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BLACK LIVES MATTER.

Individuals with Sickle Cell Disease and Sickle Cell Trait have LIVES that MATTER. They already suffer where we can't see. The color of their skin should not cause them more pain.

A Message from the President

COVID-19 remains an evolving crisis and is Killing Black People Unequally. The current state of public health with the novel coronavirus demands that at-risk populations need to be taken care of. This pandemic has amplified unequal treatment not only in access to healthcare for racial and ethnic minority communities but in every thread of our livelihood. We are quite familiar with healthcare disparities and the numerous programs, research, and policies that have evolved as a result of the 2003 report Unequal Treatment: Confronting Racial and Ethnic Disparities by the Institute of Medicine, which found that race and ethnicity remain significant predictors of the quality of healthcare a person receives. COVID-19 has revealed the paucity in the nationwide improvement of these initiatives. The Black Community is particularly suffering and accounts for a disproportionate number of the COVID-19 cases and fatalities in the United States. The disparities are striking but not surprising. Access to care remains insufficient in Black Communities. Many underlying diseases in the Black Community have been targeted as leading to worse outcomes. These diseases are often expressed as ones that can be solely modified by the individual. More exercise, less high caloric diets, etc. But we know individuals and community deficits are a combination of systemic, operational, judicial, and social inequalities that we must face. Biased systems that work in harmony can no longer be blind to a newborn hereditary disease such as sickle cell disease because it predominately impacts a race that continues to experience abuse, harm, and neglect. Healthcare is not a trusted and sacred place for individuals with sickle cell disease. Those affected continue to be treated as less than.

Early reporting of clinical data of individuals with sickle cell disease infected by the novel coronavirus shows that individuals with sickle cell disease are at increased risk for mortality and poor health outcomes. The dearth of access to care is widespread and exposed in ways that will no longer be muted, whispered about, or disguised.

A comprehensive, multi-race, multi-ethnic strategy is needed to eliminate these inequities.

Lanetta Bronté-Hall, MD, MPH, MSPH
President

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The Editor-in-Chief of Journal of Sickle Cell Disease and Hemoglobinopathies (JSCDH) would like to thank all reviewers for sharing their time, knowledge and expertise with JSCDH's authors in the evaluation of their work, without which it would be impossible to maintain the standards of our Journal.

PLATELET NUMBER IS AN INDEPENDENT RISK FACTOR FOR ACUTE CHEST SYNDROME IN SICKLE CELL PATIENTS

Authors: Crystal Wang, MD, Nataly Apollonsky, MD

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Background: Acute chest syndrome is the most common cause of death in children with sickle cell diseases. It is the second most common cause of hospitalization and increases the risk the developing debilitating chronic lung disease with recurrent disease. The pathophysiology is still not well understood, specifically the role of platelets in ACS.

Methods: A retrospective chart review was performed on patients being followed at St. Christopher's Hospital for Children Hematology department. A list of active and inactive sickle cell patients was generated by the clinic; inpatient and outpatient paper and electronic medical records were reviewed. Inclusion criteria included patients with sickle cell type SS, aged 14-24, seen from January 2012 to January 2019. Exclusion criteria included patients on chronic transfusion therapy, significant comorbid diseases, and insufficient data. Data collected included age, race, baseline CBC prior to hydroxyurea, lipid panel.

Results: 957 patients were identified as sickle cell patients followed by the clinic. Of those, 232 were between the ages of 14-24, of which 52 patients fulfilled inclusion criteria and had sufficient data for analysis. 39 were identified as patients with a history of at least one episode of ACS. 13 were identified as patients without a history of ACS. The groups were similar in gender, race, age, and percent on hydroxyurea. Patients without ACS were found to have statistically significantly lower platelet count (330) compared to those with ACS (459), based on paired t test (p value 0.00052). Lowest platelet count during admission for patients with ACS was found to be 335 (26% decrease from baseline). There was no difference between the two groups in terms of white blood cell count, hemoglobin, lipid panel, or percent of patients on hydroxyurea.

Conclusion: A higher level of circulating platelets is an independent risk factor for ACS in patients with sickle cell disease (Hgb SS). Platelets greater than 375 doubles the risk for acute chest syndrome with 91% PPV. This may support hypothesis that increased stress from a vaso-occlusive crises and more severe disease is associated with bone marrow hyperplasia, leading to thrombocytosis.

Demographics	Patients with ACS	Patients without ACS
Gender	19 female (49%) 20 male (51%)	7 female (53%) 6 male (46%)
Race	79% (31/39) Black 11% (4/39) Hispanic 5% (2/39) Unknown 5% (2/39) Other	85% (11/13) Black 14% (2/13) unknown
Sickle Cell Disease Assessment Instrument Disease Severity	18 severe (46%) (score >=2) 9 moderate (23%) (score 1) 8 mild (21%) (score 0)	2 severe (15%) (score >=2) 1 moderate (8%) (score 1) 10 mild (77%) (score 0)

	Patients with ACS	Patients without ACS	
Platelets >= 375	30	3	PPV = 91%
Platelets < 375	9	10	NPV = 55%
	Sensitivity = 77%	Specificity 77%	RR = 2.6

Authors: Lisa M. Shook, MA, MCHES (1), (2), Cami Mosley (1) , Ann M. Connelly, MSN, RN, LSN, NCSN, (3), Cheryl L. Jones, MSSA (4)

***Affiliations**: 1. Cincinnati Comprehensive Sickle Cell Center, Division of Hematology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH 2. University of Cincinnati, College of Medicine, Department of Pediatrics, Cincinnati, OH 3. Ohio Department of Health, School Nursing and Early Childhood Health Programs, Columbus, OH; 4. Ohio Department of Health, Regional Sickle Cell Services Program, Columbus, Ohio*

Background: Based on estimates from the Ohio Department of Health Sickle Cell Services newborn screening program, there are an estimated 1,200 children with sickle cell disease (SCD) attending Ohio schools (grades K – 12). SCD is an inherited blood disorder that can cause red blood cells to have a sickled shape, leading to less oxygen delivered to vital organs and clogging blood flow in the body. There are specific medical management needs that school staff need to be aware of to provide evidence-based care for these students. The objective of this study was to assess the training; self-reported knowledge, confidence and ability for school nurses to manage SCD in the school-setting, and identify continuing educational needs and preferences.

Methods: Ohio school nurses participated in one of three Ohio Department of Health sponsored school nurse conferences across the state. IRB approved surveys were distributed to 490 school nurses to complete voluntarily. Participants self-reported training, knowledge, confidence and ability to identify SCD complications and emergencies. Participants also identified preferred continuing educational content and methods.

Results: : A total of 407 (83.1%) school nurses at three conference sites completed the survey. Majority of respondents were registered nurses (63.4%) with at least a bachelor's degree (56.9%). Participants were predominantly female (99.2%) and between the ages of 40-49 (32.5%) and 50-59 (31.2%), and. worked in public schools (86.8%), with 60.2% working in more than one school location. In nearly 40% of the schools, students do not have always have access to a school nurse. Only 35% of respondents reported experience treating a student with SCD. In regards to identifying SCD complications, 46.3% of respondents reported their ability to identify splenic sequestration as "below average." Majority of participants rated their ability as "average" to identify SCD complications. Respondents ranked formats for receiving education about SCD, with the most preferred being an online module for continuing education credits (46.5%). Only 14% of nurses received continuing education about SCD in the past three years.

Conclusions: School nurses in Ohio reported varying experience, knowledge and comfort about managing SCD. Results suggest that school nurses prefer to learn about SCD when provided continuing education credit. This survey has provided a preliminary framework for developing continuing education for Ohio school nurses about SCD.

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Background: Hydroxyurea prevents vaso-occlusive crises in sickle cell disease (SCD) by increasing fetal hemoglobin levels and in turn reducing hospitalizations and mortality rates. Despite strong evidence for its use, hydroxyurea remains underutilized, due to fear of side effects, concerns regarding efficacy, or mistrust towards medical professionals. This project aimed to assess the role of patient education in improving patient knowledge and perspective of hydroxyurea, via exposure to the American Society of Hematology (ASH) Hydroxyurea Education Booklet.

Methods: This study utilized a mixed-methods approach to integrate patient responses to the ASH booklet. Targeted sampling of participants from the University of Illinois Health Systems and the Sickle Cell Disease Association of Illinois community events resulted in twenty participants, including ten adult patients with SCD and ten parents of pediatric patients with SCD. After ASH booklet exposure, participants completed a survey and semistructured interview to assess knowledge and perception of the booklet and hydroxyurea. Interview transcripts were analyzed via Dedoose, a software for qualitative analysis.

Results: After booklet exposure, the majority of participants indicated increased hydroxyurea knowledge, increased interest in taking hydroxyurea daily and a desire for more similar patient education. Survey results indicated that almost half of the respondents incorrectly believed hydroxyurea works to cure SCD crises rather than prevent them. Qualitative analysis of interview transcripts revealed three major themes. (1) Pictorial data is easily understood and preferred, which is consistent with existing literature on patient education. (2) Participants prefer realistic and diverse patient testimonials on hydroxyurea over solely positive testimonials. As one participant stated, the inclusion of only positive testimonials “underestimates the abilities of [...] patients and families with sickle cell” and seems “like an infomercial." (3) Compliance with hydroxyurea can be challenging alongside the complex management of SCD.

Conclusions: The ASH booklet was received favorably by the majority of participants. The incorrect belief that hydroxyurea works to cure sickle cell crises may be contributing to a resulting lack of faith in hydroxyurea and in the medical community that prescribed it. Exposure to solely positive testimonials in patient education may contribute to such unrealistic expectations. Therefore, this study recommends future patient education to include a pictorial focus with an emphasis on realistic testimonials, which acknowledge both positive and negative experiences with hydroxyurea. In addition, this study emphasizes a need to acknowledge and empathize with the healthcare needs of those managing SCD. These steps may positively impact patient confidence in hydroxyurea therapy

ADVANCED PRACTICE NURSE LED PRIMARY SPECIALTY CARE CLINIC IMPROVES ACCESS TO COMPREHENSIVE COORDINATED CARE FOR ADULTS WITH SICKLE CELL DISEASE IN DELAWARE

Authors: Nina Anderson, RN, DNP, Sophie Lanzkron, MD, MPH, Samir Ballas, MD, FACP, James Gill, MD, MPH, Oluseyi Senu-Oke, MD

Background: In 2009 the total hospital costs for 96 discrete adults with sickle cell disease (SCD) in Delaware (DE) reached $ 3.3 million (Anderson et al., 2014). In 2014 the TOVA Community Health launched a community-based a comprehensive adult sickle cell program in Delaware. The Delaware Department of Health and Social Services found that of these 96 individual adults in DE with SCD, they utilized hospital services 99.5% of the time for sickle cell crisis. (Anderson et al., 2014). The majority of those adults lived in New Castle County, DE. The dearth of sickle cell providers (hematologist/oncologist) for adults may drive them to seek recurrent care through the hospital system. Recognizing this as a country-wide public health crisis, the Delaware Department of Health and Social Services (DHSS) partnered with TOVA Community Health in 2014 to establish an advanced practice led adult primary specialty care clinic medical home in Wilmington, DE.

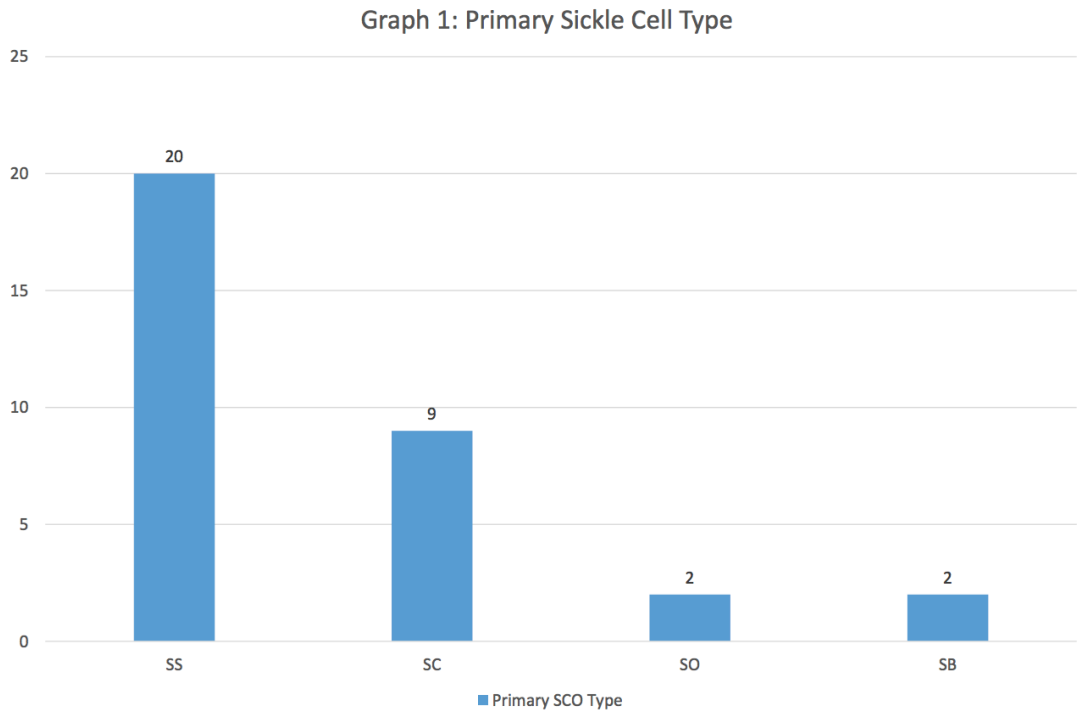
Methods: The clinic opened March, 2014. The staff included a hematologist with expertise in SCD, a primary care provider, an advanced practice nurse, a Social Worker (MSW), a nurse care coordinator, an advanced practice nurse and a community health worker funded by the SCDAA and HRSA. From 2014 to 2018 we have provided services for 33 discrete patients (Graph 1).

Results: This first cohort of patients is notable for health complications which may be due to the lack of coordinated primary specialty sickle cell care. Therapeutic counseling and support groups and preventive health maintenance services were measured by: outpatient visits to the clinic, access to hydroxyurea therapy (HU), immunizations (Pneumococcal), Depression Screens and Personalized Sickle Care Plans (Graph 2). 21 % percent of the patients had no sickle cell provider and/or hematologist/oncologist other than ED or inpatient care for the 12 months preceding their first visit to our clinic. 48% of the patients received Pneumovax 23 val (n=16/33) and Prevnar 13 (n=7/33) and three (n=3/33) received both Pneumococcal vaccines. 30% percent of the eligible patients (n=10/33 patients) seen were offered access to HU but were not on the drug. All patients did not have a Personalized Sickle Cell Care Plan prior to receiving services at the Primary Specialty Care clinic. 12% (n=4/33) patients had a diagnosis of Substance Abuse Disorder, 15% (n=5/33) had a diagnosis of Opioid Misuse Disorder and 3% (n=1/33) had both Substance Abuse and Opioid Misuse Disorder (Graph 3). 45% (n=15/33) had a Pain Management Agreement established within the time period at the primary specialty clinic.

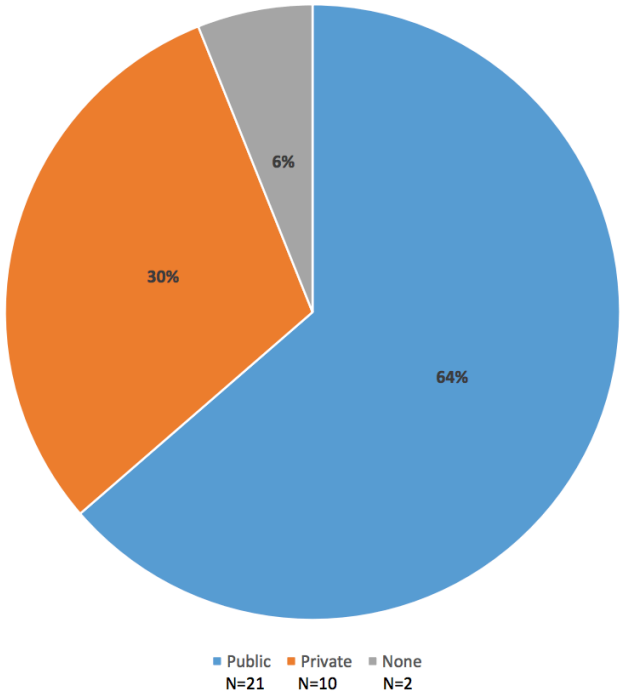
Conclusions: The creation of an nurse led advanced practice primary specialty care medical home clinic for adults with SCD in Wilmington, DE demonstrates a successful leverage of regional networks that engages academic institutions, public health, and a community based organization to develop an adult SCD community-based primary specialty care model. This safety net clinic provides team based primary specialty care to adults whose only option previously was at the hospital and/or emergency room. Our statistics reinforce the need for better access to resourced primary specialty care clinics for persons with SCD across the lifespan.

NP Project Graphs

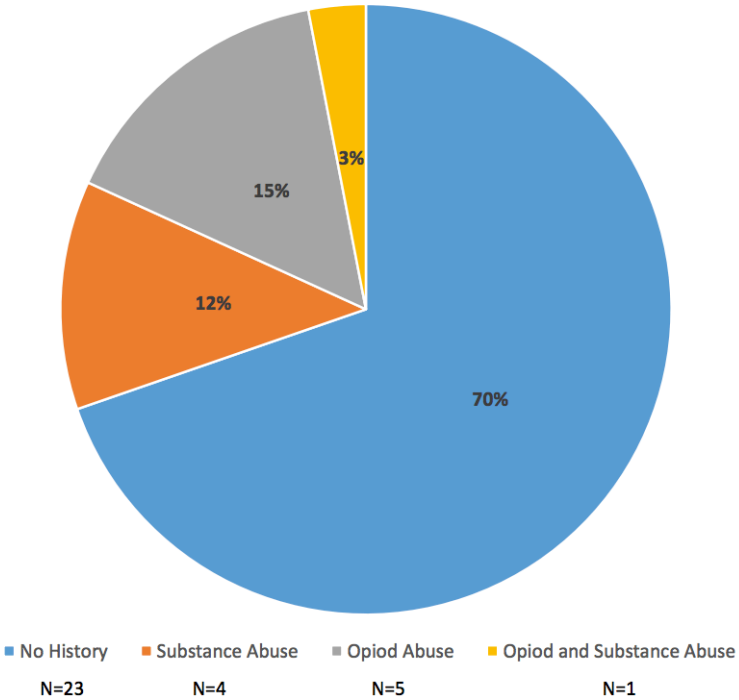
1.3.2020



Graph 2: Type of Insurance



Graph 3: History of Substance & Opioid Abuse



PREVALENCE OF DIABETES AMONG ADULTS WITH SICKLE CELL DISEASE: A SINGLE INSTITUTION EXPERIENCE

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Background: Sickle cell disease (SCD) is a heterogeneous red blood cell disorder that primarily impacts African-Americans in the United States. African-Americans also suffer from high rates of Type 2 Diabetes mellitus (T2DM). Uncontrolled, both diseases can cause vasculopathy and the prevalence of T2DM among the different genotypes of SCD remains unknown. In this study, we assessed the prevalence of T2DM among adults with various SCD genotypes at our institution.

Methods: The University of North Carolina Sickle Cell Database was used to conduct a single-institution, retrospective cross-sectional study of adult patients (≥18yo) and 2:1 age/sex/race matched controls with or without T2DM. Unadjusted statistical tests were used to examine how the group with 'more severe' SS/Sβ 0 genotypes differed from 'less severe' SC/Sβ + genotypes based on T2DM diagnosis and BMI.

Results: We identified 444 adult patients and 26 patients had a co-diagnosis of T2DM (Table 1). A higher proportion of the less severe SCD group were diagnosed with T2DM (x 2 =10.13, p = 0.001). A higher proportion of patients diagnosed with T2DM and SCD had a BMI of 25kg/m2 (i.e. overweight) or greater (76.9%) compared to matched controls) (Table 2).

Conclusions: Patients with SC/Sβ + genotypes were more likely to be diagnosed with T2DM in our cohort. Patients with SCD who are overweight may be at risk for T2DM. Further investigation is needed to determine if our findings are applicable to larger cohorts.

Table 1. Characteristics of patients with diabetes and sickle cell disease				
N	444			**p-value**
Female (N (%))	52.4% (N = 233)			
Genotype		**HbSS/HbSβ0 ('more severe')**	**HbSC/HbSβ+ ('less severe')**	
Total		N = 283	N = 161	
	Proportion with T2DM	3.2% (N = 9)	10.6% (N = 17)	0.001
	T2DM Avg. Age (SD)	45.7 (10.3)	55.6 (15.9)	0.05
	T2DM Gender (female)	56% (N = 5)	52.9% (N = 9)	0.90
	T2DM Avg. BMI (SD)	32.2 (9)	27.7 (5.5)	0.19

Table 2. Comparison of variables between cases and matched controls			
	Cases	**Controls**	**p-value**
N	26	52	
Genotype			
HbSS/HbSβ0 ('more severe')	9	18	
Female	56%	56%	n/a
Age	45.7 (10.3)	45.2 (10.8)	0.91
African-American	100%	100%	n/a
BMI	27.7 (6.2)	23.8 (4.3)	0.07
HbSC/HbSβ+ ('less severe')	17	34	
Female	52.90%	52.90%	n/a
Age	55.7 (15.8)	51.3 (13.1)	0.29
African-American	100%	100%	n/a
BMI	32.2 (9)	27.4 (5.5)	0.02

Authors: Nia Sumpter

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Objective: My objective with this paper is to give a holistic view of how Sickle Cell patients see themselves interacting with the healthcare system. This perspective should be centered at improving care for POC who have experienced the fragmentation of healthcare. This paper highlights historical trauma and how this narrative informs the healthcare choices of Black Americans. Because sickle-cell anemia disproportionately affects African Americans, it is imperative to understand patient experiences to better inform effective research agendas and hospital protocols. The objective of this analysis is to begin exploring specific experiences that alter health outcomes for sickle cell patients due to race, sexuality, gender, and socio-economic status.

Methods: In this preliminary study, I use autoethnograhpy to recount my own experiences with doctor/patient communication at various stages of my own health treatment and education. Autoethnography has proven extremely useful in helping researchers understand the details of experience and the descriptive contexts that fuel quantitative research. Specifically, in health communication, qualitative research, and more specifically autoethnography, create space for scholars to understand the exigency of patient/ healthcare provider relationships and the importance of empathy, cultural sensitivity, and inclusive practice. Autoethnography asks the researcher to be vulnerable honest, and open about individual experiences, draw connections between the personal and the political, and engage in self-reflexivity as a rigorous research act. It also requires that researchers position their own body and social identities. I am a 24-year-old Black woman from a middle-class family. I have had several experiences during childhood and through young adulthood that illuminate the discrimination and bias that occurs with sickle cell patients and primarily with white male doctors, and how that discrimination negatively affects my actual health and ability to manage my disease. However, I am a senior at Saint Louis University and have had many leadership opportunities. The way I am treated as a potential doctor and emerging leader, despite my disease, highlights an alternative experience where access is granted based on accolades, education, and ability. Using Black Feminist theory, canonical exception, and health communication theories as frameworks, I tell a series of stories to juxtapose my life as a patient managing sickle cell anemia and my life as a scholar contributing to the very field that impacts my life and how I navigate the healthcare system.

Conclusions: The overall goal of my research is to present an antithesis to philosophical methods in treating Sickle Cell Anemia patients. The naturalism approach can be erroneous when treating sickle cell anemia because it does not account for how the disease can be effected by the emotional and psychological state of the patient, things that can't be objectively measured by science. Emphasizing different approaches such as the biopsychosocial approach and armed with different theoretical lens, the doctor can understand the whole patient is effected by Sickle Cell Anemia. Evidence based medicine and other philosophical approaches to medicine can lead to negative health care outcomes because of the approach being grounded in Eurocentric epistemology that is often taught to characterize a pain crisis by numbers. A culmination of factors that govern the patient experience can be marginalizing to people that have been socially ostracized by these very policies. It is important when discussing resolutions for disparities that we include patient experiences at the center of these solutions.

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KNOWLEDGE, AWARENESS AND ATTITUDES TOWARDS SEXUAL AND REPRODUCTIVE HEALTH ISSUES IN PATIENTS WITH SICKLE CELL DISEASE AND CAREGIVERS

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Background: Adolescents and young adults (AYA) with Sickle cell disease (SCD) are a vulnerable patient population due to increased morbidity and mortality. Improving care for AYA with SCD through planned transition to adult care and better ways to address reproductive health problems related to SCD is an unmet need. The primary objective of our study was to evaluate the knowledge, awareness and attitudes towards sexual and reproductive health (SRH) issues in caregivers and patients with SCD. We sought to improve reproductive health knowledge through focused educational intervention of caregivers and patients with SCD.

Methods: We conducted a survey-based study followed by educational intervention at the Iowa State Sickle Cell symposium, which is an annual event organized by the University of Iowa Comprehensive Sickle Cell program. The survey was created based on literature review and modified based on expert opinion. We included caregivers and patients with SCD from 0-21 years of age and collected data using a 21-item questionnaire with three domains

1. Awareness of SRH issues in SCD
2. 2. Attitudes towards SRH issues and
3. 3. Knowledge of SRH issues in SCD. We provided targeted education on reproductive health with two posters, one on male fertility and another on female fertility in SCD. Knowledge component of the survey was assessed after the educational intervention and scores were compared.

Results: : Sixteen caregivers and three patients completed the pre-test questionnaire. Fifteen caregivers and one patient completed the poster-based educational session. Six caregivers completed the post-test. Our key findings are summarized below: Awareness- Only 2 out of 19 respondents (10.5%) reported having received information in all eight different areas of reproductive health in SCD. This included male fertility, menstruation, birth control methods, pregnancy, impact of treatment options on fertility (HU, transfusions and stem cell transplant) and pre-conception counseling. Attitudes- 100 percent of patients and caregivers were interested to know the effects of SCD on reproductive health. Knowledge- Pre-test and post-test questionnaires had 12 questions to assess knowledge of SRH problems in SCD, and score was given based on percentage of correct answers. Average of the pre-test score was 44.5 and average of post-test score was 65.2.

Conclusions: Caregivers and patients with SCD in our cohort were interested to learn the impact of SCD on sexual and reproductive health. Focused educational sessions are feasible and resulted in improved knowledge scores. Strategies to increase awareness and knowledge of SRH issues will lead to improved outcomes and better ways to transition AYA with SCD to adult care.

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Affiliations: *Public Health Institute*

Background: Sickle Cell Disease (SCD) is a complex disease that requires active management by medical specialists, including hematologists, to prevent serious complications that reduce life expectancy and quality of life. In the United States, SCD primarily affects people of African descent; a population that has historically encountered barriers in access to care. The objective of this analysis was to assess access to care by examining the frequency of hematologist encounters among Medicaid enrollees with SCD.

Methods: SCD patients were identified by the Sickle Cell Disease Collection Program, which links administrative, newborn screening, and clinical data sets to identify SCD patients in California. The cohort for this analysis was restricted to SCD patients with continuous Medicaid eligibility for 2016 to 2018, inclusive. The cohort was divided into pediatric (under 21) and adult (21+) based on the patient's age at the beginning of the calendar year or three-year time period. Providers are linked in Medi-Cal (state Medicaid program) data with to their National Provider Identifier, assigned by the Centers for Medicare and Medicaid Services (CMS). CMS provides look-up data for each healthcare provider, and these files were used to identify those with hematology specialty. Each cohort member's count of hematologist encounters was calculated, and results were stratified by age and sex.

Results: : There were 948 pediatric patients and 1,598 adults with SCD in California that had continuous Medicaid eligibility from 2016 to 2018. For pediatric patients, the mean age was 11.9 years and 48% were female. For adult patients, the mean age was 37.6 years and 63% were female. The proportion of SCD patients who had no encounters with a hematologist within a calendar year ranged from 50% to 55% for pediatric patients, and 70% to 72% for adults. Over the three year period, 43% (42% among female and 44% among male) of pediatric patients and 57% (58% among female and 56% among male) of adult patients were never seen by a hematologist.

Conclusions: SCD is a life-threatening blood disorder requiring specialized medical expertise; yet in California, the proportion of SCD patients with Medicaid health insurance who were not seen by a hematologist in a year was high. Even among pediatric patients, who are often thought to have better care due to comprehensive care centers, over half were not seen by a hematologist in a year. The results highlight an opportunity to improve access to specialty care for SCD patients in California enrolled in Medicaid.

Table 1. Number of Hematologist Encounters in a Year

Pediatric SCD Patients						
Year	Total Pediatric Patients	Hematologist Encounters				
		None	1	2 to 5	6 to 11	12+
2016	948	483 (51%)	63 (7%)	188 (20%)	125 (13%)	89 (9%)
2017	895	492 (55%)	50 (6%)	147 (16%)	105 (12%)	101 (11%)
2018	847	461 (54%)	52 (6%)	150 (18%)	111 (13%)	73 (9%)
Adults SCD Patients						
Year	Total Adult Patients	Hematologist Encounters				
		None	1	2 to 5	6 to 11	12+
2016	1598	1136 (71%)	113 (7%)	168 (11%)	90 (6%)	91 (6%)
2017	1651	1185 (72%)	110 (7%)	161 (10%)	86 (5%)	109 (7%)
2018	1699	1180 (69%)	113 (7%)	187 (11%)	109 (6%)	110 (6%)

INITIAL FINDINGS FROM THE LAUNCH OF THE SICKLE CELL DISEASE TRAINING AND MENTORING PROGRAM (STAMP) PROJECT ECHO FOR ADULT PRIMARY CARE PROVIDERS

Authors: Lisa Shook, MA, MCHES, DHPE Bailey House, MPH, Christina Farrell, MPH, Marsha Treadwell, PhD, Ify Osunkwo, MD, MPH John J. Strouse, MD, PhD, Julie Kanter, MD, Allison King, MD, MPH, PhD, Capt. David Wong, MD, E. Donnell Ivy, MD, Shirley Miller, MA, Taniya Varughese, MSOT, ORT/L, Shalini Vora, MPH, Sophie Lanzkron, MD, MHS and Rosalyn Stewart, MBA, MD, MS.

Affiliations: *Cincinnati Children's Hospital Medical Center*

Background: Sickle cell disease (SCD) is an inherited blood disorder affecting approximately 100,000 individuals in the US. A lack of knowledgeable providers, particularly for adult patients, has led to a significant number of adults without access to quality care. Admiral Brett Giroir, MD, Assistant Secretary for Health, recognized the need to address disparities in SCD care, which led to a partnership between the Office of Minority Health and the Health Resources Services Administration Sickle Cell Treatment Demonstration Program (SCDTDP) grantees to develop a national Project ECHO telementoring program targeting adult primary care providers (PCPs). The goals of the Sickle Cell Disease Training and Mentoring Program (STAMP) are to:

1.) Increase the number of providers trained in the evidence-based management of SCD

2.) Identify motivated PCPs

3.) Equip providers with appropriate knowledge, skills and support to effectively co-manage adult patients with SCD.

Methods: Launched in January 2020, STAMP uses Project ECHO telementoring methodology with web-based technology to deliver interactive one-hour sessions with a brief didactic to cover evidence-based practices for SCD management. Providers present de-identified patient cases in order to elicit treatment plan recommendations, both psychosocial and medical, from experts and peers attending the session. The pilot series is being offered twice monthly for six months (January – June, 2020). ECHO coordination is led by the SiNERGe SCDTDP team in the Northeast, and continuing medical education credits and Maintenance of Certification (Part II) credits are offered by the STORM SCDTDP team in the Midwest. A didactic curriculum including preventive screening and testing for adult patients, hydroxyurea, and pathophysiology of SCD-- among other topics, has been developed by all regional SCDTDP teams.

Results: : STAMP participation to date is:

1st session: 44 participants from 21 states

2nd session: 57 participants from 22 states

3rd session: 39 attendees from 16 states

Thirty-two percent of participants have attended at least two sessions. Participants included physicians, advanced practice providers, nurses, researchers, pharmacists, social workers and community based organizations.

Conclusions: STAMP has had a successful start and the potential to be a useful strategy to enhance SCD education for healthcare providers. Data will continue to be collected and analyzed through the duration of the pilot. Participants have expressed an interest in topics such as new pharmaceutical therapies for SCD, including gene therapy, which will be integrated into future sessions. Next steps include determining and coordinating co-management support across or within regions to provide additional support to STAMP participants.

MUSIC THERAPY TO IMPROVE QUALITY OF LIFE IN SICKLE CELL DISEASE (MUSIQOLS): A PILOT STUDY INVESTIGATING FEASIBILITY, ACCEPTABILITY, AND PRELIMINARY EFFICACY

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Background: Individuals with sickle cell disease (SCD) and chronic pain may benefit from adjunctive nonpharmacologic pain management strategies. Here, we investigated the feasibility, acceptability, and preliminary efficacy of a 6-part music therapy protocol on the pain, mood, quality of life, coping skills, and selfefficacy of adults with SCD.

Methods: Using a mixed methods intervention design, we randomized 24 adults with SCD and chronic pain to either 1) a 6-part music therapy protocol (MT) or 2) wait list control (WLC). The music therapy sessions were conducted at a large Midwestern hospital. Participants in MT were taught a series of music exercises for pain management that could be accessed via their own smartphones. Participants completed 2 weeks of daily electronic pain diary entries as well as measures of self-efficacy (Sickle Cell Self-Efficacy Scale), quality of life (PROMIS-29; ASCQ-Me), and coping skills (Coping Skills Questionnaire – Sickle Cell Disease) before and after study conditions. All participants in MT were interviewed following completion of post-test measures.

Results: : 28 patients were invited to participate in this study. Of those, 25 (89%) enrolled and 1 withdrew from participation before randomization. 24 participants were randomized, with 12 being assigned to each group. Baseline characteristics of the study population are described in Table 1. The mean age of all participants was 32.33 years, with the majority of participants (62.5%) being female. The mean age of MT participants was greater by about 4.5 years, but this was not significant. Of the 18 participants who reported household income, 17 (94%) reported earning less than $25,000 a year. There were no statistically significant differences in demographic characteristics between the two groups. Results indicate that the MUSIQOLS protocol and intervention were feasible for study participants. All pre- and post-test study measures and interviews were completed. There was a high rate of completed pain diary entries, with an average of 70% completed during the baseline period, and 66% completed MUSIQOLS Abstract during the follow up period. All MT participants completed all 6 music therapy sessions and reported achieving their expressed goals for therapy. All music therapy exercises deployed during the study were accessible via participants' own devices. 81% of participants reported using interventions at least once every other day. Semi-structured interviews revealed a high degree of usefulness and acceptability. There were four instances of significant improvements for MT participants compared to WLC in changes from the pre- to post-period. These included improvements in self-efficacy, sleep disturbance, pain interference, and social functioning impact (see Table 2).

