iCanCope With Sickle Cell Disease: A Mobile Pain Management Intervention for Adolescents

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PROJECT TITLE:

SCH iCanCope with SCD: *User centered design of a web- and mobile-based pain self-management program for youth with sickle cell disease*

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1. Objectives

1.1. Purpose, specific aims, or objectives:

Aim 1. To determine feasibility and initial effectiveness of *iCanCope with Sickle Cell Pain* in youth with SCD pain.

Aim 2. To test if differences in self-efficacy, self-management behaviors, goal-setting, and perceived social support will predict changes in pain intensity and coping strategies in youth with SCD.

Aim 3. To examine possible moderators of effects of *iCanCope with Sickle Cell Pain* including engagement with treatment, demographic factors (family income, age, sex), and disease characteristics (SCD pain burden).

1.2. Hypotheses to be tested:

Youth who receive *iCanCope with Sickle Cell Pain* will achieve greater increases in adaptive coping and significant reductions in symptoms of pain and pain-related disability (primary outcomes) as well as significant improvements in physical and emotional functioning and disease-specific health-related quality of life (secondary outcomes) at post-treatment and 6-month follow-up compared to youth who receive the attention-control condition. Feasibility and acceptability will be demonstrated by high levels of treatment engagement and high ratings of satisfaction with the intervention.

2. Background

2.1. Relevant prior experience and gaps in current knowledge:

Limitations of Studies to Date	**Proposed *iCanCope with Sickle Cell Pain* Study**
• Poor user adherence. • Small patient samples and included those individuals with infrequent SCD pain. • Limited pain self-management content	✓ High accessibility using virtual delivery (app, website). ✓ Targeted approach to deliver pain self-management to patients with identified pain burden. ✓ Comprehensive self-management content based on other effective CBT pain programs that we have developed ✓ Adequate sample size and inclusion of individuals with clinically relevant pain as per pain burden score.

Advances Offered by *iCanCope with Sickle Cell Pain* Program for Youth with SCD Pain
Based on completed needs assessment as well as a 2014 scoping review of pain apps,[34] the proposed *iCanCope with Sickle Cell Pain* program will be comprised of personalized goal setting to improve pain and function, CBT-based pain self-management training and rehearsal, and peer-based social support through a closed online community for youth with SCD. These components will be delivered on the *iCanCope* smartphone app and be complemented by SCD self-management education on the *iCanCope* website. The website will also include specific modules designed to empower parents and caregivers to promote disease self-management in their adolescents.

2.2. Relevant preliminary data:[1]

Evaluation of Web-Based Management of Adolescent Pain ("Web-MAP")

Dr. Palermo has developed an Internet delivered CBT pain intervention called Web-MAP that includes 8 weeks of online modules to teach relaxation skills, pain coping strategies, and parent behavioral and communication techniques to youth with mixed chronic pain conditions. In the initial RCT involving 48 youth (11–17 years) with a variety of pain conditions (e.g., headache, stomachache, musculoskeletal pain), significant reductions in pain and disability were found for youth receiving Web-MAP compared to a wait-list control group.[41] Following up on this initial trial, Dr. Palermo recently completed enrollment for a second large RCT of Web-MAP involving 273 youth (ages 10-17 years) with chronic pain (and their parents) recruited from pain centers around the U.S. and Canada.[42] Adjunctive to pain clinic treatment, youth were randomized to one of two Internet treatment conditions, Web-MAP (CBT pain intervention, n=138) vs. Web-ED (education control, n=135). In our preliminary analyses, significant group-by-time interactions were found for effects of Web-MAP on children's pain-related disability ($p = .03$), sleep quality ($p = .02$), pain-related anxiety ($p < .05$), and parent behavior ($p < .001$) and distress ($p = .002$) at 6 months. Youth receiving the Web-MAP intervention achieved greater improvements in outcomes at 6-month follow up compared to youth receiving Internet Education.

Additional preliminary data have been collected from Web-MAP in youth with SCD to address concerns raised about youth's receptivity to learning cognitive-behavioral pain management skills. Web-MAP was piloted in 12 youth (M age = 14.2, 68% female) with SCD and their parents recruited from Connecticut Children's and Emory University (proposed sites in this application). Treatment engagement was high; youth logged into Web-MAP an average of 16.7 times (SD = 10.1, range 2-38) and parents logged in an average of 17.4 times (SD = 10.8, range = 3-43) over the 8-10 week treatment period. Youth completed an average of 6 out of 8 treatment modules and parents completed an average of 7 out of 8 treatment modules. To understand participants' experience with Web-MAP, qualitative interviews were conducted with 8 parent-child dyads. Overall, participants reported that the CBT program was a helpful tool for coping with pain: "I learned a lot about pain management and things I can do to make my load a little bit easier". However, they indicated a preference for a web program that is designed specifically for youth with SCD: "I thought Web-MAP was too simple or basic to help me. I want something more interactive that is a more real world experience". When asked what could be done to improve the web program, participants suggested developing an app: "Maybe…you could make it more accessible on your phone - like an app. That would be cool because, you know, most young adults have apps and cell phones". The proposed *iCanCope with Sickle Cell Pain* intervention will build upon the CBT pain content of Web-MAP, while significantly tailoring the program for the SCD population (largely of African descent) and to add symptom and goal tracking and peer-based social support. *iCanCope with Sickle Cell Pain* will also be delivered on an integrated smartphone and web-based platform, rather than the exclusively web-based format of Web-MAP.

<u>Development and Validation of "Sickle Cell Disease Pain Burden Interview-Youth" (SCPBI-Y)</u>

The SCPBI-Y is a brief, clinically relevant, multidimensional interview that has been validated to assess pain burden in youth aged 7-21 years with SCD.[6] The construct of "pain burden" was defined to encompass pain, and its impact on physical function, social/community participation, and the emotional aspects of daily living. The SCPBI-Y was developed using a panel of field experts (physicians, nurses, psychologists, researchers), patients, and caregivers as well as review of existing functional assessment and pain impact tools in the literature. The validation study involved 129

youth recruited from the inpatient and outpatient clinics of 4 pediatric hospitals. The SCPBI-Y demonstrated strong internal consistency reliability (α=0.891; N=129), cross-informant concordance (child-caregiver; n=40, r=0.78, p<0.001), and test-retest reliability (outpatient setting; n=47, r=0.80, p<0.001). Moderate construct validity was found with validated measures of functional ability, pain, and quality of life. These findings suggest that the SCPBI-Y scores are valid and reliable for evaluating pain burden in youth with SCD and will be used to screen youth in the proposed study.

