient and provider access to the IPP is important. For providers, the EHR-embedded IPP is a crucial clinical decision support tool to facilitate treatment decisions. As demonstrated by previous research and practice, the use of clinical decision support tools integrated in the EHR affords providers person-specific information at appropriate times to enhance decision making in the clinical workflow. EHR-integrated clinical decision support has a number of important benefits across a variety of health care settings, like increased quality of care and enhanced health outcomes and improved provider and patient satisfaction.[18] For ED providers, clinical decision support tools have been found to be effective in changing physician practice with respect to process outcomes (like guideline adherence) for other diseases, and some studies have demonstrated significant positive impact for clinical care.[19,20]

The EHR-embedded IPP is an eHealth tool to help patients understand their treatment plan and communicate with providers. Through the work of our SCDIC informatics faculty and team, we have determined it is possible to provide *patients* access to their IPPs via patient portals, which are secured Internet-based platforms that offer patients access to their personal health information and the ability to communicate with their physicians.[21] Patient portals can be accessed through a website or a mobile app.

Results from a systematic review demonstrate a consistent pattern of patient portal use is associated with increased patient satisfaction.[22-24] A recent systematic review of 14 studies testing eHealth tools demonstrated eHealth tool use was associated with positive medication changes and reduction of patient symptoms.[25] Some studies with mixed results on patient outcomes associated with the effects of using the patient portal and eHealth tools may be the result of implementation fidelity. Rigorous studies that track implementation fidelity, and adaptations made during the process of implementation, are required to determine how to successfully use patient portals and other eHealth tools to maximize their effect on patient outcomes. In the proposed study we will be able to evaluate whether patients accessed their pain plan in the ED, via the EHR app on their phone, whether they showed it to the ED provider, and if their outcome improves compared to pre-enrollment. We will be able to evaluate whether the ED provider used the protocol and followed the dosing recommendations, and their self-efficacy in treating the VOE episode. In summary, the intervention for the proposed study is the EHR-embedded IPP with ED provider and patient access. A variety of implementation strategies (patient and provider) will be used and tracked to help the implementation of the intervention.[10] We will assess implementation and intervention outcomes using both qualitative and quantitative approach.

This study, in combination of the SCDIC needs assessment results, served as the basis to design, implement, and evaluate an EHR-embedded IPP for adult ED VOE treatment, which provides easy patient and provider access. Following the NHLBI guideline recommendation, the multisite collaboration will provide strong evidence of the effectiveness of the EHR-embedded IPP for the treatment of VOE in the ED.

2.2 Conceptual Models Guiding the Implementation Project

Using a Simplified Technology Acceptance Model 2 to Understand IPP Use (Figure 1)

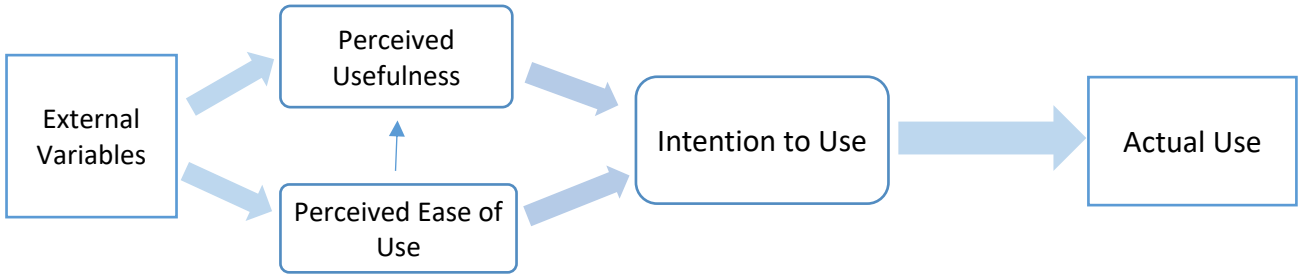
To understand the robustness of the IPP intervention, this study will use a simplified version of the Technology Acceptance Model 2 (TAM2). Developed in 1989, the original TAM is a robust and powerful model that has substantial theoretical and empirical support for its capacity to explain technology acceptance and use (accounting for about 40% of the variance).[26,27] In 2000, researchers developed and tested a theoretical extension of the TAM, which was referred to as TAM2.[26] Although TAM2 is comprehensive and offers improved capacities to predict technology acceptance and use, it has additional constructs that are impractical to be measured in the ED setting where providers are occupied, and their priority is to improve care and practice. Therefore, we will use a simplified TAM2, which uses only the main constructs from the TAM2 and their validated measurement to guide the proposed study.

The main TAM2 constructs that help predict intentions to use technology and actual use of technology are the following:

> **Perceived Ease of Use**: "the extent to which a person believes that using the system will be free of effort."[26]
>
> **Perceived Usefulness**: "the extent to which a person believes that using the system will enhance his or her job performance" is influenced by perceived ease of use and other external variables such as experience.[26]

Although the TAM2 model does not specify the differences between intention to use and actual use, as a preliminary attempt, this study will assess factors in addition to TAM2 constructs that impact the use or disuse of EHR-embedded IPP through interviews.

Figure 1. A Simplified Technology Acceptance Model 2 [26]



Readiness Assessment

Although we simplified TAM2, we acknowledge important variations in organizational settings and provider practice, knowledge, and belief among participating sites. Assessing the similarities and differences across sites is important, not only to help adopt and adapt implementation strategies but also to explain implementation and intervention outcomes.

The Centers will use a Readiness Diagnostic Scale (RDS) developed by the Consortium's Implementation Research Committee to inform the EHR-embedded IPPs' implementation and evaluation (Instrument J). The RDS is a quantitative assessment designed to capture three interrelated dimensions of organizational readiness:

1. General capacities: assess each participating ED's existing ED practice and how it functions overall.
2. Intervention-specific capacities: each participating ED's capacity to use the IPP.
3. Motivation: how well the ED facilitate physician's willingness to use the IPP.

The RDS is a multidimensional scale that assesses an organizations general capacity (24 items), innovation-specific capacities (12 items), and motivation (12 items).[28] The RDS will draw on the R = MC2 framework for organizational readiness and maintains a second-order factor structure with each component of readiness subdivided into a set of first-order factors (referred to as "subcomponents of readiness.") General capacity comprises eight distinct subcomponents, innovation-specific capacities comprises five subcomponents, and motivation comprises six subcomponents.[28] The RDS has been used in multiple high-stakes implementation projects and evaluations, including the Department of Defense Sexual Assault Prevention and Response Office, United States Air Force (with RAND corporation), Centers for Disease Control and Prevention Office on Smoking and Health, California Sage Schools Study (with the American Institute for Research funded by the National Institute for Justice), and 100 Million Lives (SCALE project with Institute for Health Improvement, funded by the Robert Wood Johnson Foundation). Preliminary validation data show favorable reliability and validity for the full scale and each respective subcomponent (data available upon request in White papers). A comprehensive validation study is currently underway, funded by NCI (#1R01CA228527-01A1; PI: Maria Fernandez, implementation scientist involved in SCDIC).

A unique feature of the RDS is its design from a formative evaluation perspective. Global measures of readiness or proxies of readiness are limited because they do not offer guidance on how to improve readiness. The RDS is based on the underlying assumption that readiness changes over time and is therefore a malleable point of intervention to improve the quality of implementation.[28] Subcomponents are distinct aspects of readiness that can be assessed and addressed to improve implementation.[29]

In this project, we will encourage five respondents from each site to respond, and responses will be analyzed at the aggregate level. We specifically probe respondents from different roles (e.g., leadership, nurses, physicians) because readiness may differ based on implementation role. Although physicians may be ready, for example, nurses may have more reservations about the protocol and therefore may be less ready. By surveying multiple respondents, we will obtain a more comprehensive picture of implementation barriers at the site level.

The results of the readiness assessment will help both the implementation and evaluation of the intervention. During the early phase of the implementation, sites will be able to view the results of the readiness assessment (anonymously) and, if needed, adjust their implementation strategies accordingly. Although general capacity of an organization may not be impacted by the intervention, sites can identify, select, and adopt strategies to boost intervention-specific capacity or boost motivation. The workgroup with the Implementation Research Committee will develop a method to document this process.

As a preliminary attempt, at the end of the intervention, the results of readiness assessment will inform our interpretation of the implementation and effectiveness outcomes. Sites with a lower level of readiness may face challenges during the implementation, which will affect their implementation outcome and intervention effectiveness.

Using the Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) for Planning and Evaluation

This study is guided by the Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) framework for intervention planning and evaluation. Developed in 1999, the RE-AIM framework assesses five dimensions of the intervention: reach, effectiveness, implementation, adoption, and maintenance.[30-32] Reach and Effectiveness dimensions usually focus on individual-level outcomes. Adoption, Implementation, and Maintenance can focus on the setting and staff level and on individual outcomes.[32] However, in this study, which operates at multiple levels, each dimension of RE-AIM will be evaluated with measures at the patient/individual, clinician/staff, or setting/site/system levels where appropriate. RE-AIM has been successfully applied in many areas of clinical investigation.[33-35] RE-AIM was selected for this intervention because of its focus on dimensions of intervention design and implementation processes that can either facilitate or impede beneficial outcomes and can be replicated and sustained in diverse clinical settings.[36-38]

Based on the simplified TAM2 and RE-AIM, the work group developed an intervention logic model to guide the planning, implementation, and evaluation of the intervention (Figure 2). It listed intervention inputs, which include human capital, physical resources, technology resources, and funding. Based on professional expertise, experiences, and stakeholder input, the workgroup has intensive discussions on required and optional strategies and activities at the patient and provider levels. The model listed the pathway between this proposed study's strategies and activities and anticipated outcomes. The outcomes are arranged by RE-AIM domains.

