Sanguine

Patient-Led Biospecimen and Data Collection

A NEW FRONTIER IN SICKLE CELL DISEASE RESEARCH

What's Inside?

Introduction

The diversity of genetic factors and symptom variability complicates translational and clinical studies related to sickle cell disease (SCD). As an autosomal recessive disorder, mutations in the ß-globin gene affect protein structure and/or expression, thereby contributing to disease severity and complexity.

The most severe form of SCD occurs when both ß-globin alleles of the hemoglobin protein have a single amino acid substitution (HbSS). Inheriting one mutant ß-S allele with other ß-globin mutations (e.g., ß-thalassemia alleles) leads to varying severity, whereas some variants, such as persistent fetal hemoglobulin (HbF) expression, can alleviate disease severity. Such confounding variables often make research study designs and data interpretation difficult.

Systemically, the central nervous system, which relies heavily on highly oxygenated blood, is vulnerable to complications both in children and adults—resulting in the need for constant monitoring and frequent red blood cell transfusions.[1] Understanding how sickling and hemolysis of red blood cells drive disease features such as vaso-occlusion, vascular damage, and inflammation has been a key focus in the field.

Did you know?

When inherited as a single heterozygous allele, the sickle cell trait (ß-globin S allele) provides a protective advantage against malarial infection because it causes increased renewal of red blood cells, disrupting the parasite's lifecycle.[2] Thought to be a form of selective pressure, the heterozygous allele has persisted in the African and Mediterranean populations where malaria infections are common.[3]

In this eBook, we rethink the well-known challenges for advancing SCD research by providing innovative solutions to patient reach, recruitment, retention, and biospecimen collection. You'll learn how Sanguine's patient-led approach provides the pharmaceutical industry with an enhanced ability to recruit study participants and collect biospecimens and data through a mobile workforce across the United States. Our leading advantage – a mobile direct-to-patient approach – brings research participation into the patient's home with a primary focus on establishing trusting relationships.

SCD Quick Facts[4]

- United States: ~100,000 patients
- Worldwide: ~3.2 million patients
- Annual incidence: ~300,000 new cases
- Sickle cell trait (mutation carriers): 43 million
- Annual SCD-related death toll: ~176,000
- Life expectancy:
  - Developed world: 40–50 years
  - Developing world: 20–25 years

CHAPTER 1

Reach, Recruit, Retain

>80% Research studies in the United States experience delays due to recruitment problems

>50% Investigative studies fail to meet enrollment requirements

~30% Average participant drop-out rate across clinical trials[5]

Participation burden represents a critical challenge in retaining SCD patients through study completion. Moreover, the added burden of a rare disease classification that affects frequently marginalized, minority patient populations dispersed across the United States complicates SCD study design and recruitment. Previous multi-centered SCD studies have taken several years to recruit sufficient participants, with ~15% of all SCD interventional trials (and greater than 50% of all prematurely terminated studies) failing due to low enrollment issues.[6–10]

Taking a Lean, Virtual Approach

With a mobile workforce of more than 135 phlebotomists nationwide **(Figure 1)**, our virtual recruitment and in-home biospecimen and data collection capabilities are designed to be minimally disruptive to patients' everyday lives. As a result, patient retention is consistently high (93%) across each study we support. Moreover, a high proportion of patients are eager to participate again and over long study periods, meaning the high scientific value of completing longitudinal studies can be realized. By working with researchers to improve study completion rates, we help minimize inconclusive findings and wasted funding, which further motivates patients to embark on the quest toward improved outcomes for SCD.

FIGURE 1. Mobile phlebotomy: U.S. Geographic Distribution. The Sanguine mobile workforce reaches 70% of the population nationwide. Our fleet consists of more than 135 phlebotomists, with 80% of patients having had the same phlebotomist throughout the duration of their participation.

As a mobile in-home research services company, we access hard-to-reach SCD patients who may otherwise be far from research sites to participate **(Figure 2)**. Our close relationship with the Sickle Cell Disease Foundation and other rare disease non-profit and patient advocacy group partnerships further supports our ability to increasingly be contracted for translational and clinical studies across this disease group. In turn, investigators benefit from expanded study recruitment reach and sample collection, ensuring continuity in research and study completion. By substantially reducing the workload on site staff and the number of sites required, researchers can expect rapid enrollment and mobilization from a leaner, virtual approach.