Development and Validation of a Web-Based Multi-Dimensional Pain Diary for Youth with SCD

This study aimed to develop and establish the content validity of a web-based multi-dimensional pain diary for young people with SCD and conduct an end-user review to refine the prototype. Diary items were adapted from the e-Ouch©, an electronic diary measure with evidence of content validity, construct validity and responsiveness in youth with arthritis.[44–46] Experts in SCD, pain, and psychometrics reviewed the items for content, language, clinical relevance, comprehensiveness, and feasibility. Two iterative cycles of expert review were conducted with 15 experts in the first cycle and 12 in the second cycle. Subsequently, two iterative cycles of in-depth cognitive interviews with patients informed the diary design and guided the modification of items to ensure they were easy to understand, quick to complete, and useful in explaining pain. These potential end-users provided positive feedback on the design and prototype of the electronic diary. The next steps for the measure will be to evaluate construct validity and responsiveness. This study provided experience in daily monitoring of pain that will inform the approach used in the proposed RCT.

"Teens Taking Charge: Managing Arthritis Online" Disease Self-Management Program

Dr. Stinson, one of the study's Co-PIs is currently completing a multi-center RCT to evaluate the effectiveness of Teens Taking Charge: Managing Arthritis Online, a 12-week multi-component web-based program consisting of disease education, self-management strategies, and social support designed for youth with arthritis and their parents.[39] The program also includes weekly contact with telephone-based coaches (trained non-healthcare professionals). This program was developed and evaluated in English and French using a sequential phased approach, including iterative development, usability testing, and outcome evaluation. The current trial involves 324 youth (12-18 years) and one of their caregivers from 11 pediatric hospitals. 330 participants were randomized to the intervention or attention-control group. We are completing outcome data on HRQL, arthritis symptoms, treatment adherence, knowledge, and self-efficacy from both groups at baseline (T1), immediately following the intervention (T2), and at 6 (T3) and 12 (T4) months. Our group is also completing an NIH-funded trial of a Spanish version of the Teens Taking Charge program (n=300), and have adapted the program to meet the self-management needs of youth with cancer (Funded by CIHR) and hemophilia (Canadian Hemophilia Society). All of these web-based interventions were built by AboutKidsHealth, the same team that will develop and ensure the sustainability of the *iCanCope with Sickle Cell Pain* website.

Needs Assessment to Inform Development of *iCanCope with Sickle Cell Pain* Program

This study aimed to qualitatively explore the perceived pain self-management needs of young people with SCD.[12] A descriptive qualitative design was used with a purposive sample of young people aged 12-29 years with SCD (n=26), parents (n=5), and healthcare professionals (HCP; n=34). Our findings demonstrated that all young people had significant disease impact from SCD on their physical, emotional, role, and future functioning. Participants also described a lack of available resources to support disease

self-management, especially pain, and indicated that the proposed *iCanCope with Sickle Cell Pain* program could address this need (See Table 2). This is one of the first studies to explore the perceived pain self-management needs of youth with SCD with the goal of informing development of a web- and app-based self-management intervention for this population. We anticipate that this early involvement of youth, parents, and HCPs will help to ensure that the content and format of the intervention is relevant, acceptable, and meets the needs of this underserved group.

2.3. Scientific or scholarly background:

Poor Pain Self-management in Youth with Sickle Cell Disease

Sickle cell disease (SCD) is the most common genetic blood disease in North America and primarily affects people of African descent.[1] The hallmark feature of SCD is recurrent episodes of acute severe pain due to vaso-occlusive crisis (VOC; blockage of red blood cells).[1,2] SCD pain is reportedly worse than postoperative pain, as intense as terminal cancer pain, and has a negative impact on all aspects of health-related quality of life (HRQL).[3–5] Youth experience increased SCD pain burden as they grow from childhood to adolescence and young adulthood.[6] In addition to acute pain from VOC, many youth with SCD also experience daily chronic pain.[7] The negative consequences of recurrent SCD pain include depression and anxiety, academic underachievement related to missing school, little or no opportunities for social interaction with peers, impaired physical activity, poor sleep, and high stress.[8,9] The vast majority of SCD pain episodes (90%) are treated in the home setting;[10] unfortunately, many of these episodes may not be optimally managed.[11,12,13] Self-management has been defined as "the individual's ability to manage the symptoms, treatment, physical, and psychological consequences and lifestyle changes inherent to living with a chronic illness".[14] The most successful self-management interventions are rooted in the principles of cognitive-behavioral therapy (CBT).[15] CBT involves normalization of the patient's experience through education, training in strategies for managing disease-related symptoms and other stressors, enhancing self-efficacy, and guidance on developing and maintaining a long-term self-management plan.[16–18] Studies in pediatric and adult SCD patients demonstrate that CBT-based therapies that promote disease self-management can lead to reduced symptoms, improved HRQL, and decreased healthcare utilization.[19] Gaining skills in monitoring and managing their SCD pain at home is particularly critical to achieve during childhood because SCD is associated with worsening pain and disability in adulthood.[19,20]

Barriers to Providing Pain Self-Management Care for Youth with SCD and their Caregivers

Home-based pain management for SCD is typically inadequate due to a lack of appropriate training for patients and parents.[11] Youth with SCD and their caregivers may be reluctant to seek out mental health services for pain management and when interested rarely have access to these services due to geographic restrictions (e.g., available only in tertiary centers), limited availability of trained clinicians to deliver the therapies, inaccessibility due to school and work schedules, as well as direct and indirect incurred costs if additional healthcare visits are used to provide this training.[21–23] Moreover, these therapies tend to be delivered in individual or group sessions in specialty clinics by highly trained personnel, and are unsuitable for widespread distribution to community and home-based settings.[24]

Rationale for Web and Mobile Technologies to Enhance Delivery of Pain Self-management Care

Web and mobile technologies can be applied to enhance the accessibility of pain self-management therapies.[25,26] In addition to improving access, these technologies can empower youth to take an active role in managing their condition by providing "in the moment" access to pain coping strategies.[27] These technologies can therefore be leveraged together to build a

tailored self-management program for youth with SCD that emphasizes empowerment, involves parents, facilitates the creation and tracking of personalized goals, and offers peer-based social support. A media-rich website delivered on a desktop/laptop computer is ideal for teaching complex CBT-related skills using animations, illustrations, and videos. Smartphones are deeply integrated into the daily life habits of most youth,[28] and therefore offer an ideal platform to prompt practice of CBT-based coping skills as needed in the moment.