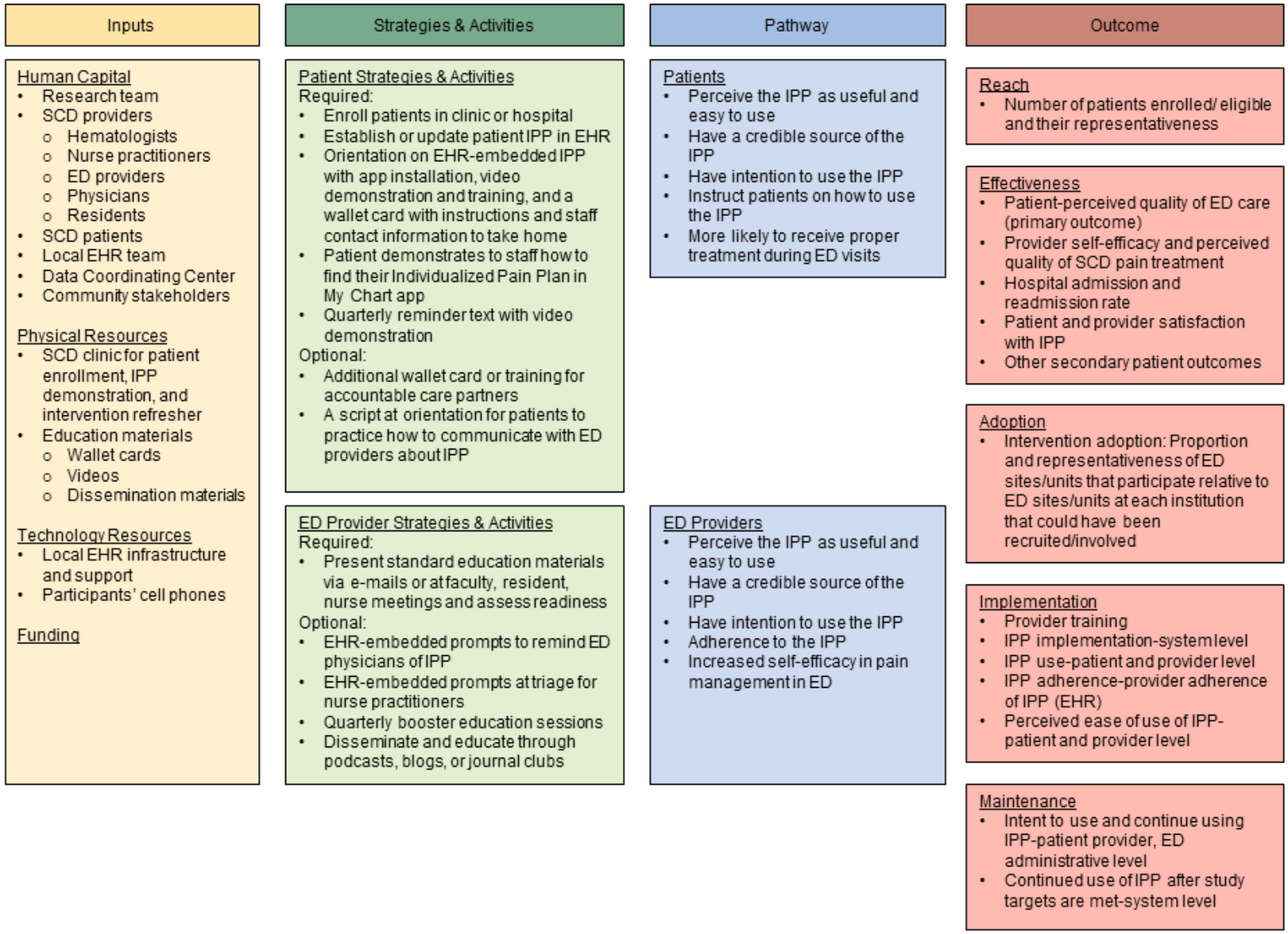
2.3 Primary Hypothesis

EHR-embedded IPP provides a credible source of pain treatment plan for both ED providers and patients. The use of EHR-embedded IPP will improve ED VOE management. Patient-perceived quality of ED pain treatment, as a patient-reported outcome, is the primary outcome for the study. At the provider level, the EHR-embedded IPP can help them make informed decisions about treating VOE and should increase self-efficacy.

Thus, we hypothesize that enrolled patients with SCD who have an EHR-embedded IPP will have 0.5 standard deviation (SD) increase in patient-perceived quality of ED pain treatment (primary outcome, composite measure) compared with baseline perceived quality of ED pain treatment for the past ED VOE visit (within 90 days prior to enrollment).

Providers who have used an EHR-embedded IPP to treat enrolled patients will have increased self-efficacy and perceived quality of ED pain treatment compared with baseline before IPP implementation.

Figure 2. ED Individualized Pain Plan Intervention Logic Model



2.4 Aims and Objectives

Our overall study purpose is to improve VOE management in adult ED units. To do this, we aim to implement the NHLBI recommendation for the use of EHR-embedded IPPs and improve IPP access by making them easily accessible to both patients with SCD and their ED providers. We will assess the effectiveness of EHR-embedded IPPs targeting patient with SCD and ED provider use of IPPs to improve patient-perceived quality of ED pain treatment, reduce unnecessary hospitalization, and improve ED provider-perceived quality of ED pain treatment and self-efficacy in SCD care. Our approach will also address and evaluate barriers and facilitators related to establishing EHR-embedded IPP in adult EDs and document the planning, implementation, and evaluation process in details to demonstrate the clinical effect of this intervention. Our findings will provide evidence to support and enhance subsequent efforts to disseminate and implement EHR-embedded IPPs in diverse clinical settings and populations. The proposed multisite study will use a pre-post study design, with a core set of mandatory patient and provider intervention strategies for each participating site, and optional strategies to allow for intervention adaptation to local needs and resources.

The aims of this study are as follows:

Aim 1: Assess the overall effectiveness of EHR-embedded IPPs on improving patient and provider outcomes associated with pain treatment in the adult ED setting. We will evaluate the effectiveness of the intervention on both patients and providers using a pre-post study design.

> **Sub-aim 1.a. To examine effectiveness of the EHR-embedded IPP on improving patients' perceived quality of ED pain treatment.** We hypothesize that among enrolled patients with at least one ED VOE visit during the intervention period, the perceived quality of ED pain treatment will increase by 0.5 standard deviation (primary outcome) after an ED VOE visit when compared with ED VOE visits made by these patients within the most recent 90 days before enrollment. We will measure change pre- and post-intervention in secondary patient outcomes, including hospital admission rate, ED VOE revisit rate, ED VOE readmission rate, and time to first dosage of pain medication provided in the ED.
>
> **Sub-aim 1.b. To examine the effectiveness of the EHR-embedded IPP on improving providers' self-efficacy in treating pain for patients with SCD and perceived quality of ED pain treatment.** We hypothesize that the intervention will increase providers' self-efficacy in treating VOEs and managing pain for patients with SCD when compared with self-efficacy before the intervention. We will also explore the effect of the intervention on ED providers' perceived quality of ED pain treatment.

Aim 2: Assess the reach, adoption, implementation, and maintenance of the EHR-embedded IPP components and implementation strategies at each participating site. We will use the RE-AIM framework to evaluate intervention outcomes in addition to intervention effectiveness.

> **Sub-aim 2.a. To assess the reach of the EHR-embedded IPP.** We will assess the reach of the intervention at the patient level by examining the proportion of patients enrolled in the study among all patients the team has recruited, and at the clinic level by examining the proportion of clinics participating in the intervention.
>
> **Sub-aim 2.b. To assess the adoption and implementation of the EHR-embedded IPP and track implementation strategies adopted by each site.** We will assess the adoption of the intervention by examining characteristics of individual EDs that participate relative to the number of individual EDs affiliated with each study site that could have been recruited. We will assess implementation fidelity and outcomes, such as the proportion of eligible hematologists and nurse practitioners who receive IPP training, number of IPPs written and included in the EHR, required and optional intervention elements that are implemented as planned, IPP use by patients and providers, provider IPP adherence to the IPP dosing recommendations, and patients' and providers' perceived ease of use of the IPPs. We will track

and report strategies used by participating sites through both quantitative data collection and interviews.

Sub-aim 2.c. To assess the intent to continue using the IPP from a multi-stakeholder perspective. We will assess patients' and providers' intent to continue using the IPP during the implementation period. At the end of the intervention, we will assess ED administrators' intent to continue using the IPP.

Aim 3: Assess organizational readiness at the beginning of the implementation and barriers and facilitators to the use of EHR-embedded IPPs. We will perform a Readiness Assessment to measure organization- and staff-level readiness at the beginning of the intervention to inform the selection and adaptation of implementation strategies. We will assess facilitators and barriers in adopting and implementing the IPPs from multiple stakeholder perspectives: patients, providers, and ED administrators.

Embedding IPPs in the EHR that are accessible to both ED providers and patients is a promising intervention to support the NHLBI evidence-based recommendations to guide treatment of VOE in the ED setting and improve quality of pain treatment in the ED and better patient outcomes. If EHR-embedded IPPs implemented and evaluated in this study show preliminary effectiveness, they could be scaled up within SCDIC centers and expanded to other institutions outside the SCDIC. The results of this proposed study will accelerate the uptake of the NHLBI recommendation and establish standardized treatment in EDs for patients with SCD.

