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Factors influencing engagement with adherence-enhancing mobile health app in sickle cell disease

Christina M Abrams[1*], Natalia Davila[2], Sherif M Badawy[3,4], Shanon Marks[5], Maura M Kepper[6], Robert W Gibson[7], Allison A King[6,8], Victor R Gordeuk[9], Chinonyelum Nwosu[10], Sophie Li[11], Jeffrey A Glassberg[12], Lisa M Klesges[13], Nirmish Shah[14], Don Brambilla[11], Jane S Hankins[15,16] and the Sickle Cell Disease Implementation Consortium[1*]

Abstract

Background Mobile health (mHealth) applications have been utilized in chronic diseases to improve medication adherence, though factors driving engagement remain understudied. We previously demonstrated the benefits of mHealth app utilization in increasing adherence to hydroxyurea. In the "Integration of mHealth into Sickle Cell Disease (SCD) Care to Increase Hydroxyurea Utilization" (meSH) study, greater engagement with the InCharge Health app increased the percentage of days covered (PDC) for hydroxyurea. However, factors influencing app engagement were not investigated. This study aimed to identify patient-level factors associated with mHealth engagement during and post-study among adolescents and adults with SCD.

Methods All meSH participants were included. The InCharge Health app use was measured for 24 weeks (study period) and 12 weeks (post-study period). Baseline demographics and validated measures of self-efficacy, financial hardship, and pain severity, impact, and frequency were evaluated as predictors of app engagement during the study period and post-study using linear models.

Results Complete app use data were obtained from 284 of 293 participants, including 150 (52.8%) females and 240 (84.8%) who were HbSS/HbSβ^0-thalassemia with a median age of 27 years. During the study period, 232 (81.7%) used InCharge Health at least once (median use excluding zeros: 26 days; IQR: 7–72 days). During the post-study period, 132 (46.5%) participants used the app at least once (median use excluding zeros: 16 days; IQR: 3–44 days). During the study period, the HbSS genotype, age > 25 years, higher education, higher self-efficacy score, and lower pain severity were associated with greater app engagement. Only age ($p = 0.0032$) and financial hardship ($p = 0.0125$) were significant in a multivariable model after backward elimination. During the post-study period, older age ($p = 0.035$), lower pain severity ($p = 0.021$) and lower frequency of pain ($p = 0.033$) predicted mHealth engagement. All three remained significant in a multivariable model after backward elimination.

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*Correspondence:
Christina M Abrams
abramsch@musc.edu
the Sickle Cell Disease Implementation Consortium
Full list of author information is available at the end of the article

Conclusions Older age, lower financial hardship, lower pain severity, and greater self-efficacy were associated with increased engagement with a mHealth intervention for improving medication adherence among people living with SCD. This research can shift future app development from focusing on factors that drive patient interaction with mHealth targeting modifiable factors influencing app engagement.

Trial registration The trial was registered with ClinicalTrials.gov. Registration Identifier: NCT04080167. Registration date: November 11, 2019.

Keywords Sickle cell disease, Adherence, Hydroxyure, Self-efficacy, Mobile health

Introduction

Sickle cell disease (SCD) is a collection of inherited blood disorders affecting approximately 100,000 individuals within the United States [1]. Current disease-modifying therapies can ameliorate SCD complications, with hydroxyurea being the most established evidence-based treatment [2–7]. Despite abundant evidence and recommendations by expert groups, adherence to hydroxyurea is low among individuals with SCD [8–10].

Adherence to medications poses a significant challenge in the management of chronic diseases, including individuals with SCD [11, 12]. Patients with SCD with low hydroxyurea adherence have worse health outcomes, increased disease complications, and lower healthcare-related quality of life [13, 14]. Barriers to daily hydroxyurea use include concern about side effects, forgetfulness, and a lack of motivation to sustain the habit [15]. These challenges can be addressed by improving access to information, providing daily reminders, and fostering the development of habitual behaviors [12, 14].