Systematic and Meta-Analytic Reviews of Internet-Based Interventions for Pain Management

Outcome data for web-based disease self-management interventions have rapidly increased over the past decade.[29–31,32] Results from systematic and meta-analytic reviews suggest consistent efficacy for symptom reduction, knowledge attainment, and improved health behaviors in individuals with painful and other chronic health conditions. In the field of chronic pain, there is emerging evidence from two recent systematic reviews in adults[32,33] (e.g., 11 RCTs with a pooled effect size of |0.285|; 95% confidence interval [CI]; |0.145 to 0.424|)[33] and one in children/adolescents[30] (4 RCTs with a pooled effect size of |0.41|; 95% CI; |0.74 to 0.07|) that self-guided treatments delivered over the Internet reduce pain intensity. However, there is little empirical data on the availability and effectiveness of web-based pain management interventions that target the unique developmental and disease-related needs of youth (aged 12-18 years) with SCD.

Systematic Reviews of Smartphone-Based Interventions for Pain Management

There are a growing number of smartphone-based pain self-management applications ("apps") available for patients to download and use on their personal mobile devices. In 2014, we conducted a comprehensive scoping review of available pain self-management apps across the iPhone, Android, Windows, and BlackBerry stores.[34] We identified 279 apps across stores with the majority (64%) designed for the Android platform. Pain self-care skill support was the most common self-management function (77.4%). Apps were also reported to provide pain education (45.9%), symptom self-monitoring (19%), social support (3.6%), and goal-setting (0.72%). No apps were comprehensive in terms of pain self-management content, with the majority of apps including only a single self-management function (58.5%). Other major limitations were noted: only 8.2% of apps included a healthcare professional in their development, patient engagement was limited, not a single app provided a theoretical rationale, and only 1 app underwent scientific evaluation.[34]

Given that successful CBT requires strong patient engagement and consistent skills practice, it is critical that intervention content and design are relevant and appealing to end-users (i.e., youth with SCD and their families).[35] There is a clear need to develop and test evidence-based apps to better support patients and families with accessible SCD pain self-management care.

Existing Pain Self-Management Programs for Youth with SCD Pain

To our knowledge, there is only one technology-based program (used in research but not publicly available) that provides pain self-management support to youth with SCD. The effectiveness of this program has been evaluated via wait-list control RCT in a sample of 46 youth (aged 8-21 years) and their caregivers.[36,37] The intervention involved a single session of in-person CBT training followed by 8 weeks of home-based practice using smartphones. In comparison to control, the primary study outcome of negative thinking in response to pain was unchanged.[37] A major study limitation was that youth did not use the smartphone app frequently. On average, youth accessed the smartphone pain coping skills on only 12% of the total days that they had the device. The range of pain frequency reported by the patient sample [mean of 15.2 pain days (SD 13.6) over 8 weeks] was relatively broad and thus some participants had relatively infrequent pain. Overall, the smartphone-assisted coping skills were used on less than 25% of total pain days. Given this low usage, the authors identified a clear need for future

studies to build strategies for increasing engagement and for properly targeting SCD patients who need pain self-management.[37]

There are currently no standardized recommendations related to the necessary content for web and app-based pain self-management programs. In our 2014 review, we catalogued existing pain apps in terms of the presence or absence of self-management functionalities based on elements that have evidence of effectiveness.[18,38–40] To assess app comprehensiveness, the following functions were assessed: **(a)** pain tracking, **(b)** ability to set goals related to improving pain and functioning, **(c)** training in CBT-based pain self-management strategies, **(d)** social support, and **(e)** disease-specific education.

Thus, while the one existing program[36,37] for youth with SCD pain demonstrates the potential of using technology to promote pain coping in this group, it is limited by: **(a)** very low patient usage, **(b)** lack of demonstrated effectiveness for improving clinical outcomes, **(c)** lack of personalized goal-setting to improve functional outcomes, **(d)** lack of social support component, and **(e)** lack of SCD education delivered on the app. Importantly, this program also required an initial in-person CBT training session, which presents barriers in terms of cost and accessibility to many patients. (See Table 1) There is currently no single technology-based program that provides comprehensive pain coping training for youth with SCD and their caregivers.

2.4. Prior approvals:

Currently participating sites received IRB approval, this is an extension of the approved study IRB #: STUDY00000693. Before beginning the referral process at any new sites, we will ensure that approvals have been obtained and we will maintain records of their approvals including all modifications.

3. Study Endpoints[2]

3.1. Primary and secondary endpoints:

Primary endpoint is greater reductions in pain-related disability. Secondary endpoint is the reduction of pain and anxiety/depressive symptoms.

3.2. Primary or secondary safety endpoints:

There are no safety endpoints in this study.

4. Drugs, Devices and Biologics[3]

4.1. Manufacturer and name of all drugs, devices and biologics:

The mobile medical application, iCanCope with Pain was developed by The Hospital for Sick Children in Ontario, Canada.

4.2. Description and purpose of all drugs, devices and biologics:

The iCanCope with Pain is a smartphone app to help young people manage persistent pain. It is comprised of personalized goal setting to improve pain and function, CBT-based pain self-management training and rehearsal, and peer-based social support through a closed online community for youth with SCD. The app provides users with reminder and positive feedback on their progress to reaching their goals. The app will provide in-the-moment access to pain coping strategies to promote positive changes in mood, behavior, and pain. The app will also allow youth to track their symptoms in real-time and generate customized reports from their data to show clinicians. The parameters that will be tracked by the app include pain, pain impact, mood, and sleep. The app will use the diary input to push relevant advice to the user.