Conclusions: Preliminary findings support the feasibility and acceptability of music therapy for home use in adults with SCD and chronic pain. Music therapy may assist adults with SCD in reducing pain interference and improving their sleep, social functioning, and perceived ability to manage their symptoms. More research is needed to determine the effectiveness of these interventions. Future studies will include a more rigorous control condition

Table 1

Demographic Variables of the Study Participants

Variables	All Participants (*n*=24)	Study Groups: Music Therapy (*n*=12)	Study Groups: Wait List Control (*n*=12)
Age (years), mean ± SD	32.33 ± 8.43	34.50 ± 9.50	30.17 ± 6.93
Gender, *n* (%)			
Male	9 (37.5)	4 (33.3)	5 (41.7)
Female	15 (62.5)	8 (66.7)	7 (58.3)
Race, *n* (%)			
Black	24 (100)	12 (100)	12 (100)
Education, *n* (%)			
< HS	1 (4.2)	0 (0.0)	1 (8.3)
HS graduate	9 (37.5)	5 (41.7)	4 (33.3)
Some college	9 (37.5)	6 (50.0)	3 (25.0)
College graduate	2 (8.3)	1 (8.3)	1 (8.3)
Refused to answer	3 (12.5)	0 (0.0)	3 (25.0)
Religious Background, *n* (%)			
Christian	15 (62.5)	7 (58.3)	8 (66.7)
None of the above	1 (4.2)	0 (0.0)	1 (8.3)
Other	1 (4.2)	1 (8.3)	0 (0.0)
Preferred not to answer	7 (29.2)	4 (33.3)	3 (25.0)
Household Income, *n* (%)			
$0 to $9,999	8 (33.3)	4 (33.3)	4 (33.3)
$10,000 to $24,999	9 (37.5)	6 (50.0)	3 (25.0)
$25,000 to $49,999	1 (4.2)	0 (0.0)	1 (8.3)
Preferred not to answer	6 (25.0)	2 (16.7)	4 (33.3)
Employment Status, *n* (%)			
Employed part time	5 (20.8)	1 (8.3)	4 (33.3)
Homemaker	1 (4.2)	0 (0.0)	1 (8.3)
Self-employed	4 (16.7)	3 (25.0)	1 (8.3)
Student	2 (8.3)	0 (0.0)	2 (16.7)
Unable to work	9 (37.5)	6 (50.0)	3 (25.0)
Unemployed, looking for work	3 (12.5)	2 (16.7)	1 (8.3)
Marital Status, *n* (%)			
Divorced	1 (4.2)	1 (8.3)	0 (0.0)
Married	4 (16.7)	2 (16.7)	2 (16.7)
Separated	1 (4.2)	0 (0.0)	1 (8.3)
Single (never married)	18 (75.0)	9 (75.0)	9 (75.0)

Table 2

Analysis of Self-Efficacy and Quality of Life Scores by Study Group

Outcome		All (*n* = 24)	MT (*n* = 12)	WLC (*n* = 12)
Self-Efficacy (SCSES)	Pre (Mean ± SD)	28.17 ± 5.14	28.25 ± 5.34	28.08 ± 5.16
	Post (Mean ± SD)	30.63 ± 5.95	33.67 ± 4.68	27.58 ± 5.66
	Change (Mean ± SD)	2.46 ± 5.69	5.42 ± 5.43	-0.50 ± 4.38
	Comparison vs. WLC[a]		**0.008**	
PROMIS Sleep Disturbance[b]	Pre (Mean ± SD)	58.03 ± 8.30	60.52 ± 7.02	55.54 ± 9.02
	Post (Mean ± SD)	59.60 ± 9.11	59.03 ± 10.00	60.18 ± 8.53
	Change (Mean ± SD)	1.57 ± 6.78	-1.49 ± 6.68	4.63 ± 5.58
	Comparison vs. WLC[a]		**0.023**	
PROMIS Pain Interference[b]	Pre (Mean ± SD)	60.15 ± 6.56	62.65 ± 6.42	57.66 ± 5.94
	Post (Mean ± SD)	61.25 ± 4.55	60.55 ± 5.68	61.96 ± 3.15
	Change (Mean ± SD)	1.10 ± 6.74	-2.10 ± 4.68	4.30 ± 7.12
	Comparison vs. WLC[a]		**0.016**	
ASCQ-Me Social Functioning Impact[b]	Pre (Mean ± SD)	47.92 ± 7.32	44.12 ± 6.94	51.73 ± 5.67
	Post (Mean ± SD)	47.27 ± 6.34	47.08 ± 6.43	47.45 ± 6.53
	Change (Mean ± SD)	-0.65 ± 7.71	2.97 ± 6.91	-4.28 ± 6.93
	Comparison vs. WLC[a]		**0.018**	

[a] Student t-test of change scores (post – pre)
[b] Raw scores were converted to t-scores using healthmeasures scoring service

OVERLAPPING GEOGRAPHIC PREVALENCE OF ASTHMA-RELATED SYMPTOMS WITH SICKLE CELL DISEASE (SCD) COMPLICATIONS OF ACUTE CHEST SYNDROME (ACS) AND VASO-OCCLUSIVE PAIN (VOE) IN METRO ATLANTA

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Background: Asthma is the one of the most common reasons for emergency department (ED) visits and geospatial hot spots have been previously been identified. Children with SCD and asthma have a higher rate of ACS events than those without asthma, however geospatial mapping has not been studied in SCD+ACS. The objective of our study is to determine the geospatial variability of ACS in metro Atlanta by identifying areas of geographic prominence in the incidence of ACS and VOE ED visits to 3 pediatric EDs for SCD compared to non-SCD asthma.

Methods: A retrospective electronic medical record (EMR) review of ED visits for children aged 2-18 years with ICD-10 codes for all SCD patients (all genotypes), ACS-related diagnoses, VOE-related diagnoses & all (non-SCD) asthma-related diagnoses from Jan-Dec 2017. Patients with both VOE and ACS, or those who developed ACS during hospitalization were included in the ACS group. Group demographic characteristics were compared using Chi-square test and two sample t-test. A geospatial comparison of non-SCD Asthma vs. all SCD, SCD+ACS & VOE alone was illustrated via heat maps. We superimposed a number of circular regions onto the study region & determined the significance of the number of cases that fall within each circle to assess cluster detection and relative risk (RR).

Results: : Over the year, 40394 unique ED visits for asthma (n=38178) & SCD (n=2216) were geocoded from the EMR (Table1). There were 1069 cases of ACS and 568 cases of isolated VOE. SCD patients are older (p<.001), had public insurance more often (p<.001), and had significantly more ED visits in our study period compared to asthma patients (mean±SD 2.8±3.3 vs. 1.5±1.1, respectively; p<.0001). In both the asthma and SCD cohort, slightly more than half were male (57% and 58%, respectively) with no significant difference in gender overall. The geospatial mapping of patient group ED visits are shown in Figure1. Although overlap is seen, a different pattern of geospatial mapping with ACS hotspots was identified in patients with SCD+ACS vs. SCD+VOE (Figure2). An overlap in census tract clusters was also identified between the asthma and ACS group that varies from the VOE group. For ACS, 8 significant cluster regions were identified (Fig3), 1 of which has a RR>5. For VOE, 14 significant cluster regions were observed, 7 with RR>5

Conclusions: Overlapping geospatial “hot spots” for ACS and asthma-related ED visits were identified, that varied from VOE. This suggests potential asthma environmental triggers in some zip code areas that may impact ACS risk. Further investigation is warranted.

Table 1. Patient characteristics by group

Variable	Asthma* (n=38178)	All SCD* (n=2216)	SCD+ACS (n=1069)	SCD+VOE (n=568)	*p-value**
Age-years (mean±SD)	8.1±4.6	11.8±5.0	11.0±5.1	13.2±4.1	**<0.001**
Sex, n (%) - Male	21893 (57%)	1281 (58%)	669 (63%)	278 (50%)	0.692
Insurance, n (%)					**<0.001**
Private	14258 (37%)	662 (30%)	310 (29%)	149 (27%)	
Public	20956 (55%)	1458 (66%)	715 (67%)	381 (68%)	
Military	302 (1%)	58 (3%)	21 (2%)	22 (4%)	
None/Other	2662 (7%)	38 (2%)	23 (2%)	6 (1%)	
# ED visits (mean±SD)	1.5±1.1	2.81±3.3	2.41±2.2	2.95±2.9	**<0.001**

"All SCD" includes all SCD visits seen in the ED regardless of diagnosis. SCD+ACS includes subgroup of patients with "ACS" as ED diagnosis and/or ACS as hospital discharge diagnosis. Patients with ICD-10 code for both ACS and VOE were included in the ACS group. SCD+VOE reflects patients with isolated pain. * *p-values* reflect differences between Asthma and All SCD.

Figure 1. Geospatial mapping of patients with Asthma vs. All SCD vs. Acute Chest Syndrome (ACS) vs. Vaso-occlusive Pain Episodes (VOE). Geospatial clusters of encounter levels are color coded. Areas shown by latitude (lat) and longitude (lon).

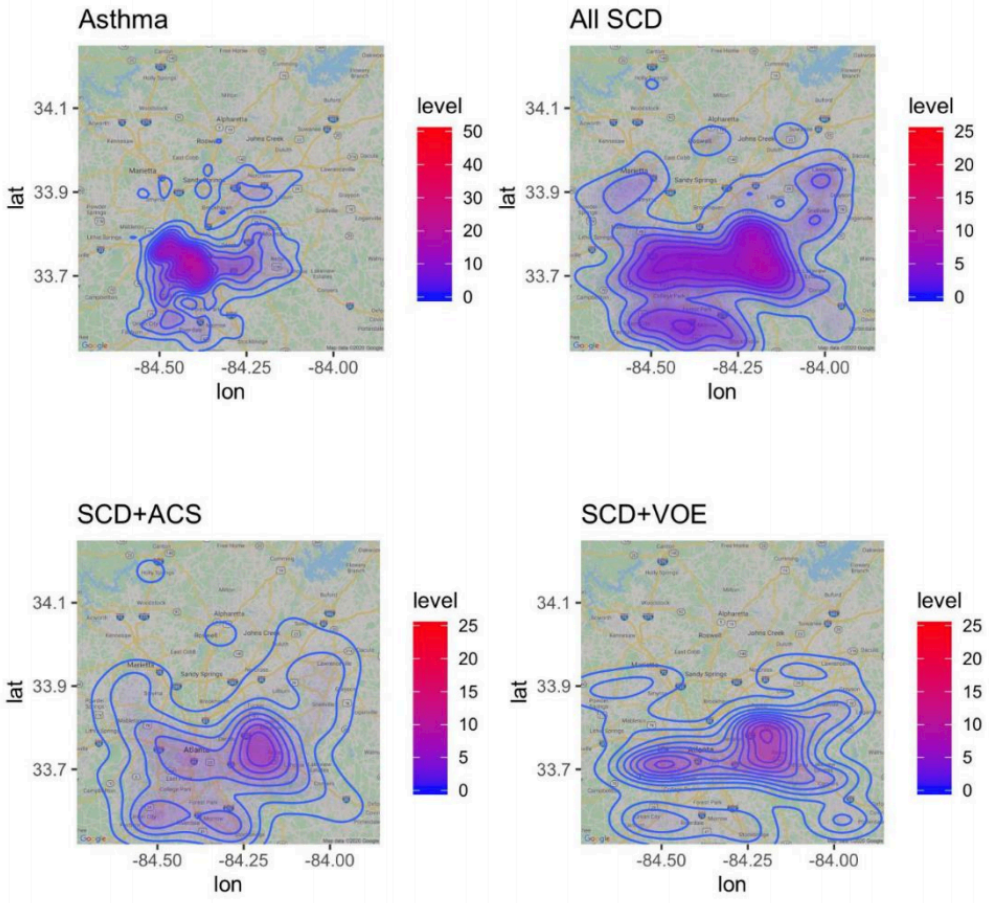
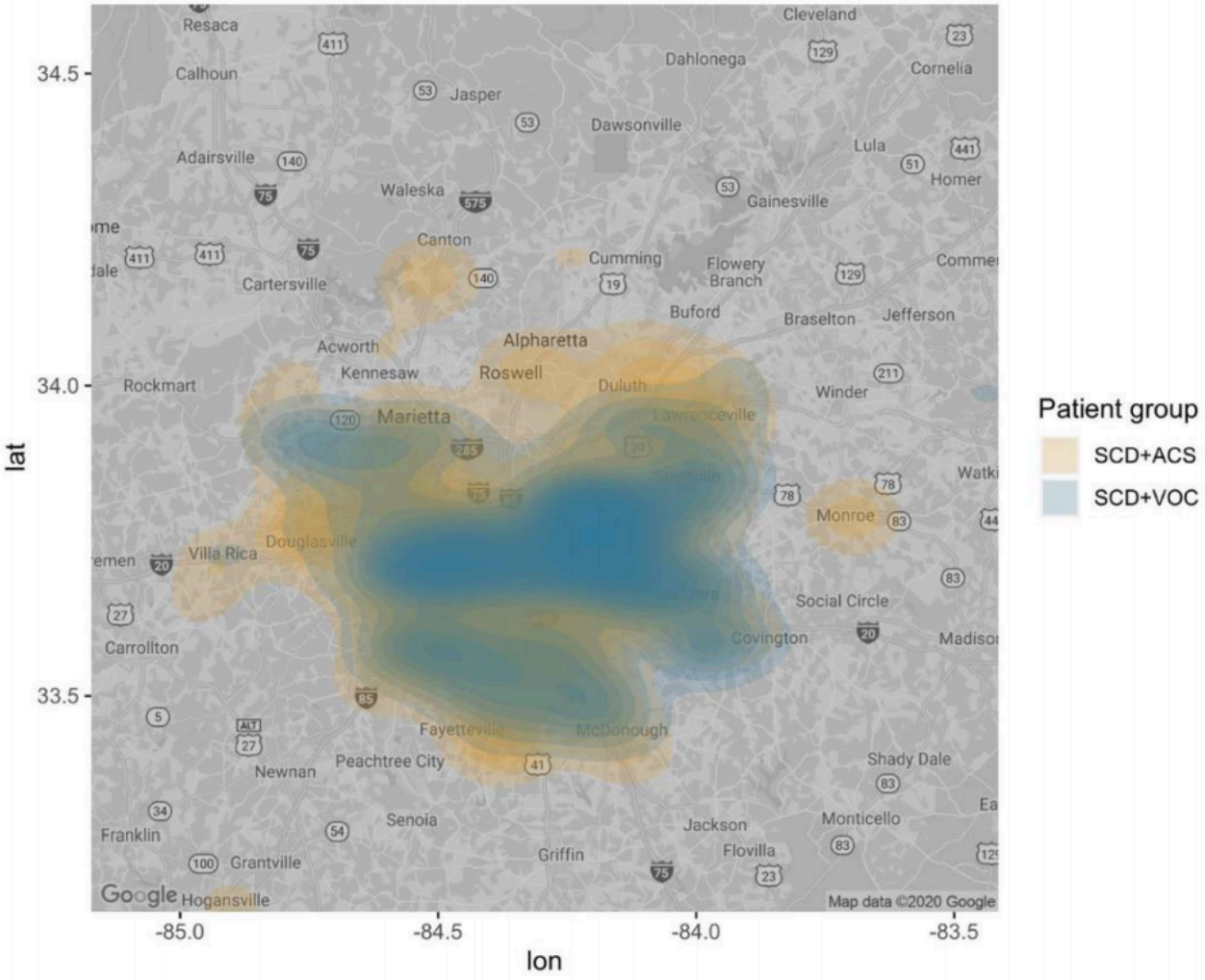


Figure 2. Geospatial map showing overlapping clusters of Acute Chest Syndrome (ACS) and Vaso-occlusive Pain Episodes (VOE). Latitude (lat) and Longitude (lon) displayed.



THE IMPACT OF VOXELOTOR TREATMENT ON LEG ULCERS IN PATIENTS WITH SCD: ANALYSIS FROM THE PHASE 3 HOPE STUDY

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Background: SCD is an inherited disorder in which pathology is driven by sickle hemoglobin (HbS) polymerization and erythrocyte sickling, leading to chronic hemolytic anemia, episodic vaso-occlusive crises, and cumulative organ damage. Leg ulcers, a chronic, painful, and debilitating complication of SCD, have been associated with severe anemia and intravascular hemolysis. Although hydroxyurea and chronic transfusions are available to treat SCD, their efficacies for treatment of leg ulcers have not been demonstrated through systematic or controlled clinical data. Voxelotor is a once-daily, orally administered HbS polymerization inhibitor that modulates hemoglobin in patients with SCD. In the HOPE trial, voxelotor demonstrated rapid and sustained improvements in Hb levels and markers of hemolysis compared with placebo. This analysis evaluated the incidence and outcomes of leg ulcers in patients from the HOPE trial.

Methods: This post hoc analysis of the HOPE trial (a phase 3, randomized, placebo-controlled study; NCT03036813) reports on the effect of voxelotor (1500 and 900 mg) versus placebo in patients aged 12 to 65 years with ≥1 report of SCD-related leg ulcers. Leg ulcers were assessed every 2 weeks (treatment day 1-week 8), 4 weeks (weeks 8-24), or 12 weeks (weeks 24-72). Severity was graded using the National Cancer Institute criteria for adverse events.

Results: : Thirteen patients (median age 24 years, 92% adults, 69% male, 92% HbSS) had leg ulcers at initiation of treatment: voxelotor 1500 mg, n=4 (2 mild severity, 2 moderate); voxelotor 900 mg, n=6 (3 mild, 3 moderate); placebo, n=3 (all mild). During the 24-week treatment period, 3 patients receiving voxelotor 1500 mg had leg ulcers resolve and 1 improved from moderate to mild, with no incidence of new ulcers. Among patients receiving voxelotor 900 mg, 4 improved during the study, 2 had no change, and 2 additional patients developed new ulcers (1 moderate severity that improved to mild, 1 unknown severity). In the placebo group, no patients had ulcer improvement and 2 Conference Abstract additional patients developed new ulcers (both moderate).

Conclusions: Voxelotor may reduce the severity of existing leg ulcers and decrease the incidence of new ones in patients with SCD. All patients receiving voxelotor 1500 mg showed improvements with no new ulcers occurring, while no patients receiving placebo had their ulcers improve and 2 developed new ulcers during the study. This analysis of an exploratory endpoint of the HOPE study suggests the potential for clinical benefit with voxelotor in patients with SCD and leg ulcers.

EFFECT OF VOXELOTOR ON HYPERBILIRUBINEMIA IN PATIENTS WITH SCD: RESULTS FROM THE PHASE 3 HOPE STUDY

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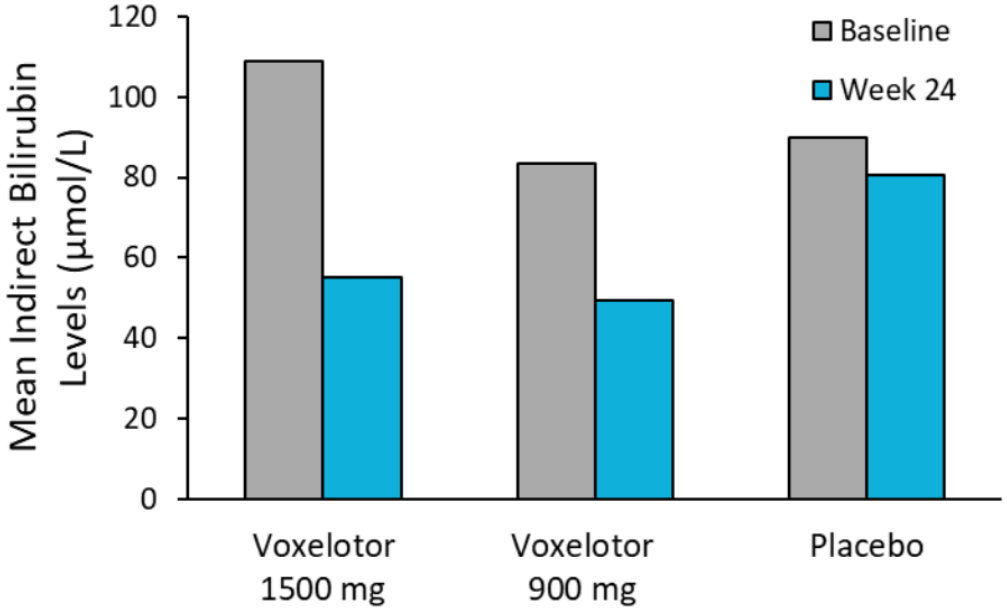
Background: Sickle cell disease (SCD) is an inherited disorder caused by sickle hemoglobin (HbS) polymerization and erythrocyte sickling, leading to chronic hemolytic anemia, episodic vaso-occlusive crises, and cumulative organ damage. Jaundice is a common symptom of SCD, which manifests as yellowing of the skin and eyes and is associated with indirect bilirubin ≥3× upper limit of normal [ULN]; i.e., ≥51 µmol/L. Jaundice can impact a patient's self-image and social relationships, and higher bilirubin levels are associated with increased incidence of pigmented gall stones. Patients with more severe hemolytic anemia experience lower hemoglobin levels and higher bilirubin levels, and extreme hyperbilirubinemia (>222 µmol/L) is associated with higher morbidity and mortality. Voxelotor, a oncedaily, orally administered HbS polymerization inhibitor, demonstrated rapid and sustained improvements in Hb levels and markers of hemolysis compared with placebo in the HOPE trial. The objective of this analysis was to evaluate changes in indirect bilirubin among voxelotor-treated patients in the HOPE trial.

Methods: This post hoc analysis of the HOPE trial (a phase 3, randomized, placebo-controlled study; NCT03036813) reports on the effect of voxelotor (1500 and 900 mg) versus placebo in patients aged 12- 65 years with elevated indirect bilirubin ≥3× ULN at baseline. This per-protocol analysis included patients who completed 24 weeks of assigned therapy and did not initiate hydroxyurea treatment after randomization. Bilirubin levels were assessed at study initiation, every 2 weeks (weeks 2-8), every 4 weeks (weeks 12-20), and at week 24.

Results: : : In the per-protocol analysis, 75 patients (voxelotor 1500 mg: n=20; voxelotor 900 mg: n=29; placebo: n=26) had indirect bilirubin levels ≥3x ULN at baseline. Patients in the voxelotor 1500 mg and 900 mg groups experienced a mean (SD) decrease of 53.4 (44.0) µmol/L and 34.2 (24.7) µmol/L in indirect bilirubin levels respectively at 24 weeks, and most patients had their bilirubin levels improve to <3× ULN (1500 mg: 55.0% [11/20]; 900 mg: 58.6% [17/29]). Patients receiving placebo experienced a 9.4 (26.3) µmol/L reduction in their indirect bilirubin and 80.8% (21/26) remained at ≥3× ULN at 24 weeks Conference Abstract (Figure 1). Analysis of the data suggests a correlation between indirect bilirubin levels ≥3× ULN and presence of sclera icterus.

Conclusions: Voxelotor led to reduced indirect bilirubin levels in patients with indirect bilirubin levels ≥3x ULN. These results suggest that the disease-modifying potential of voxelotor can ameliorate jaundice in patients with SCD, a common complication the disease, and improve their overall sense of well-being.

Figure 1. Mean Indirect Bilirubin Levels at Baseline and Week 24* Among Patients With ≥3x ULN at Baseline



*Based on average of week 20 and 24 levels. Normal bilirubin range: 3-17 µmol/L.
ULN, upper limit of normal.

JSCDH-D-20-00015

A NOVEL MICROFLUIDIC ASSAY FOR MEASURING PHYSICAL OCCLUSION AND FLOW DYNAMICS OF SICKLE CELL BLOOD SAMPLES

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Background: Sickle cell anemia is a genetic condition caused by an abnormality in oxygencarrying hemoglobin. Those affected experience clogging of the blood vessels, resulting in symptoms such as pain, anemia, and stroke, some of which are life-threatening. Quickly and cheaply detecting whether a patient is at risk for vaso-occlusion is vital for effective early intervention. In this study, we developed a microfluidic diagnostic tool for the observation and quantitative analysis of these vaso-occlusion events.

Methods: We designed and fabricated polydimethylsiloxane (PDMS) microfluidic devices based on standard soft-lithography techniques. The device has 100 repetitive parallel constriction channels (W:2.7μm, H:5.06μm) to mimic microcapillaries in the human body. We analyzed 5 controls (CT, 2 Male, 3 Females), 5 Hemoglobin SS (SS, 4 Males, 1 Female) and 5 Hemoglobin SC (SC, 1 Male, 3 Females) blood samples acquired from Yale-New Haven Hospital (YNHH). Each sample was loaded into 4 separate microfluidic devices by external pressure (10 min duration at 13cm height). While loading, each device was placed under a microscope (Leica DMi1) to record the blood flow and the number of clogging events. The percentage of clogged channels was calculated at the end of the loading period for comparison between groups.

Results: : We find the flow rate in the SC and SS group is significantly lower compared to the control group, indicating a higher system resistance caused by the patients' blood sample. In addition, we find that, compared to the control and SC groups, the percentage of clogged constriction channels is significantly higher in the SS group

Conclusions: We have developed a novel microfluidic assay that provides parallel channels to mimic capillaries in the body. This device provides an environment that may simulate vasoocclusion events in an observable manner. Our results show a significant difference in the percentage of fully-clogged channels in the SS patient group compared to the control and SC group, suggesting potential applications to detect the risk of vaso-occlusion and stroke caused by sickle cell disease and other types of diseases.

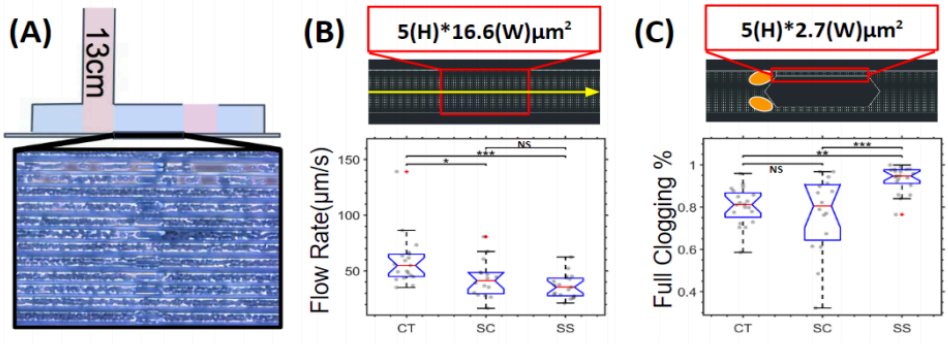

Figure1:(A) Schematic of device and loading. (B) Box plot of ANOVA post-hoc analysis of the flow rate at 8min. (C) Percentage of the 5μm channels that were completely clogged(right) at 10min.

YOUTHS' EXPERIENCES OF TRANSITION FROM PEDIATRIC TO ADULT CARE: AN UPDATED QUALITATIVE METASYNTHESIS

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Background: With increasing numbers of youth with chronic diseases living into adulthood, preparation for transition to adult healthcare settings merits attention. Poor transition can lead to higher risks of morbidity and mortality. Understanding the youths' perspectives on transition is instrumental to developing effective interventions which will be perceived by them as helpful. The objective of this metasynthesis was to synthesize qualitative research studies examining the experiences and expectations of transition to adult healthcare in youth with chronic diseases to update a previously reported metasynthesis. We determined that an update was needed given the expanded attention to this topic since the original metasynthesis publication in 2014.

Methods: We followed Sandelowski and Barroso's guidelines for synthesizing primary qualitative research. A search of PubMed, Medline, PsycINFO, and CINAHL was conducted to gather articles published after February 2011. Studies were appraised using the Critical Appraisal Skills Programme checklist. Findings of the qualitative studies were analyzed to create the metasynthesis.

Results: Of 889 articles screened, a total of 33 articles were included for final analysis. Seven main themes were induced including: cultivating transition readiness, conceiving expectations based upon pediatric healthcare, evolving parent role, evolving youth's role, finding barriers due to differences between pediatric and adult settings, lacking transition readiness, recommending improvements for transition.

Conclusions: Both pediatric and adult healthcare providers need to recognize that they have an important role in assisting youth to prepare for and to transition to the adult healthcare. Findings of this metasynthesis reaffirmed previous findings and highlighted the need to create youthcentered approaches to transition preparation. Given the consistent results of our findings with the previous metasynthesis, we believe that future qualitative research is not indicated and recommend that our findings be translated into care policies and procedures for the transition of youth with chronic diseases from pediatric to adult healthcare.

EFFICACY AND SAFETY OF RIVIPANSEL (GMI-1070) IN THE TREATMENT OF VASO-OCCLUSIVE CRISIS IN HOSPITALIZED PATIENTS WITH SICKLE CELL DISEASE: RESULTS FROM THE RESET PHASE 3 STUDY

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Background: Rivipansel, an investigational pan-selectin inhibitor, targets a key pathway in the pathophysiology of sickle cell disease (SCD) vaso-occlusive crisis (VOC). The RESET phase 3 study (NCT02187003) evaluated efficacy and safety of rivipansel for treatment of a single VOC episode in hospitalized patients with SCD

Methods: RESET was a multicenter, double-blind, placebo-controlled study conducted at 58 sites in the United States and Canada. Patients aged ≥6 years requiring Conference Abstract intravenous (IV) opioid medication and inpatient hospitalization for acute VOC were randomized 1:1 to rivipansel or placebo. Study drug began within 24 hours of first IV opioid dose. Patients aged ≥12 years weighing >40 kg received fixed-dose rivipansel (loading dose 1680 mg; maintenance doses 840 mg q12h). Patients aged 6–11 or weighing ≤40 kg received weight-based rivipansel dosing (loading dose 40 mg/kg; maintenance doses 20 mg/kg q12h). Patients received study drug until the VOC was managed with oral analgesics only or for a maximum of 15 doses. Primary efficacy end point was time from study drug initiation to readiness-for-discharge. Key secondary efficacy end points were time to discharge, cumulative IV opioid consumption, and time to IV opioid discontinuation. Efficacy analyses included all randomized patients; safety analyses included all patients with ≥1 study drug dose. A post hoc analysis examined the relationship of efficacy to time between patient-reported onset of VOC and start of study drug. Treatment comparisons for time-to-event data were based on a log-rank test and Cox proportional hazards model, stratified by age group and genotype. A rank analysis of covariance (ANCOVA) model was applied for cumulative IV opioid consumption data.

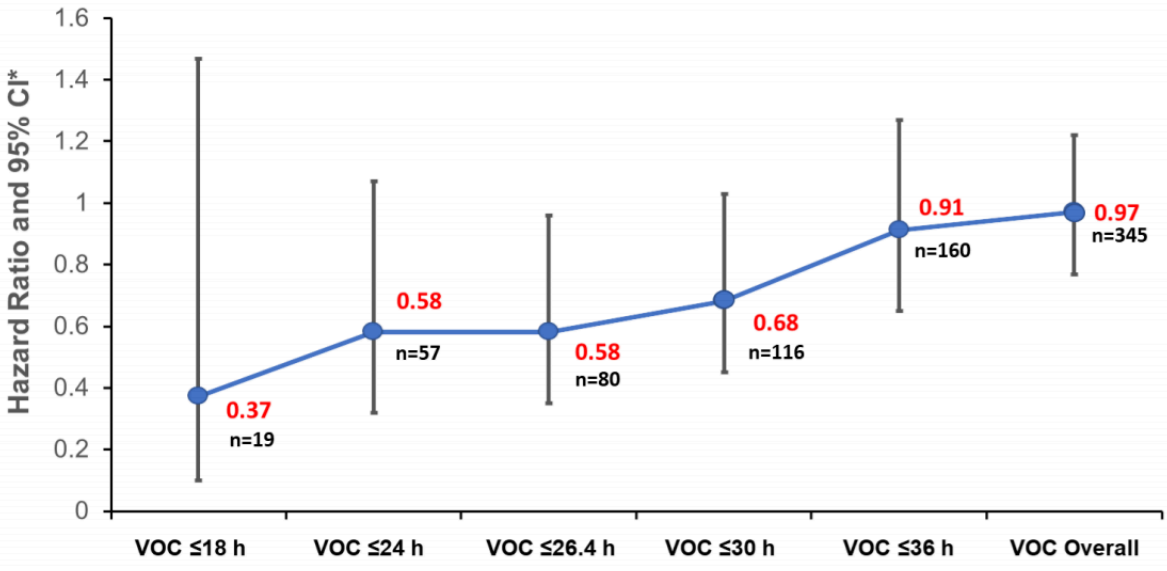
Results: In total, 345 patients were randomized (rivipansel, n=173; placebo, n= 172). Demographics and baseline characteristics were balanced between groups, except for gender (males: rivipansel 51.4%; placebo 42.4%). For both groups combined, mean age was 22 years, 94.5% of patients were black, and 66% were receiving hydroxyurea. Analysis showed a between-group difference (rivipansel vs placebo) in median time to readiness-for-discharge of -5.69 hours (hazard ratio=0.97; P=0.79). Secondary end point results were similar (Table). Analyses by age group, hydroxyurea use, genotype, and gender revealed no significant and/or clinically meaningful efficacy signals. Pharmacokinetic data indicated that rivipansel exposure was similar across age groups and consistent with prestudy modeling predictions. A significant decrease from baseline occurred in soluble E-selectin for rivipansel versus placebo (maximum mean decrease 56% at loading dose Cmax; 17%-44% decrease maintained with subsequent dosing). Post hoc analysis indicated that shorter time from VOC onset to study drug inception was associated with treatment effect for rivipansel. A significant result favoring rivipansel (P=0.03, without adjustment for multiple testing) was seen for patients treated within 26.4 hours (1st quartile) of VOC onset (Figs 1, 2A). Incidence of adverse events was similar between groups.

Conclusions: No significant or clinically meaningful efficacy signal was observed overall with rivipansel versus placebo. However, post hoc analysis demonstrated that study drug administration early during the course of VOC was associated with efficacy outcomes in favor of rivipansel, suggesting that future pharmacologic attempts to reverse vaso-occlusion should target the early stage of VOC. This study provides extensive clinical, pharmacokinetic, and biomarker data for a large group of patients with SCD treated for VOC. In-depth analyses of these data will add to a more complete understanding of VOC pathophysiology and aid in future study designs.

Table 1. Primary and Key Secondary Efficacy End Points

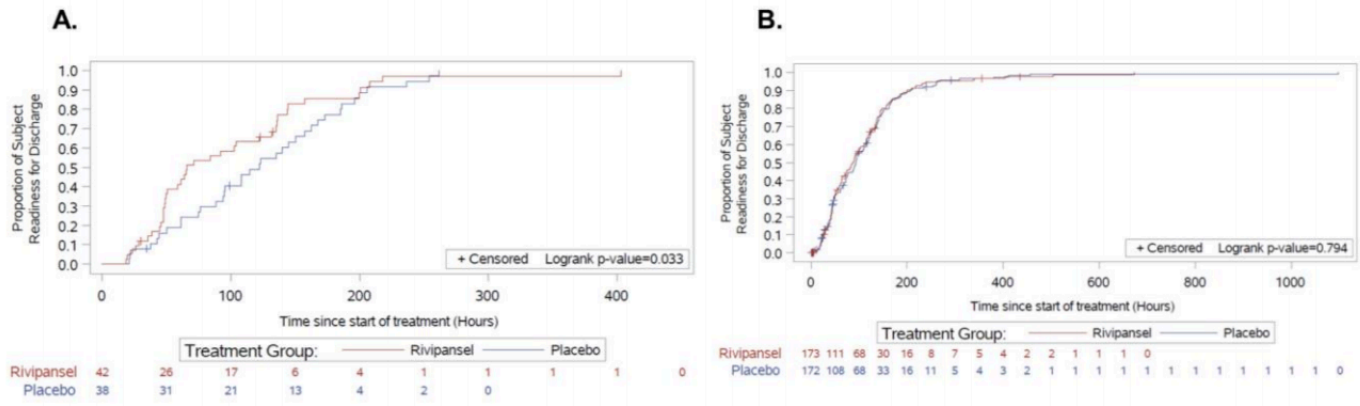
End Point	Rivipansel	Placebo	*P* Value	Hazard Ratio
Time to readiness-for-discharge from hospital, median, h (95% CI)	87.78 (65.68, 100.15)	93.47 (74.67, 109.73)	0.79	0.97
Time to discharge, median, h (95% CI)	86.75 (71.25, 98.72)	90.67 (72.10, 108.62)	0.72	0.96
Cumulative IV opioid consumption, median, morphine equivalent units/kg	2.30	2.36	0.85 (based on a rank ANCOVA model)	–
Time to discontinuation of IV opioids, median, h (95% CI)	67.20 (53.32, 80.53)	68.45 (53.75, 84.97)	0.86	1.02

Figure 1. Time From First Study Drug Dose to Readiness for Discharge from Hospital (Primary Efficacy End Point) by Time From VOC Onset to Start of Study Drug



*Hazard ratio calculated as time to readiness for discharge for placebo/rivipansel.