2.5 Study Design

Design Overview

This project will use a pre-post study design. The primary outcome, patient-perceived quality of ED pain treatment, a composite measure, will be assessed for the last ED VOE visit within 90 days of enrollment, then after each qualified ED VOE visit for one year or within 12 months post-enrollment.

Provider-perceived quality of ED pain treatment and all other secondary outcomes will be assessed in a similar manner. Table 4 lists all the outcomes that will be measured.

Design Selection Rationale

Acknowledging the limitation of a pre-post study design, the study team considered many other stronger study designs, including randomized controlled trial, stepped wedge design, interrupted time series, or adding a control group to the study. We concluded that the pre-post study design is the only feasible option given the overall length of the project and the nature of our intervention setting and data to be collected. Additionally, study site hematologists felt it was unethical to use a control group because the NHLBI recommendations of an IPP should be the standard of care.

There were several other challenges that resulted in our decision to use a pre-post study design. These challenges included (1) the inability to predict if and which patients, would have a study ED visit after enrollment (based on prior work we estimate that only half of the patients enrolled in the study will have a participating ED visit for VOE within a 12-month implementation period) and when they would have an ED visit; (2) the need to have IPP's written by the hematologist and loaded into the EHR before an ED visit; and (3) a patient's inability to consent to the study during a VOE. Although the pre-post baseline assessment suffers from self-recall bias, this is the only method to guarantee that enrolled patients will have a baseline data point for our primary patient outcome with allowed implementation period of the intervention. To minimize the effect of recall bias for patient, we will recruit patients with at least one ED VOE visit within the past 90 days of enrollment and assess their perceived quality of ED pain treatment for their last visit at enrollment. To minimize the effect of recall bias for follow-up survey, patients will receive a short text survey and providers will receive an e-mail survey about the ED care within 96 hours of an ED visit. A small number of patients (5) and providers (5) at each site will be invited to participate in a brief interview within 2 weeks of

the ED visit to include a more in-depth understanding of the ED visit and VOE management. We selected a period of 2 weeks to allow patients who may be hospitalized to be discharged home, and it is not too far from the ED visit to contribute to the inability to recall treatment.

All other designs considered (randomized controlled trial, stepped wedge design, interrupted time series, or adding a control group to the intervention groups) would require a sample size (about or over 100 per site) that would not be feasible to recruit within the study timeline.

The pre-post study design, although lacking a control (thus less robust), is the only practical choice given the constraints of the study timeline and resources. Moreover, the degree of rigor in a pre-post design is appropriate for a largely descriptive study of an intervention (EHR-embedded IPP) where implementation strategy tracking and reporting and implementation outcome assessment are also important. Given the complexity of the study question and setting, the study team is confident the proposed project and design will demonstrate how the guideline-based EHR-embedded IPP is implemented in different EDs, how implementation strategies were decided and adapted, and the effectiveness of the EHR-embedded IPP. The study team has extensive experience conducting similar projects for VOE in the ED, and the trial complexity cannot be overstated. This project will have landmark implications for VOE treatment in the ED for persons with SCD.

T0 (Preparatory Phase)

Participating sites will work with local informatics teams to determine the best way to build IPPs in their EHR system. Sites that already have an IPP infrastructure in place will revise the standard elements of the IPP if necessary. The intervention package will include an introduction of EHR-embedded IPPs, training materials, and a list of required and optional implementation strategies to make these IPPs visible to the patient and study site providers. The package will be developed with SCDIC stakeholders, including patients with SCD, hematologist, and ED providers and standardized for all sites.

Pilot Testing

After the consortium finalizes the training and intervention package, each site will perform an informal pilot testing. Research staff will have a practice session of the orientation. Feedback from the pilot testing will be used to finalize the final package. Sites will also adjust, if needed, based on the experiences of first three enrolled patients.

T1 (Active Implementation Phase)

During the active implementation phase, several strategies will roll out simultaneously.

Required Patient-related Strategies

- Enrollment of patients in clinic or hospital.
- Within 2 weeks of patient enrollment, local SCD providers establish IPPs with patients or make sure IPPs are up to date and enter them into EHR.
- An orientation session during which the research team introduces the EHR-embedded IPP to patients and helps them install the patient portal on their phone. Patients will watch a video demonstration of how to access the EHR-embedded IPP and take a wallet card with instructions and staff contact information with them upon orientation completion. Patients will be asked to show the staff how to access their pain plans via their phone (a teach-back method).

- The research team will send quarterly reminder texts with video demonstration of how to use the IPP to enrolled patients.

Required ED Provider-Related Strategies

- Training of local ED and SCD providers on EHR-embedded IPP will demonstrate how to access the IPPs. Standardized training materials will be developed by the study team to deliver the content at each site. Materials will be concise and developed in formats for education of ED physicians and nurses. The materials will include a 2-minute video addressing stigma and the actual prevalence of opioid addiction in SCD, introduction of EHR-embedded IPP, and a video demonstration of how to access the EHR-embedded IPP.

Each site can choose to perform additional strategies (see lists in Tables 2 and 3) or additional strategies not listed in the protocol but chosen with a rationale).

Readiness Assessment

The Centers will conduct a readiness assessment among ED administrators and providers after the initial training session, when they have a basic understanding of the intervention.

Based on the readiness assessment results, EDs with lower levels of readiness may choose to adopt optional patient-or provider-related implementation strategies to boost organizational and individual readiness to achieve optimal intervention outcomes.

T2 (Post-implementation Phase)

This phase reflects the maintenance, sustainability, and scalability of the interventions as reflected by patient and provider experiences during T1. ED administrators will be invited to a post-implementation interview to understand barriers and facilitators of the implementation and their experiences of the IPP and their intent to continue using the IPP in the future.

2.6 Study Setting

Eight SCDIC Centers will participate in the study (Table 1): Augusta University, Duke University, Mount Sinai, St. Jude Children's Research Hospital, University of California at San Francisco (UCSF), University of Illinois, Medical University of South Carolina (MUSC), and Washington University (Wash-U).

Table 1. Study Site Characteristics

Site	City	Estimated Population	Type of Community Setting	Academic Setting	ED Provider IPP Access	Patient IPP Access
Augusta University						
Augusta University Adult Center for Blood Disorders	Augusta	358	Urban	Academic	Have IPPs in hard copy version in the ED for future reference.	No
Duke University						
Duke University Medical Center	Durham	450	Suburban	Academic	Have EHR-embedded IPPs. IPPs do not have provider name and contact.	No
Mount Sinai						
Mount Sinai Hospital	New York	175	Urban	Academic	IPPs in clinical notes.	No
St. Jude						
Methodist University Hospital	Memphis	350	Urban	Private Hospital	IPPs in clinical notes.	No
Washington University						
Barnes Jewish Hospital Hematology	St. Louis	300	Urban	Academic	No IPPs.	No
UCSF						

Site	City	Estimated Population	Type of Community Setting	Academic Setting	ED Provider IPP Access	Patient IPP Access
UCSF Benioff Children's Hospital Oakland	Oakland	286	Urban	Academic	IPPs in clinical notes.	No
University of Illinois						
UI Hospital & Health Sciences System, Sickle Cell Center	Chicago	600	Urban	Academic	IPPs in ED and clinical notes for a few patients, not all patients.	No
MUSC						
MUSC Health Emergency Department	Charleston	400	Urban	Academic	Have EHR-embedded IPPs.	No

Eligibility Criteria

<u>Site Criteria</u>

The following inclusion criteria apply to *site* participation:

- Site hematologist or sickle cell provider willing to write an IPP for patients meeting eligibility criteria,
- Informatics resources available to support all aspects of the intervention,
- Placement of the IPP in the EHR that is accessible to both the provider and patient,
- Ability to support text messaging to patients for survey administration, and
- Support from emergency medicine and nursing leadership to agree to follow the IPP unless there is a contraindication at the time of ED VOE visit.

<u>Patient Participants</u>

The following inclusion criteria will apply to individual *patient* participants within each site:

- Confirmed SCD diagnosis. Confirmed is defined as supported by documentation in the medical record of a positive test for one of the following: Hb SS, Hb SC, Hb Sβ-thalassemia, Hb SO, Hb SD, Hb SG, Hb SE, or Hb SF. If no medical record is available, the enrolling site will conduct its own laboratory test as confirmation
- English speaking*
- Age 18–45 years**
- Access to a cellular/mobile smart phone with access to text messaging (either Android or iPhone are acceptable)
- At least one VOE visit to the participating site's ED in the past 90 days from enrollment
- At least one visit at the study site SCD clinic within the past 12 months
- Willing and cognitively able to give informed consent

*Non–English-speaking patients can be enrolled in the study if the site has the capacity to translate and provide care to these patients; to ensure implementation fidelity and that we are measuring the effectiveness of standardized care provided across sites, only English-speaking patients will be counted toward the target enrollment requirements for each site.

**This age range is set and required from the study funding source.

The following exclusion criteria will apply to *patient* participants:

- Site hematologist or sickle cell provider states patient should not have a protocol or should not be administered opioids

Provider Participants

All emergency physicians, nurses, physician assistants, or nurse practitioners who work in the study ED will have access to the EHR-embedded IPP as routine practice and asked to complete baseline surveys. There are no exclusion criteria for the providers to access the IPP.

The following inclusion criterion will apply to ED providers to participate in the follow-up study survey or interview:

- Provided pain treatment in the ED for a patient participant with a qualified ED visit (per definition supplied in Section 2.8)

A waiver of written consent will be obtained from the Institutional Review Board (IRB) for ED provider participation in surveys. Providers who participate in follow-up interviews may be asked to provide written consent.