4.3. Regulatory status of all drugs, devices and biologics:[4]

This study will be testing the initial effectiveness of the iCanCope app and website. These tools meet the definition of device because they intended to be used in the mitigation of disease. Per information found in the FDA published guidance for Mobile Medical Applications, this 'device' would be one for which the FDA would intend to exercise enforcement discretion - (meaning the FDA will not intend to enforce requirements under the FD&C Act and an IDE will not be needed for the study).

4.3.1. Drugs or Biologics:
☐ IND Exempt. Explain:[5] ✍Click here to enter text.
☐ IND.

4.3.2. Devices:
☐ IDE Exempt. Explain:[6]
☐ Abbreviated IDE / Non-Significant Risk. Explain:[7] ✍Click here to enter text.
☐ IDE / Significant Risk.

4.4. Plans to store, handle, and administer any study drugs, devices and biologics so they will be used only on subjects and be used only by authorized investigators:
N/A

5. Procedures Involved

5.1. Study design:[8]

A multi-site parallel group pilot RCT of *iCanCope with Sickle Cell Pain* versus *Attention Control Education* will be conducted with 160 youth (age 12-18) with SCD and their caregiver. The sites will include Emory/CHOA, The Hospital for Sick Children, and Connecticut Children's Medical Center, University of Mississippi, University of Florida, Boston Medical Center, Ann & Robert H. Lurie Children's Hospital of Chicago, Nationwide Children's Hospital, C.S. Mott Children's Hospital and Seattle Children's Hospital. Participants will be randomized into one of two groups; experimental group or attention control group. The intervention phase will last 6-8 weeks, with participants given a maximum of 12 weeks to complete the intervention content. This treatment period is based upon the typical duration of chronic pain intervention trials.[42,58] Outcome assessment will occur at baseline (T_1), immediately after completion of the intervention (2 months; T_2), and repeated at 6 months post-intervention (T_3) to allow for assessment of maintenance of treatment gains as youth with SCD may have fluctuations in their disease course that influence pain outcomes.

5.2. Research procedures:[9]

Experimental Group

In addition to standard medical SCD care, youth will receive the *iCanCope with Sickle Cell Pain* intervention over a period of 6 to 8 weeks. Participants will be given a maximum of 12 weeks to complete the program if delays occur. The web and app intervention will be delivered on restricted password-protected applications that will allow us to track user engagement (detailed user level and aggregate analytics). Youth will be encouraged to log onto the app (via push notifications) to track their symptoms, develop and track functional goals, access coping strategies, and socially engage in the *iCanCope* community. Youth and their caregiver will also be encouraged to access the *iCanCope* website, which will contain interactive SCD education and self-management strategies. The youth website will be organized into 6 core modules and 2 optional** modules, participants will complete one module per week (Table 3). Delivery of the optional modules will be based on response to the baseline measures. See Table 5 for a list and

description of all study measures. Eligibility to receive the option insomnia module will be based on insomnia symptoms evaluated using two questions from the Adolescent Sleep Wake Scale (ASWS) assessing difficulty falling asleep ("I have trouble going to sleep") and difficulty maintaining sleep ("After waking up during the night, I have trouble going back to sleep"). Adolescents responding "quite often," "frequently, if not always," or "always" to either of these will be judged to have symptoms of insomnia, and receive the module. Eligibility for the optional negative emotions module will be determined by the baseline score on the 4-item PROMIS depressive symptoms scale, with a score of 9 or higher indicating eligibility to receive the optional module. Eligibility for the optional modules will be sent via secure email to SickKids from Seattle Children's. Children's staff will only indicate "yes" or "no" if they meet the criteria for the PROMIS and ASWS measures. There will also be content designed for caregivers to provide instruction in the best ways to support youth's pain management skills and encourage adaptive coping, divided in to six modules (Table 3).

**optional modules for this study are potentially two additional modules that would be given to youth only if they are randomized to Group A and if their baseline scores qualify them for one or both of them. This is not optional, but an addition to their modules, similarly to how branching logic works.

Experimental Group Semi-Structured Interviews: Following the completion of the iCanCope with Sickle Cell Pain program, youth and parent participants will be invited to participate in a semi-structured interview over the phone with the research staff from SCRI. The interviews will be conducted any time between the post-treatment (T_2) and 6 month follow up assessment (T_3). All participants that are within the timeframe stated above will be asked to participate.The semi-structured interview will allow participants to qualitatively comment on the intervention. The research staff will follow a semi-structured interview guide with questions pertaining to their experience using the iCanCope with Sickle Cell Pain website and app (see attached guides in supporting documents). The interview will be audio-recorded and a research staff will transcribe the interview verbatim. The research staff will be trained on how to transcribe the interview and a different staff member will double check the transcription.

The semi-structured interviews will determine (i) participants' acceptability of and level of engagement in the iCanCope with Sickle Cell Pain program and (ii) their likes and dislikes of program, and improvements on the program content and design. The research staff will verify transcripts against the tapes and field notes taken during the interviews will be transcribed and included in the analytic process. All data will be read by multiple independent coders to obtain an overall understanding of the data and develop themes based on the research questions. This data will be used to refine the iCanCope with Sickle Cell Pain program for future trials.

Table 3. Youth Intervention Web Content: *iCanCope with Sickle Cell Pain*

Module Number	Module Title	Content/Skills
1	Introduction	Intro, SMART Goals, 3Ps pain, types of psychological treatments
2	Managing stress	Reduce negative thoughts: replace with positive and thought stopping
3	Relaxation	Relaxation: deep breathing, muscle relaxation, imagery, mini relaxation
4	Sleep	Pain and sleep, healthy sleep, ways to fall and stay asleep

5	Communication and self-advocacy	Communication skills, talking with healthcare team and school
6	Healthy lifestyle	Pacing, graded activity, hydration
7	Optional: Insomnia	Think differently about sleep, more falling and staying asleep strategies
8	Optional: Negative emotions	Identify negative emotions, schedule pleasant activities, find the positives.
Parent Intervention Web Content		
Module Number	**Module Title**	**Content/Skills**
1	Introduction	What your teen will learn, SMART goals to support your teen
2	Behavioral plans	Behavioral plans
3	Problem solving 1	Bright IDEAS problem solving system
4	Problem solving 2	Bright IDEAS problem solving system
5	Communication	Strategies that can help you talk and listen to your teen, strategies to communicate with health care providers and school staff
6	Wrap-up	Review