Sanguine Stats

93%
Patient retention rate

>500
SCD patient members

>45
SCD studies completed

Geographic Distribution of the Sanguine Sickle Cell Disease Patient Member Community

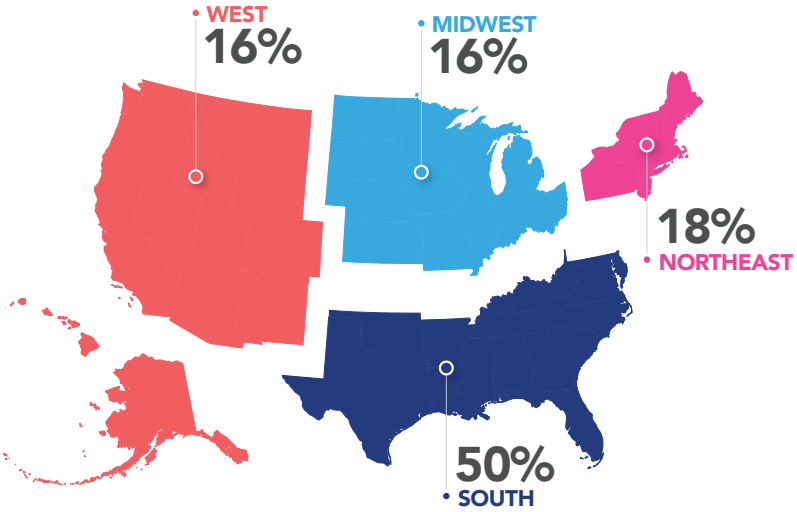


FIGURE 2. A mobile specimen collection approach means access to hard-to-reach populations. The current Sanguine sickle cell disease patient community is made up of 500 members, of which half are in the southern region of the United States. Through strategic online and social media recruitment campaigns, and partnerships with patient advocacy groups, this network is always growing.

Compliance and Quality Assured

Our model is centered around valuing our patient community's autonomy and privacy, and we focus extensively on protecting and enhancing their health. All Sanguine Bio practices and protocols are HIPAA-compliant and IRB-approved. Our informed consent protocol is 21 CFR 11-compliant; our organization maintains the gold standard AAHRPP accreditation for protecting research participants, and we exceed standards set by GCP guidelines.

HIPPA compliant | **IRB approved** | **AAHRPP accredited** | **21 CFR 11 compliant**

Let's Talk

CHAPTER 2

Emerging Therapeutics and Study Criteria

Even with modern medicine and advanced healthcare options available in high-income countries, life expectancy for SCD patients is reduced by up to 30 years, requiring ongoing pain management with limited therapeutic options.[11] At this time, only two therapeutics – hydroxyurea and L-glutamine (Endari™) – are approved for SCD disease management **(Box 1)**, both having drawbacks and less than ideal efficacy.

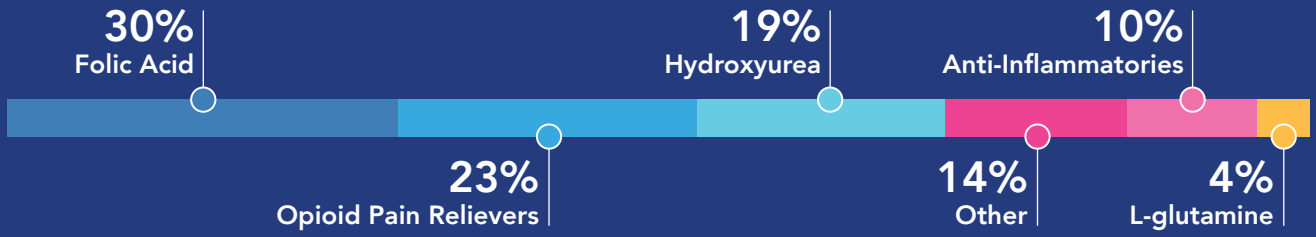
An Anti-Inflammatory Path Forward?

The role of inflammation in SCD has long been an underappreciated avenue for therapeutic discovery, only gaining traction in recent years. The repurposing of anti-inflammatories **(Box 1)** approved for use in other conditions such as rheumatoid arthritis is, for example, being actively pursued in SCD-related clinical trials.[1,12] Moreover, the emerging fields of gene editing and precision medicine promise a new era for SCD research progress, opening doors to cutting-edge therapeutics that may ultimately be real cures for the disease.

BOX.1 SANGUINE SPOTLIGHT

How Do Patients in Our Community Manage Their Disease and Symptoms?

Of the more than 500 SCD patients in our community, most rely on therapeutics outside of the currently approved hydroxyurea and L-glutamine. This attests to the complexity of current treatment decisions that tend to be individual-specific and the overwhelming need for novel treatments.