Figure 2. Kaplan Meier Curves For Time from Start of Study Drug to Readiness for Discharge From Hospital (Primary Efficacy End Point) in (A) Patients with VOC Duration ≤26.4 Hours (First Quartile) and (B) All VOC Duration



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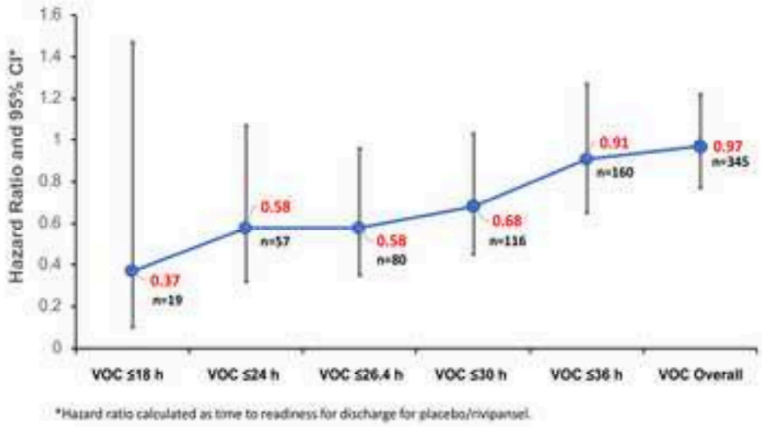

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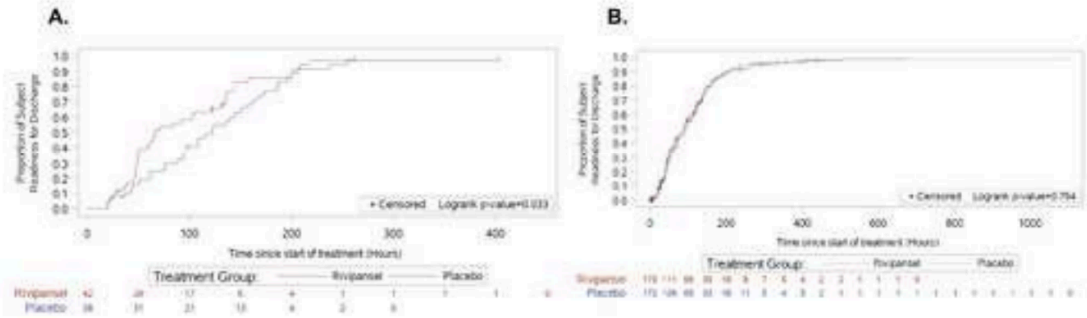

JSCDH-D-20-00018

A RESOLUTION OF SICKLE CELL DISEASE MANIFESTATIONS IN PATIENTS TREATED WITH LENTIGLOBIN FOR SCD GENE THERAPY: RESULTS FROM THE PHASE 1/2 HGB-206 GROUP C STUDY

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Background: Gene transfer of anti-sickling hemoglobin (Hb) may correct sickle cell disease (SCD). LentiGlobin for SCD contains autologous CD34+ hematopoietic stem cells (HSCs) transduced with the BB305 lentiviral vector (LVV), encoding a human ß-globin gene with the anti-sickling T87Q substitution (βA-T87Q). Safety and Conference Abstract efficacy of LentiGlobin is being evaluated in the ongoing phase 1/2 study HGB-206 (NCT02140554). Initial HGB-206 patients (Group A, N=7) were treated with LentiGlobin made from bone marrow harvested-HSCs. Modifications to the protocol and manufacturing process were introduced in Group B (N=2). Here, we describe results from Group C patients for whom HSCs were collected by apheresis following plerixafor mobilization.

Methods: Adults with SCD and complications such as recurrent severe vaso-occlusive crises (VOCs) and acute chest syndrome (ACS), received 240 µg/kg plerixafor 4 – 6 hours before apheresis to collect CD34+ HSCs. Drug product (DP) was made by transducing CD34+ HSCs with the BB305 LVV and infused into patients following myeloablative conditioning. Adverse events (AEs), laboratory parameters, and clinical manifestations were monitored. Summary data presented are median (min – max).

Results: : As of 7 March 2019, 13 Group C patients were treated and followed for 9.0 (1.0 – 15.2) months. All but 1 patient, who was not yet evaluable for engraftment as of the data cut date, achieved neutrophil and platelet engraftment at 19 (15 – 24) days and 28 (19 – 136) days, respectively. Within ~3 months postinfusion, all patients stopped receiving red blood cell (RBC) transfusions. In 8 patients with ≥ 6 months of follow-up, median HbS was ≤ 50% of total Hb and, at last visit, total Hb was 11.5 (10.2 – 15.0) g/dL, with HbAT87Q at 5.3 (4.5 – 8.8) g/dL. By month 9, on average ≥ 70% of RBCs contained ß A-T87Q . The annualized VOC+ACS rate in 6 of 8 patients with ≥ 6 months of follow-up decreased pre- to post-treatment from 5.3 (3 – 14) to 0 (0 – 2). One Grade 2 VOC was observed at 3.5 months, but no ACS or serious VOCs occurred. Lactate dehydrogenase, absolute reticulocyte count, and total bilirubin at last visit were 225.0 (130.0 – 337.0) U/L, 150.0 (42.1 – 283.0) x 109 /L, and 22.2 (3.4 – 39.3) µmol/L, respectively; all lower than at baseline. The most common non-hematologic Grade ≥ 3 AEs post-infusion were febrile neutropenia (n=10) and stomatitis (n=7). Serious AEs were reported in 6 patients, most common being nausea and vomiting. There were no DP-related AEs, graft failures, vector-mediated replicationcompetent lentivirus, or clonal dominance.

Conclusions: The safety profile of LentiGlobin for SCD remains consistent with that of single-agent busulfan conditioning and underlying SCD. Group C patients experienced high-level, sustained, nearly pancellular expression of anti-sickling HbAT87Q, with median HbS ≤ 50% of total Hb, and median total Hb > 10 g/dL in those with ≥ 6 months of follow-up. Cessation of complications and decrease in hemolysis suggest strong therapeutic effect with LentiGlobin for SCD.

DEVELOPING A GROUP HEALTHCARE MODEL WITH A PEER PATIENT ADVOCATE FOR SICKLE CELL DISEASE TRANSITION INTO ADULT CARE

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Background: Adolescent and emerging adult (AEA) patients often face challenging experiences during the transition from pediatric to adult care. This is especially true for patients with sickle cell disease (SCD) as transition often coincides with a time of rapidly increasing mortality risk. Often the healthcare system has not equipped AEAs with the appropriate skills to navigate the adult healthcare system: disease knowledge, effective communication, and advocacy. In response to this gap our team developed a group educational program, Our Hands, Our Health. Our Hands, Our Health is based on two core components of the Centering© Healthcare model: interactive learning and community building. Our Hands, Our Health included a one-on-one visit with a hematologist followed by 60 minutes of group health education enriched by interactive activities, role plays, and games. After our feasibility study (n=4) was completed, the program was expanded from six to ten sessions. For the pilot (n=13), we also added a peer patient advocate (PPA) as a co-facilitator of the program because PPAs are associated with improved case management services, offer mentorship, and experiences that could be integrated to increase relevance of the health promotion content. Our goal was to identify implementation barriers and integrate them into program revision.

Methods: Using a constant comparative technique, we reviewed the two of the three core components of the Centering model to guide the development of Our Hands, Our Health. During the feasibility and pilot studies, our mixed methods approach (observations, team debriefing, and interviews with participants and co-facilitators) allowed us to assess practical and structural implementation barriers and evaluate the group healthcare model.

Results: Feasibility The feasibility study had 4 female participants. Participants stated that they preferred group care to individual care. Qualitative feedback from feasibility participants demonstrated content weaknesses in the areas of pain, advocacy, and family planning. A peer patient advocate was incorporated into the facilitation of sessions and content development to address these content weaknesses. Additional time was needed during program development to train the peer patient advocate on specific disease knowledge and group facilitation. Additional structural changes made between pilot and feasibility study were increasing male recruitment, securing a larger room, developing an efficient process for patient registration and discharge, obtaining vital signs, and including a phlebotomist. Pilot Participants: The pilot had 12 participants; (male n= 5 and female n=7). There was only one participant who did not like meeting in a group; all others reported that they enjoyed group meetings and preferred getting their care this way. Three participants did not complete the group attributable to moving (n=2) and full-time employment (n=1). Of the eleven participants in the group, seven were interviewed upon completion of the group. Conference Abstract Interactive Learning: Participants agreed that the format allowed time to process information, ask questions, and discuss their personal experiences, which ultimately led to a better understanding of the material. Participants agreed the activities engaged them in the learning process and made topics easier to understand and apply to their own lives. Community Building: All participants reported the group setting enhanced comfort for sharing thoughts and feelings, which enhanced learning. Participants reported feeling less alone in their diagnoses. Participants reported forming friendships with other participants. Most participants reported wanting to continue attending group care sessions in order to learn more and mentor younger participants. Perceptions of Readiness to Transition to Adult Care: All participants interviewed reported ambivalence about transitioning to an adult provider. All participants interviewed reported feeling able to transition to adult care if necessary.

Conclusions: A group healthcare model with a peer patient advocate may offer a promising support system for pediatric patients transitioning to adult care. However, a multicenter trial would be needed to further investigate healthcare knowledge retention and transition readiness.

INSURANCE PATTERNS OF MEDICAID BENEFICIARIES WITH SICKLE CELL DISEASE IN CALIFORNIA AND GEORGIA, 2014-2016

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Affiliations: *(1)California Rare Disease Surveillance Program, Public Health Institute, Oakland, CA, USA (2)Georgia Health Policy Institute, Georgia State University, Atlanta, GA, USA (3)Global Blood Therapeutics, South San Francisco, CA, USA (4)University of California, San Francisco, San Francisco, CA, USA (5)Centers for Disease Control and Prevention, Atlanta, GA, USA*

Background: Sickle cell disease (SCD) is a group of inherited hemoglobinopathies characterized by hemoglobin polymerization and erythrocyte rigidity, resulting in hemolytic anemia and vaso-occlusion with ischemiareperfusion. These pathological processes can cause multisystem end organ damage (eg, stroke, renal dysfunction, cardiopulmonary conditions) leading to reduced quality of life, life-long disability, and a decrease of approximately 25 to 30 years in life expectancy. Symptoms and SCD-related comorbidities may impede educational achievement and employment among those living with the disease and their caregivers. Consequently, a high proportion of persons living with SCD are insured through Medicaid for extended periods. We present a description of the longitudinal patterns of Medicaid benefits for individuals with SCD who lived in California or Georgia during 2014 through 2016.

Methods: The California and Georgia Sickle Cell Data Collection (SCDC) programs gathered clinical, newborn screening, and administrative data. The data were then linked and de-duplicated, and a validated case definition for SCD was applied. Cases either had a physician- or newborn screening-confirmed sickling hemoglobinopathy or had three or more unique healthcare encounters in administrative data with an SCD ICD-CM classification code over any five-year period during 2004 through 2016. This analysis focuses on 2014-2016 data.

Results: The California SCDC program identified 5124 (61.5% aged 20+ years, 55% female) individuals with SCD living in the state in 2014-2016, and the Georgia SCDC program identified 9382 (52.6% aged 20+ years, 56% female). Of these patients, 3555 (69.4%) from California and 6179 (65.9%) from Georgia were Medicaid beneficiaries at any point during the study. Among patients who received Medicaid benefits in Conference Abstract California and Georgia respectively, 3352 (94.3%) and 5282 (85.5%) were beneficiaries for >50% of the study, and 2655 (74.7%) and 3768 (61.0%) were beneficiaries for the entire study. For those individuals who were Medicaid beneficiaries at any time during the study period, the mean length of continuous Medicaid coverage ranged 27.9-33.1 months across all age groups in California and 22.6-31.6 months in Georgia, with a median of 36 months in both states.

Conclusions: During the three-year study period, approximately two-thirds of individuals with SCD in California and Georgia had some Medicaid coverage. Almost 75% in California and 61% in Georgia were covered all three years. The long-term treatment needs of persons living with SCD and the cumulative burden of SCD healthcare may be important considerations for Medicaid policy makers in both states. Funding: This study was supported by Global Blood Therapeutics, Pfizer Inc., Sanofi, Doris Duke Charitable Foundation, and CDC Foundation.

GEOGRAPHIC MOBILITY AMONG MEDICAID BENEFICIARIES WITH SICKLE CELL DISEASE IN CALIFORNIA AND GEORGIA, 2014-2016

Authors: Susan Paulukonis, MA, MPH(1) ; Mei Zhou, MA, MS(2) ; Angie Snyder, MPH, PhD(2) ; Ze Cong, PhD(3) ; Irene Agodoa, MD(3) ; Nura El-Haj, MD(4) ; Mary Hulihan, MPH, DrPH(5)

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Background: Sickle cell disease (SCD) is a group of inherited hemoglobinopathies that can cause multisystem end organ damage affecting, for example, the brain, kidney, and cardiovascular system. Consequently, persons living with SCD can experience significant quality of life decrement, morbidity and mortality. A high proportion of persons with SCD are insured through Medicaid. Understanding mobility among individuals with SCD who are Medicaid beneficiaries may help inform some of the variability in access to and continuity of care. We describe the geographic mobility, at the county and zip code level, for Medicaid beneficiaries with SCD who lived in California or Georgia during 2014 through 2016.

Methods: The California and Georgia Sickle Cell Data Collection (SCDC) programs gathered clinical, newborn screening, and administrative data. The data were linked and de-duplicated, and a validated case definition for SCD was applied. Cases either had a physician- or newborn screening-confirmed sickling hemoglobinopathy or had three or more unique healthcare encounters in administrative data with an SCD ICD-CM classification code over any five-year period during 2004 through 2016. This analysis focuses on 2014-2016. Medicaid eligibility/enrollment files provided the basis for determining zip code and county mobility.

Results: The California SCDC program identified 5124 individuals with SCD living in the state in 2014-2016 and the Georgia SCDC program identified 9382. Of these, 3555 patients (69.4%) in California and 6179 (65.9%) in Georgia were enrolled in Medicaid for one or more months during this period. The mean number of changes in zip code during the follow-up period was 0.91 in California and 0.29 in Georgia. Thirteen percent of the California group and 24% of the Georgia group changed zip codes at least one Conference Abstract time. The mean (median) number of inter-county moves was 0.22 (0.0) over the 36 months of follow-up in both states

Conclusions: The majority of Medicaid beneficiaries with SCD did not relocate beyond county boundaries over three years of follow-up, suggesting that frequent mobility may not be a primary concern for SCD service planning. However, this analysis did not consider changes in the distance from care. Further studies could address other factors that might affect healthcare access for Medicaid beneficiaries with SCD, such as housing insecurity, access to transportation, and providers' acceptance of patients who are Medicaid beneficiaries. Funding: This study was supported by Global Blood Therapeutics, Pfizer Inc., Sanofi, Doris Duke Charitable Foundation, and CDC Foundation.

A SYSTEMATIC LITERATURE REVIEW OF THE BURDEN OF ISCHEMIC PRIAPISM IN PATIENTS WITH SICKLE CELL DISEASE

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Background: Ischemic or low-flow priapism is a serious condition characterized by a persistent, painful erection that lasts at least 4 hours or is unrelated to sexual stimulation. Both stuttering (repeated short episodes) and fulminant (long-lasting) priapism are prevalent in men and boys with sickle cell disease (SCD). Approximately 40% of patients with SCD will experience priapism during their lifetime. The objective of this study was to conduct a systematic literature review (SLR) to identify published studies reporting the burden associated with priapism in patients with SCD.

Methods: MEDLINE, Embase, Cochrane CENTRAL/ CDSR and 14 congresses were searched from May 9-16, 2019. Results were screened against predefined criteria by two independent researchers. Studies assessing the clinical, humanistic, or economic burden of human patients with SCD and priapism (N≥15) were included. Outcomes of interest included priapism-related symptoms, treatment-related complications, quality of life (QoL), and economic burden.

Results: The literature search identified 1236 articles; 62 full-text studies were reviewed in detail and 34 studies were included in the analysis. Most studies were retrospective observational (21), others were prospective (7 observational, 6 interventional). Study size varied widely (range: 15-10,788 patients). Of 27 studies that reported mean or median patient age, the age statistic for patients with SCD and priapism ranged from 10 to 32. Overall, 19 studies reported at least one aspect of clinical burden. Thirteen reported the rate of erectile dysfunction or impotence, ranging from 0% to 56%. Eight reported treatment-related complications, including perceived penile scarring/ deformity (19.4%) and small intrapenile hematoma (13.3%). Nineteen studies reported QoL outcomes. Eight reported physical outcomes, including a negative impact of SCDrelated priapism on sleep quality and worse scores on periodic limb movement and apnea hypopnea indices. Seven reported measures of sexual function, including low rates of satisfactory sexual intercourse. One study reported a diminished Sexual Health Inventory for Men score in patients with active priapism, and another found a statistically significant relationship between stuttering priapism and premature ejaculation. Three studies reported measures of mental function, one of which outlined increased cognitive fatigue and impaired emotional functioning among children with priapism and another reported that 36% of patients had substantial to very extreme worry regarding episodes of priapism. Use of validated measures for QoL were limited: 3 studies assessed patients with the International Index of Erectile Function (IIEF) and 1 with the Priapism Impact Profile (PIP). No studies measuring the burden to caregivers of pediatric patients with priapism were identified. Eight studies reported the economic burden of priapism in patients with SCD, including rates of emergency department visits (4 studies: 56.5% sought hospital treatment - 26/46; 49.8% admission to the hospital out of emergency department visits - 5371/10,788; 50.4% admitted at the emergency department - 930/1844; 26% vs. 11% readmission vs no readmission - p <0.001) and hospital length of stay (4 studies: mean 3.38 days; mean 3.8 days; median 2 days; median 5 days in patients who received an exchange transfusion as a treatment for priapism.). Three studies reported direct treatment costs, ranging from a mean of $4,496 (2015 USD) for patients who did not undergo penile operations to a mean of $19,670 (2013 USD) total adjusted hospital costs for patients receiving both transfusions and urologic procedures.

Conclusions: This SLR identified 34 studies reporting the burden of priapism in patients with SCD. No RCTs were identified. The use of comprehensive or validated measures of humanistic burden was limited. Manifestations of priapism are wideranging, including painful treatment-related complications, impaired sleep, and diminished physical, mental and sexual function. Patients with priapism and SCD are more likely to visit the emergency department and experience longer hospital stays compared to SCD patients without priapism. Together, the evidence identified in this SLR indicates that priapism not only can result in

erectile dysfunction but can impair multiple dimensions of a patient's physical and mental health.

INDUCTION OF FETAL HEMOGLOBIN BY A NOVEL SMALL MOLECULE

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Background: Red blood cell disorders like Sickle Cell Disease (SCD) and [?][?]thalassemias are caused by mutations within the gene for the hemoglobin [?] (HB[?][?][?]subunit. A fetal ortholog of HB[?], hemoglobin [?] (HB[?]) can prevent or reduce disease-related pathophysiology in these disorders by forming nonpathogenic complexes with the required hemoglobin [?] subunit. Globin expression is developmentally regulated, with a reduction in production of the fetal ortholog ([?][?] occurring shortly after birth and a concomitant increase in the levels of the adult ortholog ([?][?]. It has been postulated that maintaining expression of the anti-sickling [?] ortholog may be of therapeutic benefit in children and adults with SCD. Indeed, individuals with the SCD mutation who also have genetic variants that maintain HB[?] expression at clinically meaningful levels do not present with SCD-related symptoms. We have identified a biological target that when inhibited can elevate the expression of HB[?] and the resulting fetal hemoglobin (HbF) tetramer in both human CD34+-derived erythroid cells and the Townes SCD mouse model, and through medicinal chemistry design and optimization we have developed a novel small molecule, FTX-6058, as a clinical development candidate for potential treatment of hemoglobinopathies such as SCD via upregulation of HbF.

Methods: Parallel target identification efforts using CRISPR and the Fulcrum proprietary, annotated chemical probe screening set in HUDEP2 cells identified a protein complex as a key regulator of HbF expression. Inhibition of the activity of this complex induced HbF levels to ~30% of total hemoglobin. Structureguided medicinal chemistry optimization led to the design of FTX-6058. FTX-6058 treatment of differentiated primary CD34+ cells from multiple healthy donors demonstrated target engagement and potent upregulation of HBG1/2 mRNA and HbF protein. Across these multiple donors, FTX-6058 treatment resulted in a clinically desirable globin profile (e.g., ~30% HbF of total hemoglobin) accompanied by pancellular HbF expression, resembling the phenotype of SCD mutation carriers with hereditary persistence of fetal hemoglobin. FTX-6058 demonstrated a superior profile relative to hydroxyurea and other small molecule compounds or mechanisms currently under development.

Results: In in vivo preclinical studies, FTX-6058 treatment elevated fetal hemoglobin at the mRNA and protein levels at plasma concentrations predicted to be achievable in patients. FTX-6058 treatment led to elevation of the endogenous mouse hbb-bh1 mRNA in wildtype CD1 mice and, importantly, also elevation of the human HBG1 mRNA and HbF protein in the Townes SCD mouse model. In a head-tohead in-vivo preclinical study, FTX-6058 demonstrated superior activity over hydroxyurea in the Townes SCD mouse model.

Conclusions: Preclinical studies using a variety of in vitro and in vivo models have demonstrated the potential of FTX6058 as a novel HbF-inducing small molecule that could be beneficial to patients with SCD and [?][?]thalassemias. FTX-6058 was well tolerated and engaged its target in multiple preclinical rodent models with once-a-day oral dosing. IND enabling studies for FTX-6058 are currently underway.

REAL-WORLD CLINICAL BURDEN OF SICKLE CELL DISEASE IN THE US COMMUNITY PRACTICE SETTING: A SINGLE-CENTER EXPERIENCE FROM THE FOUNDATION FOR SICKLE CELL DISEASE RESEARCH

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Background: Sickle cell disease (SCD) is a progressively debilitating monogenic disease characterized by unpredictable, acute, life-threatening episodes and chronic complications such as hemolytic anemia and end-organ damage. It presents with a range of severity resulting in significant morbidity, poor quality of life, and early mortality. Real-world data on treatment patterns and clinical outcomes for patients with SCD are limited, particularly in the community care setting. This retrospective study characterized clinical manifestations and management of patients with SCD at the Foundation for Sickle Cell Disease Research (FSCDR).

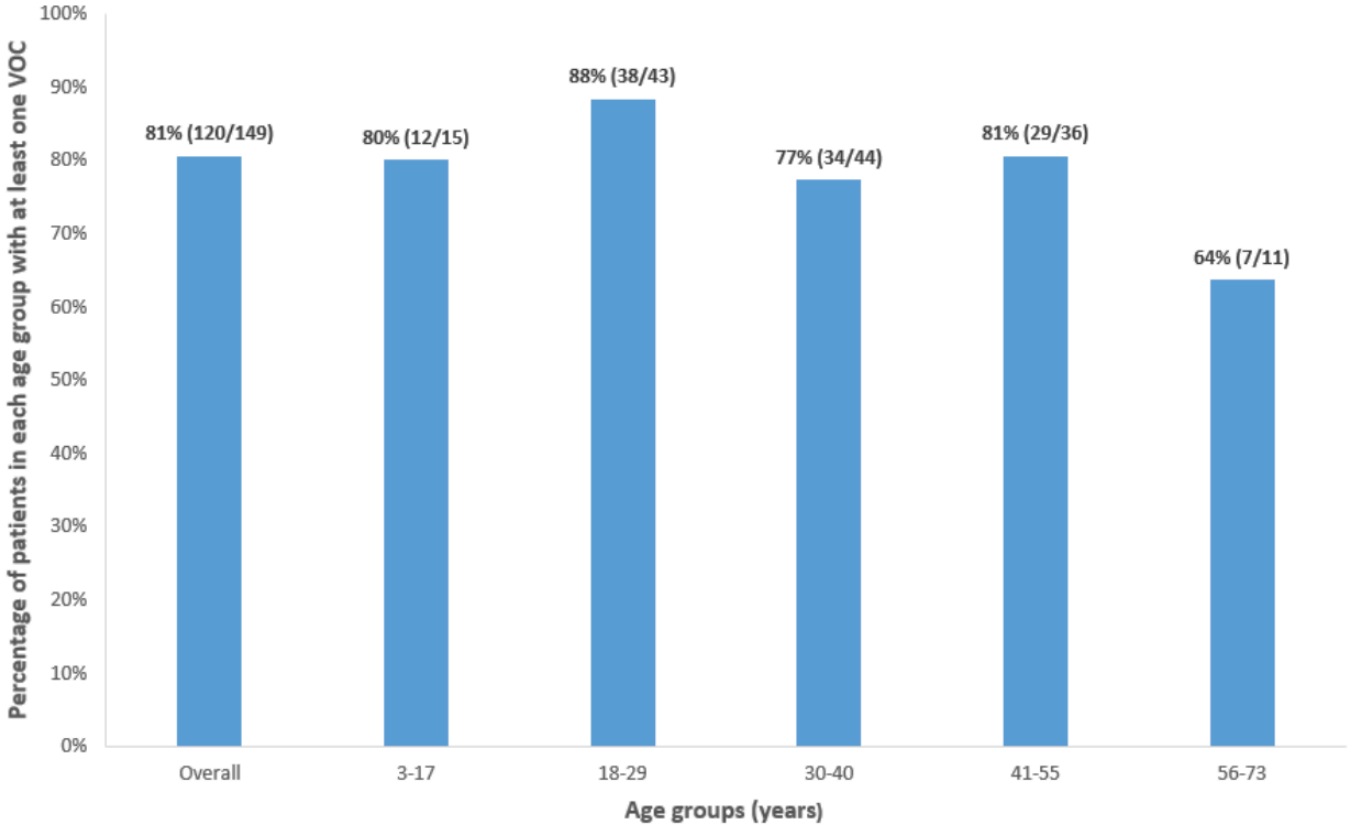
Methods: A retrospective analysis of electronic health records (EHR), supplemented with manual review of inpatient records and paper charts, from the FSCDR was conducted, with validation performed on 10% of the sample. Patient demographics, clinical characteristics, hydroxyurea (HU) prescriptions (also supported by usage notes and review of other records) and administration of red blood cell transfusions were described. Annualized VOC (defined based on keywords listed in patient records) and ACS (based on physician assessment) rates were calculated by dividing the number of events by the total follow-up duration in years.

Results: A total of 149 patients with SCD who were actively treated at the FSCDR and had clinical data from 01 January 2015 to 08 November 2019 were included. Among all patients, 92 (61.7%) were female and 142 (95.3%) were Black or African American. The median age was 33.2 years with the following age distribution: 3-17 years (n=15), 18-29 years (n=43), 30-40 years (n=44), 41-55 years (n=36), and 56-73 years (n=11). The most common genotypes were HbSS (81.2%) and HbSC (14.1%). Over a median follow-up of 3.8 years, 30 (20.8%) patients were prescribed HU and 78 (52.3%) received transfusions at least once; only 1 patient received continuous monthly transfusions for ≥ 6 months. Mean total hemoglobin (Hb) was 8.3 g/dL (standard deviation [SD] 1.6) for HbSS patients and 10.8 g/dL (SD 1.5) for HbSC patients; mean Hb values were 1-2 g/dL lower for patients who were prescribed HU or received transfusions during follow-up compared to those who did not. One hundred twenty patients (80.5%) had ≥ 1 VOC and 17 patients (11.4%) had ≥ 1 ACS during the median 3.8-year follow-up period (Figures 1 and 2). ACS occurred at a rate of 7 events per 100 person years. Three out of 15 (20%) patients aged 3- 17 years and 12 out of 87 (14%) patients aged 18-40 years had at least 1 ACS over a median follow up of 3.8 years. Patients aged 18-40 years had the highest VOC rates at almost 14 VOCs per patient per year, with over half (49/87 patients; 56.3%) having at least 2 VOCs per year (Figure 3).

Conclusions: This study provides a unique description of clinical characteristics and management of patients with SCD in a community practice setting at the FSCDR. Higher Hb levels among patients who never received HU prescriptions or transfusions during follow-up, compared to those who did receive these treatments, may reflect patient selection and adherence, rather than treatment effects. Additional studies accounting for timing of treatment and laboratory tests, and confounding factors are needed to understand treatment effectiveness. This study points to a high burden of disease as evidenced by VOC (particularly among patients aged 18-40 years) and ACS (particularly among patients younger than 40 years). Lower VOC rates among older patients do not necessarily indicate lower disease burden, and could reflect cumulative exposure to ischemia-related tissue injury and resulting end organ damage, adaptation to VOC-related pain over time or healthy survivor bias. Further investigation of VOC rates and underlying health and organ damage in older patients is needed. These findings underscore the importance of real-world data for understanding SCD treatment and clinical outcomes in community care settings. They also highlight the clinical burden of SCD and possibly higher than expected

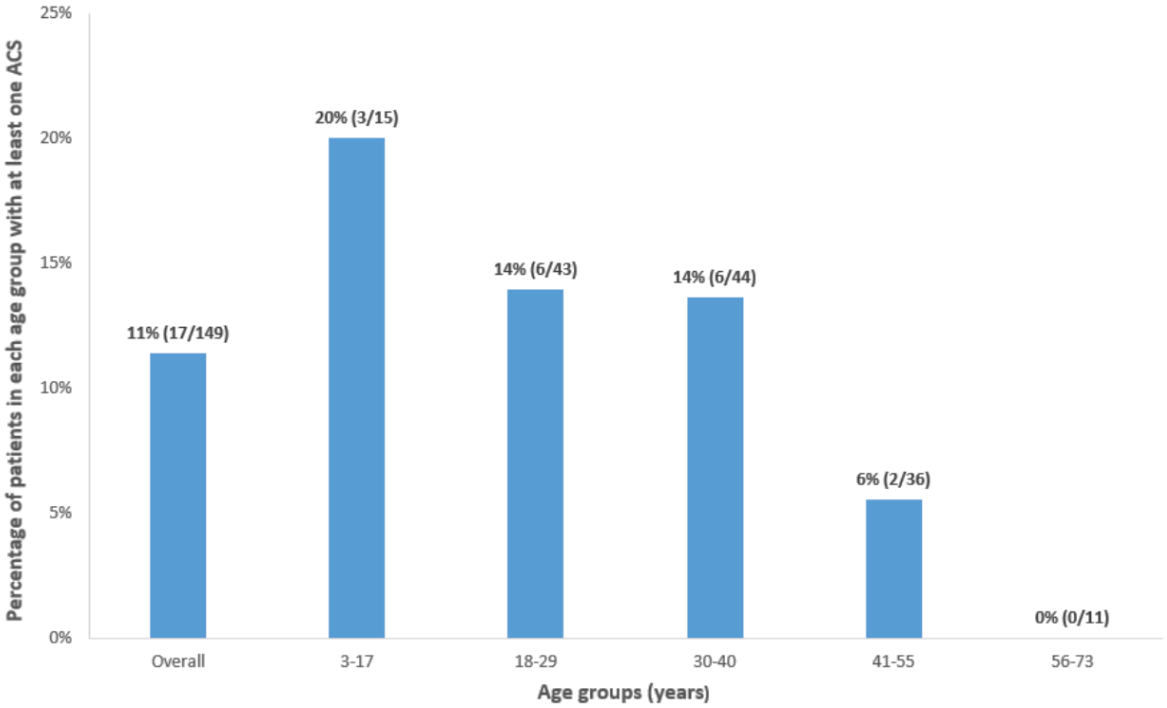
unmet need among both pediatric and adult patients in this community setting.

Figure 1. Percentage of patients with at least one VOC by age group over median follow-up of 3.8 years



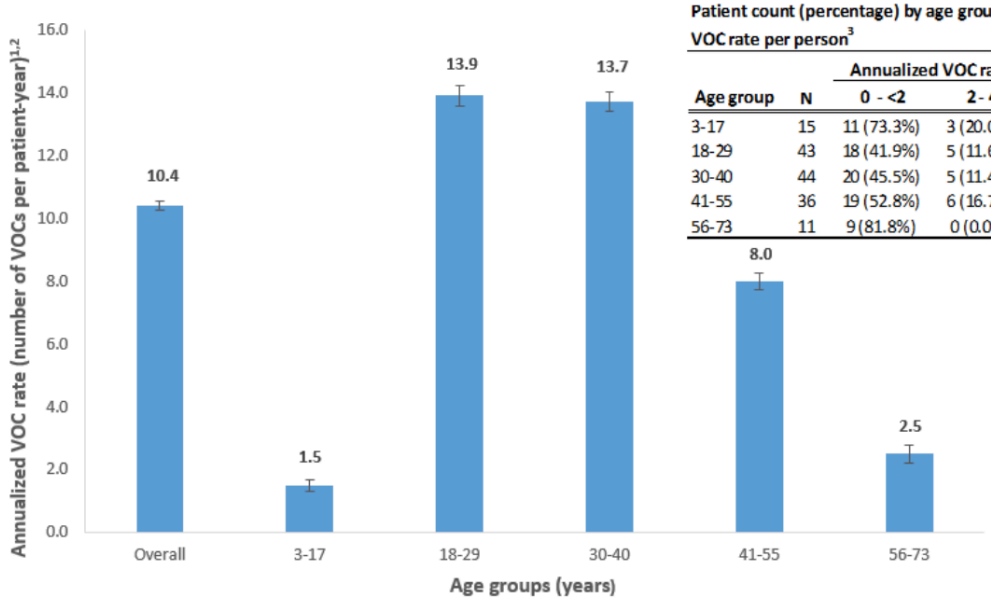
Abbreviation: VOC = vaso-occlusive crisis.

Figure 2. Percentage of patients with at least one ACS by age group over the median follow-up of 3.8 years



Abbreviation: ACS = acute chest syndrome.

Figure 3. Distributions of annualized VOC rate by age groups and per patient over the median follow-up of 3.8 years



Patient count (percentage) by age group and annualized VOC rate per person[3]

Age group	N	Annualized VOC rate per person[4] 0 - <2	2 - 4	>4
3-17	15	11 (73.3%)	3 (20.0%)	1 (6.7%)
18-29	43	18 (41.9%)	5 (11.6%)	20 (46.5%)
30-40	44	20 (45.5%)	5 (11.4%)	19 (43.2%)
41-55	36	19 (52.8%)	6 (16.7%)	11 (30.6%)
56-73	11	9 (81.8%)	0 (0.0%)	2 (18.2%)

Abbreviation: VOC = vaso-occlusive crisis.

Notes:
[1] Annualized VOC rate was calculated as the total number of VOCs experienced by all patients in the group divided by the sum of their follow-up durations in years.
[2] Error bars represent the standard errors for each annualized VOC rate.
[3] Percentages were calculated based on the number of patients in each age group.
[4] Annualized VOC rate per patient was calculated as the total number of VOCs experienced by the patient divided by the patient's follow-up duration. This ratio was standardized to a denominator of 1 year to obtain an annualized rate.

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Background: Sickle cell disease is a monogenic disease with early onset manifestations that begin in childhood and is characterized by high clinical heterogeneity, being influenced by genetic and environmental factors. Among disease modulators fetal hemoglobin and alpha thalassemia are among the most important. There is little data on these factors in sickle cell disease patients from Africa and none from Angola where the prevalence of the disease is very high. The aim of this study was to explore the possible association between alpha thalassemia, Fetal hemoglobin, hematological indices and clinical events in Angolan sickle cell disease Hydroxyurea-naïve pediatric patients.

Methods: This cross-sectional study is part of a large study in an Angolan sickle cell disease cohort conducted in the Hospital Pediátrico David Bernardino in Luanda and in Hospital Geral do Bengo in Caxito. Sampling was performed between April and August 2019. A total of 200 sickle cell disease children were included, after guardian informed consent, being 51,5% females. A venous blood sample was collected from each participant and used for hematological analyses, electrophoresis for diagnosis confirmation, Fetal hemoglobin quantification by HPLC (Bio-Rad variant II). DNA isolation was done by Qiagen blood mini kit, and the 3.7 kb alpha thalassemia deletion was studied by GAP-PCR. ANOVA, nonConference Abstract parametric tests and Chi-square tests were applied to compare the means, medians or frequencies between the three alpha thalassemia genotypes. P-value <0.05 was considered statistically significant.

Results: We observed a slight deviation from Hardy-Weinberg equilibrium regarding frequencies of 3.7 alpha thalassemia deletion with a decrease in homozygous without deletion and an increase in 3.7 heterozygous (55.0%) and homozygous (12.5%). When the frequency of deletion was compared between gender an increase in 3.7 alpha thalassemia deletion was observed in boys (17.5% vs 7.8%). Moreover, an increase in alpha thalassemia 3.7 deletion frequency was observed in children older than 5 years old (11.7% vs 13.00 %). This increase supports the hypothesis that the co-Inheritance of Alphathalassemia may improve survival of sickle cell disease patients. Further, alpha 3.7 homozygous had a significantly higher age of first manifestation (6 months vs 11 months), lower number of blood transfusions by year (0.48 vs 0.18), higher hemoglobin level (7.24 vs 7.78 g/dL), lower MCV (81.75 vs 62.73 fl), MCH (27.28 vs 20.25 pg) and number of reticulocytes (11.62 vs 6.46 103 /L). There were no differences in Fetal hemoglobin between the 3 genotypes. Moreover, the number of cases of stroke, osteomyelitis, splenomegaly, splenectomy and hepatomegaly were lower in the presence of the deletion. In sickle cell disease patients who are alpha thalassemia homozygous there was any event of stroke or osteomyelitis.

