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Keys to Recruiting and Retaining Seriously Ill African Americans with Sickle Cell Disease in Longitudinal Studies: Respectful Engagement and Persistence

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Abstract

Objectives: Sickle cell disease (SCD) is a serious illness with disabling acute and chronic pain that needs better therapies, but insufficient patient participation in research is a major impediment to advancing SCD pain management. The purpose of this article is to discuss the challenges of conducting a SCD study and approaches to successfully overcoming those challenges.

Design: In a repeated measures, longitudinal study designed to characterize SCD pain phenotypes, we recruited 311 adults of African ancestry. Adults with SCD completed four study visits 6 months apart, and age- and gender-matched healthy controls completed one visit.

Results: We recruited and completed measures on 186 SCD patients and 125 healthy controls. We retained 151 SCD patients with data at 4 time points over 18-months and 125 healthy controls (1 time point), but encountered many challenges in recruitment and study visit completion. Enrollment delays often arose from patients' difficulty in taking time from their complicated lives and frequent pain episodes. Once scheduled, SCD participants cancelled 49% of visits often

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because of pain; controls canceled 30% of scheduled visits. To facilitate recruitment and retention, we implemented a number of strategies that were invaluable in our successes.

Conclusion: Patients' struggles with illness, chronic pain and their life situations resulted in many challenges to recruitment and completion of study visits. Important to overcoming challenges was gaining the SCD patients' trust and a participant-centered approach. Early identification of potential problems allowed strategies to be instituted proactively, leading to success.

Keywords

recruitment; retention; medically vulnerable African Americans; sickle cell disease; quantitative sensory testing; QST; seriously ill

Introduction

Pain research with the 100,000 Americans with sickle cell disease (SCD) is critically important to meet the urgent need for new treatments that alter the disabling effects of the disease's most common symptom--acute and chronic pain.^{2,3} SCD, a genetic condition that in the U.S. affects people of mainly African or Latin descent,¹ is known for death at early age. Median age at death for women was 42 years and for men was 38 years.⁴ Only three treatments, hydroxyurea, stem cell transplant, and L-glutamine, have favorably impacted the disease course of patients with SCD but are not widely used.⁵⁻⁷ The Improving Patient Outcomes with Respect and Trust (IMPORT) study of 291 SCD patients' attitudes on seeking healthcare revealed that up to 92% of participants felt positive about participating in clinical trials.⁸ There is an incongruity, however, between IMPORT findings of high level of support for research studies by patients with SCD and the realities of low enrollment and retention of SCD patients in research studies.⁹ Insufficient patient participation in clinical trials is a major impediment to the advancement of SCD research.⁹ Many SCD studies are terminated due to low enrollment.^{9,10} Therefore, conducting a longitudinal study can be challenging with a population that suffers from a debilitating chronic disease, many of whom live in inner city neighborhoods, and may have complicated life situations.^{11,12} The purpose of this article is to discuss the challenges and successes of conducting such a study in a major metropolitan city.

The goal of our study was to characterize SCD pain to improve pain control in adults with SCD. We describe our challenges in conducting the study, strategies, and initiatives that led to its successful completion, and budget implications of the personnel time required to achieve success. Although many patients were interested in joining the study, the realities of their struggles with illness, chronic pain, and their life situations resulted in many challenges to recruitment and completion of the study's four visits over 18 months.

Methods

Study Design

This was a repeated measures, longitudinal study with adults of African ancestry and SCD pain to characterize the phenotypes of chronic pain and associate phenotypes with genomic

characteristics. We repeated measures every six months, in cold and warm seasons, for a total of four measures over 18 months. The study also included a cross-sectional, single session of healthy controls of African ancestry with similar measures. The study was approved by the University of Illinois at Chicago (UIC) Institutional Review Board (approval number 2014–0287). All participants provided written informed consent for participation.

Setting and Sample

Participants with SCD were recruited at the University of Illinois Hospital and Health Sciences System (UIH) outpatient adult SC clinic, which has about 600 patients. Healthy controls were recruited from the community. Study procedures were conducted at the UIC College of Nursing, located two blocks from the clinic.