Access to well-annotated samples and data, particularly the activity status of various medical treatments, is of the utmost importance when carefully considering study inclusion and exclusion criteria during the drug development process.

Start Recruiting Participants for My Study >

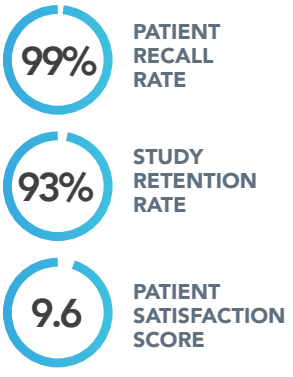
Increasingly Complex Inclusion and Exclusion Criteria

Specific exclusion and inclusion criteria (e.g., medication profiles, treatment histories) often reduce the number of eligible patients for a study, which hinders progress and statistical power. Our thoroughly curated SCD patient community is highly motivated to participate and understand scientific research. Through a patient-led approach, we drastically improve participant retention (93% compared with the 65% industry average).[5] Moreover, we pre-screen and medical record-verify patients for quick recruitment of the most eligible participants. **Table 1** highlights the common inclusion and exclusion criteria we support in SCD research.

INCLUSION CRITERIA	EXCLUSION CRITERIA
HbSS genotype	Nursing or pregnant females
HbSC genotype	Known history of HIV, hepatitis, and other bloodborne infectious diseases
HbS βTh genotype	Previously taken an investigational product in the last 30 days
+/- Sickle cell trait diagnosis	Currently taking voxelotor (Oxbryta®)
+/- Hydroxyurea	Excessive blood loss, including blood donation
Experiencing a VOC	Previously received a blood transfusion in the last three months
ABO blood type specific	Currently receiving anticoagulation therapy such as warfarin or heparin
	Previously received a bone marrow or organ transplant
	Hospitalized within two weeks of scheduled blood draw
	Hemoglobin level <4.0 g/dL in the last six months
	Tobacco use
	Substance abuse

TABLE 1. Typical inclusion and exclusion criteria supported for SCD studies. All participants enrolled in a research study are medical record-verified for their diagnosis and medical history before in-home sample and data collection.
HbSS, hemoglobin SS; *HbSC*; hemoglobin SC; *HbS βTh*, Hemoglobin S/β-thalassemia; *VOC*, vaso-occlusive crisis

Partnering with Sanguine means overcoming hurdles in study recruitment, retention, and completion through an innovative virtual model that is patient-driven to energize and engage a home-grown SCD patient community to participate. Equipped with a mobile workforce capable of in-home biospecimen and data collection, our patient community members develop trusting relationships with their phlebotomist, allowing for repeat, longitudinal collection. We reduce the burden on patients to increase recruitment capacity and improve study completion rates so that you can make meaningful conclusions that will move SCD research forward.



Make My Study Criteria Feasible >

CHAPTER 3

Vaso-Occlusive Crisis Events: A Critical Window into Disease Pathology

Vaso-occlusive crises (VOCs) represent acute, systemic, and painful lifelong events that often require emergency medical attention. They occur because of vascular aggregation of many cell types for which the triggers remain unknown. Though, evidence suggests that inflammatory or environmental stimuli, such as infection, hypoxia, or acidosis, play a fundamental role in their random episodic presentation.[1]

The chronic impact of episodic crises leads to systemic complications that ultimately reduce life expectancy. Therefore, understanding VOC pathophysiology is critical to developing therapeutic interventions that reduce severity and frequency to improve quality of life.

Event-Based Sampling: Going Direct-to-Patient

For SCD patients today, VOCs are all too common, variable in severity, and frequently debilitating. Yet, many will resist seeking medical attention to manage their symptoms. On average, only ~30% of VOC events involve healthcare utilization, with the remaining ~70% relying on self-treatment **(Figure 1)**.[13] This is a critical limiting factor in current research study designs because applying a limited VOC data subset combined with medical utilization variability from patient-to-patient can heavily skew results.