The use of mobile health (mHealth) in clinical practice has been shown to increase patient engagement and self-management of disease [16, 17], and utilization of mHealth has grown among those with SCD [16, 18–22]. While mHealth interventions gain popularity with providers and patients, barriers still exist along with concerns regarding the ability of patients to maintain engagement throughout and beyond the study period [23–25]. Perceived benefit, overall attitude toward the app, and impact of disease state have been cited as potential barriers to engagement with mHealth apps [26–29].

The multi-center Sickle Cell Disease Implementation Consortium (SCDIC) [30] study "Integration of mHealth into Sickle Cell Disease Care to Increase Hydroxyurea Utilization (meSH) [21]", tested a new mHealth intervention to improve hydroxyurea adherence among adolescents and adults with SCD, the InCharge Health app. We demonstrated that greater app use resulted in a sustained increase in the percentage of days covered (PDC) for hydroxyurea [31]. In the meSH study, adherence increased from 39.7% to 56.0% during the 6 months of study intervention and sustained at 51.4% during the 3 months post-study [31].

Although InCharge Health was associated with greater hydroxyurea adherence, the factors associated with greater mHealth use remained unclear. In this sub-analysis of meSH, we aimed to identify the factors associated with mHealth engagement, both during and after the study period. We hypothesized that patient-level characteristics (i.e., demographics, pain experience, and self-efficacy) would predict greater app use. The identification of key factors driving app engagement, both modifiable and non-modifiable, will guide future strategies to improve maintained mHealth engagement and its efficacy.

Methods

Study design

meSH was an National Heart, Lung, Blood Institute (NHLBI)-funded trial to foster greater adherence to hydroxyurea among adolescents and adults with SCD. The methods of meSH have been previously described [21]. Briefly, 7 SCDIC sites tested InCharge Health for 24 weeks in a non-randomized hybrid-effectiveness prospective trial. InCharge Health is a multi-function mHealth intervention with includes daily reminders, adherence and pain progress tracking, communication with providers and other patients, inpatient mode, educational resources, and an accountability partner. The current study is a sub-analysis of meSH that investigates the patient-level factors associated with the amount of app use during the study period and in the subsequent 3 months post-study.

Participants selection

Study participants had a SCD diagnosis, were English-speaking, aged 15–45, were treated at one of the participating sites, and owned a mobile phone. The study was approved by the IRB of all participating sites with an informed consent signed by all participants or their legal guardians.

Variable definition

Baseline demographics included age (15–24 versus 25–45 years), sex, annual income, sickle cell genotype, race, ethnicity, insurance type, occupation, highest education attained, and financial hardship. Hydroxyurea adherence was estimated by the percentage of days covered (PDC), a ratio calculated by the number of days covered by filled prescriptions to the number of days in the study period. Using validated patient-reported outcome (PRO) measures, pain experience (severity, frequency, interference) was ascertained at baseline and at 24 weeks by the Adult Sickle Cell Quality of Life Measurement Information System (ASCQ-Me) and PRO Measurement Information System (PROMIS) [32, 33], while self-efficacy was collected at baseline using the PROMIS self-efficacy measure [34]. A cumulative medical self-efficacy score was calculated as the sum of scores on 8 questions, each of which was scored on a Likert scale 0 (not confident) to 4 (very confident). Sums were categorized into 4 groups (0–8, 9–16, 17–24, 25–32). Pain severity during the last pain episode was measured on an ordinal scale, with mild pain being 0–4, moderate pain 5–7, and severe pain 8–10. Additionally, the self-reported frequency of app use was ascertained. InCharge Health engagement was measured by the number of days in the study period on which the app was accessed at least once using click-tracking data.