Inclusion criteria for patients were: (a) SCD diagnosis, (b) moderate to severe pain (3 on 0–10 scale) related to SCD within the last 12 months, (c) chronic SCD pain, defined as pain > 0 on at least half of the days during the previous 3 months, (d) spoke and read English, (e) 18 years old, and (f) African ancestry. Patients were excluded if they were legally blind, physically or cognitively unable to complete study measures, or diagnosed with a polyneuropathy or diabetes. We recruited and completed baseline measures on 186 SCD patients.

Inclusion criteria for the healthy controls were: (a) African ancestry, (b) health history negative for diabetes, hypertension, SCD, sickle cell trait (SCT), cancer, current acute or chronic pain, (c) spoke and read English; and (d) 18 years old. Controls were excluded if they were legally blind, physically or cognitively unable to complete study measures, or reported using prescription pain medications or recreational drugs. We recruited and completed the single session measures on 125 healthy controls.

Procedures

After recruitment at the UIH SC clinic or the community, potential SCD participants were scheduled for consent and baseline data collection. After informed consent, the researcher obtained blood for genetic and epigenetic analyses. The consent process stressed that participating in the study was voluntary and that samples would only be identified with a code number and participants' identifiable data would be shared only with the investigators. Then participants completed Internet-based self-report tools for pain, symptoms, health-related quality of life, and impact of pain on their lives, and completed thermal and mechanical quantitative sensory testing (QST). We conducted thermal QST using a Medoc Advanced Medical Systems TSA-II analyzer to quantify their responses to cool, warm, cold, and hot stimuli, and mechanical QST using von Frey filaments to study their response to pressure.^{13,14} For patients, blood samples and measures were obtained three more times at alternate seasons with the goal of obtaining two measures in warm/hot season and two in cool/cold season. Each visit lasted 1.5–3 hours. Participants received \$50/visit.

Results

The Research Team

Over the past 15 years, the study investigators and team members have successfully completed 13 trials with SCD patients. This study's team consisted of the same project director, and three research specialists (RSs) who have been part of the team between 8 and 15 years. The RSs were responsible for recruitment, retention and data collection. They had extensive experience recruiting for SCD research studies. Having interacted with the SC clinic physicians, staff, and patients over the years in previous studies, the RSs were familiar with many patients and had gained their trust^{12,15}. This bond facilitated approaching and recruiting them. Additionally, patients who knew the RSs often vouched for our team and encouraged other patients to join this study. This peer endorsement was invaluable in our efforts to involve new patients in our research. Having the same highly trained and efficient team with a proven record of success in SCD studies was instrumental to the success of this study.

Recruitment

SCD patients were recruited mainly in person at the SC clinic. We used Facebook to contact participants from earlier studies from whom we had permission, and contact current participants for follow-up visits. Attempts to recruit patients through Craigslist were unsuccessful. We participated in outreach activities with the Sickle Cell Disease Association of Illinois and Have a Heart for Sickle Cell Anemia Foundation (HHSCA) to build relationships with the SC community. Outreach activities included participating in Advocacy Day for SC events to lobby Illinois legislators for laws supporting SCD, and joining the executive board of HHSCA. Despite all these recruitment activities, 95% of SCD participants were recruited at the SC clinic.

Recruitment was aided by attractive flyers with our unique SCD brand,¹⁵ designed by the team's graphic designer (Figure 1). Also, a RS visited the clinic during regular hours to introduce the study to potential participants. However, patients often had to leave right after their appointments, and we often approached patients multiple times in person or by phone, since they frequently expressed interest in being contacted later. It was very time consuming and labor intensive to approach the same patients numerous times before enrollment.

The RSs divided their time between recruitment, screening, scheduling, and data collection, and we attempted to have the same RS work with the same participant at all visits. This approach was very successful for retention since participants were more likely to respond and return for follow-up visits when contacted by a more familiar RS. However, as the study progressed, the RSs spent more time on scheduling visits and completing data collection, and less time on recruitment.