2.7 Interventions

Intervention: EHR-embedded IPP

The proposed intervention is an EHR-embedded IPP accessible to patients and providers.

The IPPs are records developed by the SCD provider at each study site based on patients' outpatient chronic opioid use and analgesic agent normally required for treatment of VOE in the ED. Each site will work with its informatics team to determine the best way to make these pain plans visible to the patient and study site providers. There will be required elements that all the sites will include in their EHR-embedded IPP, and additional elements that individual sites could choose to include.

The following elements will be required as a part of the IPP:

- Genotype
- Individual pain plan—preferred analgesic agent, route, dose and dosing interval, last update time
- Name and contact information for the SCD provider

Depending on an individual site's capability, the following additional elements may be included in the IPP:

- Allergies
- Significant past medical history specific to SCD (i.e., acute chest syndrome, stroke, renal disease)
- Significant other history relative to an ED visit (i.e., patient is ultrasensitive to morphine or dilaudid)

The hematologist or SCD provider will review these protocols with the patient in the clinic. The IPP will be reviewed by the SCD provider 6 months post-enrollment and updated as needed.

If the enrolled patient has a VOE visit at a nonparticipating ED, the patient will be able to access their IPP via the web or the patient portal app through their EHR. However, data will not be collected from these visits.

Implementation Strategies

Implementation strategies are activities that each site will do to support the implementation of interventions (Byron et al.), or—in this study—*how* patients and providers will access and use the IPP. We are requiring sites to perform required strategies at the patient and provider level (see Tables 2 and 3), and will offer additional strategies as supplements. If sites want to implement additional strategies, they are free to do so.

The strategies were selected with input from multiple stakeholders, including ED physicians. They are activities that could be considered "conduct educational meetings," "develop educational materials," and "preparing patients as active consumers," as described in the most recent compilation of implementation strategies.[37] Consistent with the recommendations from the field, we are tailoring and outlining the activities from each strategy based on the context of this study.[37] Following recent recommendations from scholars in the implementation science field, a parallel study has been funded to track details about the implementation strategies (see Section 2.8)

Sites will perform required strategies described in Tables 2 and 3. Tentatively, sites have chosen selective implementation strategies listed in Tables 2 and 3. Sites can choose additional optional implementation strategies listed in Tables 2 and 3 or additional strategies not listed. All required strategies will be standardized and tracked at each site. Any optional strategies that are adopted and implemented by more than one site will also be standardized and tracked for each site. See Section 3.1 for implementation strategies tracking and reporting methods.

Table 2. Patient EHR-embedded IPP Implementation Strategies

Required	
1	At orientation • Download and install EHR patient portal app • Video demonstration of how to access EHR-embedded IPPs • Patients will be asked to show the staff how to access their pain plans via their phone (a teach-back method) • Provide a wallet card with instructions to access IPP and staff contact information to take home
2	Quarterly reminder text with video demonstration (patients could opt out of receiving reminders at enrollment)
Optional	
1	Additional wallet card or training for accountable care partners (Augusta, Chicago, Duke, MUSC, St Jude, and Wash-U)
2	A script at orientation for patients to practice how to communicate with ED providers about IPP (Chicago, Duke, MUSC, UCSF, Wash-U)

Table 3. Provider EHR-embedded IPP Implementation Strategies

Required	
Present standard education materials • A 2-minute video addressing stigma and the actual prevalence of opioid addiction in SCD • Introduction of EHR-embedded IPP and video demonstration of how to access the EHR-embedded IPP	
Optional	
1	EHR-embedded prompts to remind ED triage clinicians of IPP (Chicago, Mt. Sinai, Wash-U)
2	EHR-embedded prompts at triage for nurse practitioners (Chicago, Mt. Sinai)
3	Quarterly booster education sessions (Augusta, Chicago, Duke, Wash-U)
4	Disseminate and educate through podcasts, blogs, or journal clubs (Augusta, Chicago, MUSC, Wash-U)

2.8 Data Collection, Measures, and Outcomes

For intervention evaluation, all the measures and outcomes are organized by RE-AIM's five main domains as listed in Table 4. The primary outcome is the patient-perceived quality of ED pain treatment (composite measure). Additional secondary outcomes will be obtained as described in Table 4. For a complete set of survey instrument items matched to relevant outcomes organized by the RE-AIM domains please refer to Appendix K.

Table 4. Measures and Outcomes

RE-AIM Domain and Measurement	Level of Measurement	Measure	Baseline/Enrollment	Post–qualified ED visit		12 Months of Prospective Enrollment
				Within 96 hours	Within 2 weeks	
Reach						
Patient reach	Patient	Proportion of patients approached (denominator) and actually enrolled (numerator)	Research team tracking			
Clinic reach	Clinic sites	Proportion of clinics in each site that have at least one hematologist agree to write pain plans for enrolled patients	Research team tracking			
Effectiveness						
Patient-perceived quality of ED pain treatment	Patient	**[PRIMARY OUTCOME]** Composite measure of three questions from the needs assessment (5 categorical responses)	In-person survey	Text message	Interview	
Provider self-efficacy & perceived quality of ED pain treatment	Provider	1. Self-efficacy 2. Perceived quality of ED pain treatment	In-person survey/ E-mail	E-mail	Interview	
Hospital admission rate	System/site	All enrolled patients, VOE visits; Hospital admission rate	EHR retrieval, past 12 months			EHR retrieval, past 12 months
Other secondary patient outcomes	System	All enrolled patients, VOE visits 1. 7- and 30-day ED revisit rate 2. 7- and 30-day hospital readmission rate 3. Time to first dose	EHR retrieval, past 12 months			EHR retrieval, past 12 months
Satisfaction with IPP	Patient	On a scale of 1–7, how helpful was the pain plan in helping you get the pain treatment you needed? (1 = not at all, 7 = excellent)		Text message	Interview	
	Provider	On a scale of 1–7, how helpful was the IPP in providing care to the patient with SCD?		E-mail	Interview	
Adoption						
IPP adoption	System/site	Characteristics of participating EDs and reasons that individual EDs were not invited to participate or refuse participation	Research team tracking			

RE-AIM Domain and Measurement	Level of Measurement	Measure	Baseline/Enrollment	Post–qualified ED visit		12 Months of Prospective Enrollment
				Within 96 hours	Within 2 weeks	
Implementation						
Provider training	Provider	Proportion and representativeness of ED providers who completed a training session (numerator) among all ED providers at each site (denominator). A tracking log of provider training containing who, when, and where the providers completed the training with provider unique identify ID	Research team tracking			
IPP implementation	System	1. Number of IPPs written and when 2. Number of new IPPs available in the EHR and when				EHR review; Research team tracking
IPP implementation (parallel study)	System	Number of required and optional program elements implemented as planned in each site, reasons they were or were not implemented, and changes made during implementation	A supplement study interview site members One month into the implementation & end of implementation			
IPP use	Patient	IPP use		Text message	Qualitative interview	
	Provider	IPP use		E-mail	Qualitative interview	
IPP adherence	System/ED	1. Number of ED VOE visits when IPP is accessed/total participating sites ED VOE visits when patients have IPP in EHR 2. Adherence to Correct Drug (yes/no); Dose (within X morphine sulfate equivalents); Route		E-mail	Qualitative interview	EHR review
Perceived ease of use of IPP	Patient	TAM2 measurement Likert 1–7	In-person survey	Text	Qualitative interview	
	Provider	TAM2 measurement Likert 1–7	In-person survey	E-mail	Qualitative interview	

RE-AIM Domain and Measurement	Level of Measurement	Measure	Baseline/Enrollment	Post–qualified ED visit		12 Months of Prospective Enrollment
				Within 96 hours	Within 2 weeks	
Maintenance						
Intent to use/ continue to use IPP	Patient	Intent to use • TAM2 measurement • Likert 1–7 Intent to continue using • TAM2 measurement with revisions • Likert 1–7 • Additional qualitative questions	In-person survey	Text	Qualitative interview	
	Provider	Intent to use • TAM2 measurement • Likert 1–7 Intent to continue using • TAM2 measurement with revisions Likert 1–7 • Additional qualitative questions	In-person survey/ E-mail	E-mail	Qualitative interview	
	ED administrators (medical and nursing directors)	Intent to continue using IPP qualitative questions (e.g., Do the EDs want to continue using the program, and how would they want to adapt the program if they were to try to scale it up?)				Qualitative interviews
Continued use of IPP	System	Number of new patients at each site who are being offered access to their pain plan in the EHR after study targets are met				EHR review

Rationale of Primary Outcome Selection and Measurement

The patient-perceived quality of ED pain treatment is selected as the primary outcome based on its feasibility and importance. Patient-reported outcomes, defined as "any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else",[39] has played an increasingly important role in measuring health care outcomes. The patient-perceived quality of ED pain treatment is a satisfaction measurement that meets the aims of the intervention.

Table 5 suggests other possible measures of pain management and rationale as to why they were not selected as the primary outcome.

Table 5. Other outcomes considered for primary outcomes and reason for not choosing

Measure	Reason of not choosing as the primary outcome
Visual analogue scale (0-10) – prospectively obtained from patient during treatment for pain. (gold standard)	Sites are not equipped to obtain pain ratings during the ED visit. EDs typically have only 1-3 VOE visits/day. Given the other expectations of the SCDIC grant (ongoing registry data collection and participation in a 2nd and possible 3rd implementation science project), it is not possible to have research staff available 24/7 to obtain this data. Requiring ED providers to have that rating will add significant implementation fidelity challenges and is not feasible.
Visual analogue scale (0-10) – documented in the EHR	There is tremendous variability as to "if and when" pain scores are documented. Reliant on the EHR would result in a very large amount of missing data for the primary outcome.
Hospital admission	Hospital admission is a proxy measure of the effectiveness of pain management. We originally proposed this as the primary outcome, however the sample size was over 100 participants/site. When proposed to the sites, all eight sites stated they would not be able to participate in the project as it was not feasible to enroll 100 participants at each site.