Attention Control Group

The control group is designed to account for potential effects on outcomes of time, attention, as well as computer use during the intervention period. In addition to standard medical care, youth in the attention control group will be provided with access to a self-guided education study website, called the Sickle Cell Library, which will contain static education about SCD (no self-management skills, goal-setting, or social support content). Any site links will be monitored weekly to ensure that they do not add any "active ingredients" during the trial. We have completed a 2015 scoping review of existing SCD patient education websites (see above) to identify content to include in the control site.[47] The control condition will be delivered over 8 weeks on a restricted password-protected platform that will allow us to track usage and engagement similar to the experimental group. Participants will be encouraged to log onto the control website and complete all study outcome assessments online at the same time intervals as the experimental group. Participants in the control group will receive 4 check-in contacts (once every 2 weeks) by their preferred contact method to make sure they are not having any issues with the website and remind them to review content.

Table 4. Control Website Content for Teens and Parents: Sickle Cell Library		
Section Number	**Title**	**Education Content**
1	Introduction	Intro to program
2	About sickle cell disease	What is SCD, symptoms and complications
3	Treatments and medication	About medications, transfusions, pain medications, complementary medicines
4	Acute and chronic pain	Acute pain, chronic pain, factors that influence pain experience

5	Healthy lifestyle	Diet, exercise, alcohol and drugs, school and hospital stays
6	Looking ahead and research	Transition to adult care, clinical research

Both Groups

Both groups will complete baseline (T_1) measures online prior to randomization. Participants will be randomly allocated to either the experimental (*iCanCope with Sickle Cell Pain)* or attention control education group. Following program completion at 2 months (T_2), participants will be asked to complete post-test measures. Electronic and SMS text reminders will also be sent by the study team. Participants will be asked to complete the same measures at 6 months (T_3) following completion of the intervention or control condition. All measures will be completed online, either at home or in clinic. Paper versions of measures will be available if online access is not possible. Participants in both groups will be able to contact staff for technical problems with the app or website. Research staff will also be available at routine clinic visits during the study period.

5.3. Data sources that will be used to collect data about subjects:[10]

	Table 5. Study Measures				
Measure	**Description of Measure P=parent report, T=teen report**	**Time to Complete**	**T1**	**T2**	**T3**
	Screening and background measures				
Sickle Cell Pain Burden Interview (SCPBI)	The SCPBI will be used to screen for SCD pain burden.[6] (P, T)	2-3 minutes	X	X	X
Background questionnaire	This questionnaire will assess sociodemographic variables (including family income), pain characteristics such as intensity, location, and temporal features (T) and access / use / comfort with smartphones and internet technology. (P, T)	5 minutes	X		
Treatment expectancies questionnaire	7-item questionnaire to rate treatment expectancy. (P, T)	3 minutes	X		

Adolescent Sleep Wake Scale	2 items from the questionnaire will be used to screen for the optional website intervention module on insomnia.[61] (T)	1 minute	X		
	Primary outcome measures				
Daily pain diary (7 day)	Pain intensity (NRS-11), location, and 9-item CALI.[62] Completed daily for 7 days (T)	3 minutes	X	X	X
Coping Strategies Questionnaire for Sickle Cell Disease (CSQ)	The CSQ[63] will assess use of different strategies to cope with pain (three primary scales: coping attempts, negative thinking, passive adherence).	15 minutes	X	X	X
	Secondary outcome measures				
PROMIS-25 v1.1 Pediatric Profile	The PROMIS Pediatric Profile will be used to assess physical and emotional functioning. This is a collection of short forms containing 4 items from PROMIS domains (Depressive Symptoms, Anxiety, Mobility, Pain Interference, Fatigue, and Peer Relationships).[64] (T)	10 minutes	X	X	X
[redacted]	[redacted]	[redacted]	[redacted]		

	items comprise each subscale.[65] (P)				
[redacted]	[redacted]	[redacted]		[redacted]	[redacted]
Treatment Evaluation Inventory (TEI)	The TEI will be used to access acceptability (P, T)	3 minutes		X	
Patient's Global Impression of Change Scale	Change in global health / quality of life.[66] (T)	2 minutes		X	X
Bath Adolescent Pain Questionnaire – for parents (BAPQ-P)	The BAPQ is a measure to assess social functioning, physical functioning, depression, general anxiety, pain specific anxiety, family functioning and development. (P)	15 minutes	X	X	X
Symptom Checklist - 90	The Symptom Checklist -90 assesses a range of psychological symptoms, including obsessive compulsive, depression, anxiety, etc. (P)	12-15 minutes	X	X	X
Adult Responses to Child Symptoms (ARCS)	This 13-item questionnaire assesses parent behavior including protectiveness, minimizing, and encouraging response to children's pain behavior. (P)	5 minutes	X	X	X
Client Service Receipt Inventory (CSRI)	SCD healthcare utilization.[67] (P)	10 minutes	X		X
Adverse events self-report assessment	Adverse event form will be used.	3 minutes		X	X

5.4. Data to be collected, including long–term follow–up data:[11]
Outcome data are self-report and will be collected online using the study website (Table 5). All measures have evidence of reliability and validity in youth in this age range, and include the core measures recommended for pain clinical trials.[60] T1= pre-treatment; T2 = post-treatment (2 months); T3 = follow-up (6 months post-treatment).

6. Data and Specimen Banking[12]

6.1. Complete list of the data and/or specimens to be included in the bank:[13]
N/A

6.2. Location of data and/or specimen storage:[14]
N/A

6.3. List of those with direct access to data and/or specimens in the bank:
N/A

6.4. Length of time data and/or specimens will be stored in the bank:
N/A

6.5. Procedures for protecting the confidentiality and privacy of the subjects from whom the data and/or specimens were collected:[15]
N/A

6.6. How the data and/or specimens will be made available for future use:
N/A

6.6.1. Who can request data and/or specimens from the bank:
N/A

6.6.2. Format in which data and/or specimens will be provided:
N/A

6.6.3. Process for investigators to request data and/or specimens:[16]
N/A

6.6.4. Restrictions on future use:[17]
N/A

6.6.5. Plan for providing data results from banked data/specimens:
N/A

7. Sharing of Results

7.1. Plan to share results with subjects/others:[18]
If requested by the participant, study results will be shared with participants after participation is complete and findings are published. These results would be in the form of a letter outlining study findings.