Biostatistics considerations

Descriptive statistics for app use and various predictors included means, standard deviations and, for variables with skewed distributions, inter-quartile ranges (IQR). Predictors of app use were evaluated using linear models of days of app use during the study period (weeks 0 to 24). First, we considered a separate model for each predictor of interest (i.e., baseline PDC, demographics, baseline self-efficacy, baseline pain experience). Next, we applied backward elimination to a multivariable model that initially included all predictors under consideration. At each step, one predictor was eliminated with the predictor with the highest p-value selected for exclusion. Elimination stopped when all remaining predictors were statistically significant at $p<0.05$. The same methods were applied during the maintenance period (weeks 25 to 36).

Results

Participants' characteristics

Nine (3.1%) subjects who dropped out, died, or were lost to follow-up during the study were excluded from the analysis. The remaining 284 (96.9%) participants included 150 (52.8%) females and 240 (84.8%) with HbSS or HbSβ^0-thalassemia genotypes. Their median age was 27 years. Most individuals (146/277, 52.7%) had at least some college or vocational training. Baseline PDC was 39.7 ± 28.0%. Most had only government or public insurance (185/259, 71.4%), defined as Medicaid, Medicare, military, Indian state-sponsored, or other government. Only 150/277 (54.2%) individuals stated they were "working now" (Table 1).

Patient factors associated with app utilization during study period

Among the 284 participants, 232 (81.7%) used InCharge Health at least once during the study period (median use excluding zeros: 26 days; IQR 7–72 days). When predictors were considered individually, app use during the study varied with genotype, age, educational attainment, financial hardship, pain severity, and self-efficacy score (Tables 1 and 2). App use was, on average, greater in those with HbSS/Sβ^0-thalassemia, in older participants, in those with highest educational attainment, in those with lower pain severity, and in those with higher self-efficacy scores.

Only age ($p=0.0032$) and financial hardship ($p=0.0125$) remained in the multivariable model after backward elimination. Correlations among the predictors may explain why some that were statistically significant when considered alone were eliminated from the multivariable model. Pain severity had a borderline association with app use ($p=0.0689$). Pain severity was also weakly correlated with financial hardship score ($r=0.1174$, $p=0.0540$) but there was no difference in mean pain severity score between the two age groups (15–24 versus 25–45 years, ($p=0.81$). Self-efficacy was also found to be weakly positively correlated with age ($r=0.1253$, $p=0.0348$).

Patient factors associated with app utilization during the post-study period

Among the 284 participants, 132 (46.5%) participants used the app at least once (median use excluding zeros: 16 days; IQR: 3–44 days). When predictors were considered individually, baseline predictors of app use during the 12 weeks post-study were age ($p=0.035$), pain frequency ($p=0.033$), and pain severity ($p=0.021$) (Tables 1 and 2). Older age, lower pain frequency, and lower pain severity were associated with greater app use in weeks 25–36. All three predictors remained in the multivariable model after backward elimination.

Discussion

mHealth is increasingly used for the management of chronic diseases, but user engagement with mHealth has not been fully studied, especially beyond the study period. This is one of the first studies in patients with SCD to establish predictors for mHealth app engagement. In this multi-center, proof-of-concept, non-randomized prospective clinical trial, we found that among adolescents and adults with SCD, older age,

Table 1 Demographic characteristics associated with app engagement during study (weeks 1–24) and post-study period (weeks 25–36)