The workgroup has reviewed multiple instruments which assess patient-perceived quality of ED pain treatment. They identified The Adult Sickle Cell Quality of Life Measure (ASCQ-Me) Quality of Care (QOC) measure, which was modeled after the Consumer Assessment of Healthcare Providers and Systems (CAHPS) surveys, a tool widely used by the Centers of Medicare and Medicaid Services (CMS), Department of Defense and Department of Veterans Affairs patient-reported outcomes (PRO) in populations with SCD (both adults and children) in the U.S. The ASCQ-Me QOC measures has proven good reliability and validity.

To avoid participant survey fatigue and ensure we collect information that is most helpful and relevant, the workgroup chose three questions from the ASCQ-ME QOC to measure perceived quality of ED pain treatment. The patient-perceived quality of ED pain treatment will be measured with three questions. Question 1 seeks to address global evaluation of care for SCD in the ED. Questions 2 and 3 assess QOC-ED care.

1) How satisfied were you with the care you received?
2) How much were the emergency department doctors and nurses able to help your pain?
3) How much did the emergency department doctors and nurses believe that you had very bad sickle cell pain?

The original form of question 1 in the ASCQ-ME QOC was, how often were you satisfied with the care you received? Respondents were asked to choose from four response levels: never, sometimes, usually, and always. Questions 2 and 3 had five response levels: not at all, a little bit, somewhat, quite a bit and very much. Question 1 was reworded as listed above so that the same 5 levels of response could be used; i.e. all three questions ask for responses of similar form. Patient-perceived quality of ED pain treatment will be measured by the average of the responses to the three questions, with the responses to individual questions scores 0, 1, 2, 3 or 4.

Quantitative Assessment of Intervention Outcomes

The data coordinating center (DCC), at RTI International, will program all survey instruments into a REDCap database, and all survey data collected electronically via tablet or text message are directly uploaded and stored in that database. Surveys administered in paper form by each site will be entered into REDCap manually by the Center's study personnel.

Electronic Data Capture

The DCC will develop an electronic data capture (EDC) system for this study. Case Report Forms will reflect the data elements to be collected at each visit. Local staff at each site will collect study data and enter it into the EDC. The primary data source for the EDC will be the local EHR. Data will be entered into the EDC and uploaded to the study's central REDCap database managed by the DCC.

See Instruments A and B for the EDC.

Survey—Patient Level

All enrolled patients will complete a *baseline survey* via tablet or paper at enrollment (Instrument B & D). The patient baseline survey will assess

- patient demographic data,
- patient-perceived quality of ED pain treatment for the last ED visit (within 90 days of enrollment),
- how well they know how to use the patient portal to access IPP (after demonstration by research staff),
- perceived ease of use of the IPP, and
- intent to use the IPP for next ED VOE visit.

After an enrolled patient has an ED visit at participating ED, research staff will receive a notification from the EHR of such a visit. The research team will screen and verify **a qualified ED visit**.

A qualified ED visit must meet following criteria:

- the patient is enrolled in the study,
- the patient had an EHR-embedded pain plan at the time of the visit,
- the visit is at a participating ED and the reason of the visit is VOE, and
- it is this patient's first ED VOE visit of the month.*

*The rationale of this criterion is to alleviate the burden of data collection and retrieval if the patient has more than one visit in a month.

Within 96 hours of a qualified ED visit, the research team will send a follow-up survey through text message to the patient (Instrument E). The 96-hour follow-up survey will assess

- patients' perceived quality of ED pain treatment for this visit,
- how well they know how to use the patient portal to access IPP,
- perceived ease of use of the IPP,

- patient and ED provider use of IPP during last visit,
- satisfaction of the IPP, and
- intent to use the IPP for next ED VOE visit.

After 48 hours of sending out the follow-up survey, a text reminder will be sent to participants who have not completed the survey. The survey will close 48 hours after the text reminder being sent.

Survey—Provider Level

At the beginning of the implementation, all ED providers will be invited either in person before their IPP training session or through e-mails to complete a baseline survey (Instrument A). We will establish a subject ID for each provider. The provider baseline survey will assess

- provider-perceived quality of ED pain treatment, and
- provider's self-efficacy of manage acute pain episodes for patients with SCD.

After an enrolled patient has a qualified ED visit, the research team will retrieve the contact information of the ED provider (physician or nurse practitioner) who ordered the first analgesic for such visit. Within 96 hours of a qualified ED visit, the research team will send the ED provider a follow-up survey via e-mail (Instrument F.b).

The follow-up provider survey will assess:

- the use of IPP,
- ease of IPP use,
- IPP adherence,
- perceived quality of ED pain treatment,
- satisfaction of the IPP, and
- intent to use the IPP in the future.

After 48 hours of sending out the follow-up survey, a text reminder will be sent to participants who have not completed the survey. The survey will close 48 hours after the text reminder being sent.

2.9 Readiness Assessment

One month after the initial enrollment of patients and the beginning of provider training, the research team at each site will invite individuals to complete the readiness assessment via e-mail. We aim to have at least five completed readiness assessment surveys: one to two each from the ED administrator, study team researcher, ED physician, and ED nurse.

The readiness assessment will assess:

- ED general capacity,
- ED innovation-specific capacity, and
- motivation.

Qualitative Evaluation of Barriers and Facilitators of Implementation of the IPP

Sufficient understanding of the contextual factors in implementation of mHealth interventions is critical to ensuring future scale-up and translation of study findings to other institutional settings outside the SCDIC.[40] As such, for Aim 3, we will elaborate on the RE-AIM quantitative findings with a brief interview for a small number of patients and ED providers. Interviews will be conducted within 2 weeks of a qualified ED visit. The purpose of the interviews is to identify and address facilitators and barriers to intervention strategies and provide an understanding of the contextual factors at each site that may have influenced how and why results of individual RE-AIM domains occurred and variations in implementation across the sites.

We will purposefully sample participants for participation in a follow-up interview. Each Center will begin to invite patients and providers for interview after it has 5 patients have had qualified ED visits (post pilot). Centers will invite enrolled patients with a qualified ED visit within 2 weeks of such visit to participate in an interview (Instrument G). Centers will invite ED providers who have provided pain treatment to an enrolled patient with a qualified ED visit within 2 weeks of such a visit to participate in an interview (Instrument H). Interviews will be 30 to 60 minutes in duration and facilitated by an interviewer trained in the interview protocol. Interviews will take place in person in a clinic setting. Sites may have the option of conducting interviews by phone if an in-person session cannot be arranged. Sessions will be digitally recorded with permission.

Each participating Center will conduct at least five provider and five patient interviews. Centers will purposefully sample participants based on quantitative data provided by the first 5 qualified ED visits. Each site will select participants based on factors such as IPP use or change in primary outcome.

At the end of the project, ED administrators will be invited for a phone interview on topics including perceived barriers and facilitators to developing the intervention package with the local informatics team, barriers and facilitators to implementation, the types of strategies used, and any adaptations or modifications made to support strategies over the study period (Instrument I).

Tracking and Reporting Implementation Activities and Strategies

A parallel study has been funded to capture the planned and actual implementation strategies employed by each site (see Appendix A).[36] Semi-structured interviews with three stakeholders from each site before participant recruitment, 1 month after launching the intervention, and then at the end of the intervention will capture the barriers and facilitators of the strategies planned and whether there have been any adaptations made. Questions have been developed by the implementation and maintenance domains of the RE-AIM framework.

Examples of questions are as follows: “what options are you considering to support the use of IPP in your site?” (baseline), and “what is working well and what has been challenging?” (follow up in 1 month and at the end of the study). All interviews will be recorded, transcribed, and reviewed by the study team (the PI of the study and her mentor). For each intervention at each level (patient and providers), the transcripts will be double coded using a priori (e.g., ERIC compilation of strategies) and emergent themes. We will develop categories, themes, and subthemes that emerge from the data. A matrix of the strategies planned, used, and adapted will be developed for each site. We hope this parallel project will help delineate methodologies to capture the implementation strategies used in the consortia and contribute to both the sickle cell and implementation science field. Because the PIs of this protocol are study participants, we have not attached the interview questions to ensure confidentiality of the project and high quality of collected data.

2.10 Study Timeline

We will obtain baseline interview data for providers and patients. We will obtain specific EHR data elements outlined in Table 4 for patients, 12 months prior to enrollment. After enrollment, we will track outcomes for

12 months post-enrollment as frequently as possible. Enrollment will continue at each site until 20 unique patients/site have had at least one qualified ED visit (see sample size discussion below).

Table 6. Study Timeline

Activity	2019	2020		2021		2022
	Jun–Dec	Jan–June	July–Dec	Jan–Jun	July–Dec	Jan–June
Protocol and intervention package development						
Review & approval						
IRB						
Pilot testing						
Patient enrollment						
Data collection of all ED VOE visits for enrolled participants						
Analysis						
Manuscripts						

2.11 Sample Size

As noted in Section 2.2, the primary outcome of the study will be patient-perceived quality of ED pain treatment, measured with a composite of three questions from the SCDIC's Needs Assessment Survey. The questions will be asked of study participants who went to the participating site's ED for sickle cell–related care in the previous 90 days.