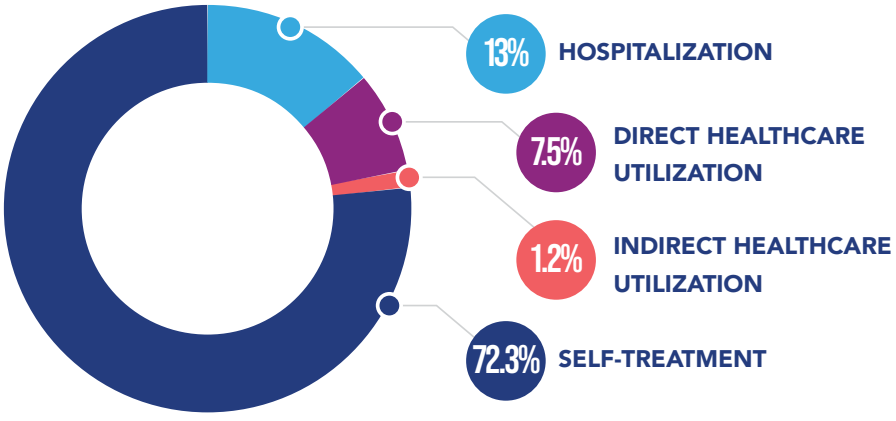


FIGURE 1. Type of treatment pursued for VOC events. Only ~30% of patient-reported VOC events could be assessed using the standard medical utilization endpoint (hospitalization/ER visit >4hrs). Data are based on 35 participants and 116 events. *Data are adapted from Sanguine Speaker Series webinar.*

Taking a direct-to-patient approach allows for the collection of comprehensive data related to a greater number of VOC events, individualized against each patient's pain thresholds for a more reliable clinical endpoint—a measurement that is incredibly difficult to capture by way of conventional study designs. Considering that many patients opt to self-treat during VOC events **(Figure 1)**, traditional endpoints focusing on hospitalization may only reveal a fraction of the effect an investigational intervention may have, masking valuable information for determining overall study success.

We partner with researchers in the pharmaceutical industry to optimize study designs and remove sample collection barriers by making it convenient for patients to participate. By adopting our direct-to-patient workflow for event-based sample collection **(Figure 2)**, researchers maximize their study's potential through increased reach for recruitment and convenient in-home sample collection for study retention. Moreover, integrating electronic surveys and questionnaires or technology-based patient-reported outcome data to supplement biological samples is entirely feasible to provide an all-inclusive view of study participants.

Event-Based In-Home Specimen Collection Workflow

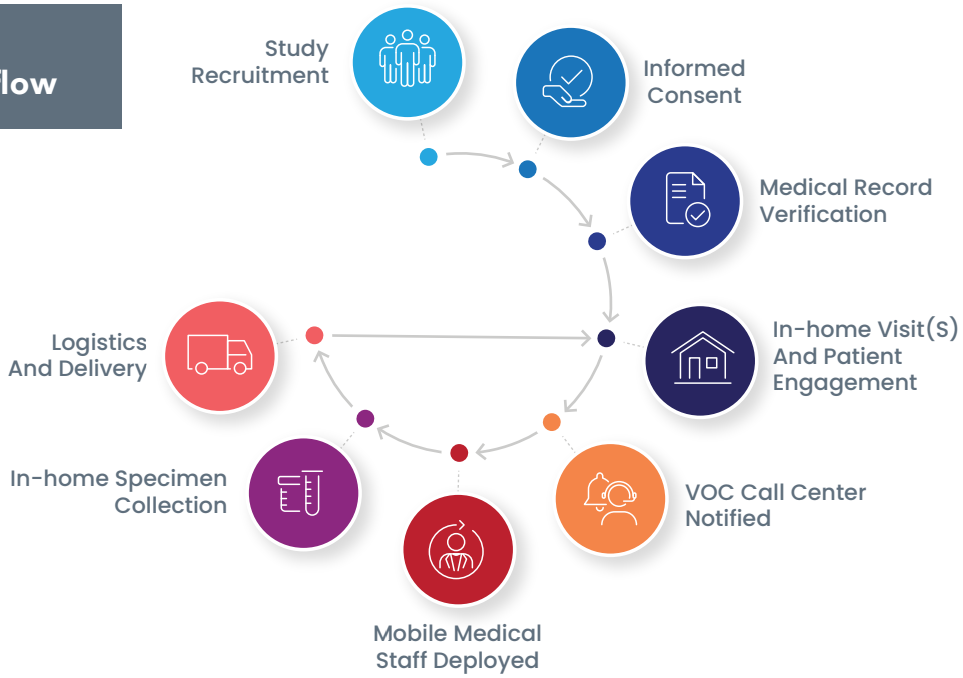


FIGURE 2. A direct-to-patient approach means access to patient samples during a VOC event. Collect samples and patient-reported outcome data during or after an acute pain episode, monitor the response or nonresponse to treatment, obtain trough and peak level biospecimens, or other event-based sample collection specific to your study.