	Days of app use during study period			**Days of app use during post-study period**	
	***n*, (%)**	**Mean (SD)**	***P***	**Mean (SD)**	***P***
Age (*n* = 284)			**0.012**		**0.035**
15–19	39 (13.7)	27.1 (35.9)		8.5 (17.9)	
20–24	73 (25.7)				
25–29	57 (20.1)	39.7 (43.5)		13.7 (21.9)	
30–34	51 (18.0)				
35–39	33 (11.6)				
40–45	31 (10.9)				
Sex (*n* = 284)			0.45		0.27
Male	134 (47.2)	32.8 (39.2)		10.2 (18.7)	
Female	150 (52.8)	36.4 (42.8)		12.9 (22.0)	
Genotype (*n* = 283)			**0.04**		0.17
HbSS/SB0-thal	240 (84.8)	37.7 (41.9)		12.9 (21.3)	
HbSC	28 (9.9)	21.6 (38.0)		5.5 (15.4)	
HbSB + -thal	12 (4.2)	16.7 (17.6)		6.3 (12.1)	
other	3 (1.1)	4 (6.1)		0 (–)	
Education (*n* = 277)			**0.04**		0.20
Less than high school	7 (2.5)	21.4 (31.5)		10.9 (27.0)	
Some high school	33 (11.9)	22.1 (30.2)		5.8 (15.2)	
High school graduate or GED equivalent	91 (32.9)	36.1 (41.4)		12.3 (21.0)	
Some college or vocational training	81 (29.2)	34.3 (42.8)		11.4 (20.8)	
College graduates	43 (15.5)	47.6 (45.5)		17.0 (23.7)	
Some graduate school or professional school	5 (1.85)	28.0 (44.7)		5.2 (9.5)	
Graduate or professional degree	17 (6.1)	40.5 (40.5)		12.9 (18.5)	
Insurance (*n* = 259)			0.55		0.87
Government	185 (71.4)	34.9 (41.9)		11.9 (21.3)	
Private	51 (19.7)	34.4 (39.6)		13.5 (20.8)	
Government & Private	14 (5.4)	37.0 (29.6)		9.4 (13.9)	
Uninsured	9 (3.5)	54.9 (51.2)		15.4 (27.0)	
Work status (*n* = 277)			0.41		0.29
Working now	150 (54.2)	38.5 (43.8)		12.5 (21.4)	
Not working (excluding retired)	119 (43.0)	31.8 (38.5)		11.8 (20.3)	
Retired	8 (2.9)	31.6 (32.0)		0.75 (2.12)	
Baseline PDC	n/a	n/a	0.30	n/a	0.25

The meSH study enrolled 293 individuals with sickle cell disease, of those, 284 had any app use data and are shown in this table

higher education, greater self-efficacy, and lower pain experience were the strongest determinants of increased mHealth engagement, though in the post-study period only older age, lower pain frequency, and lesser pain severity maintained a significant association with increased engagement. Understanding what drives app engagement is crucial in developing strategies to support maintained engagement with mHealth interventions to achieve and maximize their intended health benefits. These strategies may include ensuring that the mHealth features are engaging, are useful and appropriate for users, as well as able to support implementation strategies (e.g., care facilitation) outside of the mHealth tool.

We found that older age and lower pain experience, in addition to other variables discussed above, were associated with higher utilization of the InCharge Health app. Similarly, it was demonstrated through implementation of the InCharge Health app that predictors of increased PDC included older age, pain frequency, and pain severity [31]. In this sub analysis, there was an association between higher app use in those with lower financial

Table 2 Baseline values of self-reported outcomes related to disease vs app use during study (weeks 1–24) and post-study period (weeks 25–36)