Responses to each question will be scored 0-4 for "not at all" to "very much" and the three responses will be averaged to determine patient-perceived quality of ED pain treatment. Using the original 4 response levels for the first question and the 5 response levels to questions 2 and 3,the average score on the SCDIC's Needs Assessment Survey was 2.22. The standard deviations (SDs) for responses to the individual questions were 0.96, 1.09 and 1.19 respectively. Correlations between response ranged from 0.56 for questions 1 and 3 to 0.67 for questions 1 and 2. On the Needs Assessment Survey, the SD for patient-perceived quality of ED pain treatment, which depends on the SDs for the three questions and the correlations between responses, was 0.93. For the power calculations, we assumed the effect of modifying question 1 and rescaling the responses from levels to 5 was to increase the mean by 25%, from 1.66 to 2.07, and to increase the SD from 0.96 to 1.2, which is slightly greater than the SDs for questions 2 and 3. We assumed that the correlations between responses would not change. With these modifications, the mean for patient-perceived quality of ED pain treatment increased from 2.22 to 2.35 and the SD from 0.93 to 1.0. We therefore conducted a simulation study to determine statistical power to detect a treatment difference of half a standard deviation, or 0.5.

We plan to use a linear mixed model (LMM) for data analysis. Suppose that Y_{ijt} is the composite score in the i^{th} patient at the j^{th} site at time t. Then the analytic model is

$$Y_{ijt} = \mu + \alpha_j + \beta X + b_j X + v_{ij} + \varepsilon_{ijt}$$

where μ is the pre-intervention mean patient-perceived quality of ED pain treatment; α_j is the random site effect; X is the pre- and post-intervention indicator (= 0 pre-intervention and = 1 post-intervention); β is the average change in score attributable to the intervention; b_j is a random effect to account for site-to-site variation in average change score, v_{ij} is a random effect for participant; and ε_{ijt} is individual-level residual noise. For this study, site should be assumed to mean ED. It is assumed that α_j, b_j, v_{ij} and ε_{ijt} are normally distributed and uncorrelated, given the model fixed effects. For the Sickle Cell Disease Implementation Study, $\mu + \beta$ is mean post-intervention patient-perceived quality of ED pain treatment. Also, the model assumes that the intervention effect will vary by site as indicated by $b_j X$.

Using the above parameterization, sample size calculations were carried out by simulation in SAS. The following assumptions were made in the simulations:

1. Each of the eight sites will recruit and consent at least 40 study participants at baseline who had at least one ED VOE visit in the preceding 90 days.

2. At least 50% of the study participants will have at least one qualified ED visit after the intervention has been implemented.

3. The mean baseline level (μ) of patient-perceived quality of ED pain treatment is assumed to be 2.35 on the composite variable based on data from the needs assessment discussed above. This estimation is based on patients having at least one qualified ED visit within a year.

4. As a result of the intervention, the average patient-perceived quality of ED pain treatment is expected to increase one half a standard deviation post-intervention, meaning that β =0.50. This means that the average composite score will increase to 2.85 post-intervention.

5. The model also assumes that the intervention effect will vary across sites with the standard deviation for the random intervention effect set at 0.447 (i.e. the variance was set at 0.2).

6. Within-site correlation (commonly referred to as inter-cluster correlation) of baseline measurements, calculated as the ratio of site level variance (i.e., variance of α_j) over the total variance (sum of the variances of α_j, v_{ij} and ε_{ijt}) is set at 0.10.

7. Within-participant correlation, calculated as the ratio of individual-level variance (i.e., variance of v_{ij}) over total individual variance (i.e., the sum of variances of v_{ij} and ε_{ijt}) is set at 0.50, reflecting the expectation that pre-intervention composite score is predictive of post-intervention score.

8. A two-sided p-value > 0.05 for rejecting the null hypothesis of no intervention effect.

9. Finally, the simulation assumes that about 20% of the participants will be lost to follow-up and provide no posttest data.

Because of the first two assumptions, it was assumed that 40 patients would be recruited at each site and, on average, 20 of 40 would have at least one post-intervention ED visit each. However, because of assumption 9, it was assumed that data from the post-intervention visit would be missing with probability 0.20. The average sample size in the simulations was therefore 320 participants with pre-intervention measurements and 128 participants with post-intervention measurements. A total of 1,000 simulated datasets were generated based on assumptions 1–9. The LMM was fitted to each dataset and power was estimated as the proportion of datasets for which a statistically significant improvement in average patient-perceived quality of ED care was detected; i.e. the proportion for which the null hypothesis that $\beta = 0$ was rejected. The results indicate that the study will have >90% power to reject the null hypothesis when the intervention results in an average improvement in patient-perceived quality of ED care of 0.5 standard deviations under the assumed conditions. Given the distribution of the scale (0–4), the study team came to a consensus that a 0.5 SD would be a clinically significant improvement in perceived quality of pain treatment.

Assumption 6, regarding site-to-site variation in baseline scores, was based on the results of the Needs Assessment Survey. In that survey, site-to-site variation in the responses, using the original 4-level coding for question 1, was 6% of the sum of between-site and within-site variance. Statistical power to detect a treatment effect tends to be sensitive to the variance of random effects, so the proportion of variance attributed to site was set at 0.10, which is higher than the proportion of 0.06 in the needs assessment survey.

To investigate the sensitivity of the power calculations to the values in assumptions 1-9, we recalculated statistical power after modifying the assume values. The calculations appear to be quite robust. For example, when we increased total baseline variance from 1.0 to 1.25, the proportion of baseline variance attributable to site from 0.1 to 0.5, and site-to-site variance of the treatment effect from 0.2 to 0.4, power remained slightly above 88%. The power calculations are robust to fairly large departures from the assumptions underlying them.

2.12 Recruitment

Patient Recruitment and Procedures

All patients enrolled in the SCDIC registry and screened eligible will be contacted by research staff for participation on the ED project. Additional participants meeting criteria at participating SCDIC sites, previously not enrolled in the registry, are also eligible and may be recruited either in clinic, during hospitalizations, with opt-out mailing, or at community events by research staff. Each site will keep a tracking log (Appendix L) of individuals being contacted, including their name, whether they are eligible of participating, date of contact, method of contact, if they consented or not, and reason for refusal (optional).

At enrollment, participants will provide consent to participate in the study. Patients will provide consent for the research team to review their EHR for utilization data 12 months before and after enrollment, to receive a brief text message survey within 96 hours of a qualified ED visit, a reminder text message to fill in the follow-up survey 48 hours after receiving the follow-up survey, and being invited to participate in an interview two weeks after a qualified ED visit.

The research staff will schedule a face-to-face orientation with patient and provide instructions on how to find their EHR-embedded IPP via the web or patient portal app and possible optional strategies outlined in Table 2. Patients will complete the baseline survey at the orientation.

Provider Recruitment

All ED providers will be invited to participate at ongoing staff meetings and resident conferences. All ED providers will be able to access the EHR-embedded IPP and will receive basic education about the protocol. All ED providers will be invited to complete a baseline survey at enrollment. All ED providers will receive an e-mail to a brief survey within 96 hours of caring for a patient with a qualified ED visit. Providers will be given the option of being contacted to participate in a brief interview within 2 weeks of providing care to a patient with a qualified ED visit. Changes in the new Common Rule do not require written consent of providers for survey participation; a waiver of written consent will be obtained by the IRB.

3. Methods: Data Management and Analysis

3.1 Data Management

All study data will be managed and stored at the DCC and accessible to the study team through the SCDIC secured website. Quantitative data captured in the EDC system and surveys will be maintained in a REDCap database. Qualitative data in the form of audio recordings, transcripts, notes, and code summaries will be stored in a secure location at each of the participating centers.

Manual of Operations

The DCC will prepare a manual of operations (MOO) specifying the procedures for data collection to maximize harmonization of effort. The MOO will include procedures for recruiting and enrolling participants and collecting or abstracting, checking, and transferring data. The DCC will conduct a MOO training for the study coordinators annually at the in-person meeting or virtually as needed for new staff.

3.2 Methods of Analysis

Quantitative Data

A characterization of the study's patients by their demographic characteristics, genotype, baseline patient-perceived quality of ED pain treatment of last ED VOE visit, hospital admissions and ED VOE visits in the past 90 days, satisfaction with IPP, and use of IPP during qualified ED visits 12 months after enrollment (as detailed in Table 4) will be provided for all patients combined and across sites.

The analysis of the reach, adoption, implementation, and maintenance outcomes will be descriptive. For implementation strategies, a matrix with clear definitions of the components of the implementation strategies will be developed to inform how we can capitalize on what is already happening in the SCDIC ED. We will base the matrix on detailed information regarding the forms of the implementation strategies that we will collect from the study sites. Such a matrix will help us understand whether we need to scale up strategies that are already happening or develop new strategies to target the determinants of the intervention.

The effectiveness outcomes listed in Table 4 will be analyzed as detailed below. The primary outcome is patient-perceived quality of ED pain treatment, measured with a composite of three questions from the Needs Assessment Survey, as described in Section 2.11. Given the assumptions of independence and normality of the variance components α_j, b_j, v_{ij}, and ε_{ijt}, in the LMM in Section 2.11, the impact of the intervention (β) on the primary outcome will be estimated using standard statistical software for mixed-effects models such as PROC MIXED in SAS. A three-level model with a random effects for site, participants nested within site, and site-to-site variation in the treatment effect, and a fixed effect for treatment response will be specified to assess the impact of the intervention. *The primary analysis will be based on the pre-intervention composite score and the score at one ED visit per participant, using the first visit for those with more than one.* The model can accommodate multiple visits per participants by adding a covariance matrix to account for the repeated observations. We plan to include additional visits in another analysis. We are aware, however, that the results may be difficult to interpret, depending on the relationship between pain frequency, satisfaction with care and response to the intervention. Additional predictors can be added to the model to evaluate the effect of other variables, such as site provider IPP access prior to the intervention, site readiness, on response to the intervention. Such an analysis will involve interactions between the added predictors and treatment to determine if the treatment difference varies with the values of the other predictors. If there is evidence of implementation heterogeneity across sites, the random effect for sites can be removed from the model, and five dummy variables, for all but one site, can be created and interacted with the treatment variable to test for treatment heterogeneity across sites, controlling for time.