Conclusions: For the first time in an Angolan population, the results obtained reveal that alpha thalassemia deletion in sickle cell disease influences the hematological and clinical aspects and produces a mild phenotype. Sickle cell disease is well characterized in high-income countries but not in sub-Saharan Africa where it is most prevalent. These results were concordant with other studies performed in other areas and could be consequence of a reduction in hemolytic rate due to a lower HbS production and consequent lower cell sickling.

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PRELIMINARY ANALYSIS OF NEUROLOGIC OUTCOMES IN SICKLE CELL DISEASE (SCD) PATIENTS WITH CONDITIONAL TRANSCRANIAL DOPPLER (TCD) ULTRASOUND VELOCITIES: A SINGLE CENTER EXPERIENCE

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Background: Women with Sickle Cell Disease (SCD) are at an increased risk for pain associated with their menstrual cycle. Sickle cell vaso-occlusive crises are associated with increased rates of hospitalizations and early mortality. Little data exists on the frequency and impact of menses associated pain crises.

Objective: The Consortium for the Advancement of Sickle Cell Research (CASIRE) is an international collaborative research group with sites in the United States, Europe, and Africa. Using data from the CASIRE Cohort we sought to determine the frequency and impact of menstruation-associated pain crises in an international cohort of women with sickle cell disease in the United States and Ghana.

Methods: The CASiRe database includes 6 sites in the U.S. (Univ. of Michigan, Rainbow Babies & Children's Hospital, Promedica Toledo Children's Hospital, Children's Hospital at Montefiore, Connecticut Children's Medical Center, Univ. of Connecticut Health Center), 2 in Ghana (Ghana Institute of Clinical Genetics, Pediatric SCD Clinic at Korle Bu Teaching Hospital), 2 in Italy (Univ. of Campania Luigi Vanvitelli, Univ. of Padua, Italy), and U.K.(Guys & St. Thomas Hospital, Evelina Children's Hosp). Between 2011 and 2017, after obtaining IRB approval at each site and written informed consent, demographic, clinical and laboratory data were collected by interviewing the patient and/or parent/guardian. This analysis includes only the 3 U.S. sites(Michigan, Promedica Children's Univ of Connecticut)and the 2 Ghanaian sites. 178 participants with SCD US (n = 24), Ghana (n = 154)] completed a self-reported medical history. Data was collected in a clinic setting.

Results: Genotype was 75.8% (N=135) Hgb SS, 22.5% (N=40) Hgb SC, and 1.7% (n=3) Sickle Beta Thalassemia Plus. Out of the 178 participants, 39% (N=70) reported that menstruation has triggered pain crises in the past. 8.9% (N=16) of women were on some form of contraception; 11.8%(N=8) of women reporting Menses triggering pain crises were reported using contraception. Patients with menstruation-associated pain were seen in the emergency room at a higher rate (1.85 vs 2.52 ER/ Day Hosp pain crises/yr., p=0.147) and was more likely to require hospitalization (0.75 vs 1.71 pain crises requiring hospitalization/yr., p=<0.002) in the past year compared to patients without menstruation-associated pain. Within the past 6 months, 33.7%(N=60) reported Menses triggering pain crises. While 12.9% reported menses triggering pain crises once in the past 6 months, 24% reported menses triggered pain crises at least 4 times within the same time period. Further, 35% reported the intensity of the pain as moderate -severe.

Conclusions: Patients with menstruation-associated pain were more likely require hospitalizations in the past year in our international cohort of SCD women. At least one-third of patients reported moderate to severe pain with menstruation associated pain crises. Additional studies are need to evaluate pain and quality of life with women with menses associated pain crises. While a small number of women were on contraceptives, more studies are needed to examine the relationship between contraceptive use and sickle cell-related menstrual pain.

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CHRONIC PAIN IN CHILDREN AND ADOLESCENTS WITH SICKLE CELL DISEASE

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Background: Recent advancements in the treatment of Sickle Cell Disease (SCD) have led to a decrease in the morbidity and mortality. With longer lifespan, chronic pain has been increasingly recognized, impacting up to 50% of adults with SCD. The ACTTION-APS Pain Taxonomy Initiative (AAPT) Diagnostic Criteria for Chronic SCD Pain, published in 2017, provides diagnostic criteria for chronic pain in the setting of SCD. The purpose of this study was to 1) determine the prevalence of chronic pain in children and adolescents with SCD, 2) divide them into chronic pain categories as set out by AAPT Diagnostic Criteria for Chronic SCD Pain and, and 3) further describe this sample using validated measures. This will aid in improved understanding and management of complex pain in SCD.

Methods: This is a single center prospective study at Connecticut Children's, approved by Connecticut Children's IRB. 159 patients aged 7-21 years old with SCD from Connecticut Children's Hematology Sickle Cell Database were screened for suspected chronic pain based on 2 ED visits for pain, any in-patient admission for pain, or 2 or more opioid prescriptions during January 1- December 31, 2018. Patients with suspected chronic pain were approached to confirm chronic pain defined as greater than 50% of days, in pain, utilizing the following criteria: pain 4 or more days per week over the past 6 months and/or Sickle Cell Disease Pain Burden Interview-Youth (SCPBI-Y)score of 7 or greater. All enrolled patients were given the following 5 surveys: Peds Quality of Life SD, Child Activity Limitation Interview (CALI) 21, PROMIS 37, Centralized Pain Inventory, and PROMIS Neuropathic scale. Descriptive statistics were performed on data collection from chart review that included ethnicity, gender, age, insurance type, SCD subtype, co-morbid diagnoses, SCD treatment, ED VOC visits, VOC admissions, number of opioid prescriptions, alternative pain treatments, other medications, and the 6 surveys.

Results: Out of 149 patients in the database, 59 screened positive for suspected chronic pain. Of these, 29 were enrolled as chronic pain (19.5% of all patients screened), 14 confirmed as not chronic pain, and 16 patients were not approached due to logistics. 16 males and 13 females, ranging from 8-22 years old at time of enrollment. 19 patients had Hemoglobin SS, 4 had Hemoglobin SC, 3 had Hemoglobin Sβ0 thalassemia, 2 had Hemoglobin S β+ thalassemia, and 1 patient had Hemoglobin S Quebec-chori. Per the AAPT diagnostic criteria, patients were divided into 3 core groups based on presence of contributory disease complications (e.g. avascular necrosis); 22 patients did not have contributory disease complications and 7 patients had contributory disease complications as well as pain at other sites and were therefore classified into the mixed pain contributory disease group. There were no patients in the contributory disease complication group without mixed pain. The two groups had the same number of mean pain sites, 6.8 (range from 0-19), and similar opioid use (13.3 opioid prescriptions per year in the mixed pain group, 12.5 in the non-contributory group). Medical and psychiatric comorbidities were common in both groups. 52% of patients had psychiatric conditions, with slightly higher prevalence in the mixed pain group vs the non-contributory group (57% vs 50%). 22 patients had public insurance and 7 had private insurance. Patients had high pain burden with mean SCPBI-Y scores (maximum possible 28) of 16.1 in the mixed pain group (range 10-21, SD 3.4) and 12.6 in the nocontributory disease group (range 8-23, SD 4.3). Average QL score was 115.9 (SD 19) in the mixed group and 101.5 (SD 30.2) in the non-contributory group. CALI score was similar between the two groups with an average of 31. Most patients did not have high scores on the Conference Abstract PROMIS Neuropathic scale with an average of 9.4 (maximum possible 28), however, the centralized pain index scores averaged 13.6 (max possible 31).

Conclusions: The AAPT diagnostic system can be used to classify children and adolescents with SCD and chronic pain. The prevalence of chronic pain in youth is lower than that reported in adults. Most patients had pain at multiple sites, some with contributory disease complications and others without. Patients with SCD and chronic pain experience multiple medical, psychological, and social comorbidities that can impact their pain and quality of life.

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Background: Numerous studies have established NSAIDs, opioids, and acetaminophen as first-line pain management therapies in the acute management of sickle cell disease vaso-occlusive pain crises. Muscle relaxant use has been acknowledged as an adjuvant for pain management in patients with vaso-occlusive pain crises, however no specific outcomes have been reported with muscle relaxant use as part of a pain management regimen. Despite the lack of formal studies, many providers utilize muscle relaxants on a case-by-case basis for patients with sickle cell vaso-occlusive pain crises with pain characteristics such as muscle tightness and cramping, with some benefit often reported. This study sought to examine if the use of muscle relaxants as part of the treatment regimen for pediatric sickle cell disease vaso-occlusive pain crises leads to better outcomes.

Methods: A retrospective chart review was conducted to assess individual vaso-occlusive crisis episodes. Subjects were collected from the database of sickle cell disease patients followed by the Sickle Cell & Hemoglobinopathy Center of WNY. The charts of 188 subjects were reviewed from the Kaleida Health electronic medical record. A total of 207 vaso-occlusive pain crisis hospitalizations amongst 54 patients were examined. Subjects were separated into two groups: those who received cyclobenzaprine during hospitalization and those who did not receive cyclobenzaprine during hospitalization. Patients under the age of 21-years-old who were admitted to Oishei Children's Hospital or the former Women and Children's Hospital of Buffalo within the 36-month period between January 2016 to December 2018 for vaso-occlusive pain crisis were included in the study. Pregnant patients upon admission and any patient admitted with or who developed acute chest syndrome, stroke, or TIA during hospitalization were excluded. Length of hospital stay, 30-day readmission rate, and mean and median morphine equivalent (mg/kg/day) were examined between the 2 groups.

Results: The results of the study showed that patients who received cyclobenzaprine during hospitalization had almost twice the length of hospitalization, almost twice the rate of readmission within 30 days for vaso-occlusive pain crisis, and 2.5x more daily opioid dosage requirements. An intrapersonal comparison for patients who received cyclobenzaprine during some hospitalizations but not others displayed similar results in favor of not receiving the drug.

Conclusions: Cyclobenzaprine may have no benefit and possibly even a negative impact on patient hospitalizations for sickle cell disease vaso-occlusive pain crises. Cyclobenzaprine may not be an effective adjunct for pain relief and did not show to improve hospital outcomes as measured by length of hospital stay and 30-day readmission rate. The data is limited by selection bias between the 2 study groups, as cyclobenzaprine was prescribed to those patients complaining of muscular pain whose standard treatment regimen was subtherapeutic. Thus, those with responsive standard therapy did not require cyclobenzaprine unless it was already a home medication continued upon admission. However, there may be factors within the medication that contribute with poor outcomes in sickle cell disease vaso-occlusive pain crises

"JUST DO IT" IMPLEMENTATION OF "GOT TRANSITION" IN A LIMITED RESOURCE SETTING

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Background: Identification of infants with sickle cell disease through newborn screening has driven the creation of a healthcare system designed to provide comprehensive care. The success of these programs and advances in the treatment of sickle cell disease has created a population of adults with SCD for which the healthcare system was not designed. Many young adults are lost to comprehensive care when they leave their pediatric medical home. These young adults use the ED for their primary source of care resulting in increased cost, morbidity, and mortality. The problem of healthcare transition (HCT) is not unique to SCD and can be found with many serious, chronic, childhood-onset diseases. To address this problem, the American Academy of Pediatrics (AAP), American College of Physicians, and American Academy of Family Practioners developed a framework for HCT called "Got Transition." They identified 6 core processes: 1) develop transition policy, 2) maintain system of tracking, 3) assess transition readiness, 4) transition planning, 5) transfer of care, and 6) assess transfer completion. When met, their recommendations have improved outcomes. The problem is how to implement HCT in a clinic standard workflow. Our objective was to create a change package that could be implemented with minimum resources.

Methods: We reviewed the "Got Transition" website (www.gottransition.org), online transition courses, ASH SCD initiative (www.hematology.org/Advocacy/4329.aspx), and we extracted the minimal clinical actions needed to implement a HCT program for our clinic.

Results: Our change package is shown in the table. We implemented this change package with a "just do it" approach for our pediatric SCD center. We believed this approach was most appropriate because of the strong evidence for HCT and low risk for future implementation if we failed. Our providers began transitioning with the next eligible patient, on the next routine healthcare visit. Our process measure for each core element was the percent completed for the eligible patients. These transition visits are well Conference Abstract received by patient and family, taking about 20-25 minutes. These transition visits are planned for twice a year.

Conclusions: Implementation is hard, requiring resources, time, effort, leadership commitment. HCT for sickle cell varies greatly across centers, depending on their resources. Our change package represents a simple doable HCT which we are now spreading across the public hospitals within our system through our Project ECHO Sickle Cell Disease Learning Collaborative.

Core Element (Driver)	Clinical Activity	Tools
Transition Policy	Handout and discuss transient policy	Sample Transition Policy (https://www.gottransition.org/resources/index.cfm)
Transition tracking	Fill out tracking form	Tracking form or registry (https://www.gottransition.org/resources/index.cfm)
Assessment of transition readiness	Discuss results of assessment and proceed to planning goals	ASH SCD transition readiness assessment form (https://www.hematology.org/Clinicians/Priorities/5573.aspx)
Transition planning	Defined transition goals for the year Yearly annual review	"Go Transition" Resources (https://www.gottransition.org/resources/index.cfm) ASH SCD Clinical Summary (https://www.hematology.org/Clinicians/Priorities/5573.aspx)
Transfer	Help family select physician and support transfer of care	ASH SCD Clinical Summary (https://www.hematology.org/Clinicians/Priorities/5573.aspx)
Assess transfer completion	Follow-up call with family	

Table: Change Package

THE EFFECT OF UTILIZATION OF INDIVIDUALIZED PAIN PLANS ON PATIENT SATISFACTION IN PATIENTS WITH SICKLE CELL DISEASE

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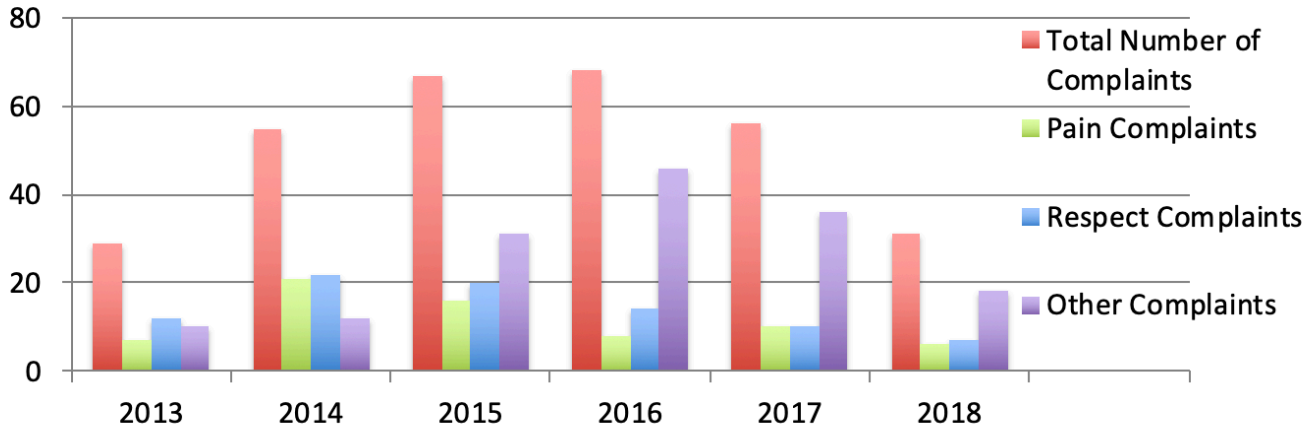
Background: Sickle cell disease is an inherited blood disorder that affects millions of people worldwide, with approximately 100,000 Americans affected (Center for Disease Control, 2017). Sickle cell disease results in over 200,000 emergency department visits in the U.S. annually, with pain as the most common complaint (Lanzkron S, et al 2010). Unfortunately, patients with sickle cell disease have experiences of hospital care that are characterized by mistrust, stigmatization, control, and neglect. Patients report feeling that healthcare providers frequently doubt the legitimacy of their pain and they are often stigmatized as drug seeking (Maxwell, K et al 1999). One of the most significant complaints voiced by patients is being insufficiently involved in care decisions (Lattimer, L et all 2011). At The Ohio State University Wexner Medical Center, a comprehensive sickle cell center was developed. During its development, patients with sickle cell met with their hematologist and jointly determined an individualized pain plan to be used when they present to the emergency department in vaso-occlusive crisis (VOC).

Methods: A multidisciplinary group was formed in order to enact a protocol to implement individualized pain plans for sickle cell patients who presented with VOC. Sickle cell patient complaint data from the patient experience team was collected from 01/01/2013 through 12/31/2018 to determine the effect of customized pain plans on patient satisfaction. Total number of complaints as well as types of complaints (pain, respect, other) was collected to determine if there was a change in number of complaints and type of complaints. Other complaints include complaints about parking, accommodations, and food.

Results: Utilization of individualized pain plans led to a decrease in patient complaints over time with a peak in 2014 (Figure 1). Of the years during protocol implementation, 2015 had the most complaints about pain management with the majority being made early in the year during the initial phases of enactment. After successfully integrating use of custom pain plans, a steady decrease in complaints was noted with the fewest complaints about pain or respect being noted in 2018. There was a Conference Abstract decrease of 28.6% in the average annual complaints on pain management and a 70% decrease in the average annual complaints about respect.

Conclusions: Patient satisfaction improves with use of individualized pain plans as demonstrated by the patient experience data. Press-Ganey surveys were not a robust way of gathering data and were thus excluded. Improvement in satisfaction is likely from a combination of expectations of care being met as well as patients feeling as though they have some control in their care. By allowing patients to participate in determining their pain plan along with a medical specialist, patients can feel as though they are being heard. Using a custom pain plan designed in part by the patient also leads to less confusion as to which pain regimen is most effective. With a standardized protocol and individualized pain plans, patients feel more respected in the hospital. In the future, gathering data from the security department on the number of times security had to be involved in patient interactions could provide further insight into the patient experience. From an alliance with the emergency department, the hematologist, and the patient, the patient experience can be significantly improved.


80
60
40
20
0
2013
2014
2015
2016
2017
2018
Total Number of Complaints
Pain Complaints
Respect Complaints
Other Complaints

SICKLE CELL INTRAHEPATIC CHOLESTASIS

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Background: Sickle cell disease (SCD) is a hemoglobinopathy that is caused by an inherited mutation of the beta-globin chain in hemoglobin (Hb). In deoxygenated states, the mutated Hb undergoes polymerization causing erythrocytes to undergo a morphological alteration and aggregation. This aggregation can subsequently lead to acute vaso-occlusion and multi-organ damage commonly affecting the kidneys and liver. With less than 50 cases reported in literature, Conference Abstract sickle cell intrahepatic cholestasis (SCIC) remains a rare and life threatening complication that occurs secondary to hepatic ischemia caused by sickled erythrocyte-mediated occlusion of the hepatic sinusoids. SCIC is clinically characterized by acute right upper quadrant abdominal pain, hepatomegaly, severe hyperbilirubinemia, and transaminitis. To mitigate progression to hepatic failure and decrease mortality, SCIC is treated by plasma exchange transfusion. Here we present the case of SCIC in a 60 year old patient with SCD co-morbid with glucose-6 phosphate dehydrogenase deficiency (G6PD).

Case: A 60 year old African-American man with a past medical history of SCD, hiatal hernia, stage chronic kidney disease, G6PD, and a chronic non-healing lower extremity ulcer presented to the emergency department with generalized myalgias, cough productive of yellow sputum, dark colored urine, and progressively worsening scleral icterus that began following administration of the influenza and pneumococcal vaccine ten days prior. He denied recent illness or travel and also denied any night sweats, fevers, chest pain, hematochezia, or melena associated with these symptoms. His surgical history was remarkable for a splenectomy and cholecystectomy which were both completed without complication. His home medications were cyanocobalamin, montelukast, triamcinolone ointment. Since his last sickle cell crisis, 12 months ago, he has been generally well. He does not use hydroxyurea. The patient denied any tobacco product, alcohol, or illicit drug use. On presentation, his vitals were unremarkable with the exception of tachycardia. His complete blood count demonstrated normocytic anemia (Hb: 6.3 g/dl, MCV: 96.8 fL) and thrombocytopenia (146×10^3/μL); no leukocytosis was observed (WBC: 8.7×10^3/μL). Elevations in reticulocyte count (12.7%) and serum nucleated red blood cells (43) were observed while serum haptoglobin was decreased (<30 mg/dL). His comprehensive metabolic panel was remarkable for hyponatremia (Na: 132 mEq/L), hyperkalemia (5.0 mEq/L), azotemia of 45 mg/dL, and a transaminitis was observed with elevations in AST (165 U/L), ALT (68 U/L), and ALP (172 U/L). His total bilirubin was elevated to 49.5 mg/dL and his direct bilirubin was elevated to 26.23 U/L. Serum lipase was elevated (120 U/L) as was serum creatine kinase (81 U/L) and serum uric acid (8.5 mg/dL). Coagulation studies demonstrated a prolonged PT of 44.7 seconds and INR of 3.8 seconds. Influenza A/B, infectious mononucleosis, Legionella urine antigen, serum Mycoplasma IgM, HIV1/2 antibody and antigen, and blood cultures were negative. Chest X-ray demonstrated a right lower lobe opacity suspicious for pneumonia and computed tomography of the abdomen demonstrated hepatic scarring. Subsequent doppler ultrasound of the liver demonstrated normal hepatopedal flow in the main portal vein and no evidence of thrombosis. The patient was subsequently given cefepime and azithromycin and was admitted to the intensive care unit. Throughout the admission, the patient's condition continued to deteriorate as his mentation became severely altered and his Hb decreased to 4.0 mg/dL. He received an exchange transfusion and after this he went into respiratory distress and was intubated and unfortunately died 7 days later.

Conclusions: SCIC represents a significant diagnostic challenge as it must be differentiated from other more common hepatic sequelae (hepatic sequestration, hepatic crisis) of SCD. While early plasma exchange is the current first line therapy for SCIC, mortality continues to be as high as 64% in patients with severe disease. In patients with

severe disease that did not respond to exchange, such as the patient presented here, there is an even higher rate of mortality. Therefore, this case emphasizes the continued need for a better understanding of the pathophysiology behind SCIC to improve outcomes.

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QUALITY IMPROVEMENT: YET ANOTHER SICKLE CELL DISEASE HEALTHCARE DISPARITY

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Background: Sickle cell disease is an orphan disease affecting about 100,000 individuals in the US and results in poor quality of life and premature death. Disparities in SCD quality of care, funding, and research have been well documented compared to similar orphan disease. In general, quality improvement (QI) studies are making a significant difference in healthcare quality. This has been demonstrated for another orphan serious genetic disease, cystic fibrosis (CF) which affects about 1/3 the number of individuals. Our objective is to compare published QI for studies CF and SCD.

Methods: A PubMed literature search from 2000 to 2019 was conducted using the search terms “quality Improvement” with either “cystic fibrosis” or “sickle cell”. The abstracts were identified and the papers addressing specific outcomes were selected. Clinical trials and publications where CF or SCD were co-morbidities in a larger study were excluded.

Results: In the search we found a total 114 articles for CF and 52 for SC. Those using defined QI methodology were 50 and 29, respectively. In general, the numbers of QI studies per year increased for both CF and SCD. For chronic disease, QI studies address issues of acute care, adherence to recommended maintenance care or practice guidelines, transition of care, and communication and use of registry. For CF there was a balance of studies looking at the components of quality care. For SCD, 66% of the studies looked at improving pain management. For CF there was greater balance between all these issues with the largest number of studies improving adherence as measured by clinical outcomes.

Conclusions: To close the gap in quality of care for sickle cell disease we need to increase the number and types of QI studies done. Yet to do this requires a driving force - QI costs time and money. For CF the driver has been the CF foundation. For sickle cell disease, we need all the stakeholders to be involved including community groups, hospitals, insurers, and national organizations.

SECRETORY PHOSPHOLIPASE A2 IN EXHALED BREATH CONDENSATE FROM SICKLE CELL PATIENTS WITH ACUTE CHEST SYNDROME: A FEASIBILITY STUDY

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Background: Acute chest syndrome (ACS) is a potentially life-threatening complication of sickle cell disease (SCD). While ACS is defined by the presence of a particular grouping of clinical signs and symptoms, the underlying pathophysiology is varied. Many triggers have been described including local or systemic infection, fat emboli, and asthma exacerbation. Most current techniques to identify underlying triggers for ACS or study inflammatory lung damage are uncomfortable for the patient and/or invasive and are limited in scope. Plasma levels of secretory phospholipase A2 (sPLA2) are significantly elevated in patients with SCD during ACS compared with levels during vaso-occlusive crisis and at baseline.1 While plasma sPLA2 may prove to be an effective biomarker to aid in ACS diagnosis and monitoring of disease progression and response to therapy, its measurement requires frequent blood draws from already anemic patients in sickling crises. Exhaled breath condensate (EBC) collection is simple, non-invasive, and contains many biomarkers with properties similar to those of sPLA2. EBC has not previously been used to evaluate sPLA2. We hypothesized that sPLA2 will be measurable in EBC from patients with SCD during ACS.

Methods: In this single-institution feasibility study, plasma and EBC levels of sPLA2 from pediatric and adult patients with SCD were measured during ACS episodes and at baseline clinical status. The definition of ACS used for this study required a new radiographic pulmonary infiltrate of at least one complete lung segment, and two or more of the following symptoms: fever, chest pain, dyspnea, tachypnea, hypoxia. Within 48 hours of ACS diagnosis, three patients with SCD (type HbSS) each had three EBC samples collected (at least one hour apart). A plasma sample was obtained from each subject at the time of the first EBC collection. Additionally, three SCD patients at baseline clinical status Conference Abstract had one collection of EBC and plasma for comparison. Human sPLA2 Type IIa levels were measured in all samples by a commercially-available ELISA

Results: Of nine subjects screened, seven were enrolled and five completed the study. Only one of the subjects who completed collection during ACS returned for baseline sample collection. An additional two subjects were enrolled for baseline EBC and serum sample collection. Incidentally, all participating subjects were female. The subjects enrolled for baseline-only collection were adults (both 25 years of age). All other subjects were children (ages 8-12 years). All participants tolerated sample collection well. sPLA2 reached level of detection in the subject with ACS who had the largest radiographic pulmonary infiltrate and also reached the highest level of respiratory support when compared to the other ACS subjects. This patient also had the highest level of plasma sPLA2.

Conclusions: It is feasible to measure EBC sPLA2 levels in SCD patients with acute chest syndrome. sPLA2 is detectable in EBC. Further studies are warranted to evaluate measurability and reproducibility of sPLA2 in EBC as well as its relationship to disease states.

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IMPROVING SICKLE CELL DISEASE CARE: THE SICKLE CELL DISEASE TREATMENT DEMONSTRATION REGIONAL COLLABORATIVES PROGRAME

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Background: Since the Sickle Cell Treatment Act of 2003, The Sickle Cell Disease Treatment Demonstration Regional Collaborative Program (SCDTDP), funded by the Health Resources and Services Administration (HRSA) has established regional sickle cell partnerships. There are five regions: Northeast, Southeast, Midwest, Heartland, and Pacific. The collaborative program focuses on promoting best practice treatments, offering provider education, and increasing access to high-quality care for individuals living with sickle cell disease (SCD) in the US. The SCDTDP regional directors share the vision of transforming SCD care by providing quality care to more individuals with SCD over this next decade, thereby increasing lifespan, enhancing quality of life and minimizing morbidity. The goals of the SCDTDP Program are:

- To improve health outcomes in individuals with SCD
- To reduce morbidity and mortality caused by SCD
- To reduce the number of individuals with SCD receiving care only in emergency departments
- To improve the quality of coordinated and comprehensive services to individuals with SCD and their families

This session will highlight the impact and accomplishments of the SCDTDP to date. A panel including presenters from the five current sickle cell regional collaboratives will describe their regional work and share their collective results.

Methods: The five regional collaboratives created networks of SCD experts in each state and District/ Territories in the US. The networks include providers, community based organizations, state and federal entities, and other key stakeholders. These collaboratives include:

- Heartland|Southwest Sickle Cell Disease Network- serving AR, IA, KS, LA, MO, NE, OK, and TX
- Sickle Treatment & Outcomes Research in the Midwest (STORM)- serving IL, IN, MI, MN, ND, OH, SD, and WI
- Sickle Cell Improvement across the Northeast Region through Education (SiNERGe) collaborative serving CT, DC, DE, MA, ME, MD, NH, NJ, NY, PA, RI, VA, VT, WV, U.S. Virgin Islands, and Puerto Rico
- Pacific Sickle Cell Regional Collaborative (PSCRC)- serving AK, AZ, CA, CO, HI, ID, MT, NM, NV,OR, UT, and WA
- Education and Mentoring to Bring Access to Care for SCD (EMBRACE) sickle cell consortium- serving AL, FL, GA, KY, MS, NC, SC, and TN

The collaboratives are actively advocating for support of programs and initiatives that benefit care of individuals with SCD and conduct a number of activities to meet the objective of increasing access to quality care for individuals living with SCD. The regional collaboratives have established learning networks that share information and data to identify, develop, implement, and track quality improvement initiatives. Each region has also established free telementoring programs for healthcare providers to improve provider knowledge regarding guideline-based care for individuals with SCD. They have also developed strong relationships with community-based organizations to increase patient access to SCD care.

Results: The combined efforts of SCDTDP have improved access to care, increased prescribing of Hydroxyurea for patients with SCD, and increased the number of providers knowledgeable about SCD. Some of the SCDTDP success includes:

- More than10,000 patients with SCD are receiving care within the SCDTDP networks
- Increased Hydroxyurea use across the US
- Over 500 providers have utilized telementoring sessions

- Collaboration with community based organizations has increased
- State and regional actions plans have been developed
- Quality improvement initiatives impacting sites' quality of care
- The SCDTDPs developing one voice for the national SCD provider community

Conclusions: The regional collaboratives of the SCDTDP continue move the national sickle cell initiative forward by continuing previous work to ensure continued improvements in provider knowledge, attitudes, and skills resulting in increased accessibility and delivery of high quality care to individuals with sickle cell disease.

EVALUATION OF PSYCHOLOGY REFERRALS AND HEALTH CARE UTILIZATION PATTERNS IN CHILDREN AND ADOLESCENTS WITH SICKLE CELL DISEASE

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Background: Mental health challenges are prevalent among patients managing sickle cell disease (SCD) due to the nature of the illness (Stollon et al., 2015; Toumi, Merzoug, & Boulassel, 2018). Particularly, adolescent patients with SCD have been found to display an increase in mental health needs when the frequency of SCD complications increase (Stollon et al., 2015). In addition the physiological complications, patients' perceptions of their illness process, and ability to prevent SCD complications have been found to impact their mental health as well (Elander, Lusher, Bevan, Telfer, & Burton, 2004). Mental health declines have been associated with more frequent complications of SCD which results in increased hospital utilization (Carroll, Carlton, Fagan, & Lanzkron, 2009). Increased untreated mental health challenges could indirectly cause an increase in hospital utilization for patients with SCD. In 2017, Texas Children's Hospital's (TXCH) Hematology center implemented a program to identify patients with SCD with high health care utilization. The goal of the program was to decrease health care utilization by developing individualized care plans to provide holistic support and alleviate social and environmental challenges outside of the disease process. Psychological services were identified as a key component of the care plan, but the process of referring a patient was not standardized. Therefore, we aimed to establish the role of age and health care utilization pattern as predictive factors in the existing referral pattern to psychology for patients with SCD. The objectives of this study were to identify an association between provider initiation of psychology referral and health care utilization, and to identify an association between provider initiation of psychology referral and patient age. We hypothesize that provider initiation of psychology referral will have a significant association with patient age and with higher health care utilization patterns.

Methods: We employed a cross sectional study design to conduct a secondary analysis of electronic medical record (EMR) data for patients followed by TXCH Hematology. Each EMR was reviewed from the August 2017-August 2018 utilization report to determine the presence of psychology referrals, number of outpatient and inpatient psychology encounters and patient age at the time of the report. Psychology outpatient and inpatient encounters were excluded from the model because these measures do not reflect the providers' actions of referring patients to psychology. Health care utilization patterns were categorized as: high (≥4 emergency (EC) or inpatient encounters per year), intermediate (2-3 EC or inpatient encounters per year), and low (≤ 1 EC or inpatient encounter per year). A multilevel logistic regression model was used to define the associations between provider psychology referral and health care utilization pattern, and between referral and age.

Results: Sixty-three SCD patients were included in the SCD health care utilization report. The mean age of the cohort was 10.63 years (range 0.00 to 20.00 years). The mean age of high utilization group was 12.35 years (n=33), intermediate utilization group was 8.16 years (n=19), and for low utilization group was 9.73 years (n=11). The difference in age for each utilization Conference Abstract group was found to be significant (p=0.02). For each year increase in age, a patient had a 1.43-fold higher likelihood of being referred to psychology when utilization category was fixed (p=0.009). Compared to those with low utilization, the intermediate utilization group had 1.73- fold higher likelihood of being referred to psychology (p=0.74) and high utilization group had 3.84-fold higher likelihood of being referred to psychology (p=0.41). There was not enough evidence to conclude the variance in psychology referrals across providers was significant despite the trend being notable (variance=3.59 95% CI 0.39-33.08).

Conclusions: Among children with SCD, there was not a significant association between health care utilization pattern and provider's referral to psychology. However, there was a significant association between age and provider's referral to

psychology. The current study is limited because of the small population included in the sample as well as the limited predictors included in the model to predict provider psychology referral. More analysis is required in order to get a better understanding of the factors that influence the initiation of a psychology referral. A standardized practice guideline to initiate a psychology referral including age and other factors may lead to improved quality of life and improved mental health outcomes.

CHARACTERISTICS AND POTENTIAL TREATMENT OPTIONS FOR PATIENTS WITH MICROVASCULAR ISCHEMIA ON CARDIAC MRI IN SICKLE CELL DISEASE

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Background: Microvascular ischemia leading to myocardial injury or infarction is an underrecognized problem in patients with sickle cell disease (SCD) presenting with chest pain. Initial data from our study suggests 18% SCD patients have troponin elevation suggesting myocardial injury and it is associated with higher all-cause mortality. There is limited data on management of microvascular disease and myocardial infarction in SCD patients. In this analysis we aim to explore the characteristics of patients with microvascular ischemia on cardiac MRI and our approach to managing these patients.

Methods: We conducted a retrospective chart review of patients with SCD seen at OSU Wexner Medical Center from July 2005 to July 2015 to identify patients who had cardiac MRI performed. Clinical and laboratory data around the time of cardiac MRI was collected. Abnormal cardiac MRIs were divided in two groups 1) Microvascular disease was defined by presence of subendocardial or myocardial perfusion defects and myocardial scarring. 2) Myocardial disease otherwise includes other findings suggestive but not specific for myocardial ischemia including left ventricular dysfunction, midmyocardial fibrosis, inflammation and regional wall motion abnormalities. Fisher's exact test and Wilcoxon rank sum test were used for data analysis for categorical and continuous variables respectively.

Results: Forty-seven out of 373 SCD patients had cardiac MRI done during this period. Cardiac MRI was abnormal in 51% patients (n=24, median age 35.5 years; 46% male; genotype Hb SS 83%, SC 13% and Sβ-thal 4%) with findings specific for microvascular disease (group1) in 14/47 (30%) MRIs. Following electrocardiographic findings were present: T-wave inversion in 4, ST elevation in 1, ST depression in 1 and remaining 14 EKGs had non ischemic findings like normal EKG (n=5), sinus tachycardia (n=4), non-specific ST-T wave changes (n=4), LVH and atrial fibrillation. Cardiac catheterization was available in 9 of 24 patients, 8/9 showed clean coronaries and one patient had triple vessel disease. Following medications were used in management along or in different combinations: Aspirin (n=15), nitrate (n=6), beta blockers (n=7), ACE inhibitors (n=5), spironolactone (n=1), clopidogrel (n=1). Two patients with concurrent troponin elevation received simple transfusion.