Additionally, as the patients who were more interested in participation had joined, it became more difficult to recruit new participants from the large but limited clinic pool. In the first four months of the study our SCD recruitment rate was 11.8 participants/month. Over the next 12 months, recruitment decreased to 6.2 participants/month and in the next 9 months to 3.7 participants/month. As the study progressed, and there were fewer patients available for

recruitment and the RSs were less able to focus on recruitment, we temporarily assigned another RS to recruit full-time at the clinic during the last few months. With this focused effort, recruitment increased 2.5 times, averaging 9.3 participants/month.

We recruited healthy controls from the community, through Craigslist, referrals from SCD patients, and word of mouth. Recruitment of healthy controls was easier due to a much larger pool of potential participants who did not suffer from the crippling effects of SCD.

Scheduling, cancellations, rescheduling, and missed visits

One of our biggest challenges was scheduling and completing study visits. Visits were usually scheduled by phone or text messages, and most took multiple attempts to be scheduled. Once scheduled, we had an inordinate number of cancellations; 49% of the SCD visits were cancelled. By contrast, 30% of those with healthy controls were cancelled.

The primary reason for cancellation by SCD participants was that they were in pain or in pain crisis, in the emergency department (ED), or admitted to the hospital. Other reasons for missed visits included lack of transportation or childcare, work issues, and bad weather, which could lead to pain crises. Some could not be reached or did not return calls before the scheduled visit despite many contact attempts. Most participants rescheduled their visits, although rescheduling also presented challenges since we had to contact them additional times. The main reasons for cancellation by the healthy controls were because of work or family complications, or losing interest in participation.

To facilitate attendance, the RSs scheduled visits on evenings and weekends, as needed. When participants were dealing with illness, as well as work, school, family, childcare, and other life issues, the RSs flexibility facilitated their continued participation. Equally important, when they cancelled visits, often multiple times, the RSs were understanding, at no time pressuring participants. To minimize cancellations, we entertained children when parents lacked childcare, secured wheelchairs for people with mobility challenges, picked up participants at the clinic or other UIC location, among other initiatives.

Other strategies for success

Continuous monitoring of recruitment and data collection progress was essential in this process. Recruitment and retention progress was a standing agenda item for the weekly team meetings. This monitoring allowed us to modify our processes and re-plan as necessary to ensure proper progress of the study. Other strategies that aided success included the RSs receiving additional training, as needed. For example, the study involved blood draws for genetic analyses, but going to the phlebotomy lab was complicated and time consuming. The RSs received phlebotomy training to remove this barrier. To dispel patients' concerns about the length of the study or the possibility of the procedures causing pain, we prepared a short video where a participant well known to most clinic patients talked about her participation. Another initiative was providing parking close to the study site. In a big city and with a participant population living with a chronic condition, convenient parking facilitated participation and was genuinely appreciated. Finally, participants received \$50 for every completed study visit in compensation for their time and expenses.

As in any longitudinal study, we were concerned about retention. To facilitate retention, we obtained the participant's phone number and other contact methods like email address, alternate phone and Facebook. We gave them a certificate of completion at study end (Figure 2). They were pleased to receive this token of our appreciation for their contribution to the scientific understanding of SCD pain.

Recruitment and Retention Outcomes of Strategies

A total of 354 SCD patients and 233 healthy controls were screened, and 325 SCD patients and 201 controls were eligible. SCD patients who were eligible but did not join the study (n=139) were either not interested (n=43) or expressed interest but never scheduled the first visit (n=96). Major ineligibility reasons among the SCD patients were low pain scores (n=15) and diabetes (n=9), and for the healthy controls were SCT (n=8), hypertension or diabetes (n=8), or pain (n=7). We successfully recruited and completed baseline measures on 186 SCD patients and 125 healthy controls, surpassing our targets of 180 and 115, respectively. We were also successful in recruiting patients who had not joined our previous SCD studies. Of 186 participants, 110 (59%) were new. It is also notable that 76 participants (41%) had joined at least one previous study in which SCD pain was a focus. We have collected the same pain measures over time, up to 10 years in some cases, for this group.