	Number of individuals	**Days of app use during study period**		**Days of app use during post-study period**	
	***n* (%)**	**Mean (SD)**	***P***	**Mean (SD)**	***P***
Financial Hardship (*n* = 268)			0.052		0.14
After paying the bills, you still have enough money for special things that you want	80 (29.9)	42.0 (42.3)		13.2 (20.4)	
You have enough money to pay the bills, but little spare money to buy extra or special things	115 (42.9)	34.6 (40.5)		12.7 (21.9)	
You have money to pay bills, but only because you have to cut back on things	42 (15.7)	30.7 (41.7)		9.9 19.9)	
You are having difficulty paying the bills, no matter what you do	31 (11.6)	27.2 (35.4)		7.3 (17.0)	
Health Literacy (how often did you need to have someone help you…) (*n* = 273)			0.58	***n* (%)**	0.66
Never	165 (60.4)	39.2 (43.6)		13.0 (20.9)	
Rarely	65 (23.8)	21.1 (31.1)		7.9 (17.4)	
Sometimes	32 (11.7)	43.3 (41.5)		16.5 (26.5)	
Often	5 (1.8)	27.0 (33.2)		0.40 (0.89)	
Always	6 (2.2)	42.8 (51.9)		12.3 (20.8)	
Pain frequency (*n* = 277)			0.24		**0.03**
I did not have a pain attack in the past 12 months	37 (13.4)	40.5 (47.9)		15.6 (25.7)	
1	36 (13.0)	45.8 (50.9)		17.8 (24.1)	
2	46 (16.6)	25.1 (30.3)		10.5 (20.2)	
3	32 (11.6)	44.2 (46.9)		12.4 (18.8)	
4 or more	126 (45.5)	32.5 (37.4)		9.5 (18.3)	
Pain Severity of most recent pain episode (*n* = 273)			**0.01**		**0.02**
No to mild pain (0–4)	17 (6.2)	61.4 (47.6)		25.9 (27.8)	
Moderate pain (5–7)	68 (24.9%)	38.4 (40.8)		12.1 (19.1)	
Severe pain (8–10)	188 (68.9%)	32.0 (40.2)		10.8 (20.3)	
Self-efficacy cumulative scores (8 questions, lowest 0 to highest 32, *n* = 284)			**0.01**		0.15
Group 1 (score: 0–8)	14 (4.9%)	13.8 (22.8)		8.4 (19.2)	
Group 2 (9–16)	18 (6.3%)	25.5 (37.7)		7.8 (14.0)	
Group 3 (17–24)	72 (25.4%)	29.6 (37.7)		9.9 (18.3)	
Group 4 (25–32)	180 (63.4%)	39.3 (43.1)		13.0 (21.9)	

The meSH study enrolled 293 individuals with sickle cell disease, of those, 284 had any app use data and are shown in this table

hardship, which is likely interlinked with previous findings showing that private health insurance plans were associated with increased PDC [31]. We know social determinants of health (SDOH), income, and disease severity are connected [35–37] and likely influencing behavior in consumption of health products. It is well established that SDOH affect health outcomes in SCD [38, 39], and during the study period, this work suggests that mHealth app engagement could similarly be affected by financial and educational attainment.

The frequency of app engagement declined as well in relation to reported disease severity (severity of pain along during the study period and both frequency and severity in post-study period), which is in line with our previous finding that decreased hydroxyurea adherence was associated with greater pain severity and pain frequency [31]. These results, along with the evidence of the impact of SDOH on app utilization, underscore the fact that there is likely a complex interplay of disease severity with financial wellbeing. In our study, higher rates of pain severity were associated with those who reported higher rates of financial hardship as well. A survey of patients with SCD demonstrated that most individuals have been prevented from attending work (44%), prevented from progressing in their career (42%), unable to keep a job (38%) or to find a job (38%), or prevented from attending (46%) or performing (37%) in school [36]. In this same survey, 27% of those with SCD, felt their disease limited the ability to progress further in their education. This study also reported that those with high impact of SCD on their daily life, school, or emotional health had significantly more acute pain in the preceding 12 months, demonstrating the significant interconnection of all aspects of life in those with SCD [40]. Work from the SCDIC, concurred with this association as well. The risk of unemployment increased with both pain frequency and severity, while the risk of depression increased with the frequency of painful episodes [41], suggesting that the impact of pain spans the life of those with SCD.