Conclusions: Myocardial ischemia due to microvascular disease is prevalent in patients with SCD presenting with chest pain whose management remains unclear. Aspirin, long acting nitrates, beta blockers and ACEIs are potential areas of treatment. Further research is warranted to evaluate for the effect of these medications or other sickle cell disease modifying therapies on clinical outcomes.

STUDYING THE PREVALENCE OF CANNABIS USE IN TEENAGERS WITH SICKLE CELL DISEASE, AN UPDATED ANALYSIS

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Background: There are protean manifestations of Sickle Cell Disease (SCD), but the primary issue of this debilitating disease is severe pain that occurs in both acute and chronic settings. Patients with SCD require both the use of NSAIDs and opioid pain medication to manage their pain. However, this combination often does not provide the relief that patients need, forcing patients to look for alternative and adjunct forms of pain control. With the recent legalization of marijuana in Michigan, we aim to determine the prevalence of marijuana use in adolescents and teens with SCD, to aid in tracking this longitudinally. As of today, there is no data on the use of marijuana in this age group of patients with SCD. Objective: To assess the current practices and prevalence of marijuana use amongst teenagers with sickle cell disease.

Methods: A seven-item survey was created and distributed to patients presenting to clinic for annual visits, transfusions, and/or patients admitted to the hospital for sickle cell pain crises or fevers. This survey posed questions about marijuana usage including- frequency of use, form of marijuana used, purpose of use (medical or recreational), and lastly, perception of pain reduction.

Results: At this time, 50 surveys were collected and scored. Of which, 15 (30%) had positive screens for marijuana use. Of those using marijuana, 50% were using marijuana products at least once per week. The most common form of isolated use was inhalational (33%), followed by edible (20%). 47% of patients using marijuana were combining various forms of it. Results were similar amongst boys and girls as 53% of boys and 47% of girls in this study were using marijuana. Finally and most importantly, 93% of patients who were using marijuana found that it helped to alleviate their pain.

Conclusions: Several teenagers with SCD are using marijuana in various forms, most of whom are using it recreationally in an inhaled form. We as practitioners need to acknowledge that our patients with SCD are using these products and counsel accordingly. As this is an pilot study, further studies need to be done to assess its role on pain control in patients with sickle cell disease.

MORE THAN PAIN: THE EMOTIONAL ASPECT OF SICKLE CELL VIDEO

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Background: Although pain is often the main complaint of patients, those with sickle cell can suffer from a multitude of other conditions as a result of their condition, which can affect all organ systems. As patients and their physicians must focus on all the pathophysiological aspects of the disease, the emotional impact of the disease is often not discussed in clinical settings.

Methods: Sickle cell patients were consented to be interviewed, as well as 2 physicians who care for sickle cell patients. Patients were all asked similar questions, but the interview was allowed to get "off script", as the patients had different experiences with the condition. There was also an interview guide for the physicians, which differed from the patient questions. Interviews were then examined, and it was noted whenever the topic of the interview changed, what it changed to, and the time in the interview. This was used to edit the video together, which was done using Adobe Premiere, with audio edits made with Adobe Audition.

Results: The result was a 9 minute and 30 second video titled "More than Pain: The Emotional Impact of Sickle Cell Disease" (link: https://youtu.be/2UjInocLG2A). The video starts with a physician discussing an aspect of depression in sickle cell patients. 2 patients then share stories of how the conditions has impacted their friends and family. A patient then discusses how the disease can cause anxiety that impacts her daily life. Both physicians and patients discuss the impact of prognosis, and it is finished by talking about the III and Long Foundation, and a clip of a patient talking about what she would do if she didn't have sickle cell.

Conclusions: Sickle cell disease has impacts on a patient that are far deeper than blood. Patients often have concerns that impact their daily activities. Anxiety and depression can be common in this population, but is often not talked about. Hopefully this video can be used to educate both students and current healthcare professionals on the complexity of these patients. This video can teach that pain is not the only symptom of sickle cell disease, but is often the only thing people associate with the disease. Caring for a patient means not only checking levels and keeping symptoms in check, but making sure the patient is as healthy physically as they are mentally and emotionally. By educating those who care for these patients about how patients may feel, we can wish for a better understanding between professionals and patients, as well as a more holistic approach to care for this patient population.

PERCEPTION OR REALITY: PAIN AND SICKLE CELL VIDEO

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Background: In 2016, there were over 63,000 drug overdoses in the US, and almost 66% of these involved a prescription or illicit opioid. The increase in abuse of these drugs have led to caution on the side of physicians to prescribe them. Opioids are a common treatment for sickle cell patients, many of whom start at an early age. Although patients with sickle cell may be exposed to more risk factors for opioid misuse, rates of addiction do not appear to be above the general population. This finding however has not stopped sickle cell patients from being stigmatized as patients who seek opioids for non-medical reasons. This effect hurts patients, and decreases the trust in the patient-doctor relationship.

Methods: Sickle cell patients and physicians who work with sickle cell patients agreed and were consented to an interview about their condition, including a discussion on opioids, pain, and stigma around their prescriptions. The interview would cover specific topics, but patients were allowed elaborate or skip topics if desired. Once interviews were conducted, they were analyzed, noting times whenever a topic changed, and what the topic was. Some of these notes were then organized into a proposed order, and clips were edited together using Adobe Premiere, with audio edits made with Adobe Audition.

Results: The resultant video is 8 minutes and 33 seconds, titled “Perception or Reality? Pain and Sickle Cell” (link: https://youtu.be/MtudEs5JWQ0) video starts with 2 clips describing a pain in sickle cell. This leads to a patient, then a doctor, state that race still plays a role in the medical field, and how it can affect the health of an individual. The explanation of the fear patients have of being a drug seeker is discussed by 3 patients over the next few minutes. This is partially interrupted by physicians elaborating on how opioid legislation has affected the patient population, leading to an increase in this fear. The video ends with a patient discussing how to better the opioid conversation between a patient and doctor, followed by a physician emphasizing that when in doubt, believe the patient.

Conclusions: In addition to the pain many patients struggle with, they must now worry about the possibility of being labeled a drug seeker. To better the patient-doctor relationship, physicians must be sure to use a kind tone, encourage dialogue between healthcare professionals and those they care for, and believe the patient when there is no outstanding reason not to. This video could help educate current and future healthcare professionals on the issues sickle cell patients face. Incorporation not only into hospital resources, but into classrooms of students could lead to change of perception of both opioids and sickle cell. By spreading awareness about the stigma sickle cell patients receive in relation to their medications, we can aim to reduce it.

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VASCULAR ACCESS COMPLICATIONS IN SICKLE CELL DISEASE PATIENTS ON RENAL REPLACEMENT THERAPY: EXPERIENCE AT A SINGLE INSTITUTION

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Background: Sickle cell nephropathy is common in sickle cell disease (SCD) patients. Some patients develop end stage renal disease (ESRD) and require renal replacement therapy. SCD patients are more likely to have difficult vascular access and subsequent complications including infection and thrombosis. The goal of our study is to identify complications associated with vascular access needed for renal replacement therapy.

Methods: : We performed a retrospective chart review of SCD patients at Ohio State University Wexner Medical Center from 2009 to 2019 to identify patients with ESRD. Electronic medical records were reviewed and clinical and laboratory data was collected and stored in a secure database. SCD was defined based on hemoglobinopathy evaluation and ESRD identified as patients with need for renal replacement therapy.

Results: 432 SCD patients were identified at our institution the past ten years. Eleven patients (64% male, 73% Genotype SS, 18% Genotype SC, 9% Genotype S-Beta 0 Thalassemia disease) met criteria for SCD and ESRD. All patients started on hemodialysis. The median age at time of dialysis was 37 (age range 20-64). Nine out of eleven patients (81%) had seen an outpatient nephrologist before initiating dialysis. Ten out of eleven patients (91%) started dialysis with a tunneled dialysis catheter. The most common complication of dialysis catheters was infection (50%). Other complications associated with dialysis catheters include thrombus (20%) with one patient developing SVC syndrome as a result, bleeding (20%) and accidental removal of catheter (20%). One patient has had a dialysis catheter for more than a year and has declined fistula or graft when recommended. All other patients have had a fistula or graft. Complications associated with arteriovenous fistulas include stenosis (3), hematoma (2), infection (2), fistula not maturing (2) and steal syndrome (1). Patients who had arteriovenous grafts had stenosis (2), infection (2), thrombosis (1), steal syndrome (1), hematoma (1) and retained graft (1). One patient was transitioned to peritoneal dialysis but returned to hemodialysis after about 27 months due to peritonitis and adhesions. In addition, one patient in our cohort received a renal transplant and is doing well ten years post-transplant. Six out of eleven patients (55%) were deceased at time of chart review. The average time spent on dialysis before death was 54 months (range: 27 months to 130 months).

Conclusions: Over a ten year period, 11 sickle cell disease patients had renal replacement therapy at our institution. Every patient had a vascular access complication, and ten out of eleven patients initiated dialysis with a tunneled catheter rather than an established permanent Conference Abstract vascular access. In this population, vascular access complications are particularly common. More information is needed to develop strategies to establish and manage vascular access for ESRD in SCD patients.

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DELINEATING MECHANISMS INVOLVED IN HYDROXYUREA-MEDIATED REDUCTION IN RED-CELL ENDOTHELIAL INTERACTIONS IN SICKLE CELL DISEASE

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Vaso-occlusion is the hallmark of sickle cell disease (SCD) resulting in severe pain, multi-organ dysfunction, and increased mortality. Sickle red blood cells (SSRBCs) contribute to VOEs by participating in a series of adhesive events mediated by cell surface adhesion molecules elevated in the SCD microenvironment. Hydroxyurea (HU), the standard of care for SCD management, reduces VOEs, in part, by reducing adhesion receptor expression and red cell-endothelial interactions however these mechanisms are not well defined. Very late antigen-4 (VLA-4), the most characterized adhesion receptor in SCD, is well characterized in supporting avid interactions between SSRBC and endothelial vascular cell adhesion molecule-1 (VCAM-1), as well as, SSRBCs and white blood cells. VLA-4 exists in multiple activation states and is functionally regulated by rapid, cell signaling pathways to activate ligand binding. We have demonstrated that HU modulates VLA-4-mediated adhesion in whole blood samples collected from pediatric SCD patients, within minutes, suggesting rapid, erythroid signaling pathways may be involved. Ongoing studies will utilize flow cytometric approaches to determine the activation status of VLA-4 on SSRBCs from SCD patients on/off HU therapy using a conformation sensitive antibody against VLA-4. Flow adhesion assays will be run in parallel. These studies are aimed at establishing the relationship between VLA-4 activity and binding affinity in SSRBCs in response to hydroxyurea therapy. .

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NOVEL APPROACH TO IDENTIFY THERAPEUTIC TARGETS THAT REDUCE ADHESION-MEDIATED VASO-OCCLUSIVE EPISODES IN SICKLE CELL DISEASE

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Red blood cell (RBC) adhesion contributes to morbidity and mortality in sickle cell disease (SCD) by causing frequent and unpredictable vaso-occlusive episodes (VOEs). Hydroxyurea (HU), the mainstay therapy for SCD, reduces the frequency of VOEs, in part, by decreasing adhesion receptor expression and red cell-endothelial interactions. Very late antigen-4 (VLA-4), the most characterized adhesion receptor in SCD, is highly expressed on reticulocytes (immature RBCs) from SCD patients with frequent VOEs and decreased in HU-treated patients. VLA-4-dependent adhesive interactions are rapidly and reversibly modulated by cell signaling pathways in white blood cells and other inflammatory diseases however these mechanisms are not well defined in RBCs or SCD. Preliminary data from our lab indicate that VLA-4-mediated adhesion is decreased within minutes of HU treatment, suggesting rapid, erythroid cell signaling pathways may be involved. Using mass spectrometry (MS), we identified a novel approach to elucidate HU- and erythroid-signaling pathways that modulate VLA-4 function in sickle reticulocytes to aid in the development of alternative therapies to reduce VOEs in SCD. Post-acquisition analysis of raw MS data will identify VLA-4 protein interactions in SCD patients on/off HU therapy.

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TRANSFUSION TRANSMITTED INFECTION (TTI) SCREENING IN CHRONICALLY TRANSFUSED ADULTS WITH SICKLE CELL DISEASE

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Background: Sickle cell disease (SCD) patients maintained on chronic transfusion therapy (CTT) are exposed to a large volume of blood products. Early identification of transfusion transmitted infections (TTIs) including HIV, Hepatitis B (HBV) and Hepatitis C (HCV) is important. This study was conducted to determine the current status of screening for TTIs in SCD patients on CTT in the Adult Sickle Cell Center and to determine the prevalence of HBV immunity.

Methods: A retrospective study was conducted to assess TTI screening status. TTI status was determined using 4th Generation ELISA for HIV, Enzyme-Immuno Assay for anti-HCV antibody for HCV and EIA for HBsAg for HBV infections. HBV immunity was determined by the presence of Anti-HBs antibody titres by Immunometric assay.

Results: The study included 144 patients. The median age was 32 years (IQR 20-66) and 47% were males. No one was screened annually, and 116 patients (80.5%) were screened for HIV, 102 patients (70.3%) for HCV and 85 patients (59%) for HBV infections at least once in the study period. Of those screened, 4 patients were newly diagnosed with HCV infection, 1 patient with HBV infection and none with HIV infection. Only 59 patients were tested for anti-HBs antibody titres, and 28(47.4%) did not have protective titres against HBV.

Conclusions: Despite low screening rates, the incidence rates of new HCV and HBV infections were high in this cohort, which warrants a screening protocol for TTI. Low rates of immunity against HBV infection suggests the need for an improved vaccination strategy.

TABLE 1: Baseline Characteristics for the participants included in this study (N=144)

Sl. No.	Characteristics	All patients (N=144)
1.	Age	34.97 ± 12.16
2.	Sex (M:F)	62 : 82 (43%:56.9%)
3.	African- American (%)	131 (97%)
4.	Duration of chronic transfusion 1 year 2 years 3 years 4 years ≥5 years	 43 (29.86%) 12 (8.33%) 16 (11.1%) 18 (12.5%) 55 (38.19%)
5.	Average number of pRBC units received per month < 2 units 3-8 units > 8 units	 39 (27.08%) 79 (54.86%) 26 (18.05%)

TABLE 2: Screening and test results for HIV, HBV and HCV among the participants(N=144)

Sl. No.	Tested for	Tested at least once during the study period		Tested any time before the study period		Never tested
		No. tested	Positive	No. tested	Positive	
1.	HIV	116 (80.5%)	0	14 (9.7%)	2	14 (9.7%)
2.	HCV	102 (70.8%)	4	26 (18.05%)	2	16 (11.1%)
3.	HBV (HBsAg)	85 (59.02%)	1	30 (20.8%)	0	29 (20.13%)
4.	HBV (Anti-HBc)	58 (40.2%)	5	24 (16.6%)	1	62 (43.05%)

Figure 1: No. of patients screened for the TTIs at least once in the last 5 years (n=144)

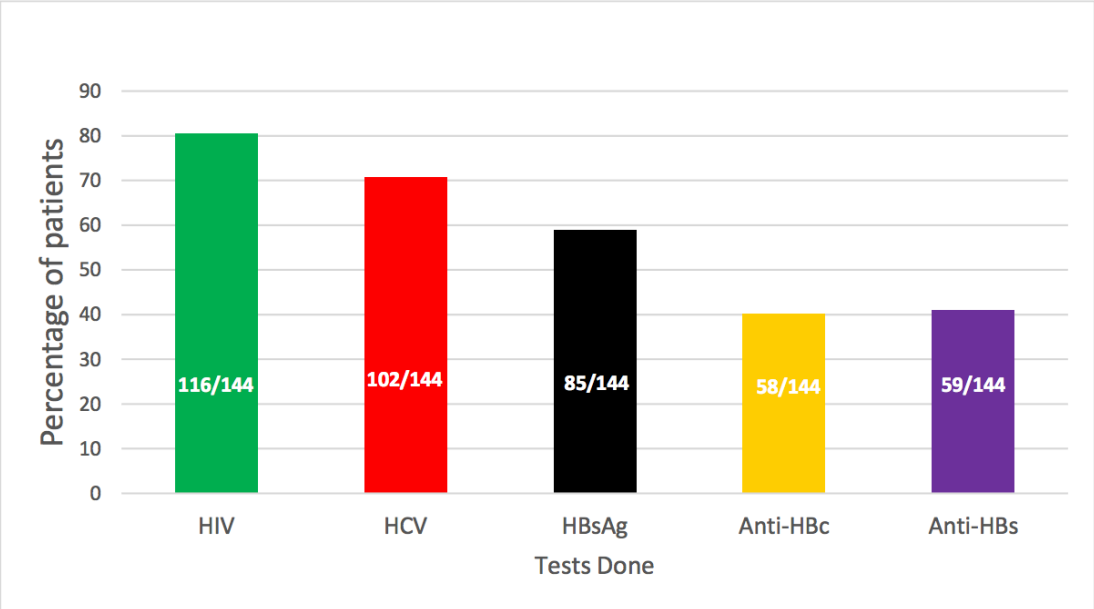
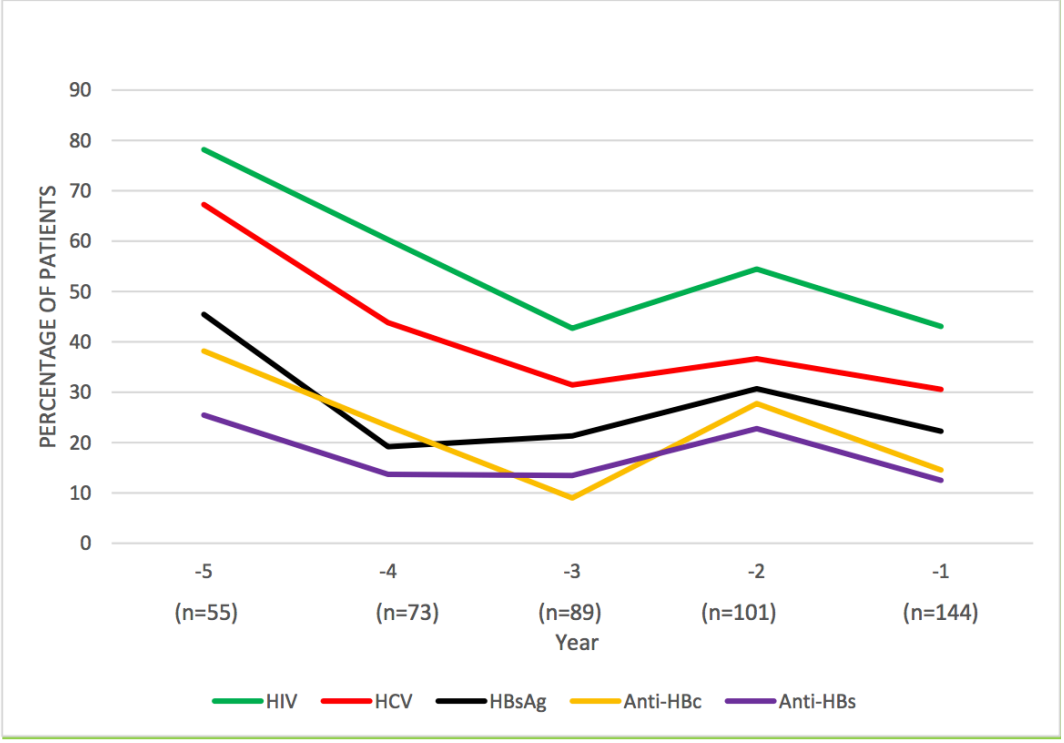


Figure 2: Trends of testing for the TTIs in the last 5 years (n=144)



IMMUNIZATION KNOWLEDGE AND BELIEFS OF CAREGIVERS OF CHILDREN WITH SICKLE CELL DISEASE

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Background: Sickle cell disease (SCD) is a genetic blood disorder affecting red blood cells. One potential complication of children with SCD is overwhelming sepsis, which may result in death. As a result, immunizations are one of the most impactful preventive measures available to children with SCD. The National Heart Lung and Blood Institute has implemented evidence-based recommendations for immunizations, along with the US Advisory Committee on Immunization Practices (ACIP) that has developed pneumococcal and meningococcal vaccine schedules. It is also recommended children with SCD have annual influenza vaccines. Despite these recommendations, it is believed that large percentages of children are not up-to-date with immunizations, and there is growing attention to parent/caregiver refusal of vaccines due to "vaccine hesitancy." The overall purpose of this project is to collect data about the caregiver beliefs, attitudes and knowledge about immunizations for children with SCD.

Methods: A survey was administrated to collect parent/caregiver demographics, along with the administration of a modified version of the validated Parent Attitudes about Childhood Vaccines Survey (PACV), to explore caregiver beliefs, attitudes and knowledge about immunizations. The IRB approved study was administered in a pediatric sickle cell clinic and patient education event. Inclusion criteria included all English-speaking caregivers of children with any SCD genotype, ages newborn – 18 years old. Responses were collected and entered into REDCap.

Results: Eighty-five caregivers have completed the survey to date: mothers (67%), fathers (26%) and grandmothers (6%). The majority had a GED/high school diploma (27%), college diploma (27%), or had completed some college classes (20%); while 12% had a 9th -10th grade education. The mean parent age was 39.4 years old, while the mean patient age was 9.5 years old. The majority of the children have hemoglobin SS (67%); hemoglobin SC (24%), sickle beta plus thalassemia (3.7%) and sickle beta zero (3%). The majority of caregivers (80%) report clear understanding of the importance of immunizations for their child with SCD, but only 40% strongly agree that an influenza shot is both safe and necessary for their child with SCD. Despite those concerns, 70% of caregivers make sure their child has an influenza shot annually and nearly 60% agree that the flu can be serious for children with SCD. One possible barrier to the flu shot is that over 30% of the caregivers are unsure if children with SCD are more likely to get the flu than other children and only 50% of caregivers feel that the flu vaccine is effective at preventing the flu. Nearly half of the caregivers were unsure whether a vaccine made from a live weakened virus is more effective than a vaccine made from a dead virus, and 40% would be concerned if the flu vaccine was made from a live, weakened virus. Only a small percentage (less than 5%) were concerned the influenza vaccine may cause autism, but 10% were concerned the flu vaccine may cause other chronic diseases, such as asthma. Moreover, 40% of caregivers believe there is a high chance of side effects from the flu vaccine. Regarding patient education, 60% of caregivers trust the information they receive from their healthcare providers about immunizations, and 80% feel they can openly discuss their vaccine concerns with their child's healthcare provider. More than half of the caregivers feel many of the illnesses that Conference Abstract immunizations prevent are severe. Less than 10% of caregivers feel that it is better for their child to develop immunity to illnesses by getting sick, rather than getting an immunization

Conclusions: Preliminary data shows that the majority of caregivers of children with SCD believe that immunizations, including influenza shots, are necessary for preventing complications as well as their child's well-being. The majority of caregivers trust the educational information that they receive from their healthcare providers. In the next phase of the study, immunization adherence rates will be analyzed in order to identify factors that may be correlated to acceptance or hesitancy of immunizations. An electronic medical record review will be conducted to assess if the child is up-to-date on the recommended, age appropriate vaccination scheduled for children with SCD. The study will also be expanded to two additional clinical sites.

30 YEARS OF NEWBORN SCREENING FOR HEMOGLOBINOPATHIES IN OHIO

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Background: Since March 1990, all infants born in Ohio are mandated to be tested with newborn bloodspot screenings for sickle cell disease (SCD), sickle cell trait (SCT), and other hemoglobinopathies. The primary purpose of is to identify infants with SCD in order to initiate penicillin prophylaxis, which substantially reduces mortality from pneumococcal sepsis. The landmark penicillin study by Dr. Marilyn Gaston in Cincinnati in the 1980's, led to a partnership with the Ohio Department of Health (ODH) to begin newborn screening (NBS). The ODH funds a regional network of six sickle cell projects based in pediatric hospitals (Cincinnati, Dayton, Columbus, and Akron) and community-based agencies (Toledo and Cleveland). Projects are funded to provide coordination and follow-up of abnormal NBS results; hemoglobinopathy counseling for patients and families; referrals to specialized medical teams, and outreach education activities for healthcare providers and the public. The ODH Public Health Laboratory notifies the sickle cell programs of all presumptive positive abnormal hemoglobin results for follow-up services in partnership with the newborn's physician of record. In recognition of the 30th anniversary of newborn screening for hemoglobinopathies in Ohio, a retrospective data analysis was done to analyze trends

Methods: NBS was obtained from the Ohio Public Laboratory. Due to changes in data systems over time, only data from the last nine years was analyzed.

Results: From 2010 - 2019, there have been 1,247,232 babies tested in the NBS program; with 31,694 newborns having an abnormal hemoglobinopathy alert; 30,528 of those cases having presumed hemoglobin trait. There were 1,168 newborns with a presumed hemoglobin disease alert: (361 presumed cases of hemoglobin SS; 185 presumed cases of hemoglobin SC; and 61 cases of sickle beta thalassemia). Lost to follow-up for presumed disease cases was less than 3%, including babies that expired.

Conclusions: The ODH Newborn Screening Program is a complex system that provides diagnosis of hemoglobinpathies, particularly to ensure newborns with SCD receive early intervention with appropriate medical care and enables confirmatory testing of SCT to ensure that unusual or unstable hemoglobin variants are detected. As a next step, further analysis of this data will identify other trends, such as growing incidence in outlying areas, which will provide the opportunity to use targeted strategies to educate healthcare providers and general public, about hemoglobin disorders.

HOW COMFORTABLE ARE MEDICAL RESIDENTS WITH TREATING SICKLE CELL DISEASE?

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Background: Sickle cell disease (SCD) occurs due to an inherited defect in the hemoglobin betaglobin subunit that causes an alteration in erythrocyte morphology leading to aggregation. It is clinically characterized by hemolytic anemia, end organ damage, and chronic pain syndromes. Given the challenges of its clinical syndrome, resource limitations, and inconsistent training in SCD management, medical management of this patient population is widely considered to be suboptimal. The purpose of this investigation was to identify the specific challenges of SCD treatment among medical residents (MR) at an institution with a large SCD patient population and how MR confidence with SCD management changed over the course of their graduate medical training

Methods: This investigation was undertaken at a suburban 214 bed community hospital south of Chicago, Illinois that experiences >100 admissions related to acute SCD crises annually. A written survey was provided to MR from postgraduate years (PGY) 1 to 3 and asked respondents to quantify the number of SCD patients they had treated thus far in their training. Comfort with current medical management practices among respondents was assessed by having them rank their comfort level (CL) on a 0 to 10 scale where 0 represented no confidence and 10 represented maximal comfort with medically managing one of the four investigated facets (general SCD management, pain management, inpatient SCD management, and patient controlled analgesia pumps (PCA)) of SCD-related care. Respondents were also asked whether the terms “sickler” and “frequent flyer” held a positive, negative, or neutral connotation when referring There were a total of 27 respondents, all of whom were currently enrolled in either an internal medicine, family medicine, or emergency medicine residency. 55.5% of respondents were in their first year of training, 25.9% were in their second year, and 18.1% were in their third year. The mean number of SCD patients treated by PGY-1 residents was 2.07 (STD: 1.07), 6.85 (STD: 4.01) for the PGY-2 respondents, and 5.6 (STD: 4.16) for the PGY-3 respondents. Among PGY1 respondents, 57.1% reported that the terms “sickler” and “frequent flyers” represented neutral categorizations of patients while 42.9% reported that this terminology carried a negative connotation. Among PGY-2 respondents, 71.4% believed that this terminology was negative while 14.3% characterized these terms as neutral. Within the PGY-3 respondent subpopulation, 50.0% thought that the terminology carried a negative connotation while 50.0% thought it represented a neutral characterization of patients.

Table 1: Comfort levels with sickle cell disease care among medical residents

	Comfort level with treating SCD (STD)	Comfort level with pain management (e.g. IV narcotics) (STD)	Comfort level with inpatient management of SCD (STD)	Comfort with level patient controlled analgesia (STD)	Composite Score (MCCI)	Comfort with treating SCD/ MCCI (%)
PGY-1	7.00 (2.56)	4.87 (2.62)	4.33 (2.35)	2.67 (2.38)	18.87	37.10
PGY-2	6.29 (1.38)	5.71 (1.89)	6.00 (0.58)	1.86 (1.07)	19.86	31.66
PGY-3	8.00 (0.70)	8.00 (1.00)	8.00 (0.71)	3.80 (2.78)	27.80	20.14

CL for the investigated parameters of SCD care are summarized in Table 1. CL for pain management and inpatient SCD management increased with each year of training while CL for general SCD management and PCA dipped in PGY-2 before increasing to their respective maximums in PGY-3. It is expected that residents will gain confidence with treating an increasing range of medical conditions as their medical training progresses. To this end, a mean composite comfort index (MCCI) was calculated for each PGY subpopulation whereby the mean CL for each clinical management survey question was added together. MCCI was found to increase as MR progressed through their training (Table 1). However, despite the increase in this composite index of comfort with every year of additional training, the relative contribution of comfort with treating SCD relative to the MCCI dwindled as residents progressed through their training (37.1% in PGY1, 31.7% in PGY-2, and 20.1% in PGY-3). Most respondents, independent of level of training, identified that differentiating between SCD or its complications and malingering represented a significant challenge. Respondents also noted that the lack of a protocolized approach to pain management also further complicated SCD patient management.

Conclusions: SCD treatment represents a persistent challenge to medical residents despite increased confidence in other areas of clinical medicine. Given these challenges, our institution has introduced a SCD care initiative to improve resident education, comfort with management, and patient outcomes.

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UTILIZATION OF EVIDENCE BASED ORDER SET IN THE INPATIENT CARE OF SICKLE CELL PATIENTS

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Background: Comprehensive sickle cell care is usually limited to academic centers and access to health care is very limited in the community setting. Often times sickle cell patients utilize acute care settings (emergency room, urgent care, hospitals) for sickle cell care. About 73% of primary care physicians believe that more education and support tools would help avoid complications in managing SCD. More than 80% of primary care physicians report feeling uncomfortable treating patients with SCD. The purpose of this study was to improve the quality of care in the management of hospitalized sickle cell patients. We hypothesize that utilizing an evidence based order set (EBOS) would help providers improve their clinical practice and hence enhanced care for acute complications of sickle cell .

Methods: This study was done at a community teaching hospital located in the south suburbs of Chicago with about 206 active beds. All sickle cell encounters were recorded between January 2018-December 2018. Data was collected on each patient to determine LOS, total actual charges, readmissions and initial care plan. An EBOS was implemented to help improve the quality of care for sickle cell patients at this institution. The EBOS specifically addressed the following: pain management with an emphasis on daily evaluation of pain needs and sedation scoring by nursing, hydration with recommendations of initial maintenance intravenous fluids (hypotonic solutions) in the first 24 hours with prompt reassessment in order to avoid fluid replacement related complications, incentive spirometer (IS) use every 2 hours and with narcotics along with documentation, utilization of 2 view x-rays with suspicion of respiratory pathology, venous thromboembolism prophylaxis, hydroxyurea continuation, and antipruritic therapies, and supportive care including bowel and anti-nausea regimen.

Results: There were a total of 124 admissions during 2018; 70 of these patients were admitted as inpatient status and 54 were in observation beds. Average length of stay for the inpatient group was 4.17 days. The observation group was generally discharged within 48 hours. The sum of total actual charges was $3,287,005.52. Average length of stay for all medicine patients at this facility was 4.58. Readmission rate among the sickle cell patients was 18.5%. All 124 patients were admitted through the ED for sickle cell pain episodes with the exception of one patient who was status post transplant and no longer had sickle cell related pain was admitted due to pneumonia. The most important finding from our study was that only about 24% (n=30) of the admitted patients received a routine incentive spirometer (IS) during their admission prior to EBOS implementation. Of these 30 patients only 20 had recorded IS use. Once the EBOS was implemented, if the primary provider utilized the EBOS every admitted patient received an IS and IS use was documented by nursing on a routine basis.

Conclusions: Implementation of the EBOS has helped standardize the care sickle cell patients receive at our facility. However, at present time we continue to struggle with physician compliance with Conference Abstract utilization of the EBOS. Only about 40% of our providers are utilizing EBOS for admission orders. Resident physicians were more likely to use EBOS compared to attendings. We continue to educate physicians at our facility regarding the EBOS and encourage its utilization. In the next phase of our project we hope to utilize physician and nursing education through grand rounds and case presentations to raise awareness regarding evidence based guidelines for management of sickle cell patients. Utilization of a standard protocol helps with consistency of care and helps improve the quality of care these patients receive during their hospitalization.

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Background: Sickle Cell Disease (SCD) is a blood disorder affecting over 1 million people globally. This analysis is to explore pain burden in SCD in 2 different geographical distinct populations: the United States and Africa (Ghana). The Consortium for the Advancement of Sickle Cell Research (CASiRe) was created to better understand the clinical severity of patients with sickle cell disease on a global scale. Within this study the validated Sickle Cell Pain Burden Interview (SCPBI) was used to assess the impact of pain on physical, emotional, and social function

Methods: The CASiRe database includes 6 sites in the U.S. (Univ. of Michigan, Rainbow Babies & Children's Hospital, Promedica Toledo Children's Hospital, Children's Hospital at Montefiore, Connecticut Children's Medical Center, Univ. of Connecticut Health Center), 2 in Ghana (Ghana Institute of Clinical Genetics, Pediatric SCD Clinic at Korle Bu Teaching Hospital), 2 in Italy (Univ. of Campania Luigi Vanvitelli, Univ. of Padua, Italy), and U.K.(Guys & St. Thomas Hospital, Evelina Children's Hosp). Between 2011 and 2017, after obtaining IRB approval at each site and written informed consent, demographic, clinical and laboratory data were collected by interviewing the patient and/or parent/guardian. This analysis includes only the 6 U.S. sites and the 2 Ghanaian sites. With existing IRB approved SCD registries data were abstracted directly from their respective databases. Descriptive statistics were performed on a subset of data that included: ethnicity, gender, genotype of SCD, prior medical diagnosis, and SCPBI. The validated SCPBI is comprised of seven items rated on a five-point Likert scale (total score 0= no pain burden, 28= highest pain burden), with higher scores indicating a greater impact of pain.

Results: We analyzed 298 patients; 97% were Black or African American, 36% resided in America, and 64% resided in Ghana. 41% of the cohort were men, while 59% of the cohort were women. There was no significant difference in pain burden between men and women in the entire cohort, p=.307. There was no significant difference in pain burden within the cohort across age groups, p=.842. The mean pain burden score for SCD patients in US was 6.53(±5.885), while the mean for patients in Ghana was 4.04(±5.100), p=.000. US men had a mean score of 6.74 (±5.68), while men from Ghana had a mean score of 3.54 (±4.46), p=.003. Women from US had a mean score of 6.37(±6.06), while women from Ghana had a mean score of 4.44 (±5.54), p=. 03. Across the entire cohort the mean score for patients with a mild SCD genotype of SCD was 3.55 (±5.079), while it was 5.36 (±5.575) for patients with a severe SCD genotype, p=.015. Geographical differences in pain burden were evident regardless of severity genotype, mild genotype patients from US vs. Ghana (5.40 (±5.29), v. 2.82 (±4.86) p=.054); severe genotype US vs. Ghana (6.79 (±6.012), vs. 4.49 (±5.13), p = .003). Pain burden across Conference Abstract the cohort is significantly higher in those patients with the following co-morbidities: History of Stroke, Asthma, Depression, than those without these conditions.

Conclusions: The SCPBI is a simple validated pain assessment tool which is feasible to administer in a variety of settings which can be incorporated into routine clinical care. US patients with SCD have a higher pain burden when compared to patients from Ghana. Further study should clarify the underlying contributors to pain burden in these populations and understand the etiology of geographic differences in pain.