8. Study Timelines

8.1. Duration of an individual subject's participation in the study:
Subjects will be participating in the study for approximately 10 months.

8.2. Duration anticipated to enroll all study subjects:
Approximately 3.5 years.

8.3. Estimated date for the investigators to complete this study:
We estimate that December 2022 will be the final data collection date for primary outcome measure and will be conducting data analysis for another 1-2 years.

9. Study Population[19]

9.1. Inclusion criteria for each subject population (e.g., patients, parents, providers):
Inclusion Criteria: Youth will be eligible if they (a) are aged between 12-18 years, (b) are diagnosed with any type of SCD, (c) are able to speak and read English, (d) score at least 4 on

the Sickle Cell Pain Burden Interview (SCPBI) [6], and (e) have access to the internet on a smartphone. Parents or caregivers will be eligible if they (a) are able to speak and read English and (b) have access to the internet on a smartphone or computer.

9.2. Exclusion criteria for each subject population:

Exclusion Criteria: Youth will be excluded if they have significant cognitive limitations that would impair their ability to use and understand the *iCanCope with Sickle Cell Pain* program, as per their healthcare provider or parent. Youth will also be excluded if they have previously received more than 4 sessions of outpatient psychological therapy for pain management in the 6 months prior to the time of screening.

9.3. Vulnerable populations involved in the study:[20]

☒ Children/Teenagers[21]

Risk assessment specific to this vulnerable population and additional safeguards:[22]

The research is considered minimal risk as the probability and magnitude of psychological and physical risks anticipated in this research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. The relaxation skills and pain coping strategies taught in the online program is comparable to what is taught within clinical programs. The participant has the option of withdrawing participation at any time during the study. Knowledge gained through this research will guide future research and interventions to help adolescents with SCD.

☐ Children who are Wards of the State[23]

Risk assessment specific to this vulnerable population and additional safeguards:

✍Click here to enter text.

☐ Adults Unable to Consent[24]

Risk assessment specific to this vulnerable population and additional safeguards:

✍Click here to enter text.

☐ Neonates of Uncertain Viability or Non–Viable Neonates[25]

Risk assessment specific to this vulnerable population and additional safeguards:

✍Click here to enter text.

☐ Pregnant Women[26]

Additional safeguards:

✍Click here to enter text.

☐ Prisoners[27]

Additional safeguards:

✍Click here to enter text.

10. Number of Subjects

10.1. Total number of subjects to be enrolled locally:[28]

60 dyads: children with SCD and their parents will be enrolled from Seattle Children's Hospital.

10.2. Total number of subjects to be enrolled across all participating sites:[29]

160 dyads: children with SCD and their parents will be enrolled from participating sites.

10.3. Number of screened subjects versus the actual number enrolled in the research:[30]

Participants will be recruited from pediatric centers with SCD patient populations. The patient populations at these centers provide access to about 500 patients who are likely eligible for recruitment into this study based on proposed inclusion criteria. We anticipate a 30-40% refusal rate based on our experience recruiting in this population.

10.4. Power analysis:

Based on prior and current study experience, and the pool of available study candidates, we plan to enroll a total of 160 subjects into the pilot RCT. With attrition conservatively estimated at 20% we expect a final sample size of 128. This proposed sample size is based on the following power calculation using preliminary data from investigator experience with prior pain trials and published trials in SCD:

Calculations are based on expected differences in youth pain-related disability and pain intensity. Group sample sizes of 52 and 52 achieve 84% power to detect a difference of 1.0 in pain-related disability between the two treatment conditions, with three assessments, AR(1) covariance structure, SD=4, ICC=0.2, and alpha=0.05. If the difference is 1.5 between treatment arms, then 52 per group achieves 99% power with the same assumptions. For pain intensity, group sample sizes of 49 and 49 achieve 80% power to detect a difference of 0.75 in pain intensity (average over three time points) in a design with 3 repeated measurements having a AR(1) covariance structure, SD=2, ICC=0.2 and 0.05 alpha.

11. Withdrawal of Subjects

11.1. Anticipated circumstances under which subjects will be withdrawn from the research without their consent:

The PI may decide to withdraw participants from the study if a family is not able to comply with study procedures or do not understand study instructions.

11.2. Procedures for orderly termination:

If a participant must be withdrawn from all study procedures the study staff would contact the family to explain the cause for study withdrawal and finalized study termination.

11.3. Procedures that will be followed when subjects withdraw from the research, including partial withdrawal from procedures with continued data collection and withdrawal from data/specimen banking:

Full Withdrawal: If a participant must be withdrawn from all study procedures the study staff would contact the family to explain the cause for study withdrawal and finalized study termination.

Partial Withdrawal: If a participant partially withdraws from the procedures, study staff would contact the family to discuss family's interest in participation. If the family is interested, the study procedures will be continued, if the family is not interested, this will be considered a full withdrawal.

12. Risks to Subjects

12.1. Reasonably foreseeable risks to subjects (include each study population, each arm, and optional procedures):

This study is minimal risk. There are potential risks around emotional distress, time commitment, and confidentiality. Although asking about physical symptoms and mood/behavior does not typically result in any distress, there is a small risk of emotional

distress. There is a potential risk of loss of confidentiality. Some of the questionnaires include questions that could uncover depression or suicidal ideation. See below for plan.

12.2. Procedures with unforeseeable risks:

There are no anticipated harms associated with participating in this study. Participants may get upset when talking about their pain from SCD. This risk will be discussed when consent is provided, and participants will be reminded that if they become upset at any time during the course of the study they can talk to the research assistant and their health care team (for example, nurse, social worker, or psychologist). Participants may be inconvenienced with the amount of time required to participate in the study (2 months + 6 month follow up).