The secondary outcomes of hospital admission rate (a count outcome as multiple hospital admissions are possible), 7-day ED VOE revisit (a dichotomous outcome), and time to first dose (also likely a count outcome) will be analyzed with generalized linear mixed models (GLMM), where the outcome will be specified as a Poisson or binomial variable with a logit function as needed by the data type of outcome. The GLMM models would follow the same format as the LMM above with fixed effects for time, intervention, and covariates and random effects for participants within sites. Such models can be fit with standard statistical software like PROC GLMMIX. The secondary outcome of satisfaction with IPP, measured with a single Likert scale question for both patient and provider, will be analyzed as a continuous outcome with an LMM as detailed above for the primary outcome. In all cases, the analysis will estimate an intervention effect (β) that will compare the secondary outcome at baseline to after the intervention is delivered (posttest). Power calculations indicate that the study sample will be too small to detect statistically significant differences in these noncontinuous variables, but estimates will be provided to inform future research.

Qualitative Data

Each study site will record the interviews using method of their choice that complies with the Health Insurance Portability and Accountability Act (HIPPA). Recordings will be transcribed via a HIPPA compliant transcribing service or by study site research members. All deidentified transcriptions will be sent to RTI through an sFTP site for analysis. RTI will be responsible for the analysis of transcripts and notes. Key team responsibilities will include preparing an analytic plan, coding scheme, training coders, conducting inter-rater reliability checks, reviewing coding summaries, and preparing coding reports and visualizations.

Thematic analysis will be conducted through deductive coding of the transcripts. The RE-AIM framework depicted in Table 4 will inform the coding structure and common codebook. Using a deductive approach, the codebook will create an initial list of codes to be used in the analysis and include operationalized examples on how to apply the code. Analysts will revise the codebook as necessary to hone definitions to increase consistency in coding across the research teams. The use of a common qualitative software will facilitate the coding of the transcripts and identify emergent patterns and themes in the data. Any discrepancies in coding and analysis will be identified and resolved collectively among the analysts. Data will be compiled into different stakeholder groups (patients, providers) by themes and analyzed across the study sites.

4. Methods: Monitoring

4.1 Data Monitoring and Quality

Local research coordinators, under the supervision of a local Principal Investigator (PI), will monitor and ensure data quality at each site. The DCC is responsible for assuring the quality of the data received and will conduct standard quality checks of the data like reviewing for completeness, accuracy, and item missingness; conducting audits; and double-entering a sample of paper-based surveys. The DCC-based operations manager will meet regularly with the data coordinators at each center to review data output, quality metrics, and data collection procedures.

4.2 Harms

This study does not involve a drug intervention, device intervention, or highly invasive data collection procedure. However, recognizing that unanticipated events can occur in the course of any study, even one with minimal risk, the following reporting protocols will apply. The site PI or designee will assess the event to evaluate whether it is unanticipated (i.e., unexpected), related to the study, places the participant or others at risk, or is serious enough to decide whether it should be reported to the local IRB, DCC, and sponsor IRB.

Adverse Events and Unanticipated Problems

This study will collect the following information:

- unanticipated and related adverse events (possibly related, probably related, or definitely related to study participation), and
- unanticipated problems that may involve risk to participants or study staff but do not necessarily result in an adverse event (i.e., harm).

Unanticipated adverse events are new or greater than previously known events in terms of nature, severity, frequency, or occurrence, as documented in the protocol, consent, or other study documents approved by the IRB.

An example of an unanticipated problem that may not result in an adverse event (i.e., harm) is misplacement of a participant's research record containing personally identifiable information such that the risk of loss of confidentiality is introduced. This event is reportable regardless of whether the confidentiality is breached or not breached. If the PI or designee identifies the adverse event or unanticipated problem as meeting the following criteria, it will be reported to the local IRB within 5 business days and to the DCC within 10 business days: involves substantive harm (or genuine risk of substantive harm) to the safety, rights, or welfare of the site's research participants, research staff, or others.

Otherwise, the site will report the events to the local IRB and Steering Committee (if applicable) on an annual basis at the time of continuing review.

4.3 Auditing

Clinical research monitors will review records of up to 10% of the study participants annually for appropriateness of the informed consent process, eligibility, serious adverse event reporting, and patient protocol status. Additional information may be monitored at the request of NHLBI, Central IRB, or other institutional administration. The monitor will generate a formal report, which is shared with the PI, study team, and NHLBI.

Continuing reviews by the IRB will occur at least annually. In addition, serious adverse event reports are reviewed in a timely manner by the IRB and NHLBI. Monitoring of this protocol is considered to be in the "low-risk" risk category.

5. Ethics and Dissemination

5.1 Research Ethics Approval

No data collection activities will begin at an individual SCDIC participating clinical center until approvals from site IRBs have been granted. The SCDIC clinical centers will concurrently submit the protocol, consents, and data collection forms to their respective IRBs for review. Site IRBs will focus on data security (receipt, storage, sharing, and protection of breach) and determine procedures related to direct patient interaction. All participating SCDIC clinical centers and the DCC have a Federal Wide Assurance issued through the U.S. Office of Human Research Protections, which ensures that the organizations comply with all federal regulations to protect research participants.

Risks and Benefits

The data collected for this study may come from medical record abstraction, self-reported information, and the EHR system. The study is not considered greater than minimal risk as mentioned in Section 4.1. Some patients may benefit from participating in the study having an updated pain plan or an improved understanding of pain management for SCD. Some patients may benefit from knowing they are helping to advance knowledge for future patients with their condition.

Unbiased Recruitment

All eligible participants will be recruited without bias. Adolescents, women, and minorities will be included as they represent the patient population of each Center.

5.2 Protocol Amendments

Modifications to the protocol or consent form that impact eligibility criteria, outcomes, or analyses will be submitted to DCC's and each site's IRB for approval prior to implementation. Protocol modifications and consent form changes will be submitted to the appropriate oversight committees according to the timetables set forth by those committees.

5.3 Consent or Assent

Patient Participants

Patient participants will be recruited by local clinical or research staff from all participating centers who will consent participants at the community clinic sites or during inpatient hospitalizations. This protocol includes individuals with SCD ages 15–45, and the interventions are implemented in the site ED.

After detailed discussion of the protocol, participants will be given a copy of the informed consent document for review. Participation will be voluntary and participants may withdraw from the study at any time. Participants will receive a set amount of compensation for the orientation visit, the baseline survey completed, and each follow-up survey completed. Participants and families will be informed of any information that becomes available during the study that might impact their continued participation. There will be a consent form specific to the protocol.

With changes in the Common Rule, baseline and follow-up surveys will be exempt from requiring written consent. However, we anticipate that individual IRBs may handle this differently. Each site will obtain IRB approval and follow site-specific requirements for obtaining consent.

Provider Participants

ED physicians will receive an e-mail asking them to complete a baseline survey of instruments per Table 4. This design will request a waiver of documentation of informed consent from the IRB and is in accordance with the new Common Rule regulations, which do not require written consent for surveys. Research staff will track ED VOE visits and e-mail a follow-up survey to the ED physicians who provided care to the enrolled participants within 96 hours of the qualified ED visit. Physicians will be invited to participate in a brief

interview to obtain a better understanding of facilitators and barriers experienced when using the IPP. Research staff will follow up with the providers and schedule an interview for those indicating they would like to participate in an interview. Each site will decide if, and how much, providers will be provided with an incentive to participate in the survey and interview.

5.4 Confidentiality

Patients' pain plan information will be collected and stored in the local EHR system. Additional information collected by local sites will be securely stored according to IRB protocol. All study data will be collected by local study coordinators with the supervision of the local study leaders and sent via EDC to the study database, which is a secure web-based data management system managed by the DCC. Full names and other identifying information, excluding date of birth, will be retained only by the centers. Participants' data will be labeled and stored with coded identification numbers that can be linked to names only by the corresponding center to protect patient identity. The DCC will receive data coded with participant identification numbers for tracking and linkage only with no identifying information. Once data collection is complete, an analysis file will be provided to begin analysis. Data will be encrypted to protect against loss of confidentiality.

All collected data will be kept confidential to the extent permitted by law. The DCC will not be able to link an individual to their identifying information.

5.5 Access to Data

Access to the data management system will be restricted to the local study leaders (PIs) and designated research staff and will be password-protected. Study coordinators will maintain a list to allow linkage to participant identity; this list will be restricted to designated study staff (PIs and research coordinators) and to entities that may need access to verify accuracy and completeness of data (local IRBs and study monitors).

5.6 Dissemination Policy

Concepts of manuscripts of this proposed study will be reviewed and discussed by the SCDIC Publications Committee. All manuscripts must be approved by the Committee prior to submission for publication. In addition to presenting results through conferences and publications, the research team will disseminate research results to local clinics and EDs to share findings and lessons learned of this project.