MULTIDISCIPLINARY QUALITY IMPROVEMENT INTERVENTION TO DECREASE LENGTH OF STAY FOR ADULTS WITH SICKLE CELL DISEASE

Authors: Justin West, BSN, RN; Dale Wright, MS, RN; Daniel Sop, MS, Wally Smith, MD

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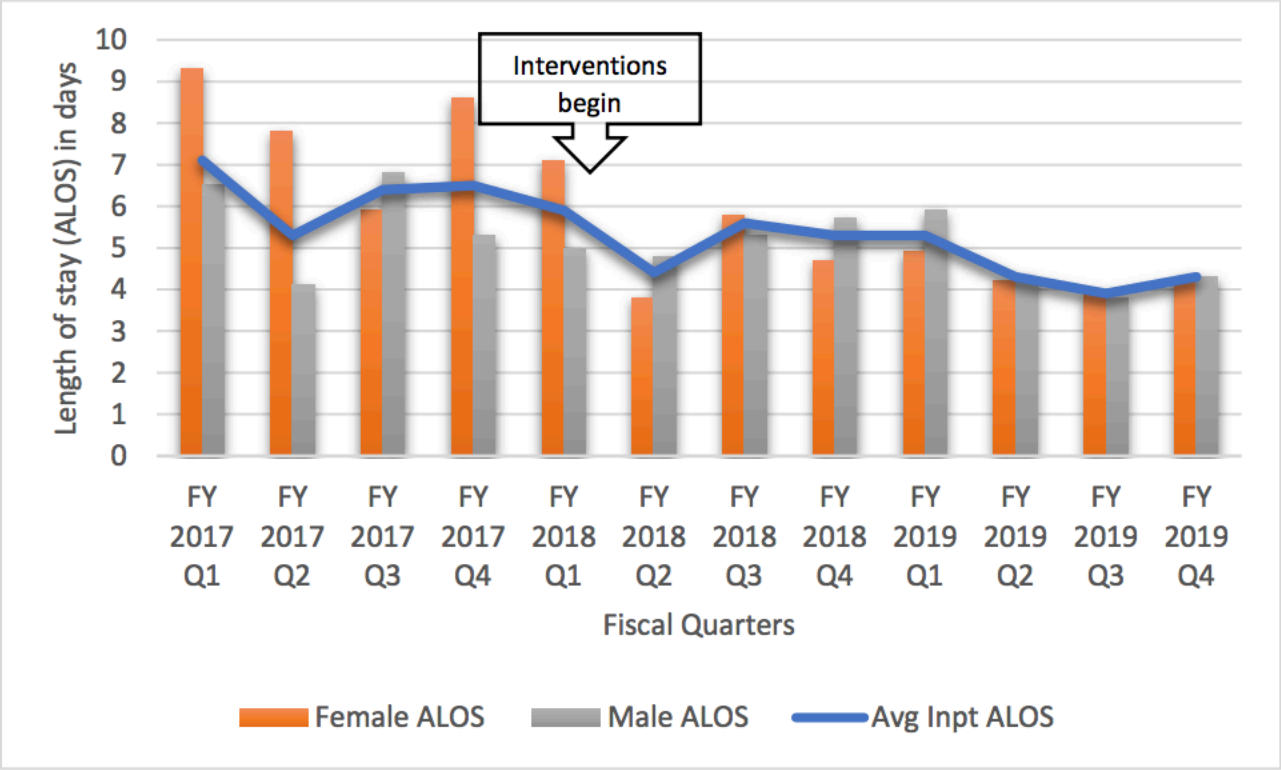
Background: Patients with sickle cell disease (SCD) face many barriers when hospitalized for vaso-occlusive crisis, including provider bias and lack of specialized education that can lead to mistrust and inconsistencies in care. In addition, hospitalized patients with SCD are also at heightened risk of life-threatening complications such as venous thromboembolism and acute chest due to reduced mobility and pain or opioid-induced hypoventilation. At an urban academic medical center, an increasing average length of stay (ALOS) well above the national average of approximately 5 days for inpatient admissions related to SCD prompted a project to reduce ALOS and improve quality of care for inpatients with SCD.

Methods: The intervention utilized the Plan-Do-Study-Act cycle method, at Virginia Commonwealth University Medical Center. The patient population consisted of adults age 18 or older admitted to a single adult inpatient hospital nursing unit to the hospitalist medicine team for SCD vaso-occlusive crisis and acute chest syndrome. Early in fiscal year 2018 (FY18), an environmental scan by an interprofessional team of hospitalist physicians, nurse practitioners, pharmacists, and nurses from bedside and management roles revealed a lack of consistency and structure to care for SCD inpatients, The planning team anecdotally observed frequent disagreements and conflicts between nurses, providers, and patients regarding opioid dosing, readiness for discharge, and perceptions of attitudes of care. The team met on a regular basis to identify, develop, and evaluate evidence-based interventions to improve quality and consistency for SCD-related admissions. Nurses on the unit were given education on SCD, discussing pathophysiology and highlighting potential complications and common misconceptions. Patients were also individually counseled on the rationale for the changes being made. A nursing care plan was drafted and revised iteratively through Plan-Do-Study-Act cycles. The care plan included checklists for nurses to complete on admission and then on a daily basis, emphasizing the encouragement of the use of incentive spirometry and mobility goals to reduce the risk of acute chest and venous thromboembolism. Also, additional patients, including some who were identified as high utilizers, were specifically targeted to the pilot unit for increased cohorting of patients with SCD. The team performed a retrospective analysis of internal VCU admissions/discharge/transfer claims data to review ALOS before, during, and after the intervention period.

Results: There were a total of 185 SCD-related admissions on the pilot unit in the nursingfocused intervention period of FY18 (46% female, 54% male). As a percentage of total adult inpatient sickle cell-related admissions on hospitalist/ internal medicine services (26.3%), this was an increase from FY17 (20.4%). Due to encouraging results and further interventions, sickle cell inpatient cohorting on this unit increased to 45% in FY19. Average ALOS on the unit decreased from 6.3 days in FY17 (7.5 days for females, 5.6 days for males) in the preintervention period to 5.3 days in FY18 (negligible gender difference). Compared to the ALOS for SCD-related adult admissions on other units in the hospital, the decrease was more significant (a decrease of 1 day on the intervention unit versus 0.37 days for the other units combined). Conference Abstract Limitations: This quality improvement project occurred on a single inpatient nursing unit without a control group, at a single academic medical center.

Discussion: The one day decrease in average ALOS observed was likely due in part to the culture change that occurred over the course of the year for nurses as well as the patients. The nursing care plan improved structure, accountability, and consistency while also encouraging regular communication with patients and providers. In addition, the resulting increased awareness from nursing and trust from patients helped pave the way for further initiatives to improve inpatient sickle cell care such as the Tiered Oral Therapy Protocol implemented during the following year that led to additional reductions in ALOS.

Conclusions: In one academic medical center on one nursing unit, length of stay, percentages of admissions, and attitudes about quality of care for SCD were each improved via a multidisciplinary team intervention.


Length of stay (ALOS) in days
10
9
8
7
6
5
4
3
2
1
0
Interventions begin
FY 2017 Q1
FY 2017 Q2
FY 2017 Q3
FY 2017 Q4
FY 2018 Q1
FY 2018 Q2
FY 2018 Q3
FY 2018 Q4
FY 2019 Q1
FY 2019 Q2
FY 2019 Q3
FY 2019 Q4
Fiscal Quarters
Female ALOS
Male ALOS
Avg Inpt ALOS

SICKLE CELL PAIN: INTERVENTION WITH CAPSAICIN EXPOSURE (SPICE)

Authors: Alexander Glaros, MD, Michael U. Callaghan, MD, Ahmar U. Zaidi, MD

Affiliations: Detroit Medical Center

Background: Pain is the most common of many potential complications of sickle cell disease (SCD), and unfortunately is the most stigmatizing in the current social climate. The opioid crisis has made it increasingly difficult for people with SCD to obtain much needed relief from this debilitating sequela that can be acute or chronic, and nociceptive or neuropathic in nature. Alternative therapies are therefore needed, especially for chronic and neuropathic pain, for which treatment with opioids is not always effective. Topical capsaicin for neuropathic pain relief in adults has been studied extensively, but it has not been investigated for SCD-related pain. We describe our safety and feasibility investigation of high dose (8%) topical capsaicin for the treatment of neuropathic pain in children with SCD. The primary objective was to assess drug safety. Secondary objectives were to assess the feasibility and optimal utilization strategy of various measures of neuropathic and chronic pain states, and to obtain preliminary efficacy data based on those measures.

Methods: Eligible participants were patients between ages 14-21 years with SCD and reported symptoms of neuropathic pain. 7 visits were planned at 6 week intervals over 9 months. During each visit, mechanical quantitative sensory testing (QST) was conducted using an electronic von Frey instrument (Bioseb Instruments) at a control site (thenar eminence) and the two most common sites of vaso-occlusive pain as reported at enrollment. Additionally, participants completed the PainDETECT® pain questionnaire (Pfizer) for assessment of neuropathic pain. After testing during visits 1, 3, and 5 an 8% capsaicin patch was applied to the previously established most common site of pain following pretreatment with 5% topical lidocaine. Safety was evaluated via analysis of adverse events both in real time and retrospectively at study completion, with a plan to suspend study activities for CTCAE grade 3 or greater adverse events attributable to the drug. Efficacy was primarily evaluated by improvement in mechanical pain threshold at the site of most frequent pain (treated with capsaicin) relative to the 2nd most common site of pain (not treated). Trends in PainDetect scores also contributed to a preliminary understanding of capsaicin efficacy.

Results: Planned enrollment of 10 participants (5 male, 5 female) was completed within 8 weeks after 13 patients were approached about the study. To date, 8 participants have completed visits 1-5, and 4 have completed visit 6. There have been no CTCAE grade 3 adverse events attributable to capsaicin. One participant requested during her second patch application that the patch be removed early due to intolerance of the expected burning sensation during contact with the patch. She subsequently did not have the third patch applied at visit 5. All participants were informed at enrollment of the likelihood of this side effect, which was nearly universal among participants but generally well tolerated. The other 9 participants completed all planned study activities and felt the second patch application caused less discomfort. Subjectively, 6 participants felt after 2 treatments that the treated area was no longer their most common site of pain, and this was supported by more objective measures. The average difference in pain threshold as measured by QST between the two painful sites (QSTTreated - QSTuntreated) was used to Conference Abstract evaluate a beneficial effect of capsaicin. This difference from visit 1 to visit 5 changed from -31.94g to +13.75g over the first 5 visits for an average improvement in pain threshold at the treated site relative to the untreated site of +45.7g (p=0.05) (Fig. 1), indicating that by visit 5 the threshold was higher at the treated site than the untreated site, a reversal from visit 1.

Conclusions: An interim analysis of data from our ongoing pilot study indicates 8% topical capsaicin is a safe and feasible treatment for children with SCD. The data indicates this therapy may be efficacious in ameliorating neuropathic pain for this population and warrants further investigation in a follow-up efficacy study, the planning of which is underway.

Figure 1.

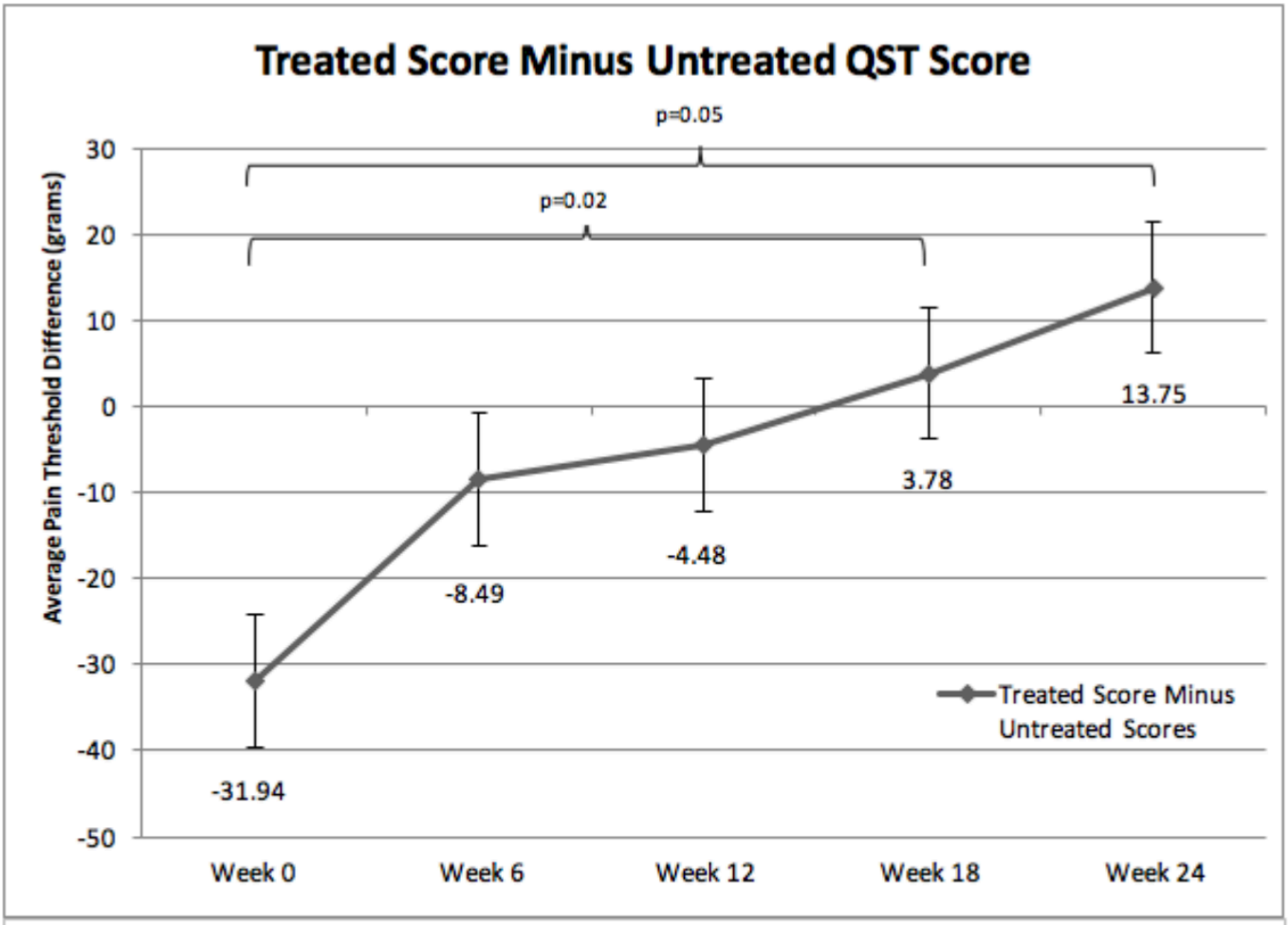


Figure 1. Difference in pain threshold by mechanical quantitative sensory testing (QST) between the most common and second most common sites of vaso-occlusive pain at time of enrollment, as indicated by participant report. Most common site of pain at enrollment was treated with high dose (8%) capsaicin after QST measurement at weeks 0, 12, and 24. Trend indicates an overall improvement in pain threshold at the treated area with an average improvement in pain threshold differential from Week 0 to Week 18 of 35.7g (p = 0.02), and from Week 0 to Week 24 of 45.7g (p=0.05). Of note, week 24 data was available for only 8/10 participants at time of abstract submission.

ANALYSIS OF HYDROXYUREA IMPLEMENTATION IN A PEDIATRIC SICKLE CELL PROGRAM OVER A TENYEAR PERIOD

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Background: The benefits of Hydroxyurea (HU) in sickle cell disease (SCD) have been well demonstrated in multiinstitutional adult and pediatric studies. However, HU usage in community practices has not been uniform.

Objective: Demonstrate the feasibility and report on the effectiveness of hydroxyurea implementation in a community pediatric hematology practice.

Methods: In October 2011, the Center for Cancer and Blood Disorders of Northern Virginia initiated a program to place all patients with genetically severe forms of SCD age 9 months and older on HU. A longitudinal database tracked clinical status and outcomes. Data were analyzed for a total of 10 years in 2-year periods from 2011-13, 2013-2015, and again for 2018-19, using data from 2009-2011 as historical controls. Patient outcomes included total hemoglobin (Hgb), fetal hemoglobin (Hgb F), hospitalization rate, treat-and-release ED visits, and transfusion rates

Results: Data are presented for patients with Hgb SS, HgbS/beta0 thalassemia, HgbSOArab, Hgb SCHarlem, ranging in age from infancy to young adulthood in the mid-20s, excluding those on chronic transfusions. Cohort size increased over time, with 86 in 2011, 109 in 2013, 130 in 2015, and 147 in 2019. The male/female ratio was consistent from 1.2 to 1.3. HU usage rate increased from 33% in 2011 to 93% in 2019. From the beginning of the HU program in 2011 to 2019, average Hgb increased from 8.3g/dL to 9.9g/dL ($p<0.01$)(Table 1). The percentage of patients with Hgb > 9g/dL rose from 23% to 72% ($p<0.01$) (Graph 1). Average Hgb F increased from 13% to 26.2% (Table 1). The percentage of patients with Hgb F > 20% was 27.6% in 2011 and 70% in 2019 ($p<0.01$), while those with Hgb F > 30% increased from 6.6% to 42% (Graph 2). Hospitalizations decreased 3-fold from 0.77 admissions/person-year in 2009-2011 to 0.26 admissions/person-year in 2018-19 ($p<0.01$) (Graph 3), and the percentage of patients with no hospitalizations in a two-year period increased from 43% to 74% ($p<0.01$) (Table 2). While 15/86 (17%) patients were on chronic transfusions in 2009-2011, the rate decreased to 4/153 (3%) by 2019 (Table 2). Patients who received any sporadic transfusion in a 2-yr period decreased from 38% to 5% ($p<0.01$) (Table 2). There was no significant change in the rate of treat-and-release ED visits, which remained approximately 0.6/person-year (Table 2).

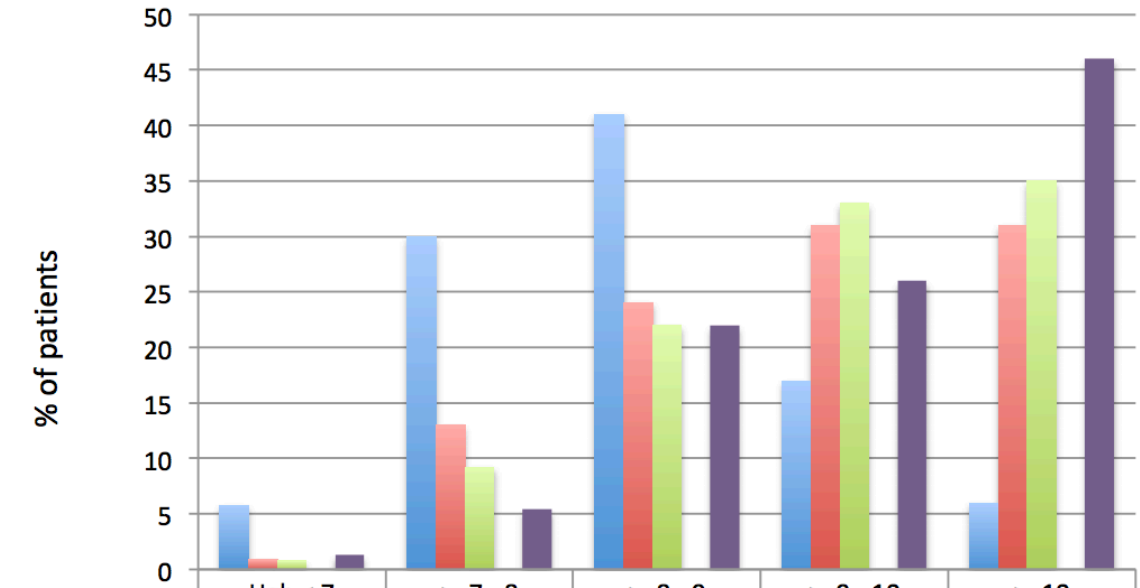
Conclusions: Rigorous HU prescription and enforcement in a pediatric community hematology sickle cell program led to HU usage rate of approximately 80% after 2 years and 90% after 8 years. Hgb, HgbF, hospitalizations, and transfusion rates improved significantly within the initial 2 years and continued to improve over the subsequent 6 years, resulting in a majority of patients having Hgb > 9, Hgb F > 20%, needing no hospitalizations and receiving no transfusions.

Table 1 Average Hgb and Hgb F

	2011		2013		2015		2019	
	HU elig SCA* n=86	taking HU n=28	HU elig SCA n=109	taking HU n=86	HU elig SCA n=130	taking HU n=107	HU elig SCA n=147	taking HU n=136
average Hgb ± stdev	8.3 ± 0.98	8.9 ± 0.76	9.4 ± 1.3	9.5 ± 1.2	9.5 ± 1.3	9.7 ± 1.2	9.8 ± 1.3	9.9 ± 1.3
average Hgb F ± stdev	13 ± 8.7	18.2 ± 8.3	24.3 ± 9.0	25.2 ± 9.4	24.0 ± 9.5	25.4 ± 8.5	26.2 ± 10	27.5 ± 9.1

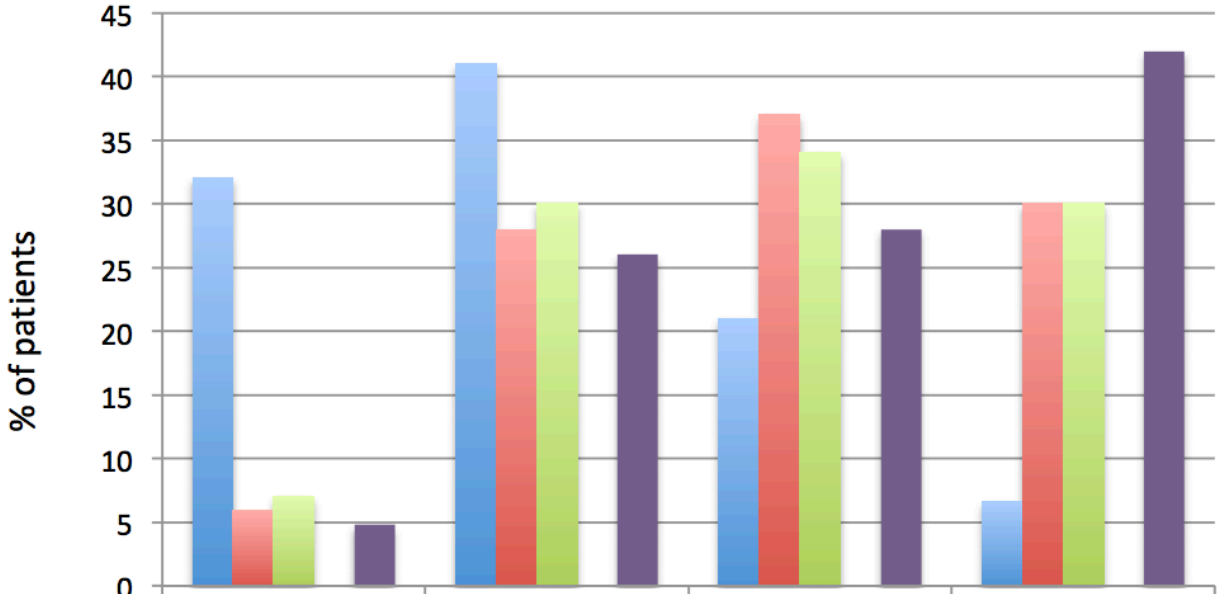
- HU elig SCA: Patients with sickle cell anemia, defined as a genetically severe form of sickle cell disease, including Hgb SS, Sbeta0, SC-Harlem, SO-Arab, who are age ≥ 9 months and not on chronic transfusions, therefore are eligible for HU.

Graph 1 Percent of Patients at each Hemoglobin level



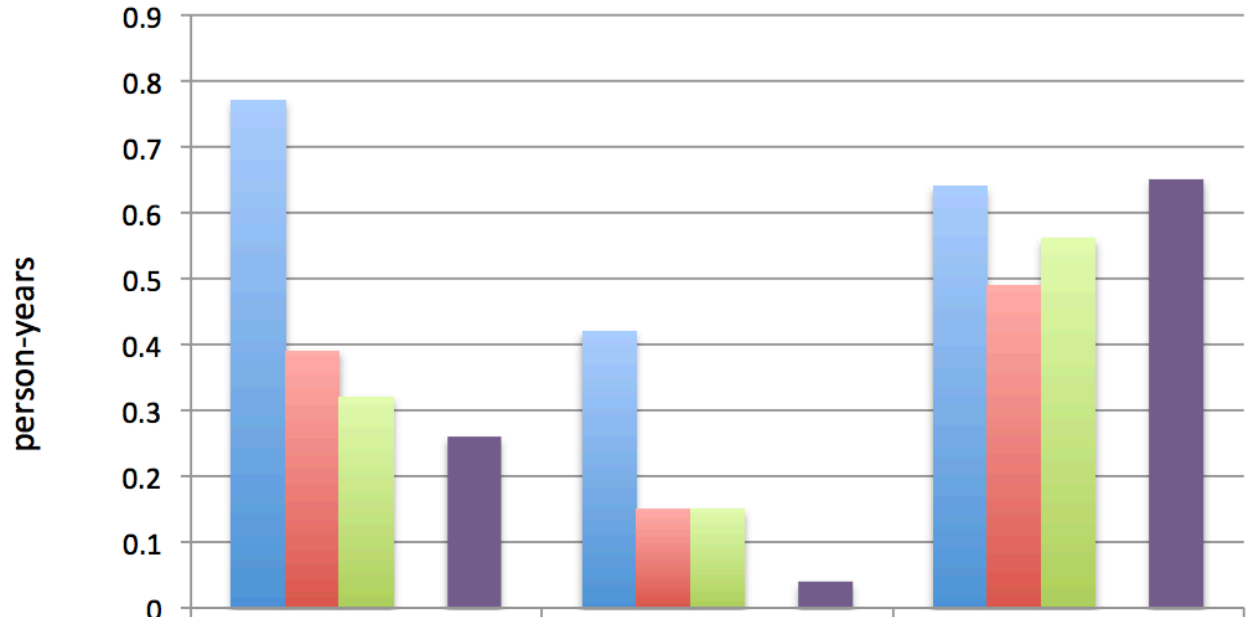
	Hgb < 7	>=7 - 8	>=8 - 9	>=9 - 10	>=10
2011 (n=86)	5.8	30	41	17	6
2013 (n=109)	0.9	13	24	31	31
2015 (n=130)	0.77	9.2	22	33	35
2019 (n=147)	1.34	5.4	22	26	46

Graph 2 Percent of Patients at each Hemoglobin F level



	Hgb F<10%	>=10-20%	>=20-30%	>=30%
2011 (n=76)	32	41	21	6.6
2013 (n=101)	5.9	28	37	30
2015 (n=128)	7	30	34	30
2019 (n=147)	4.8	26	28	42

Graph 3 Hospitalization, transfusion, and ED visit rates



	Hospitalizations	Transfusions (sporadic)	ED (treat-and-release)
2011 (n=86)	0.77	0.42	0.64
2013 (n=109)	0.39	0.15	0.49
2015 (n=130)	0.32	0.15	0.56
2019 (n=147)	0.26	0.04	0.65

Table 2 Percent of patients with no hospitalizations, no transfusions, no ED visits, and on chronic transfusions

% patients with	2011 n= 86	2013 n=109	2015 n=130	2019 n=147
No hospitalizations	43%	57%	63%	74%
No sporadic transfusions	62%	75%	82%	95%
No ED visits	51%	50%	48%	44%
Chronic transfusions	17%	14%	9%	3%

JSCDH-D-20-00053

PHASE 1 SINGLE (SAD) AND MULTIPLE ASCENDING DOSE (MAD) STUDY OF THE SAFETY, PHARMACOKINETICS (PK) AND PHARMACODYNAMICS (PD) OF FT-4202, A PKR-ACTIVATOR, IN HEALTHY AND SICKLE CELL DISEASE SUBJECTS

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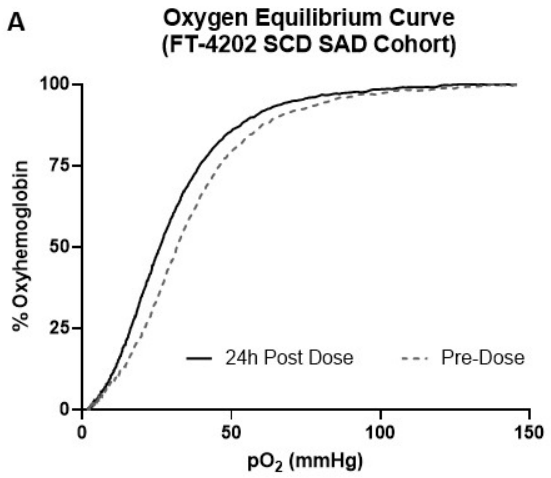
Background: The hallmark of sickle cell disease (SCD) is hemoglobin S (HbS) polymerization upon deoxygenation, resulting in red blood cell (RBC) sickling and subsequent oxidative/membrane damage, hemolysis, inflammation and vasoocclusions. Exacerbating the pathogenesis of SCD, the HbS RBC has 1) increased (↑) 2,3-DPG with decreased (↓) oxygen affinity (↑ p50) and 2) ↓ RBC ATP. FT-4202 is a novel, small molecule allosteric activator of erythrocyte pyruvate kinase (PKR) and functions as an RBC metabolic modulator causing ↓ 2,3- DPG and ↑ ATP levels in RBC. A first-in-human Phase 1 study evaluating FT-4202 in healthy subjects (HS) and subjects with SCD has been initiated [NCT03815695]. The aims of this study are to evaluate the safety and PK/PD of FT-4202 in healthy and SCD subjects

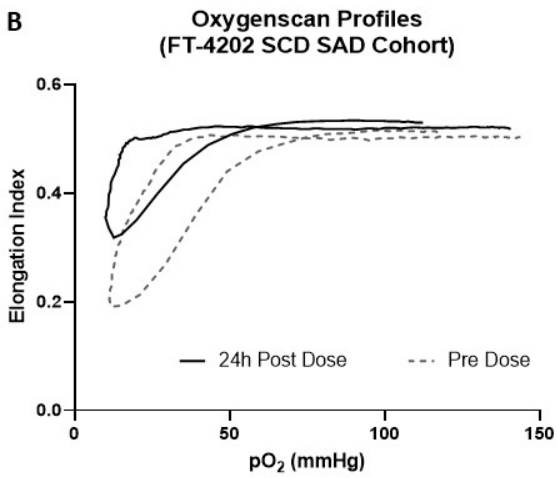
Methods: In this study, SAD/MAD cohorts are randomized (3 to 1) to receive FT-4202 or placebo (P). FT-4202 was evaluated first in four healthy SAD cohorts and four healthy MAD (14-day dosing period) cohorts. Based on the safety, and PK/PD profile from HS, FT-4202 is then evaluated in one SCD SAD cohort and 2 SCD MAD cohorts. Safety assessments include adverse events (AEs), vital signs, ECGs and laboratory parameters. PK/PD blood sampling was performed on Day 1 (SAD/MAD) and Day 14 (MAD) and up to 72h after the last dose. PD parameters included 2,3-DPG, ATP, and p50 in all cohorts with additional PD studies (including oxygen scan) performed only in the SCD cohorts.

Results: To date, FT-4202 has been evaluated in the HS SAD/MAD/Food Effect cohorts (n=90) and in the SCD SAD cohort (n=6). In HS studies, FT-4202 was well tolerated with Grade 1 headache as the most common AE reported in HS receiving a single dose (4%) or 14 days (28%) of FT-4202 and in 1/6 SCD subjects receiving FT-4202/P (blinded). The PK profile of FT-4202 was similar in HS and SCD subjects. FT-4202 was rapidly absorbed with a median Tmax of 1h post-dose, a T1/2 of ~10-13h, and an AUC0-24 ~7000 h.ng/mL. In the HS studies, the PD activity of FT-4202 was observed at all dose levels after 24h (↓ 2,3-DPG, $p<0.0001$) and after Conference Abstract 14-days (↑ ATP $p<0.0001$) of dosing. The biologic consequence of this PD response was an increase in oxygen affinity (↓ p50, $p<0.0001$) within 24h of FT-4202 dosing and a decrease in absolute reticulocyte counts ($p<0.0001$) with a slight increase in hemoglobin levels (ns) by Day 4 of the dosing period in all FT-4202 dose cohorts. Biologic activity has been observed in SCD subjects receiving a single dose of FT-4202, demonstrating the PKR enzyme in the SCD RBC is functional and responds to an allosteric PKR activator. Figure 1 shows the effects of FT-4202 on a SCD subject's RBCs, 24h after FT-4202 dosing. 1A: Increased oxygen affinity of HbS, similar to HbA; 1B: A left shift in the point of sickling (PoS) with an increase in the EImin. The median change in p50 and PoS in all FT-4202 treated SCD subjects are provided.

Conclusions: FT-4202 has a favorable safety profile and has demonstrated PD activity after a single dose or after multiple daily doses in HS. Early single dose studies in SCD subjects show an acceptable safety profile with evidence of PD activity translating into favorable biologic effects of increased oxygen affinity with a shift in the PoS to lower oxygen tensions and improved membrane deformability of sickle RBCs. 2-week SCD/MAD cohorts are ongoing to further evaluate the effects of FT-4202 on hemoglobin, inflammation and RBC metabolomics. A 12-week dosing cohort to further characterize the effects of chronic PKR-activation on the pathophysiology of SCD will be evaluated if the 2-week MAD studies are supportive.

Figure 1. FT-4202 Increases Oxygen Affinity and Decreases Point of Sickling (PoS) in SCD RBC's After a Single Dose





p50 (mmHg) Pre Dose	p50 (mmHg) 24h Post Dose
30.6 ± 1.8	25.9 ± 0.5

Median p50 ± SD (n > 3)

PoS (mmHg) Pre Dose	PoS (mmHg) 24h Post Dose
37.0 ± 3.3	26.8 ± 6.2

Median PoS ± SD (n > 3)

LEFT VENTRICULAR NON-COMPACTION IN SICKLE CELL DISEASE IN THE PEDIATRIC POPULATION

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Background: Left Ventricular Non-Compaction (LVNC) is a congenital cardiomyopathy resulting from the arrest of myocardial compaction during embryogenesis. It is frequently detected in young African American children with Sickle Cell Disease (SCD). We hypothesize that the non-compaction is a benign condition resulting from increased myocardial stress due to chronic anemia, rather than a true cardiomyopathy.

Methods: A retrospective chart review was performed in children with diagnosed SCD and echocardiography within the last 2 years. LVNC was diagnosed using the Jenni criteria and ratio>2.3 between compacted and non-compacted myocardial layers.

Results: 17 out of 52 children with SCD met the criteria of non-compaction syndrome. Of these, 40% were female, 60% were male and all 17 patients were African American. A decrease in the myocardial thickness from the posterior free wall to the apex in all of the patients was noted. Despite these findings, there were no signs of poor cardiac function.

Conclusions: LVNC leads to cardiac arrhythmias and mural thrombus formation [8]. Chronic anemia of SCD is associated with an increased left ventricular preload and a high cardiac output [4]. In this study, we sought to determine whether this increased preload plays a role in the development of LVNC. We report that 32.7% of children with SCD in our study population have features of Left Ventricular Hyper-Trabeculation (LVHT) on echocardiogram. When compared to 28% of adults with SCD who have evidence of LVHT, the percentage of affected children in our clinic is comparable. This lends to our hypothesis that LVHT may be an exaggerated physiological response to the increased LV preload [3], LV stress present from birth, and continues into adulthood. LVNC is a rare cause of sudden cardiac death in this population, however when discovered, this condition should be thoroughly investigated to prevent the long-term outcomes. A thorough family history of non-compaction is imperative in LVNC diagnosis. Meticulous testing involving a two-dimensional echocardiogram [10], cardiac MRI and LV angiography as well as monitoring of systolic and diastolic functions, LV dimension and chronological progression of the disease are integral components for a definitive diagnosis. Although there are rare cases of LVNC causing sudden death, the noncompaction seen in most of SCD cases is a benign condition resulting from increased myocardial stress due to chronic anemia, and not a true cardiomyopathy.

DEFINING AN "UNAFFILIATED PATIENT" FOR SICKLE CELL DISEASE HEALTHCARE INTERVENTION STUDIES IN THE US SICKLE CELL DISEASE IMPLEMENTATION CONSORTIUM

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***Affiliations**: (above)*

Background: Sickle cell disease (SCD) is a global health issue with recent rapid progress in therapy. Despite knowledge of how to help individuals with SCD, evidence-based guidelines are rarely followed in practice. Many individuals with SCD are not followed by SCD specialists or knowledgeable primary care physicians. The Sickle Cell Disease Implementation Consortium (SCDIC), founded in 2016 by the National Heart, Lung and Blood Institute, is a national consortium that uses implementation science to identify and address barriers to quality care in SCD. The SCDIC seeks to understand how and why patients become unaffiliated from SCD care and determine strategies to identify and connect these patients to care. A challenge with facilitating this work, however, is the lack of a definition for unaffiliated among experts or in the empirical literature. We hypothesized that, by using a systematic, consensus building process, an expert group of SCD providers could come to agreement about a definition of a person with SCD who is unaffiliated from SCD-specific care.