12.3. Procedures with risks to an embryo or fetus should the subject be or become pregnant:

N/A

12.4. Risks to others who are not subjects:

N/A

12.5. Procedures performed to lessen the probability or magnitude of risks:

Participants will be advised they can skip any questions they feel uncomfortable answering. To support confidentiality, adolescents will be asked to complete questionnaires independently. We will make every effort to protect this data. For example, all data will be coded with a unique ID number. Participants will be informed of their right to refuse to participate in any part of the data collection and given the phone numbers of the PI and the Seattle Children's IRB in the event that they desire further information or would like to issue a formal complaint. In the course of the study, we may become aware that participants are an imminent threat to themselves. The PI will be available 24 hours a day to be called via cell phone to address crisis questions and the study team will follow the Critical Incident Protocol. Crises that are high risk and imminent will be acted upon immediately with staff linking participants to appropriate crisis services. Parent contact information will be used when appropriate. Lower risk and less imminent cases are also reviewed by the clinically responsible PI. All actions taken will be documented on a case report form and reported to the IRB.

13. Potential Benefits to Subjects

13.1. Potential benefits that individual subjects may experience from taking part in the research:[31]

No immediate and direct benefits to individual participants are expected. However, some participants may improve their pain self-management skills from participating in education control or active intervention. The information acquired from this study also will allow researchers and health care providers to have a better understanding of the psychosocial factors associated with pain and functioning in SCD and how to best teach self-management skills. The information from this proposed project may be useful to clinicians who deal with SCD patients and families, who often request information about how to better manage pain and in the design of future interventions.

14. Data Analysis/Management

14.1. Data analysis plan, including statistical procedures:

Data analyses will be performed using SPSS v20.0 and SAS v9.3. Distributions of primary and secondary outcome variables at each time point (and on difference scores between time points) will be examined first with summary statistics and graphical tools. For outcome variables with highly skewed distributions, we will either apply transformation or non-parametric test procedures. Preliminary work will also involve computation of scale reliabilities (e.g., internal consistency using Cronbach's alpha) of all of the self-report measures. The pilot RCT analysis will be an intent-to-treat analysis including all randomized subjects.

Analytic plan for Aim 1

Feasibility will be determined by calculating rates of accrual, drop out, compliance, and missing data with 95% CI's. Criteria for feasibility success will be based on previous studies by our group[39,72]: accrual rates >70%, attrition rates <20%, minimal technical difficulties (i.e., reported by <10%), high acceptability and satisfaction (item mean score of 4 on AES), adherence rates >80%, and minimal missed responses. In Aim 1, we will also determine preliminary efficacy of the intervention. To account for clustering due to repeated assessments within individuals, generalized estimating equations (GEE) will be used. Interaction terms will be used to compare the mean change from pre-treatment to post-treatment for the *iCanCope* group with the corresponding mean change for the *Attention Control Education* group. Single degree of freedom contrasts will test if there is a statistically significant change in pain and coping from pre-treatment to immediate post-treatment for the two groups separately; additional contrasts will be computed to test if there is a statistically significant mean change from baseline to the 6-month follow-up for each group. Secondary treatment outcomes (physical and emotional function, HRQL) will also be examined using GEE to test significant mean changes over time and between groups by using interaction terms and contrasts. Treatment fidelity will be assessed by examining differential attrition (completers vs. non-completers) between and within groups using chi-squared tests and logistic regression models.

Analytic Approach for Aim 2 and 3

Our working hypothesis related to Specific Aim 2 is that differences in self-efficacy, self-management behaviors, goal-setting, and perceived social support will predict changes in pain intensity and coping strategies in youth with SCD. The test of this hypothesis will follow the recommendations for testing "moderated mediation" models described by Bauer, which permits specification of a single equation that furnishes the coefficients necessary for estimating total, direct, and indirect effects in a multilevel mediation model.[84] The single equation is made possible by creating a new outcome variable ("Z") that comprises both the outcome variable of interest ("Y") and mediating variable ("M") simultaneously; the two are distinguished by creating two specification variables ("S") that take on the value of 0 and 1 depending on whether the new outcome variable "Z" represents the mediating variable or outcome variable. The single model is then specified as:

$$Z_{ij} = S_{M_{ij}}(d_{M_j} + a_j X_{ij}) + S_{Y_{ij}}(d_{Y_j} + b_j M_{ij} + c'_j X_{ij}) + e_{Z_{ij}}$$

. The model permits the estimation of the indirect effect $(a_j b_j)$ as a random effect, and by expressing this random effect as a linear function of a Level 2 variable (in this case, treatment group), it is possible to evaluate group differences in the proposed meditational model (i.e., "moderated mediation"). The models will be specified with "time" as a predictor ("X") of the outcomes pain intensity and coping strategies, with the self-efficacy, self-management behaviors, goal-setting, and perceived social support variables included as mediating variables ("M"). The indirect effect of time will then be specified to be predicted by treatment. As such, this model will allow a test of whether an individual's changes over time in pain outcomes are partly explained by changes in the

hypothesized mediators and whether the strength of this indirect effect varies depending on group.

To address Specific Aim 3, exploratory analysis will be used to examine possible moderators of effects of *iCanCope with Sickle Cell Pain* including engagement with treatment, demographic factors (family income, age, sex), and disease characteristics (SCD pain burden). To assess the moderation effect an interaction term will be included for each separate moderator variable and key predictor of interest (two-way interaction between moderator and group for cross-sectional analysis and three-way interaction between moderator, group and time for longitudinal analysis) in the regression models and test its significance using Wald t-test.

14.2. Quality control procedures for collected data:[32]

The PI will supervise the study coordinator in collating and storing data and overseeing the integrity of study records. Data will be maintained on a network server with password protection and daily backup of data performed. The primary source of data will come from online assessments conducted on the REDCap website provided through ITHS at UW. REDCap has extensive security precautions appropriate for the storage of PHI. REDCap was developed specifically around HIPAA-Security guidelines and is recommended for use by researchers. In 2010 the Institute of Translational Health Sciences Biomedical Informatics Core (ITHS BMI) began supporting an installation of REDCap (Research Electronic Data Capture), which is software specifically designed for electronic data capture (EDC) for clinical trials. REDCap features include differentiated user roles and privileges, user authentication and authorization security, electronic signatures, SSL encryption, and comprehensive auditing to record and monitor access and data changes. PIs can configure REDCap User Rights and Data Access Groups to provide granular study data access to authorized study personnel. Access to servers is restricted to authorized ITHS BMI support personnel. The servers are located on ITHS-owned hardware in a secure server room at the University of Washington. This server room meets the technical requirements for HIPAA compliance and hosts other servers containing Protected Health Information (PHI). The Operating System of each server will be kept fully patched and firewalled in accordance with UW Medicine Information Security Policy. All identifying information will be removed from all electronic data, thus protecting the identities of participating families. Data will be kept for a minimum of seven years.