Evidence from the Field

Researchers who partner with us take advantage of direct-to-patient event-based sampling for capturing a range of baseline and VOC measurements over an extended period of time. By enabling longitudinal sampling, this virtual model provides researchers with valuable benchmarks for comparing individual baseline phenotypes and VOC events within translational, and therapeutic interventional or observational studies. For example, to identify biomarkers in SCD associated with both VOC and non-VOC events, Pfizer researchers demonstrated significantly altered biomarkers during VOCs, compared with non-VOC baseline data, all collected in an at-home setting **(Box 1)**.[13]

BOX.1 Research in Focus

Evaluation of Longitudinal Pain Study in Sickle Cell Disease (ELIPSIS)[13]

Working together with Pfizer to longitudinally collect patient samples and data from a cohort of 36 patients, researchers evaluated what biomarkers may be associated with VOC events. The published work focuses on a full spectrum of samples and data (e.g., electronic patient-reporting, actigraphy, VOC event sampling, baseline sampling) made possible via our direct-to-patient model.

CONCEPTUAL STUDY DESIGN VALUE:

Identification of biomarkers related to VOCs: utilizing molecular endpoints can increase clarity and precision of interventional readouts

Understanding of individual variability: longitudinal study designs enable natural history data collection and establish baseline values unique to each participant

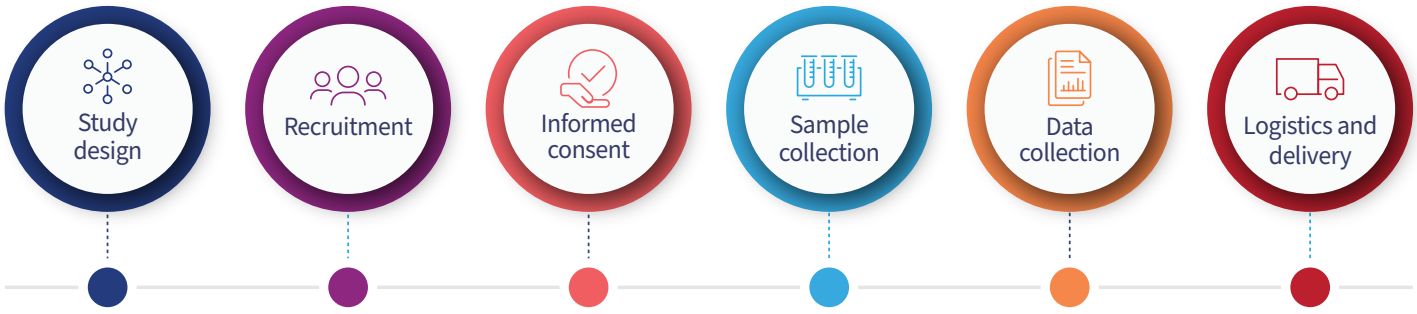
The remote model implemented in the highlighted work increases confidence in the early stages of a clinical trial and reduces costs while increasing participant retention—problems that so often plague clinical research. Additionally, the ability to collect daily patient activity data and electronic patient-reported outcomes generates a rich collection of information that could ultimately be utilized to predict event onset, severity, and/or resolution. With this recently established framework, the SCD field is better poised to execute strategically designed interventional studies and identify novel therapeutics successfully.

Get Started Today >

Conclusion

Conducting rare disease research comes with a high cost and a high study drop-out rate, but working with Sanguine sets your study up for the greatest chance of success. The complexities of SCD disease manifestation and their incorporation into study designs and achievable endpoints requires a partner who offers a tailored approach. Working together, we can ensure efficient recruitment, retention, and engagement coupled with high-quality longitudinal sample collection during key physiological disease events. We bridge researchers with patients—giving you access to a powerful platform for advancing biomedical research and having a tangible effect on patients' lives.

Get to market faster with a fully integrated services solution



About Us

Sanguine Bio is a pioneer of in-home biospecimen collection and a leader in direct-to-patient recruitment and digital health innovation. We partner with researchers to expedite and complete studies across various medical conditions, supporting complex inclusion/exclusion sample and data collection criteria for longitudinal and cross-sectional study designs. Our growing community is made up of more than 30,000 medical record-verified, highly engaged, patient members, and more than 100 advocacy groups, allowing us to seamlessly work with the pharmaceutical industry on more than 600 pre-clinical and clinical condition-specific research studies to date. Learn more: researcher.sanguinebio.com/direct-to-patient-research-services/

Sanguine

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