Methods: The Delphi process is an approach for arriving at group consensus by providing participants with rounds of questionnaires. Three rounds of questionnaires were distributed electronically and anonymously in 2019 to a group of SCD practitioners. Practitioners were asked to rate their agreement with a series of questions related to unaffiliation of SCD patients. Items reflected three primary domains: 1) duration of time since last medical visit; 2) the type of provider needed to be seen; and 3) what constitutes an expert provider. In subsequent rounds, group ratings were shared and respondents re-rated in the context of this new information. A consensus was defined as 80% or more of respondents agreeing on a given item.

Results: Twenty-eight SCD practitioners participated: 65% were SCD focused researchers, 60% were healthcare providers, 30% were working on developing SCD care guidelines, 68% spent greater than half their time caring for patients with SCD. After 3 rounds, 20-23 participants reached consensus on the following definitions. An unaffiliated patient was defined as "a person with SCD who has not been seen by a sickle cell specialist outside of the emergency department or urgent care setting in at least a year". A sickle cell specialist is someone who meets the following criteria: 1) knowledgeable of the 2014 NIH Guidelines "Evidence-based management of SCD; 2) trained in hydroxyurea management; 3) trained in management of blood transfusions; 4) trained on screening for organ damage in SCD; 5) aware of psychosocial and cognitive issues in sickle cell; 6) experienced in working with SCD patients; 7) trained in pain management and on sickle cell emergencies; 8) attends sickle cell disease conferences regularly; 9) mentored by an SCD specialist; and 10) obtains Continuing Medical Education every 2 years.

Conclusions: This study has strong implications for future research, practice, and policy related to SCD. From a research perspective, this work helps future researchers more specifically define unaffiliation so that interventions to connect these patients to specialized care are more effective. From a practice and policy perspective, this study yields numerous implications and directions for future work including: 1) how can we establish networks of providers to scale the reach of SCD experts (particularly in remote areas); 2) how do we support SCD specialist networks through improved payment plans (for third party payers); and 3) how can we support the dissemination of SCD-specific knowledge to assist in co-management with non-expert providers. This study lays the foundation for a breadth of work related to reconnecting patients with SCD to high quality care.

A PILOT PROGRAM OF STABILIZATION OF HOUSING AND CASE MANAGEMENT REDUCES HEALTHCARE UTILIZATION FOR HIGH-UTILIZING ADULTS WITH SICKLE CELL DISEASE

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Background: Adults with sickle cell disease (SCD) may face not only the biological ravages of their chronic illness, but also a plethora of adverse social determinants of health (SDoH), resulting in higher health care utilization. One often-overlooked SDoH in adults is homelessness or housing instability. Interventions to stabilize housing have been shown to lower utilization in veterans, substance misusers, and other vulnerable adults. We therefore hypothesized that eliminating housing instability would lower healthcare utilization among high-utilizing SCD adults.

Methods: Virginia Supportive Housing and the Adult Sickle Cell Medical Home at Virginia Commonwealth University collaborated to institute a pilot housing program in 2019 for five selected SCD adults enrolled in the Medical Home and assigned a patient navigator, each with unstable housing, high healthcare utilization, and possibly high opioid use or suspicion of opioid misuse or diversion. To be invited, patients either: 1) had been deemed homeless by Federal guidelines; 2) had reported that they were living temporarily with others and moving repeatedly (aka sofa surfing); 3)lived in a rooming house that could make it challenging to sustain medical adherence or safe storage of their opioids; 4) had been recently released from jail but had no support system or housing, or; 5) underwent medical or cognitive assessment leading to the conclusion that their current housing posed a physical or medical threat. We followed patients for a range of three to nine months. Medical care continued with the same providers during this period. Patient navigators met with and supported patients throughout their entry into and stay in the housing unit, and patients were the subject of weekly case management and care coordination meetings, visits from the patient navigators in their homes and assistance with other community services. Virginia Supportive Housing staff were tasked with developing individualized self-improvement, care transition, and housing transition plans for each patient, though VCU did not co-develop or monitor these. Reported utilization occurred within the VCU health system. Utilization data was collected for 5 months pre-program and 8 months post-program for each patient.

Results: Three men and two women agreed to enter the housing program (9 were invited). For these five patients, compared to 2017-18, total 2018-19 hospital charges decreased by 44%, and 3-day ED return rates decreased by 13%. Thirty-day readmission rates decreased by 74%. Inpatient average length of stay decreased by 25 %. Inpatient visits decreased by 34%. In contrast, ED visit return rates increased by 5.4 %. Total 2018 hospital days were 448 days, and total charges were $843,498.44. These decreased to 107 days and $319,257, respectively in 2019 after placement, for a Conference Abstract savings of $524,241. Anecdotally, patients self-reported increased wellness days, decreased opioid utilization and dependence, increased safety, and increased engagement in seeking or obtaining employment.

Limitations: This was a pilot program with a small number of carefully selected patients at one institution, for a limited time period.

Conclusions: Similar to results with other vulnerable populations, a pilot program featuring housing stabilization and intense case management reduced health care utilization and charges for 5 selected high-utilizing adults with SCD. Future studies should further test this intervention, and should develop a list of key learnings and best practices for housing programs in this population.

DECREASED UTILIZATION THROUGH STANDARDIZATION: A MULTI-INTERVENTION APPROACH TO MANAGING SICKLE CELL DISEASE IN THE EMERGENCY DEPARTMENT

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Background: Sickle cell disease (SCD) is a chronic progressive medical condition and patients who suffer from the disease may become high utilizers of both emergency department (ED) and inpatient hospital care. Several prior studies have investigated the impact of care plans on inpatient or emergency department lengths of stay. Our goal was to study the impact of a bundle of interventions on key inpatient and ED metrics.

Methods: Our institution is an urban academic facility with approximately 80,000 adult emergency department visits a year with approximately 3,000 of these being for SCD related complaints. Starting in July of 2018 a series of interventions were undertaken at our institution including the formation of an ED sickle cell committee, change in the triage process for sickle cell patients presenting to the emergency department, and implementation of comprehensive sickle cell pain treatment and disposition plans (created by the inpatient/ outpatient sickle cell team, for use in the emergency and inpatient settings). The triage process was designed to screen for life threats and allow initial management in the waiting room when bed space was not available. The comprehensive plans standardized pain medication routes and dosing across all ED and inpatient providers. The goal was to provide high-quality, timely, and consistent care for patients while reducing inpatient utilization. Data was collected for 24 months prior to implementation and we compared key metrics for the 19 months following the intervention. Key metrics included the average ED length of stay (LOS), admission rate, inpatient LOS, and rate of 72 hour returns to the ED. Statistics were descriptive and differences in means or proportions were generated with 95% confidence intervals.

Results: The mean age of patients presenting to the ED was 38 years old with approximately 58% being female. Prior to the interventions there were 3,352 ED visits by 681 patients. After the interventions, this number decreased to 2,518 visits among 659 patients (Table 1). There was a non-statistically significant increase in the length of stay in the emergency department from 2.3 to 2.5 hours (difference of 0.1 95%CI -0.1 to 0.4), but a statistically significant decrease in the inpatient length of stay from 137.3 hours to 107.9 hours (difference of -29.4 hours 95%CI -15.7 to -43.1 hours) (Table 2). In addition, while the percentage of patients returning to the ED within 72 hours increased from 14.1% to 17.7% (difference of 3.6% 95%CI 1.4% to 5.9%), the number of admissions from the ED to the hospital decreased from 19.3% to 15.2% (difference of -4.1% 95%CI -1.8% to -6.4%).

Conclusions: Following a multi-modal intervention involving formation of an ED sickle cell committee, revision of the triage algorithm for sickle cell patients, and implementation of patient specific care plans, there was a decrease in number of ED Conference Abstract visits, percentage of patients admitted to the hospital, and hospital LOS with a small increase in 72 hour returns to the ED.

Table 1: Demographics

	Pre-Intervention	Post-Intervention
Age in years, mean (SD)	38 (14)	38 (14)
Female n (proportion)	395 (58%)	389 (59%)
Total ED visits per year	3,352	2,518
Unique patients per year	681	659

Table 2: Key Metrics

	Pre-Intervention	Post-Intervention	Difference (95% CI)
ED length of stay, mean (hours)	2.3	2.5	0.1 (-0.1 to 0.4)
Admitted (%)	19.3%	15.2%	-4.1% (-1.8% to -6.4%)
Inpatient LOS, mean (hours)	137.3	107.9	-29.4 (-15.7 to -43.1)
ED returns within 72 hours of discharge (from ED or hospital)	14.1%	17.7%	3.6 (1.4% to 5.9%)

INTEGRATIVE SERVICES AND OUTCOMES FOR PATIENTS WITH SICKLE CELL DISEASE

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Background: Pain is the signature manifestation in sickle cell disease (SCD). Opioids are the current mainstay therapy for acute and/or chronic pain despite being associated with adverse effects including potential for tolerance, dependence and opioid induced hyperalgesia. Pain in SCD can span over an individuals' lifetime, therefore additional strategies are needed for pain control that can help minimize use of opioids. The CDC recommends using non-opioid, non-pharmacologic therapies for pain. There is a growing body of literature to support non-pharmacological therapy for pain management; however, there is a lack of evidence-based studies to support the use of these modalities in patients with sickle cell disease. The Integrative Sickle Cell Pain Clinic was launched at Children's National Hospital, after reviewing emerging beneficial data on integrative approaches and pain in non-SCD patient population. Results from our SCD family education symposium survey indicated interest in learning more about integrative therapies and non-pharmacological approaches for managing SCD related pain. This is a multidisciplinary clinic that provides a hematology visit, acupuncture, pain management, psychotherapy and counseling, physical therapy, aromatherapy, and healing touch. These services are offered to the patients during an admission for pain or by referral from their primary hematologist. The aim of this clinic is to empower patients to cope with pain and to give them access to non-pharmacologic means to treat their pain.

Objective: The primary goal of the study is to determine the experience and satisfaction of patients/ parents who have received integrative therapies for pain associated with SCD.

Methods: This study was approved by the Children's National Institutional Review Board. Patients seen in the integrative clinic were approached to participate in this study using questionnaires to evaluate their experience before and after alternative therapies. Written informed consent was obtained before the interventions.

Results: Thirty-seven patients have been seen in the Sickle Cell Integrative Pain Clinic in the past year. Twenty-four patients have been admitted for pain since being seen in the Integrative Clinic and 33% of the patients have requested integrative services during their admission. Patients who attend this clinic range in age from 11-22 years. The average age is 15.35, 67.5% were female and 8 of the patients have returned to the clinic 2-4 times over the past year. Twenty-six patients who attended clinic consented to participate in the study and completed surveys. Genotypes were; 57.69% with HbSS, 34.6% HbSC and 7.7% HbSβ0. The patients followed in clinic were admitted to the hospital an average of 2.4 times in the preceding month. Eighty percent of the patients were taking hydroxyurea (SCD disease modifying agent), and 65% of the patients were taking opioids (short or long acting). The pediatric pain screening tool suggested that 52 % of patients were at medium risk for developing chronic pain. Twenty one patients Conference Abstract completed a treatment satisfaction survey after attending integrative clinic or after receiving integrative therapies (i.e. acupuncture) while admitted to Children's National. Seventy-one percent of patients agree that integrative therapy was an acceptable way of treating adolescent's pain, and believed it was likely to be an effective treatment for sickle cell pain. The vast majority (90%) of the patients had a positive experience with the therapies.

Conclusions: We demonstrated that patients who attended our integrative clinic found these alternative methods to be an acceptable and effective way to treat their sickle cell pain. They expressed an overall positive experience. More studies are needed to provide scientific evidence for advocacy for reimbursement for integrative therapies.

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OCULAR MANIFESTATION OF SICKLE CELL DISEASE IN A TEENAGE MALE WITH HOMOZYGOUS SICKLE CELL DISEASE AND G6PD DEFICIENCY

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Background: Sickle Cell Disease (SCD) is one of the most common inherited blood disorders worldwide. A single point mutation in the beta globin chain leads to the formation of the abnormal sickle hemoglobin which results in clinical manifestations in multiple organs It is a complex disorder which affects the structure and function of hemoglobin, reduces the ability of red blood cells to transport oxygen and progresses to chronic vascular disease. Ocular manifestations of sickle cell disease may affect any vascular bed in the eye. Sickle cell retinopathy is the most significant and may be classified as proliferative or non-proliferative sickle cell retinopathy. This may lead to irreversible blindness in advanced stages secondary to vitreous hemorrhage or retinal detachment. Glucose-6-phosphate dehydrogenase deficiency is an X linked hemolytic anemia and occurs predominantly in the same ethnic groups that are affected by SCD, such as African American and Middle Eastern. We report the case of a 13-year-old male with sickle cell disease SS type and concomitant G6PD deficiency with retinopathy.

Methods: A retrospective review of the patient's records was conducted in February 2020.

Results: We report the case of a 13-year-old male with sickle cell SS disease, G6PD deficiency, status post cholecystectomy, splenectomy, and history of mild persistent asthma. The patient presented with blurred vision and flashes of light in the left eye. He noticed a grey halo surrounding objects. The vision change was associated with lightheadedness. No other neurological symptoms were reported. He denied any concurrent vaso-occlusive pain. The patient had a similar episode two years ago affecting his right eye. A brain magnetic resonance imaging (MRI) and head and neck magnetic resonance angiogram (MRA) showed signal abnormality in the right frontal periventricular white matter which was attributed to gliotic changes secondary to old infarcts. There were no acute vascular infarcts or hemorrhage. He was evaluated by a retina specialist and diagnosed with sludging in the optic vein and arterovenous crossing changes similar to those seen in hypertensive retinopathy. Visual acuity was tested by the Snellen eye chart and no acute change from baseline was found. Hemoglobin/hematocrit was 7.1 g/dl/ 20.2% and the reticulocyte count was 16.7%. His comprehensive metabolic panel was within normal limits except for a total serum bilirubin of 12 mg/dl and direct bilirubin of 0.41 mg/dl. The patient was hydrated and transfused. The hemoglobin and hematocrit post-transfusion were 9.0 g/dl and 26.2 %, respectively. His lightheadedness and vision changes in the left eye resolved during the admission. Brain MRI on admission showed no acute intracranial hemorrhage, territorial infarction, intracranial mass lesion, or acute hydrocephalus. The head and neck MRA on admission showed normal intracranial and cervical arterial vasculature, without hemodynamically significant stenosis, occlusion, or other abnormality. The fundoscopic examination did not reveal any abnormality in Conference Abstract the left retinal vessels or optic disc. Outpatient ophthalmology examination revealed mild AV crossing changes in the retinal blood vessels. The patient was discharged on hydroxyurea and folic acid supplementation. Chronic transfusion was recommended but declined by the family.

Conclusions: Early screening for sickle cell retinopathy is recommended to prevent progression of the disease. Patients with early-stage sickle cell retinopathy should be followed by a multidisciplinary team including pediatric hematology and pediatric ophthalmologist to optimize care. Red cell exchange transfusions are beneficial. Surgical options such as vitrectomy are also indicated in selective patients. New agents such as intravitreal Ranibizumab and Bevacizumab provide additional treatment options.

IMPACT OF SICKLE CELL DISEASE ON PATIENTS' DAILY LIVES IN THE US: RESULTS FROM THE SICKLE CELL WORLD ASSESSMENT SURVEY (SWAY)

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Background: Sickle cell disease (SCD) is the most common single-gene disorder, affecting amino acid composition of hemoglobin and shortening life expectancy. The Sickle Cell World Assessment Survey (SWAY) is a worldwide survey assessing the impact of SCD on the daily life of patients, including physical symptoms, emotional well-being, and school/work performance. Here, we describe the impact of SCD on pediatric and adult patients' daily lives in the United States (US). Understanding the burden of SCD on patients can inform management of the disease and improve quality of life.

Methods: SWAY was a cross-sectional survey of 2,145 SCD patients and 365 healthcare professionals (HCPs) across 16 countries. Here we present data from US pediatric (aged 6-17) and adult (aged ≥ 18) patients, who were recruited via their treating HCPs and patient association groups. The survey captured demographics, symptoms, impact Conference Abstract of disease and use of a caregiver, impact on work/finances/education, disease management/treatment approaches, and patient–physician relationship, with data collected using self-completed or proxy surveys, whereby a parent, guardian or caregiver completed the survey on the patient's behalf. Where relevant, questions include a 7-point severity scale for each statement; a score of 5–7 indicates 'high severity/impact'.

Results: The survey included 77 US SCD pediatric patients and 307 adult patients. 47% and 65% female respectively. A high impact on emotional well-being (60% pediatric vs 64% adult), family/social life (51% pediatric vs 53% adult) and relationship with other family members (45% pediatric vs 45% adult) was reported by patients. Impact on family/social life was considerably lower for the global sample (40% pediatric and 41% adult). Both pediatric and adult patients reported high impact in terms of frustration with having to endure their symptoms (60% and 79% respectively) and worry that their SCD will get worse (53% and 72% respectively). Patients reported avoidance of intense (70% pediatric and adult), moderate (49% pediatric vs 44% adult) and mild (48% pediatric vs 35% adult) physical activity. Avoidance of mild physical activity was considerably lower for the global sample (30% pediatric and 23% adult). Both pediatric and adults' patients reporting worrying about painful episodes when exercising (64% and 66% respectively). Other concerns during exercise include worry about exhaustion (60% pediatric vs 63% adult) and dehydration (53% pediatric vs 62% adult). A high impact on travel was reported with patients limiting long distance travel (42% pediatric vs 33% adult), walking (40% pediatric vs 42% adult), and travelling by airplane (40% pediatric vs 27% adult), although this was notably lower for adults. The majority (92%) of pediatric patients require some level of support for their daily activities due

to their SCD, predominantly provided by parents (77%). This is lower for adults (75%), support was mainly provided by parents (38%) and spouse/ partner (33%). Access to healthcare (73% pediatric vs 45% adult), transportation (73% pediatric vs 65% adult), and emotional (70% pediatric and adult) support are the leading types of help provided. Pediatric patients received an average of 23.0 hours (SD 29.6) help/support per week, this was higher for adults with an average of 28.6 hours (SD 35.2), although not statistically significant. 48% of pediatric patients received professional emotional support (e.g. psychiatrist, psychologist, counseling), this was lower for adults (41%), Nearly half of patients reported a desire to receive additional emotional support (47% pediatric and 48% adult respectively). Pediatric patients reported that SCD had a high impact on attendance (52%) and performance (51%) at school. Caregivers reported a predicted high impact (88%) on the patient's future transition to adulthood, this is considerably higher in comparison with the global sample (66%). Adult patients reported a high impact (50%) on career progression and patients missed an average of 7.4 hours work during the past 7 days, as a result of problems associated with their SCD.

Conclusions: The SWAY survey demonstrates the substantial impact of SCD on both pediatric and adult patients' daily lives, including emotional and physical well-being, relationships and academic/ professional development. Improved understanding of SCD burden can enhance patients' quality of life at home and achievement at school/work. Caregivers expressed concern with the process of pediatric patients' transition to adulthood, highlighting the need for enhanced transition research to improve health and key outcomes.

MANAGEMENT STRATEGIES AND SATISFACTION LEVELS IN PATIENTS WITH SICKLE CELL DISEASE IN THE US: RESULTS FROM THE SICKLE CELL WORLD ASSESSMENT SURVEY (SWAY)

Authors: Biree Andemariam(1) , John James(2) , Baba Inusa(3) , Fuad El Rassi(4) , Beverly Francis-Gibson(5) , Alecia Nero(6) , Caterina Minniti(7) , Cassandra Trimnell(8) , Miguel R. Abboud(9) , Jean-Benoît Arlet(10) , Raffaella Colombatti(11) , Suman Jain(12) , Wasil Jastaniah(13) , Laurie DeBonnett(14) , Ifeyinwa Osunkwo(15), Olivera Rajkovic-Hooley, PhD, Nicholas Ramscar

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Background: Sickle cell disease (SCD) is a complex genetic disorder affecting mainly people of African origin. A hallmark of SCD is vaso-occlusive crisis (VOC) – this event is acutely painful and the primary cause of hospitalization in SCD patients. VOCs can lead to life-threatening acute complications. SCD is also associated with chronic complications, increased risk of end organ damage and shortened life expectancy. Therefore, effective management and treatment strategies are essential to reduce burden of illness and lead to high quality of life for the patient. The SWAY survey assessed the treatment and management strategies used by US patients with SCD and assessed patient satisfaction levels.

Methods: : SWAY was a multi-country, cross-sectional survey of SCD patients and treating physicians. The survey, conducted online and in print, includes 6 categories: demographics, symptoms, impact of disease on patient and their caregiver, impact on work and finances, disease management/treatment approaches, and patient-physician relationship. Where relevant, questions include a 7-point severity scale for each statement; a score of 5–7 indicates 'high severity/impact'. Patient enrollment is via treating physicians and patient association groups

Results: The survey included 384 US SCD patients, 61% female, mean (SD) age 30.1 (13.4) years. When considering the main person responsible for SCD treatment and management, patients primarily reported management by an SCD specialist (72%). Most patients were satisfied with the frequency of interaction with their doctor (83%) and reported they are confident they are being assessed and treated properly (76%; based on high-impact scores 5–7). Accordingly, 75% of patients (scoring 5–7) reported sharing the same goals for SCD management and treatment as their doctor. The most common treatment goals for patients are to improve quality of life (53%) and prevent SCD worsening (42%). Patients reported receiving ongoing treatment with opioids (63%), folic acid (58%), over-the-counter pain medication (49%), anti-inflammatory medication (47%) and hydroxyurea (36%). 73% of patients have previously received surgery or a medical procedure to manage their SCD, with port placement (42%) and gall bladder removal (37%) being the most frequent. Although 72% of patients (scoring 5–7) indicated satisfaction with their treatments' control of their SCD, 66% of patients (scoring 5–7) report worrying about the long-term side effects of their treatment. The majority of patients, (76%) agreed (scoring 5–7) they would like an alternative treatment to their current pain management medication. The majority of patients (64%) reported high severity/impact of SCD on their overall emotional well-being. In the 12 months before survey completion, 2738 VOCs were reported (mean (SD) of 7.1 (5.7) VOCs per patient); 4% of patients experienced 0 VOCs, 38% experienced 1–4 VOCs and 59% experienced ≥5

VOCs. Of all VOCs, 52% of VOCs led to inpatient hospitalization, 22% were managed at home, 13% were treated in the emergency room, and 13% required a health care provider (HCP) visit. The main reasons that 3 patients chose to manage their VOCs at home include a previous poor experience at ER or hospital (50%), the perception that medical professionals do not understand SCD (32%) and the opinion that medical assistance was not required (26%). Selfmanagement of VOCs varied considerably by age. 91% of adult patients (aged 18+) managed by drinking fluids versus 59% of pediatrics (aged <18), while 89% adults did so with rest/sleep versus 69% pediatrics, 80% adults managed VOCs with opioidbased analgesia in comparison with 49% pediatrics.

Conclusions: The survey included 384 US SCD patients, 61% female, mean (SD) age 30.1 (13.4) years. When considering the main person responsible for SCD treatment and management, patients primarily reported management by an SCD specialist (72%). Most patients were satisfied with the frequency of interaction with their doctor (83%) and reported they are confident they are being assessed and treated properly (76%; based on high-impact scores 5–7). Accordingly, 75% of patients (scoring 5–7) reported sharing the same goals for SCD management and treatment as their doctor. The most common treatment goals for patients are to improve quality of life (53%) and prevent SCD worsening (42%). Patients reported receiving ongoing treatment with opioids (63%), folic acid (58%), over-the-counter pain medication (49%), antiinflammatory medication (47%) and hydroxyurea (36%). 73% of patients have previously received surgery or a medical procedure to manage their SCD, with port placement (42%) and gall bladder removal (37%) being the most frequent. Although 72% of patients (scoring 5–7) indicated satisfaction with their treatments' control of their SCD, 66% of patients (scoring 5–7) report worrying about the long-term side effects of their treatment. The majority of patients, (76%) agreed (scoring 5–7) they would like an alternative treatment to their current pain management medication. The majority of patients (64%) reported high severity/impact of SCD on their overall emotional well-being. In the 12 months before survey completion, 2738 VOCs were reported (mean (SD) of 7.1 (5.7) VOCs per patient); 4% of patients experienced 0 VOCs, 38% experienced 1–4 VOCs and 59% experienced ≥5 VOCs. Of all VOCs, 52% of VOCs led to inpatient hospitalization, 22% were managed at home, 13% were treated in the emergency room, and 13% required a health care provider (HCP) visit. The main reasons that 3 patients chose to manage their VOCs at home include a previous poor experience at ER or hospital (50%), the perception that medical professionals do not understand SCD (32%) and the opinion that medical assistance was not required (26%). Selfmanagement of VOCs varied considerably by age. 91% of adult patients (aged 18+) managed by drinking fluids versus 59% of pediatrics (aged <18), while 89% adults did so with rest/sleep versus 69% pediatrics, 80% adults managed VOCs with opioidbased analgesia in comparison with 49% pediatrics.

THE E-SELECTIN INHIBITOR GMI-1687 RESTORES NORMAL BLOOD FLOW IN A MOUSE MODEL OF SICKLE CELL VASO-OCCLUSION

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Background: In sickle cell disease (SCD), recurrent episodes of vaso-occlusive crisis (VOC) contribute to morbidity and accelerated mortality due primarily to ischemic irreversible end-organ damage. VOC, which is precipitated by inflammation, is due largely to sickle red blood cell (SS-RBC) adhesion in the vasculature. While both P-selectin and L-selectin likely contribute to the underlying inflammatory cascade leading to VOC, previous studies have shown that E-selectin expression on the vascular luminal surface appears to be crucial for adhesion of SS-RBC and leukocytes to the endothelium. GMI-1687 is an innovative potent E-selectin specific antagonist that demonstrates high bioavailability following subcutaneous (SC) administration. SC injection of GMI1687 shows significant activity in preclinical models previously reported for parenteral administration of uproleselan (GMI-1271), but at approximately 250-1000-fold lower dose. In the present investigation we report in vitro and in vivo studies evaluating the activity of GMI-1687 in a SCD mouse model of VOC.

Methods: To define KDs, the binding activity of GMI-1687 to selectins was assessed using microscale thermophoresis. An in vivo model of SCD was used where two hours post TNF[?] treatment, nude mice with dorsal skin-fold window chamber implants were infused with human SS-RBC. Adhesion to inflamed venules and development of VOC was recorded using intravital microscopy. The in vivo activity of E-selectin inhibition with GMI-1687 was assessed following intravenous (IV) and subcutaneous (SC) injection in the mouse model of SCD.

Results: The KD of GMI-1687 binding to E-selectin was 41 nM. In contrast, the KD of GMI-1687 binding to L-selectin was 750,000 nM, with no observable Pselectin binding (KD>10 mM). In vivo, beginning immediately after SS-RBC infusion (t0) and 30 minutes later (t30), mice were injected IV with saline or GMI1687 (20 [?]g/kg or 40 [?]g/kg). As expected, mice treated with saline alone showed marked adhesion of human SS-RBC to venules (56% and 61% occlusion of the total vessels recorded at t0 and t30, respectively) with evident blood stasis. In contrast, administration of GMI-1687 at 40 [?]g/kg had marked anti-SS-RBC adhesive activity (80% inhibition at both t0 and t30; p<0.0001 compared to control saline treatment), with only 4% of analyzed venules showing VOC. The reduction of SS-RBC adhesion obtained with GMI-1687 was doseConference Abstract dependent (42% inhibition at t30 with 20 [?]g/kg, p=0.0008 compared to control saline treatment), while the lack of observable occluded venules (2% with 20 [?]g/kg) was equivalent to the 40 [?]g/kg dose. As a result of reduced sickle cell adhesion and VOC, the number of circulating SS-RBC increased by approximately 10-fold and 16-fold in mice treated with two doses of 20 [?]g/kg and 40 [?]g/kg (p=0.03) GMI-1687, respectively. In a subsequent study, IV treatment with GMI-1687 was initiated 30 min post infusion of SS-RBC (t30) into TNFtreated mice, a time during which sickle cells are adherent to inflamed venules and VOC is established, and repeated 30 minutes later (t60). Under these conditions, GMI-1687 at 40 [?]g/kg significantly reversed SS-RBC adhesion and VOC at both t30 and t60 (p=0.002 and 0.0073, respectively, compared to saline treatment). This led to restoration of blood flow in 85% of the venules in GMI1687 treated mice vs. 18% of vessels with normal blood flow in the control saline treated group, and a 6-fold (p=0.0002) increase in the number of circulating human SS-RBC. We next assessed the activity of SC administration with 40 [?]g/kg GMI-1687 on human SS-RBC adhesion and development of VOC. Similar to the IV experiments, GMI-1687 initiated at t0 and t30 post SS-RBC infusion significantly reduced SS-RBC adhesion in inflamed vessels (69% reduction at t0, and 63% at t30,p=0.0001). The reduction in SS-RBC adhesion led to a lower incidence of VOC (2% compared to 30% of vessels in mice injected with saline), and a 5.1-fold improvement (p=0.0315) in the number of circulating human SSRBC. It is noteworthy that the effective dose of GMI-1687 used in these studies resulting in the restoration of normal blood flow was approximately 500-fold less than that reported for rivipansel.

Conclusions: These data demonstrate that the administration of the E-selectin specific compound

GMI-1687 was effective in restoring blood flow in a mouse model of SCD, and support the development of GMI-1687 as a SC treatment for VOC and potentially other inflammatory diseases where endothelial activation plays a central role.

ASSESSING CURRENT NONPHARMACOLOGIC PAIN MANAGEMENT PRACTICES IN ADULTS WITH SICKLE CELL DISEASE

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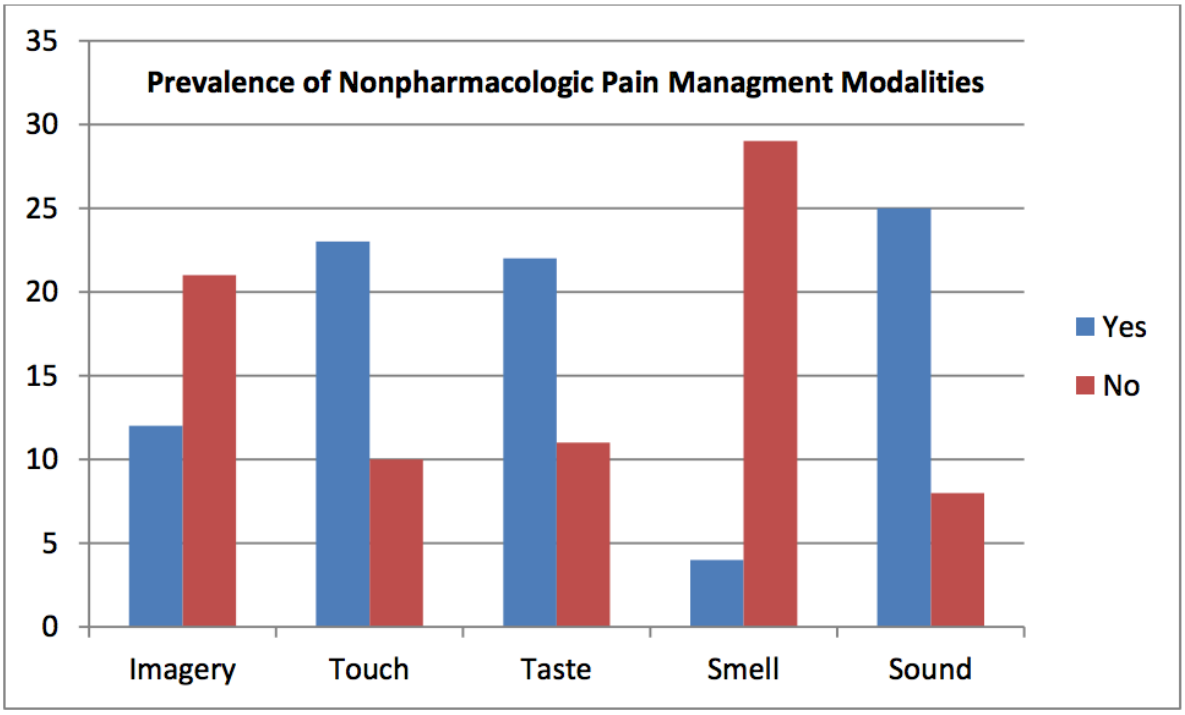
Background: Sickle cell disease, the most common inherited hemoglobinopathy, causes a spectrum of micro and macrovascular complications over the lifespan, most commonly pain. This pain can either be acute episodic called a vaso-occlusive crisis (VOC) or chronic pain, often daily and debilitating. The Pain in Sickle Cell Epidemiological Study (PiSCES) followed 232 patients with sickle cell disease and demonstrated chronic pain was even more common than acute pain (Smith, Penberthy, & al., 2008). Both acute and chronic pain, typically treated with opioid therapy due to a lack of other effective options, drive emergency department visits as well as subsequent hospitalizations. There is little evidence to support long-term effectiveness of chronic opioid therapy which conveys significant risks including hyperalgesia, and overdose (Carroll, 2019). Managing both the acute and chronic pain of SCD becomes a challenge that requires both pharmacologic and nonpharmacologic interventions. Some research suggests efficacy of peer-mentored group programs in managing pain in other chronic diseases. There is little research on current nonpharmacologic pain management practices among patients with sickle cell disease. Furthermore, it is not clear if patients desire a peer mediated group intervention for chronic pain. In order to evaluate current practices and assess interest in a peer mediated group, we conducted qualitative interviews with adult patients at the ChristianaCare Sickle Cell Program.

Methods: Participants were recruited during clinic visits at the Sickle Cell Program at the Center for Special Health Care Needs. All patients 18 years of age or older; with the following genotypes SS, SC, SB+, SB0 were eligible. After informed consent was obtained, research personnel conducted semi-structured interviews. Questions were both quantitative and qualitative, focusing on patients' nonpharmacologic pain management practices as well as their interest in a chronic pain self-management program. Interviews were recorded and then transcribed. Descriptive statistics were conducted to describe the frequencies of specific pain management modalities. For open-ended questions regarding pain description, pain triggers, and coping skills., qualitative analyses were conducted using NVIVO. Themes were identified with a modified grounded theory approach.

Results: Thirty-four interviews were completed. Participants were 39.4% male (13/33) and 60.6% female (20/33) and an average of 27.8 years old (19-55 years). Utilization of nonpharmacologic pain management techniques was common among participants, most commonly sound and taste, described as hydration. 81.8% of respondents (27/33) identified a connection between their stress levels and their pain. When assessing interest in a peer mediated intervention for chronic pain, 84.9% (28/33) were interested in participating, with 85.7% (24/28) wanting either an exclusively in person or mixed in-person and electronic modality. Additionally, 61.9% of respondents indicated a desire for the intervention to include peer moderators in addition to a medical professional. Themes for pain description were severe bone pain, sharp and shooting pain, and throbbing and aching body. External factors like cold weather and internal factors like dehydration were identified as pain triggers. Themes for coping skills included pharmacologic and nonpharmacologic methods. Pharmacologic methods included adhering to prescribed medications and taking over the counter supplements, such as Alka-Seltzer. Nonpharmacologic skills consisted of ways to stay warm and hydrated, like water consumption and hot showers, or mental approaches to coping like reflection and relaxation techniques. Additional analysis of the interviews is ongoing.



Conclusions: Patients with sickle cell disease already employ a variety of nonpharmacologic pain management techniques, but express significant interest in learning more about these techniques. Many patients are interested in participating in a group chronic pain intervention with peers as co-facilitators. Information included in such an intervention should be specific to sickle cell disease as well as culturally relevant, a curriculum which does not currently exist. Future research should continue to evaluate the prevalence and effectiveness of a variety of nonpharmacologic pain management techniques in order to improve quality of life and decrease acute care utilization.