Contrary to much of the literature, in our study, older individuals were more likely to engage with mHealth. Most other research demonstrates mHealth engagement is more common in young individuals [42–44], though there is increasing use across the age spectrum [43–45]. In our sample, older patients had higher levels of self-efficacy. Correlations between self-efficacy, age, and disease management have been reported in this population [46–48]. These correlations demonstrate a subset of young adults with SCD often lack the self-efficacy and disease self-management skills necessary to manage their disease, thus leading to difficulty in managing their symptoms [46–50]. In contrast, those with increased self-efficacy and motivation have more positive health outcomes [42, 45]. Reports in patients with SCD have demonstrated that app use engagement has predicted self-efficacy and improved outcomes [17]. This finding has an impact on SCD given the increasing population of aging individuals with SCD [51] as we must determine the best way in which to support this population in managing their disease.

In our study, individuals who rated themselves as more self-efficacious were more likely to engage with the app than those who were less self-efficacious. While other studies have looked at the role of self-efficacy in SCD and disease management, this association of self-efficacy with medication adherence is not singular to SCD [52–55]. Often, individuals, especially in the adolescent and young adult age groups, do not find themselves engaged in managing their disease [19]. If self-efficacy is associated with improved health literacy and medication adherence [12, 25], it implies a greater willingness to engage with other forms of "treatment," such as mHealth interventions targeting medication adherence. Greater self-efficacy predicts greater app utilization, which, in turn, predicts greater adherence to medication [31], resulting in better control of disease and outcomes [50]. Disease self-efficacy has been positively correlated and disease severity has been negative correlated with healthcare-related quality of life in those with SCD [56]. This study highlights areas of future investigations related to promotion of self-efficacy among adolescents and young adults with SCD. As targets of future intervention, this could lead to greater engagement with tools, such as mHealth applications, to promote medication adherence and ultimately boost their treatment effects.

Sustainability of app engagement is not commonly addressed after active mHealth interventions. Two other reports describe decreased app use post-study [17, 57], and we found a similar trend, which is often referred to as "the law of attrition [58]". During the post-study period, older age, less frequent pain, and lower pain severity continued to drive app utilization. Far fewer variables maintained influence in the post-study period compared within the study period (genotype, education, self-efficacy, and financial hardship). Despite decreased utilization, we previously demonstrated that the increase in PDC during the study period persisted in the post-study period with a PDC of 51.4% and mean difference from baseline 11.65% post-study [31]. Limited literature exists to discuss how often or how long an app needs to be used to continue generating behavior change, though the longer length of interventions likely correlates with more persistent behavior change [59, 60]. Unfortunately, abandonment of apps is often found once the novelty effect wears off [61]. What is also suggested by the literature is that a decline in usage can be associated with acquiring the knowledge and skills needed to continue to engage in behavior (such as continued adherence to hydroxyurea [60, 62], supporting the continued increase in PDC in the post-study period in our patients. Increasing internal motivation by targeting introduction of continued novelty through the addition of new features could be an area of interest for future iterations of the app based on participant perceived areas of importance within the app.

Limitations

Incomplete follow-up led to the exclusion of a small proportion of subjects, while varying levels of missing data on predictors reduced sample sizes to a varying extent. This is balanced by the fact that the missing data is relatively small. This study has a large sample size with several participants from a wide variety of institutions, helping to improve its generalizability. Other studies suffered from small sample sizes, precluding testing of covariates of mHealth engagement [25]. Because we had a large sample size, we could test the interactions between the covariates and app engagement. Generalizability outside of the SCD patient population can be limited given the tailoring of this app to SCD; however, key features related to demographics and patient-reported outcomes can be extrapolated from this population to similarly affected groups. This study also examined both objective and subjective predictors, including demographics and patient reports of the impact of disease, which can help us further understand the complex nature of determinants of mHealth engagement within this population. Days of app use were limited to only a single interaction on a given day with the app. We did not quantify interactions with each feature (i.e., time spent with each app feature). Future studies should quantitatively evaluate patterns of app use relative to clinical outcomes to understand the amount of each feature (i.e., dose) is necessary for the outcome of interest. Finally, the post-study follow-up was short (12 weeks), therefore, future studies with longer post-study passive observation period is planned to examine factors associated with sustained mHealth engagement.