We also completed 498 SCD follow-up visits at approximately 6, 12, and 18 months after baseline (809 total visits). Between 3/2015 and the end of the study on 2/2019 we scheduled 1,531 study visits, including those for the healthy controls, but conducted only 809. The 722 visits cancelled included in many cases multiple cancellations for the same subject, although most cancelled visits were rescheduled. The majority of visits were cancelled at the last minute or participants did not show up. Since the visits were 1.5–3 hours long, we scheduled 3 hour slots to ensure completion without interruption. Last moment cancellations meant that the instruments and resources were idle during that time since it was extremely difficult to schedule another visit at short notice.

Despite the enormous challenges in completing study visits, our overall attrition was low. Of the 186 SCD patients enrolled, 151 completed all four data collection points, exceeding our target of 150 patients with full data, while 17 completed three data collection points, 11 completed two, and 7 completed only the baseline visit. The 35 patients who missed visits included 7 SCD participants who while in study died due to their illness. The attrition for the healthy controls was 5%. This indicated commitment to the study, in many cases because of an interest in helping others with SCD, since many were referrals from SCD patients or knew people with this disease. Healthy controls responding to Craigslist appeared to be more interested in the \$50 stipend.

Discussion

We encountered many challenges in our recruitment, retention and visit completion with individuals suffering from SCD, and used a number of strategies that were invaluable to our successes in this longitudinal study. SCD patients were in general interested in joining the study as evidenced by the fact that only 12% of approached patients expressed no interest in participation.⁹ The difficulty in recruitment often arose from patients' difficulty in making

time from their complicated lives to schedule the first visit, especially because they may have been in pain.

Also essential was having a well-trained and experienced team of RSs, who had gained the trust of the SCD patients through previous interactions, who were highly perseverant in their attempts to recruit and schedule participants, and allowed flexibility to ensure maximum convenience for participants. Constant monitoring of recruitment and data collection status enabled early identification of potential problems and allowed us to proactively institute the strategies that led to success. Once the SCD patients entered the study, they tended to remain, probably assisted by the commitment of our study personnel.

One major implication of our successful strategies is that it can be extremely costly in terms of personnel time to successfully complete a longitudinal study with a population suffering from a debilitating disease. Although we did not track the time invested in enrolling each individual subject and successfully scheduling each data collection point, the numerous times we had to approach many potential participants before enrollment and numerous cancellations and rescheduling of visits required an extraordinary amount of time and full attention of our three RSs. Success comes with a lot of effort, particularly when dealing with a population living with a chronic condition, many of whom had complicated lives. When developing a research budget, investigators need to account for additional time and labor costs necessary to re-approach patients to enroll them in a study.

A limitation was that we did not keep specific records as to why each participant missed appointments. Anecdotally we know that many of the SCD participants did not keep their appointments due to pain, and we recommend specifically documenting the reasons why each study session is missed in future studies. Sufficient study personnel is needed to address the unique needs of SCD study participants, including a liaison function to the SC clinic to coordinate analgesic needs.

Conclusion

The clarification of processes for successful recruitment of patients into SCD studies is important as they have been plagued by low recruitment and retention. Our research team has discovered successful approaches and a proven track record of strong and experienced leadership and recruitment in SCD studies. Our monitoring processes and kind, professional, and consistent approach are necessary components of performing a research study with this chronic pain population.

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Figure 1.
Study flyers in sickle cell clinic exam rooms

CERTIFICATE OF COMPLETION

Presented to

Participant's Name

You played a huge part in advancing science to improve care
for sickle cell pain! We appreciate your participation and
contributions to the QST Sickle Cell Pain Study.

*With our sincere thanks,
The QST Sickle Cell Team*

Figure 2.
Certificate of completion