De-identified patient-level data will also be made available to researchers outside the SCDIC through an application and approval process as part of the SCDIC's Ancillary Studies Policy and Data Dissemination Plan. To protect the confidentiality and privacy of the participants, investigators granted access to the limited access data must adhere to strict requirements incorporated into a standard Data Use Agreement. In accordance with NHLBI policy, outside researchers will also be required to submit an approval from their IRB.

6. References

1. Center for Disease Control and Prevention. Sickler cell disease (SCD). Data and statistics on sickle cell disease. August 9. Available at https://www.cdc.gov/ncbddd/sicklecell/data.html

2. Payne AB, Mehal JM, Chapman C, et al. Mortality trends and causes of death in persons with sickle cell disease in the United States, 1979-2014. *Blood.* 2017(130):865.

3. Quinn CT, Rogers ZR, McCavit TL, Buchanan GR. Improved survival of children and adolescents with sickle cell disease. *Blood.* 2010;115(17):3447-3452. doi:10.1182/blood-2009-07-233700. PMID: 20194891. PMCID: PMC2867259.

4. Ware RE, de Montalembert M, Tshilolo L, Abboud MR. Sickle cell disease. *Lancet.* 2017;390(10091):311-323.

5. Haywood Jr C, Tanabe P, Naik R, Beach MC, Lanzkron S. The impact of race and disease on sickle cell patient wait times in the emergency department. *American Journal of Emergency Medicine.* 2013;31(4):651-656.

6. Jenerette CM, Pierre-Louis BJ, Matthie N, Girardeau Y. Nurses' attitudes toward patients with sickle cell disease: a worksite comparison. *Pain Management Nursing.* 2015;16(3):173-181.

7. Glassberg JA, Tanabe P, Chow A, et al. Emergency provider analgesic practices and attitudes toward patients with sickle cell disease. *Annals of Emergency Medicine.* 2013;62(4):293-302. e210.

8. Haywood C, Lanzkron S, Hughes MT, et al. A video-intervention to improve clinician attitudes toward patients with sickle cell disease: the results of a randomized experiment. *Journal of General Internal Medicine.* 2011;26(5):518-523.

9. National Heart L, Institute B. Evidence-based management of sickle cell disease: expert panel report, 2014. *Washington, DC: National Institutes of Health.* 2014.

10. Tanabe P, Silva S, Bosworth HB, et al. A randomized controlled trial comparing two vaso‐occlusive episode (VOE) protocols in sickle cell disease (SCD). *American Journal of Hematology.* 2018;93(2):159-168.

11. Krishnamurti L, Smith‐Packard B, Gupta A, Campbell M, Gunawardena S, Saladino R. Impact of individualized pain plan on the emergency management of children with sickle cell disease. *Pediatric Blood & Cancer.* 2014;61(10):1747-1753.

12. Kato-Lin Y-C, Krishnamurti L, Padman R, Seltman HJ. Does e-pain plan improve management of sickle cell disease associated vaso-occlusive pain crisis? A mixed methods evaluation. *International Journal of Medical Informatics.* 2014;83(11):814-824.

13. Schefft MR, Swaffar C, Newlin J, Noda C, Sisler I. A novel approach to reducing admissions for children with sickle cell disease in pain crisis through individualization and standardization in the emergency department. *Pediatric Blood Cancer.* 2018:e27274.

14. Middleton B, Bloomrosen M, Dente MA, et al. Enhancing patient safety and quality of care by improving the usability of electronic health record systems: recommendations from AMIA. *J Am Med Informat Assoc.* 2013;20(e1):e2-e8.

15. Chaudhry B, Wang J, Wu S, et al. Systematic review: impact of health information technology on quality, efficiency, and costs of medical care. *Annals of Internal Medicine.* 2006;144(10):742-752.

16. Jones SS, Rudin RS, Perry T, Shekelle PG. Health information technology: an updated systematic review with a focus on meaningful use. *Annals of Internal Medicine.* 2014;160(1):48-54.

17. Henry J, Pylypchuk Y, Searcy T, Patel V. Adoption of electronic health record systems among US non-federal acute care hospitals: 2008-2015. *ONC Data Brief.* 2016;35:1-9.

18. HealthIT.gov. Clinical decision support. Available at https://www.healthit.gov/topic/safety/clinical-decision-support.

19. Patterson BW, Pulia MS, Ravi S, et al. Scope and influence of electronic health record–integrated clinical decision support in the emergency department: a systematic review. *Annals of Emergency Medicine.* 2019.

20. Bennett P, Hardiker NR. The use of computerized clinical decision support systems in emergency care: a substantive review of the literature. *Journal of the American Medical Informatics Association.* 2016;24(3):655-668.

21. HealthIT.gov. What is a patient portal? Available at https://www.healthit.gov/faq/what-patient-portal.

22. Kruse CS, Bolton K, Freriks G. The effect of patient portals on quality outcomes and its implications to meaningful use: a systematic review. *Journal of Medical Internet Research.* 2015;17(2).

23. Mold F, de Lusignan S, Sheikh A, et al. Patients' online access to their electronic health records and linked online services: a systematic review in primary care. *British Journal of General Practice.* 2015;65(632):e141-e151.

24. Ammenwerth E, Schnell-Inderst P, Hoerbst A. The impact of electronic patient portals on patient care: a systematic review of controlled trials. *J Med Internet Res.* 2012;14(6):e162. doi:10.2196/jmir.2238. PMID: 23183044. PMCID: PMC3510722.

25. Lancaster K, Abuzour A, Khaira M, et al. The use and effects of electronic health tools for patient self-monitoring and reporting of outcomes following medication use: systematic review. *Journal of Medical Internet Research.* 2018;20(12).

26. Venkatesh V, Davis FD. A theoretical extension of the technology acceptance model: Four longitudinal field studies. *Manag Sci.* 2000;46(2):186-204.

27. Davis FD. Perceived usefulness, perceived ease of use, and user acceptance of information technology. *MIS quarterly.* 1989:319-340.

28. Scaccia JP, Cook BS, Lamont A, et al. A practical implementation science heuristic for organizational readiness: R = MC(2). *J Community Psychol.* 2015;43(4):484-501. doi:10.1002/jcop.21698. PMID: 26668443. PMCID: PMC4676714.

29. Hajjar L, Cook BS, Domlyn A, Alia Ray K, Laird D, Wandersman A. Readiness and relationships are crucial for coalitions and collaboratives: concepts and evaluation tools. *New Direction in Evaluation.* in press.

30. Glasgow RE, Vogt TM, Boles SM. Evaluating the public health impact of health promotion interventions: the RE-AIM framework. *American Journal of Public Health.* 1999;89(9):1322-1327.

31. Tabak RG, Khoong EC, Chambers DA, Brownson RC. Bridging research and practice: models for dissemination and implementation research. *American Journal of Preventive Medicine.* 2012;43(3):337-350.

32. Glasgow RE, Harden SM, Gaglio B, et al. RE-AIM planning and evaluation framework: adapting to new science and practice with a twenty-year review. *Front Pub Health.* 2019;7:64.

33. Damschroder LJ, Moin T, Datta SK, et al. Implementation and evaluation of the VA DPP clinical demonstration: protocol for a multi-site non-randomized hybrid effectiveness-implementation type III trial. *Implementation Science.* 2015;10(1):68.

34. Wozniak L, Soprovich A, Mundt C, Johnson JA, Johnson ST. Contextualizing the proven effectiveness of a lifestyle intervention for type 2 diabetes in primary care: A qualitative assessment based on the RE-AIM Framework. *Can J Diab.* 2015;39:S92-S99.

35. Blackman KC, Zoellner J, Berrey LM, et al. Assessing the internal and external validity of mobile health physical activity promotion interventions: a systematic literature review using the RE-AIM framework. *Journal of Medical Internet Research.* 2013;15(10).

36. Proctor EK, Powell BJ, McMillen JC. Implementation strategies: recommendations for specifying and reporting. *Implementation Science.* 2013;8(1):139.

37. Powell BJ, Waltz TJ, Chinman MJ, et al. A refined compilation of implementation strategies: results from the Expert Recommendations for Implementing Change (ERIC) project. *Implementation Science.* 2015;10(1):21.

38. Carlfjord S, Andersson A, Bendtsen P, Nilsen P, Lindberg M. Applying the RE-AIM framework to evaluate two implementation strategies used to introduce a tool for lifestyle intervention in Swedish primary health care. *Health Promotion International.* 2011;27(2):167-176.

39. US Food and Drug Administration (FDA). Guidance for industry patient-reported outcome measures: Use in medical product development to support labeling claims. *US: Department of Health and Human Services Food and Drug Administration*. Available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM193282.pdf.

40. Bakken S, Ruland CM. Translating clinical informatics interventions into routine clinical care: how can the RE-AIM framework help? *J Am Med Inform Assoc.* 2009;16(6):889-897. doi:10.1197/jamia.M3085. PMID: 19717799. PMCID: PMC3002125.

41. McNall M, Foster-Fishman PG. Methods of rapid evaluation, assessment, and appraisal. *American Journal of Evaluation.* 2007;28(2):151-168.

42. Neal JW, Neal ZP, VanDyke E, Kornbluh M. Expediting the analysis of qualitative data in evaluation: A procedure for the rapid identification of themes from audio recordings (RITA). *American Journal of Evaluation.* 2015;36(1):118-132.

43. Vindrola-Padros C, Vindrola-Padros B. Quick and dirty? A systematic review of the use of rapid ethnographies in healthcare organisation and delivery. *BMJ Qual Saf.* 2018;27(4):321-330.

44. Hamilton AB. *Qualitative methods in rapid turn-around health service research: VA HSR&D National Cyberseminar Series: Spotlight on Women's Health*. Washington, DC: US Department of Veterans Affairs; 2013.