Conclusion

This work is the first to investigate factors driving engagement with a medication adherence-enhancing mHealth intervention among individuals living with SCD. Age, self-efficacy, financial hardship, and pain experience seemed to drive mHealth engagement most strongly in individuals with SCD, with some factors more influential in sustaining app engagement. Informed by this work, we hope to improve the app and target individuals who could benefit from increased drug adherence. Future research should improve mHealth design features to improve the implementation of this app further and support those with greater financial hardship and pain, thus translating into improved health outcomes.

Abbreviations

App	Application
ASCQ-ME	Adult Sickle Cell Quality of Life Measurement Information System
IQR	Interquartile range
IRB	Institutional Review Board
meSH	Integration of mHealth into Sickle Cell Disease Care to Increase Hydroxyurea Utilization
mHealth	Mobile health
NHLBI	National Heart Lung Blood Institution
PDC	Percentage of days covered
PRO	Patient reported outcome
PROMIS	Patient Reported Outcome Measurement Information System
SCD	Sickle cell disease
SDIC	Sickle Cell Disease Implementation Consortium
SDOH	Social determinants of health

Supplementary Information

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Supplementary Material 1.

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Authors' contributions

CMA participated in design of study concept, drafted manuscript, interpreted data, edited, and reviewed manuscript. SM lead the app development team and reviewed manuscript. JSH and NS developed the study concept, enrolled participants, and participated in manuscript writing. DB conducted the statistical analysis and reviewed the manuscript. ND, SMB, MK, RG, AAK, VRG, JAG, LMK, SL reviewed and edited the manuscript. CN enrolled participants and reviewed manuscript. All authors have accepted responsibility for the content of the manuscript and approved its submission after reviewing the final version of the manuscript.

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Data availability

Original data will be made available in BioLINCC after the publication. For further details, please contact corresponding author. De-identified participant data access can be accessed through https://biolincc.nhlbi.nih.gov/home/, when available.

Declarations

Ethics approval and consent to participate

All research was carried out in accordance to the Declaration of Helsinki, relevant guidelines and regulations. The study was approved by the IRB for 7 of the participating sites (St. Jude Children's Research Hospital, Duke University, Medical University of South Carolina, Augusta University, Washing University in St. Louis, Icahn School of Medicine at Mount Sinai, University of Illinois at Chicago) with an informed consent signed by all participants or their legal guardians. Assent was provided by those individuals ages under 18 years of age. Participation in this study was voluntary.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Pediatrics, Division of Hematology-Oncology, Medical University of South Carolina, 125 Doughty Street, Suite 520, Charleston, SC 29403, USA. [2]College of Nursing, Medical University of South Carolina, Charleston, SC, USA. [3]Division of Hematology, Oncology, and Stem Cell Transplant, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA. [4]Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL, USA. [5]Agency 39a, Culver City, CA, USA. [6]Prevention Research Center, The Brown School, Washington University, Saint Louis, MO, USA. [7]Department of Emergency Medicine, Medical College of Georgia, Augusta, GA, USA. [8]Department of Pediatrics, Washington University in St. Louis, St Louis, MO, USA. [9]Sickle Cell Center, University of Illinois at Chicago, Chicago, IL, USA. [10]Department of Hematology, St. Jude Children's Research Hospital, Memphis, TN, USA. [11]Research Triangle Institute International, Research Triangle Park, NC, USA. [12]Department of Emergency Medicine, Icahn School of Medicine at Mount Sinai, New York, NY, USA. [13]Division of Public Health Sciences, Department of Surgery, Washington University, Saint Louis, MO, USA. [14]Department of Pediatric Hematology and Oncology, Duke University, Durham, NC, USA. [15]Departments of Hematology and Global Pediatric Medicine, St. Jude

Children's Research Hospital, Memphis, TN, USA. [16]Center for Sickle Cell Disease, University of Tennessee Health Science Center, Memphis, TN, USA.

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