CORESCD: DEVELOPING A CORE OUTCOME SET FOR CLINICAL TRIALS OF NEW SICKLE CELL DISEASE INTERVENTIONS

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Background: After decades of limited treatment options for individuals living with sickle cell disease (SCD), a much-needed surge in therapeutic innovation is currently underway. Encouraging developments include US Food and Drug Administration (FDA) approval of three new SCD therapies within the past three years. In addition, rapid advancement in gene therapy for SCD holds the promise of a cure. With multiple new therapies in the pipeline, the timing is ideal to determine how best to assess the impact of these new treatments. Alignment across experts and stakeholders is needed on which study outcomes are most important to patients, regulators, and payers to demonstrate the efficacy, comparative effectiveness, and value of therapies for SCD. Development and use of a core outcome set (COS) can help by serving as an agreed-upon minimum set of outcomes to be measured and reported in all clinical trials for SCD. Use of a COS allows for better-informed comparisons of treatment options and expedited treatment availability for patients. We used a structured, multi-stakeholder consensus process to identify two core sets of outcomes that should be used in trials of disease-modifying therapies and of acute interventions for SCD respectively.

Methods: The coreSCD COS were developed using a modified Delphi process that involved SCD patients and advocates, clinicians, payers and health technology assessors (HTA), regulators and other government representatives, and representatives from life science companies. A targeted literature review and environmental scan were used to create a candidate outcome list which was supplemented with stakeholder input. Following orientation and training, participants completed three rounds of online voting in which they rated each outcome on a scale of 1-9 (should not be included in COS to critical to include in COS). Outcomes were retained for further consideration if at least 70% of voters rated the outcome from 7-9. In the first two rounds of voting, outcomes were also retained if they were rated 7-9 by at least 70% of patients and advocates, even if this threshold was not reached for the group as a whole. The "patient-important" criterion was removed for the final round of voting and outcomes were only retained if they reached the 70% consensus threshold for the entire group. Following the second round of online voting, an in-person meeting of the Delphi participants was convened in Baltimore, MD in October 2019. This provided an opportunity for attendees to discuss the outcomes that remained on the list, sharing their perspectives and developing a better understanding of the views of other stakeholders prior to the final round of voting.

Results: Forty-two participants completed the Delphi voting process (11 patients/advocates, 9 clinicians/researchers, 9 HTA/payers, 3 government representatives, and 10 industry representatives). A decision was made prior to the first round of voting to create two separate core outcome sets – one for trials of disease-modifying therapies and one for trials of acute interventions. The initial survey included 85 outcomes for trials of disease-modifying Conference Abstract therapies and 36 outcomes for trials of acute interventions across five domains (Biomarkers, Physiological/Clinical, Functioning, Resource Use, and Mortality/Survival). Among other topics at the in-person meeting, there was discussion regarding the multiple pain outcomes that were retained for trials of disease-modifying therapies following the second round of voting (including pain frequency, pain intensity, pain duration, vaso-occlusive crisis, pain interference/impact, and chronic pain). The group agreed to include three outcomes related to acute sickle cell pain in the final voting round (frequency, intensity, and duration) as well as chronic pain. Of these four outcomes, only acute sickle cell pain frequency was retained in the final core set. The group also agreed that pain interference/impact is critical to include in SCD trials and recommend that this outcome be measured as part of health-related quality of life (HRQOL) assessments. Full results from the final round of the Delphi survey are currently under review and COS recommendations are pending.

Conclusions: If consistently used and reported, the coreSCD core sets can help to ensure a more useful body of evidence for newly developed and future SCD interventions, facilitating value assessments, comparisons, and systematic reviews based on stakeholder-relevant outcomes. This will result in a

stakeholder-important base of evidence to inform decision-making across the product lifecycle for regulatory approval, market access, and clinical use.

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A COMMUNITY BASED PARTICIPATORY RESEARCH APPROACH IN PRIORITIZING SELF-MANAGEMENT NEEDS FOR YOUNG ADULTS LIVING WITH SICKLE CELL DISEASE

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Background: Despite advances in healthcare, people with sickle cell disease (SCD), continue to experience health disparities, poor health outcomes, and limited access to care and resources. Young adulthood is a life-stage of increased vulnerability to morbidity and mortality for people with SCD. Challenges include loss of access to care, stigma, poor preparation for transition, and inadequate preparation for self-management. The purpose of this study was to use a Community Based Participatory Research (CBPR) approach to understand the prioritized areas of need from the perspectives of young adults living with SCD to improve their self-management. The CBPR approach allows the research to begin with a topic that is of significance to the community. Findings can be applied towards developing culturally relevant interventions with potential to build greater trust between researchers and communities and develop interventions that improve patient outcomes.

Methods: This Community-Based Participatory Research study was conducted in partnership with young adults living with SCD, parents of individuals with SCD, health professionals, and faith leaders to explore how sociocultural contexts impact self-management, and to identify and prioritize areas of need for interventions to promote self-management. We identified adults from the community by sharing a flyer with community organizations. Adults identified also shared the focus group information with other adults living with SCD of which some were enrolled. Data were collected through focus group interviews with young adults with SCD and community stakeholders.

Results: Fourteen young adults participated. All were African American with a mean age of 22.6 years (SD= 3.14) and 11 were female (79%). Two parents, two health professionals, and three faith leaders participated, and all were between the ages of 50 and 60 years of age. Through collaborative data-analysis and using the Sickle Cell Disease Transition Curriculum as a guide, three domains were identified as priority areas: Medical/ preventative care including complications, pain management, and mental health; Social including sexuality/reproduction, sickle cell awareness, and coping; and Academic which included college preparation and career readiness. During the fourth focus group, young adults finalized the topics for a six-week pilot support group that will be held at a central city faith-based setting within the community.

Conclusions: Knowledge of the priorities and context for those living with SCD is critical. Using a Community Based Participatory Research approach to develop, implement, and evaluate culturally relevant interventions can support self-management and improve patient outcomes for young adults living with SCD.

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RATE OF INFLUENZA VACCINATION IN PEDIATRIC SICKLE CELL PATIENTS FROM 2017-2019 AT ROBERT WOOD JOHNSON UNIVERSITY HOSPITAL

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Background: Children with sickle cell disease (SCD) are at high risk for influenza-related complications such as secondary bacterial infections with encapsulated organisms and acute chest syndrome, causing a rate of hospitalization 56 times higher than the healthy population. Despite widespread recommendations that these patients receive annual vaccination, reported immunization rates remain under 50%. Ensuring timely vaccination against influenza may decrease admission rates and duration of illness in these immunocompromised children.

Objectives: To measure rate of influenza vaccination in sickle cell patients at RWJUH (Robert Wood Johnson University Hospital) and Rutgers Cancer Institute of NJ (RCINJ) from 2017- 2019. The use of this data will hopefully propel utilization of the influenza vaccine administration in the outpatient setting.

Methods: We performed a multi-center (RWJUH and RCINJ) outcomes retrospective chart review study of 200 patients with sickle cell disease between the ages of 6 months to 21 years, generated from a list of eligible patients at Rutgers Cancer Institute of New Jersey. Between two flu seasons, August 1, 2017-March 31, 2019, investigators reviewed data from both inpatient and outpatient records to determine vaccination compliance and environment of administration (Inpatient administration vs. outpatient), while also collecting demographic such as age and sex.

Results: Ninety-three patients were documented as not receiving the vaccine. Ninety -four patients did receive the vaccine; the vast majority being given in the inpatient study. There were thirteen patients whose vaccination status could not be determined.

Conclusions: The findings in this study display show that approximately 50% of our patients with SCD are unvaccinated against influenza. Of note, the majority of patients that are vaccinated received the vaccine in the inpatient setting. During data collection, it was noticed that there seems to be limitations in both the inpatient and outpatient EMR regarding the documentation of both vaccination inquiry and details regarding environment of vaccination, date, and provider. Achieving appropriate vaccination compliance in children with SCD, especially on an outpatient basis, can reduce the monetary burden to both their families and medical system by reducing admission rates, length of stay, and complications. Previous studies have shown quality improvement measures, such as implementation of a vaccination database, can show significant improvement in vaccination rates. In further studies, we will be looking to implement and record the efficacy of these measures, especially in the outpatient setting.

THE ROLE OF A DEDICATED NURSE PRACTITIONER FOR ADULTS WITH SICKLE CELL DISEASE: INCORPORATING CONTINUITY OF CARE AND INTEGRATIVE SERVICES WITHIN A COMPREHENSIVE SICKLE CELL DISEASE TEAM

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Background: Individuals with sickle cell disease (SCD) that are admitted acutely for pain management require coordination of care due to the complexities of disease management. Inadequate pain control can lead to increased length of stay and/or increased readmission rates. Recent data suggest that one-third of adults with SCD admitted for an acute pain crisis had a readmission within 30 days. Among inpatient stays for adults with SCD, the mean length of stay was around 5 days 1 . The introduction of continuity of care throughout the outpatient and inpatient experience of care can improve patient care and lead to decreased length of stay and readmissions. The Inpatient SCD Continuity Nurse Practitioner (NP) provides care across the continuum, and serves to close the gap between inpatient providers and the outpatient clinic.

Methods: Beginning in January 2017, the Inpatient SCD Continuity NP provided consultations across the continuum of care for adults with SCD at a large Midwestern comprehensive cancer center, which included inpatient care, an outpatient clinic, and a day hospital for the management of acute pain. The Inpatient NP monitored frequent admissions to identify opportunities for interventions including developing care plans and incorporating strategies to manage pain such as palliative care consults, pain anesthesia consults for chronic pain, music therapy, art therapy, acupuncture, social work, and psychiatry. This service also ensured that patients who were failing prescribed treatments and who required multidisciplinary care, including patients with significant untreated cardiac and pulmonary conditions, were referred to appropriate specialists. A medical record review of all patients with SCD admitted to the hospital were reviewed by an internal SCD quality committee to determine any changes in readmission rates and length of stay. Additionally, a medical record review was conducted to determine changes in patient-reported outcomes of pain and anxiety as a result of music therapy and/or acupuncture services.

Results: : With the introduction of the Inpatient SCD Continuity NP, the mean readmission rate decreased from 41% in 2018 to 32 % in 2019. Mean length of stay for admissions for a vaso-occlusive crisis decreased from an average of 5-7 days in January 2017 to 4-6 days in September 2019. Pre- and post-intervention data from Conference Abstract inpatient music therapy and acupuncture sessions revealed clinically meaningful reductions in pain and anxiety within individual treatments.

Conclusions: Nurse practitioners provide an integral role in improving the coordination of services and efficient use of resources for adults with SCD, leading to decreased length of stay and readmissions.

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NEUROCOGNITIVE TESTING IN PEDIATRIC SICKLE CELL DISEASE: FULL SCALE IQ ASSESSMENT MAY NOT TELL THE WHOLE STORY

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Background: Sickle Cell Disease (SCD) is a chronic, congenital hemoglobinopathy characterized by progressive multiorgan dysfunction (Vichinsky, ASH proceedings). The brain is one of the major organs affected by SCD. While it is known that neurocognitive defects can be seen even in the absence of overt stroke and silent cerebral infarcts, there are no specific guidelines for performing neurocognitive assessments on patients with SCD. We report our findings in 20 patients that received neurocognitive testing at our institution within the last 3 years.

Methods: Eligible participants were identified through the Chicago Sickle Cell Disease Research Group (CSCDRG) Registry in conjunction with the SCD medical team and pediatric psychologist. Enrolled subjects took part in child/caregiver interviews, caregiver questionnaires, and review of relevant medical and school records. Participants and caregivers completed a baseline neuropsychological evaluation, which included the Wechsler Intelligence Scale for Children (WISC). Questionnaires were also sent to participants' teachers. Medical chart review was used to collect information about genotype and relevant imaging.

Results: Neurocognitive testing was performed on 20 (Male-13, Female-7) pediatric patients ranging in age from 6 to 14 years. The majority of patients had sickle cell genotype Hgb SS (n=16, 80%). 15 of the 20 patients had a baseline MRI. Of the 15, only five patients (33%) had abnormalities noted on MRI. Brain abnormalities included CVA (n=2), Moya Moya (n=2), and T2 signal intensity (n=4). Cohort average full-scale IQ was 75. Interestingly, average full-scale IQ scores did not differ between patients who had a known brain abnormality (75) and patients who did not have a known brain abnormality (76) prior to testing. Most of the patients (n=15, 75%) were in the grade appropriate for age. Additionally, we also found that prior to neurocognitive testing, only one patient had a known Diagnostic and Statistical Manual of Mental Disorders fifth edition (DSM-5) diagnosis. Following testing, we identified ten more patients who met criteria for at least one DSM-5 diagnosis. The diagnoses fell under primarily three categories including Neurodevelopmental Disorders (i.e., Attention-Deficit Hyperactivity Disorder, Specific Learning Disability in Mathematics), Trauma and Stressor Related Disorders (i.e., Adjustment Disorder with depressed mood), and Disruptive, Impulse Control and Conduct Disorders (i.e., Oppositional Defiant Disorder).

Conclusions: We have described the differences in a pediatric sickle cell patient population who underwent neurocognitive testing. Our cohort of children with sickle cell disease exhibit significant neurocognitive deficits even in the absence of overt imaging findings or clinical stroke. Our findings also suggest that patients with SCD maybe at a higher risk of clinically significant mental health disorders, and these need to be addressed with specific interventions to maximize scholastic and occupational achievement. Furthermore, neurocognitive testing should be a part of routine evaluation in patients with sickle cell disease.

Figures:

Table 1. Cohort Demographics			
Variable	**n (% when applicable)**	**Mean (Median)**	**Range**
Subjects	20	-	-
Age at Testing in Years	-	10.71	6-14
Gender (Male)	13 (65%)	-	-
Grade Appropriate for Age (Yes)	15 (75%)	-	-
IEP Prior to Testing (Yes)	11 (55%)	-	-
Overall Cohort Full Scale IQ	20 (100%)	76 (75)	57-101
DSM Diagnosis (except SCD)			
Pre Test	1 (5%)	-	-
Post Test	11 (55%)	-	-
Imaging			
TCD prior to testing	15 (75%)		
MRI prior to testing	15 (75%)		
History of Abnormal TCD	0 (0%)	-	-
History of Abnormal MRI/MRA	5 (33%)	-	-
Brain Abnormalities			
CVA	3 (15%)	-	-
Moya Moya	2 (10%)	-	-
T2 Signal Intensity	4 (20%)	-	-
Genotype			
HbSS	16 (80%)	-	-
HbSC	3 (15%)	-	-
HbBeta-0	0 (0%)	-	-
HbBeta+	1 (5%)	-	-

Table 2. Imaging Findings and IQ		
	n	Full Scale IQ
History of Brain Abnormality	5	75 (57-92)
No History of Brain Abnormality	15	76 (60-101)

CHRONIC PAIN IN CHILDREN AND ADOLESCENTS WITH SICKLE CELL DISEASE

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Affiliations: *Cyclerion Therapeutics*

Background: Sickle cell disease (SCD) is an inherited blood disorder that impacts multiple organs leading to variable clinical presentation. In addition to severe pain episodes, SCD is characterized by chronic symptoms reportable only by patients (e.g. pain, tiredness). It is important to involve SCD patients during drug development to ensure accurate capture of the patient experience and seek ways to address patients' pressing needs. One way of involving patients is to seek to understand the patient experience and assess what is relevant and important to them using patient reported outcome (PRO) instruments.

Methods: Literature and PRO instrument review of other studies in SCD provides information on patients' concerns and how they have been assessed. One-on-one interviews and focus groups with patients document first-hand how patients talk about their experiences with SCD. Interviews with SCD patients' clinicians provide additional perspective on the patient experience. These components help identify relevant and important patient experiences that can be used to develop a PRO instrument for use in clinical trials and potentially be useful for regulatory approval decisions. We conducted literature/instrument reviews, and interviews with patients to assess the patient experience in SCD.

Results: Literature review conducted in 2017 revealed that SCD results in emotional impacts (anxiety, sadness/depression, anger, worry) and social impacts (difficulty forming and maintaining relationships with family/friends). During interviews with older adolescents and adult (≥16 years old) patients, patients identified SCD symptoms such as pain, tiredness, joint stiffness, vision issues, breathing issues, decreased appetite, insomnia, fever, numbness/tingling, swelling, difficulty concentrating, headache, and joint swelling. Pain and tiredness were rated as highly bothersome. Patients also talked about impacts of SCD on their lives, including a reduced ability to participate in social activities, difficulty walking, impact on physical activities, and not being able to attend school or work.

Conclusions: It is important to evaluate relevant and important SCD patient experiences in a way that can demonstrate treatment benefit when measured in an interventional clinical trial. Instruments developed for this purpose should ensure that concepts being measured are clinically relevant and important to patients. The findings from the instruments used in a regulated clinical trial may then be communicated in labeling in a way that is accurate, interpretable, and not confusing. Our research revealed that SCD disrupts patients' lives in a major way. Therefore, medicines that can address the relevant symptoms and impacts of the disease will go a long way in helping patients.

FRACTURE OF THE FEMUR IN A PREMATURE INFANT- AN UNUSUAL ASSOCIATION WITH SICKLE CELL DISEASE AND OSTEOGENESIS IMPERFECTA

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Background: Bone health is impacted by multiple factors such as certain genetic disorders and treatment modalities . Osteogenesis Imperfecta (OI) and Sickle Cell Disease (SCD) are two such disorders. OI is a genetic disorder which may be autosomal recessive or dominant inheritance. It is caused by mutations in genes encoding type 1 collagen which is known to synthesize bones, skin and other connective tissues. Defective collagen synthesis can lead to brittle bones and other abnormalities. Patients present with fractures without a history of preceding trauma. Severe cases of OI may also cause respiratory problems and cardiac complications such as cardiac valve insufficiency. SCD is an autosomal recessive genetic disorder. The substitution of valine for glutamic acid in the sixth position of the beta globin chain leads to the formation of sickle hemoglobin which results in a hemolytic anemia. Increase in blood viscosity and sickling of red blood cells lead to complications such as painful vaso-occlusive crisis, dactylitis, acute chest syndrome, strokes, and avascular necrosis of bones.

Case Presentation: We present a rare case of an infant with OI and SCD. The patient was born at 26 weeks gestational age and admitted to the Neonatal Intensive Care Unit (NICU). The patient's treatment plan included caffeine, vitamin D supplementation and TPN. Newborn screening reported SCD, SS type. At 84 days of age while in the NICU, the patient was noted to have swelling and decreased movement of the left lower extremity and an x-ray showed a femoral fracture. Blue sclerae were also noted on physical examination, which prompted further investigation. Genetic testing showed COLA1A mutation which confirmed diagnosis of OI. Currently the patient is twelve months of age and is in the 13th percentile for height and below the 3rd percentile for weight. There have been no additional fractures although an episode of sickle cell related pain crises occurred at one year of age. The patient presented with irritability and inability to bear weight on the right lower extremity. There was minimal swelling of the knee and foot. Imaging did not reveal new fractures of either extremity.

Conclusions: Premature infants are at a higher risk for decreased bone density. There are other co-morbidities such as SCD and use of caffeine which compound this risk. There are multiple interventions such as monitoring calcium and phosphorus and supplementation with vitamin D, which optimize bone health and help mitigate complications from decreased bone density. Despite that, fractures Conference Abstract still occur. This case report emphasizes the importance of a thorough physical examination and a high index of suspicion to determine the contributing factors to a fracture in a premature infant. Even though there is not much research on SCD and OI occurring together, we are aware of the symptom overlap. The impact of these two diseases on clinical features, outcomes, and challenges to care remains to be seen. The possibility for cure for both disorders with stem cell transplant or gene therapy offers hope and impetus for future research and clinical trials

EXPLORING TRANSITION READINESS FROM THE PATIENT AND PARENTAL PERSPECTIVE

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Background: Medical advances in sickle cell disease have thankfully changed the continuum of care landscape for patients with this chronic illness. Progress in pharmacologic treatment begets increased psychosocial strategies for implementation of transition programs now designed to prepare pediatric patients for the eventual high-risk stage of young adulthood, and transfer to an adult provider. Typical aspects of transition prep include disease education, management, and increased understanding of one's condition. Although often overlooked, a critical component of this process is parental inclusion since their participation correlates with increased disease management skills in children. As providers, it's imperative to utilize tools which foster family wide communication, understanding, collaborative treatment planning, and the identification of knowledge enhancing opportunities. The Got Transition Sample Readiness Assessment is one such user -friendly instrument that gives providers a backdrop for discerning the distinctive views of a child's readiness for adult care from both the patient and parent perspective.

Methods: As part of a standard of care transition program during pediatric sickle cell clinic afternoons, quizzes, surveys, modules and resources are often distributed to patients 12 years of age and older at the Novak Center for Children's Health in Louisville, KY. Completed forms are entered into a Red-Cap database for the purposes of tracking the transition curriculum and tweaking future care plans. Got Transition's Readiness Assessment Survey for Youth and Parents have been given to patients, ages 16 to 18, and their parents, during regular clinic visits. Each question highlights a topic of importance pertaining to the either the patient such as, "I can explain my medical needs to others", or to the parent such as, "My child knows his/her medical needs". The respondent is asked whether they, or their child, "knows this", "needs to learn this", or needs to know "who does this". Upon submission into Red Cap, retrospective data analysis occurred to discern gender, parent, and child related parallelisms, differences and any other valuable information which can improve patient cTo date, thirty-six surveys without identifiable information have been completed: 8 female adolescent patients (SS=3, S Beta Zero=3, SC=2), 10 male adolescent patients (SS=7, S Beta Zero=1, SC=2), 17 mothers and 1 father. The two highest "red flag" topics for both genders and their parents are "knowing how to get referrals to other providers" (25% of girls- 25% of girl parents-30% of boys-10% of boy parents) and having a "current copy of care plan" (25% of girls-25% of girl parents-50% boys-20% boy parents). A breakdown of 21 questions for both genders and their parents yielded the following overall confidence indicative percentages: Boys-72%, Boy Parents- 64%, Girls-60%, Girl Parents -53%. The chart below illustrates an abbreviated version of all questions and results.

%Difference in Female Pt Score compared to her parent	% of Female Pt Parents who answered - Yes, she knows this	% of Female Pts who answered – Yes, I Know This	Abbreviated Survey Topic	% of Male Patients who answered- Yes, I know this	% of Male Pt Parents who answered- Yes, he knows this	%Difference in Male Pt Score compared to his parent
0	25	25	Referrals	30	10	+20
0	25	25	Copy of Current Plan	50	20	+30
-12.5	50	37.5	Questions for Dr	50	60	-10
0	37.5	37.5	Plan at 18 for Ins	60	70	-10

Conclusions: Utilization of this tool generates eased identification of similarities, differences, and informational gaps in patient, parent and provider communication. On average boys and their parents tend to be more confident in the child's readiness, (Boys 12% higher than girls – Boys Parents 11% higher than Girls Parents), and both genders' assessment of their readiness was higher on average than their parents (7% for girls – 8% for boys), all of which warrant further exploration. With the inclusion of parents' perspectives in the assessment of transition readiness, providers can outline strategies to better prepare not only the patient, but also the parent, in effort to sustain long term disease management endeavors and a more seamless family-oriented road to adult care.

VIRTUAL REALITY IMPROVES PAIN SCORES PREFERENTIALLY IN ADOLESCENT BOYS WITH SICKLE CELL DISEASE RELATED ACUTE VASO-OCCLUSIVE EPISODE

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Background: Pain is a hallmark of Sickle Cell Disease (SCD) resulting in significant physical, psychological and financial burden to the patient and hospital system. Management relies heavily on drug analgesics however non-pharmaceutical interventions are increasingly being explored. Virtual reality (VR) has recently shown promise as an adjunctive solution. The primary objective of this study was to assess the feasibility and acceptability of virtual reality experiences to decrease non-procedural pain and anxiety in pediatric patients with SCD and an acute vaso-occlusive crisis (VOC).

Methods: A prospective feasibility study evaluated patients with SCD between the ages of 8 and 21 who were being treated for VOC in the day hospital or inpatient unit. A total of 36 subjects participated. Patients chose from an art, relaxation, or game VR experience. Validated self-report pain and anxiety surveys were administered pre and post a 15-minute VR experience. To measure the effect of VR on the sympathetic nervous system an Empatica watch was worn by each subject. Minimally invasive physiologic sensors within the watch measured heart rate, electrodermal response, acceleration and skin temperature. Side effects of VR were evaluated using simulator sickness surveys. Qualitative feedback was also obtained. Bivariate analyses comparing pain, anxiety and sickness scores were performed using parametric paired ttests or non-parametric Wilcoxon paired signed rank tests.

Results: Subjects were 44% male with a mean age of 15(±3) years. The majority (68%) of participants chose the game experience. A significant decrease in median pain scores from 7/10 pre-intervention to 6/10 post intervention was found ($p < 0.01$). After stratifying by age, a significant decrease in pain scores was observed in adolescents, however in children less than 13 years old, there was no significant change in pain scores ($p = 1.0$). Differences in gender were also observed. In males, pain scores decreased significantly ($p < 0.02$), however this finding was not observed in females ($p < 0.10$). Mean anxiety scores pre and post intervention did not change significantly however the anxiety scores were low at baseline. When asked to describe how much they liked the VR experience, 34 of the participants had a positive response and minimal side effects were reported. Empatica watch data analysis is currently ongoing

Conclusions: A statistically significant decrease in pain was seen after use of VR. Interestingly, after stratifying by age and gender, this finding was maintained only in adolescent boys. Our study offers further support for VR as a novel and feasible approach to decreasing pain in patients with SCD and VOC. Larger studies are needed to confirm differences seen within age and gender subgroups, as well as evaluating impact on total opioid dose and length of stay. Given the ubiquitous availability of cell phones worldwide, VR could be an adjunctive non-pharmacologic approach for treatment of SCD related acute pain in low resource settings as well.

AN INTENSIVE TRANSITION NAVIGATOR INTERVENTION IMPROVES TRANSITION READINESS TO ADULT CARE IN YOUTH WITH SICKLE CELL DISEASE

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Background: Recent advancements in the treatment of Sickle Cell Disease (SCD) have led to a decrease in the morbidity and mortality. With longer lifespan, chronic pain has been increasingly recognized, impacting up to 50% of adults with SCD. The ACTTION-APS Pain Taxonomy Initiative (AAPT) Diagnostic Criteria for Chronic SCD Pain, published in 2017, provides diagnostic criteria for chronic pain in the setting of SCD. The purpose of this study was to 1) determine the prevalence of chronic pain in children and adolescents with SCD, 2) divide them into chronic pain categories as set out by AAPT Diagnostic Criteria for Chronic SCD Pain and, and 3) further describe this sample using validated measures. This will aid in improved understanding and management of complex pain in SCD.

Methods: This is a single center prospective study at Connecticut Children's, approved by Connecticut Children's IRB. 159 patients aged 7-21 years old with SCD from Connecticut Children's Hematology Sickle Cell Database were screened for suspected chronic pain based on 2 ED visits for pain, any in-patient admission for pain, or 2 or more opioid prescriptions during January 1- December 31, 2018. Patients with suspected chronic pain were approached to confirm chronic pain defined as greater than 50% of days, in pain, utilizing the following criteria: pain 4 or more days per week over the past 6 months and/or Sickle Cell Disease Pain Burden Interview-Youth (SCPBI-Y)score of 7 or greater. All enrolled patients were given the following 5 surveys: Peds Quality of Life SD, Child Activity Limitation Interview (CALI) 21, PROMIS 37, Centralized Pain Inventory, and PROMIS Neuropathic scale. Descriptive statistics were performed on data collection from chart review that included ethnicity, gender, age, insurance type, SCD subtype, co-morbid diagnoses, SCD treatment, ED VOC visits, VOC admissions, number of opioid prescriptions, alternative pain treatments, other medications, and the 6 surveys.

Results: Out of 149 patients in the database, 59 screened positive for suspected chronic pain. Of these, 29 were enrolled as chronic pain (19.5% of all patients screened), 14 confirmed as not chronic pain, and 16 patients were not approached due to logistics. 16 males and 13 females, ranging from 8-22 years old at time of enrollment. 19 patients had Hemoglobin SS, 4 had Hemoglobin SC, 3 had Hemoglobin Sß0 thalassemia, 2 had Hemoglobin S ß+ thalassemia, and 1 patient had Hemoglobin S Quebec-chori. Per the AAPT diagnostic criteria, patients were divided into 3 core groups based on presence of contributory disease complications (e.g. avascular necrosis); 22 patients did not have contributory disease complications and 7 patients had contributory disease complications as well as pain at other sites and were therefore classified into the mixed pain contributory disease group. There were no patients in the contributory disease complication group without mixed pain. The two groups had the same number of mean pain sites, 6.8 (range from 0-19), and similar opioid use (13.3 opioid prescriptions per year in the mixed pain group, 12.5 in the non-contributory group). Medical and psychiatric comorbidities were common in both groups. 52% of patients had psychiatric conditions, with slightly higher prevalence in the mixed pain group vs the non-contributory group (57% vs 50%). 22 patients had public insurance and 7 had private insurance. Patients had high pain burden with mean SCPBI-Y scores (maximum possible 28) of 16.1 in the mixed pain group (range 10-21, SD 3.4) and 12.6 in the nocontributory disease group (range 8-23, SD 4.3). Average QL score was 115.9 (SD 19) in the mixed group and 101.5 (SD 30.2) in the non-contributory group. CALI score was similar between the two groups with an average of 31. Most patients did not have high scores on the Conference Abstract PROMIS Neuropathic scale with an average of 9.4 (maximum possible 28), however, the centralized pain index scores averaged 13.6 (max possible 31).

Conclusions: The AAPT diagnostic system can be used to classify children and adolescents with SCD and chronic pain. The prevalence of chronic pain in youth is lower than that reported in adults. Most patients had pain at multiple sites, some with contributory disease complications and others without. Patients with SCD and chronic pain experience multiple medical, psychological, and

social comorbidities that can impact their pain and quality of life.

RANDOMIZED PHASE 2 TRIAL OF INTRAVENOUS GAMMA GLOBULIN (IVIG) FOR THE TREATMENT OF ACUTE VASO-OCCLUSIVE CRISIS IN PATIENTS WITH SICKLE CELL DISEASE: LESSONS LEARNED FROM THE MIDPOINT ANALYSIS

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Background: Sickle cell Disease (SCD) is associated with chronic hemolytic anemia, recurrent pain episodes, cumulative organ damage and a shortened lifespan. The most frequent clinical manifestation of this disease is the recurrence of vaso-occlusive “crises” (VOC) for which there is currently no therapy other than supportive care and analgesics. Studies using a mouse model of SCD suggest that leukocytes (WBCs) play a key role in vascular occlusion by interacting with sickle red blood cells (sRBCs). In search for the molecular mechanisms responsible for these interactions, it was reported intravenous immune globulin (IVIG) had a profound effect on interactions among RBCs, WBCs, and the endothelium, improved blood flow and impacted on the overall survival of sickle cell mice. Currently there exist no targeted therapies for the treatment of acute VOC. We are evaluating the use of IVIG as a disease modifying novel therapy for the treatment of acute VOC in patients with SCD.

Methods: A Phase 2 randomized, double-blind, placebo-controlled, single dose study of IVIG (Gamunex-C, Grifols, Clayton, NC) in children (ages 8-21 years) with HbSS or Sß0-thalassemia hospitalized for an uncomplicated acute pain crisis is ongoing. A pre-specified age stratified midpoint analysis was conducted after enrollment of 37 patients and is reported here. Subjects were randomly assigned 1:1 to receive either a 400mg/kg dose of IVIG or placebo, administered in less than 24 hours after presentation to the ED, in addition to standard care. Clinical safety outcome variables monitored include treatment-emergent adverse events (TEAEs) and SCDassociated complications followed through 30 days after hospital discharge. Efficacy outcomes analyzed were length of VOC and neutrophil activation markers of adhesion and inflammation (activated Mac-1 and aged neutrophil numbers by flow cytometry)

Results: : Study drug was well tolerated with no Grade 3 or higher TEAE’s. Neutrophil activation biomarkers showed significant improvement in the treatment cohort compared to the patients in the placebo arm. There was a striking, statistically significant reduction in number (59.3 ± 39.6 versus 189.1 ± 146.8, p=0.01) and percentage (85.7 ± 48.2 versus 150.7 ± 135.9, p=0.05) of aged neutrophils, potential novel biomarkers of inflammation in SCD. Activated Mac-1 showed a trend towards improvement, 94.7 ± 44.2 in the treatment arm versus 152.6 ± 109.7 in the placebo arm (p=0.29). Conference Abstract There was no reduction in length of VOC in age group >=14 years old, but there was a nonsignificant trend towards a benefit for the intervention group in the <14-year-old stratum. The younger age group median (range) length of VOC in the intervention group (n=7) was 59.65 (48.52, 69.97) hours compared to 78.30 (59.21, 106.02) (p=0.13) for the control group (n=9).

Conclusions: These findings support the continued investigation of IVIG during acute VOC in the younger cohort. The opportunity for reversibility may be greater in younger subjects with decreased organ damage and chronic pain and these subjects are often not included in early phase studies. The pronounced effect of IVIG on aged neutrophil numbers might inform future studies of novel neutrophil activation assays as validated biomarkers.

Table 1A. Baseline Subject Traits

	IVIG n=18	Placebo n=19	P value
Age (year)	14.4 ± 3.58 14.5 (11, 18)	13.8 ± 3.9 15 (10, 18)	0.68
Female (%)	55.6	36.8	0.33
Hispanic Ethnicity (%)	22.2	31.6	0.71
African-American (%)	82.4	94.7	0.46
Hb genotype SS (%)	100.0	89.5	0.49
Hydroxyurea (%)	77.8	78.9	>0.99
1-year prior pain crisis admissions (n)	1.8 ± 1.7 1.5 (0.75, 2.25)	1.3 ± 1.34 1.0 (0, 3)	0.38

Values are mean ± sd,and median (25th,75thpercentiles) for continuous variables and % for categorical variables. P values comparing intervention to control with Mann-Whitney U test (continuous) or Fishers exact test (categorical)

Figure 2: Cohort Diagram

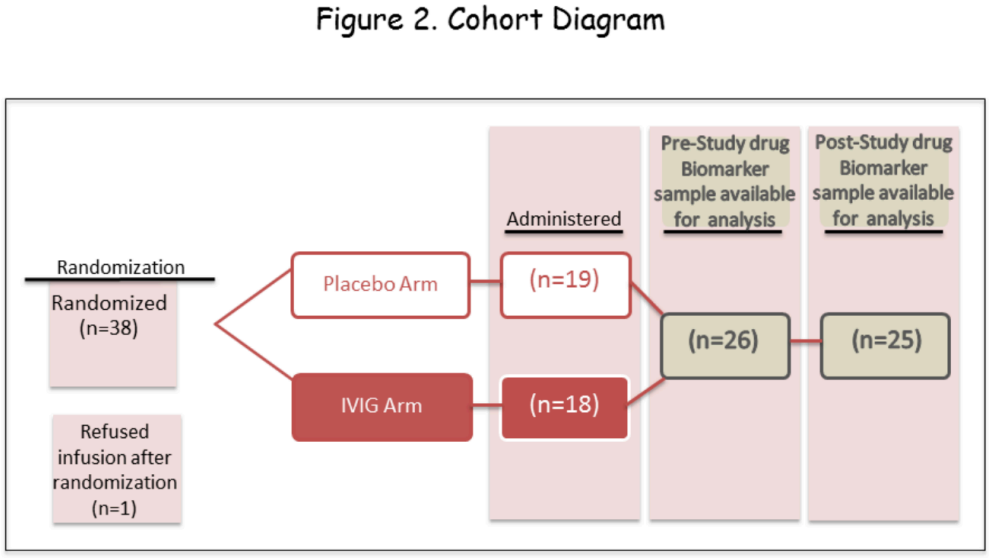
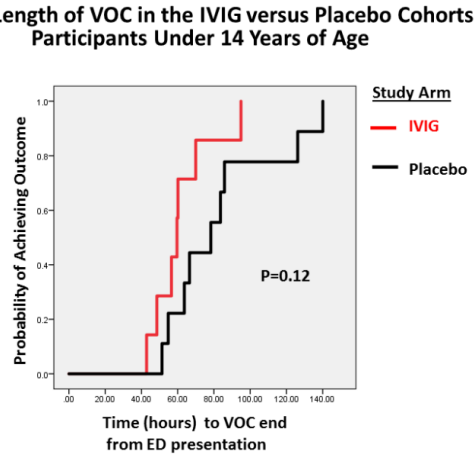


Figure 3: Length of VOC in the IVIG versus Placebo Cohorts Under 14 Years of Age



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