To ensure the accuracy of the data the following processes will be implemented:

- The study coordinator will check all data from REDCap questionnaires for completeness.
- REDCap will be exported directly to SPSS statistical software, to ensure the participant's responses are accurately entered into the database used for analyses. This will be secure and stored locally at Seattle Children's.

iCanCope Program- The Toronto site will be responsible for maintaining the study iCanCope smartphone app, which will be used for some online data entry by study participants. The iCanCope app will be hosted at the Centre for Global eHealth Innovation at University Health Network (UHN). Data stored on the iCanCope server will be protected from data corruption as per policies of the UHN data center. Regular backups will be performed in order to prevent against unrecoverable corruption issues. All processes will be PHIPA compliant.

15. Confidentiality[33]

15.1. Procedures to secure the data and/or specimens during storage, use, and transmission:

All participant data will be coded with a unique identification number, thus ensuring the subject's identity as a participant in this study will remain confidential. The research records will be kept confidential and protected health information will be safeguarded as required by Seattle Children's IRB and HIPAA regulations. The research staff and Seattle Children's IRB will be allowed to inspect the information collected from this study. Data collection online through REDCap will also be private and confidential. REDCap was developed specifically around HIPAA-Security guidelines and is recommended for use by researchers. In 2010 the Institute of Translational Health Sciences Biomedical Informatics Core (ITHS BMI) began supporting an installation of REDCap (Research Electronic Data Capture), which is software specifically designed for electronic data capture (EDC) for clinical trials. REDCap features include differentiated user roles and privileges, user authentication and authorization security, electronic signatures, SSL encryption, and comprehensive auditing to record and monitor access and data changes. PIs can configure REDCap User Rights and Data Access Groups to provide granular study data access to authorized study personnel. Access to servers is restricted to authorized ITHS BMI support personnel. The servers are located on ITHS-owned hardware in a secure server room at the University of Washington. This server room meets the technical requirements for HIPAA compliance and hosts other servers containing Protected Health Information (PHI). The Operating System of each server will be kept fully patched and firewalled in accordance with UW Medicine Information Security Policy.

No personally identifying health information is stored in the app. Users are given unique login IDs and use nicknames as usernames in the app. All participant data will be coded with a unique identification number, thus ensuring the subject's identity as a participant in this study will remain confidential. The research records will be kept confidential and protected health information will be safeguarded as required by Seattle Children's IRB and HIPAA regulations. The research staff and Seattle Children's IRB will be allowed to inspect the information collected from this study. All contact information and identifying data will be stored in a secure computer file within Dr. Palermo's research lab at SCRI. Participant contact information and PHI will be sent to SickKids Toronto and it would be stored in a secure, password protected computer file within Dr. Stinson's lab at SickKids.

15.2. Location where the data and/or specimens will be stored:

All contact information and identifying data will be stored in a secure, password protected computer file within the PI's research lab at Seattle Children's. Participant contact information and PHI will also be stored in a secure, password computer file within Dr. Stinson's lab at SickKids for purposes of setting up the login information for the app and website and for programming the iCanCope 'optional' modules.

15.3. Length of time data and/or specimens will be stored:

Data will be kept for a minimum of seven years

15.4. Individuals with access to data and/or specimens:

Only the research staff and Seattle Children's IRB will be allowed to inspect the information collected from this study.

15.5. Process for the transmission of data and/or specimens outside Seattle Children's:

15.5.1. List of data and/or specimens that will be transmitted:

Participant contact information is being sent to Sickkids Toronto so they can provide login information to the website and app. Seattle will also send information about ASWS and PROMIS depression score to Sickkids Toronto for programming the iCanCope 'optional' modules.

15.5.2. Individual(s) who will transmit data:

Study coordinators at Seattle Children's and SickKids Toronto will send this information in a secure email. Study staff at Seattle Children's will comply with the Electronic Communication of PHI policy and procedures.

16. Provisions to Monitor Data to Ensure the Safety of Subjects[34]

16.1. Plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe:[35]

N/A

16.2. Data reviewed to ensure safety of subjects:

N/A

16.3. Safety information collection procedures:

N/A

16.4. Frequency of cumulative data review:

N/A

16.5. Conditions that trigger an immediate suspension of the research:

N/A

17. Use of Social Media

17.1. Types of social media to be used and how:

We will be using Instagram and Facebook for recruitment purposes only. It will be used to share the study flyer, information and provide a link to the REDCap referral form where potential participants may contact the SCRI study team.

17.2. Measures in place to protect the privacy or confidentiality of subjects:[36]

Community members may voluntarily disclose their information on social media if they choose to because the comment section will be open to the public. Their participation in the study may also be disclosed if they choose to disclose that information. Participants will be encouraged to use the online referral form or email the study team instead of Instagram to contact the study team so that we can protect their privacy.

17.3. Types of communications that will be submitted to the IRB for review:[37]

All Instagram and Facebook study flyers will be uploaded for IRB review.

17.4. If user-generated content will be active, how it will be monitored and what actions will be taken to ensure subject safety and study integrity:

N/A

18. Research Related Injury[38]

18.1. Available compensation in the event of research related injury:

N/A

19. Recruitment Methods[39]

19.1. When, where, and how potential subjects will be recruited:

At Emory/CHOA, The Hospital for Sick Children, and Connecticut Children's Medical Center, the potential subjects are recruited at their Sickle Cell clinics. Local study staff will mail a study introduction letter and follow up with a phone call. Study staff may also make an in-person clinic visit during the patients' appointments. Once eligibility is confirmed and documented on the eligibility checklist, consent/assent will be obtained by a trained member of the research team. Consent/assent will preferably be obtained in person, or by telephone if the patient is not able to come to the hospital. If the patient is not able to come to the hospital in person to sign the consent forms, the research staff will review the forms over the phone with the patient and provide instructions to send the signed consent form back either by mail, fax, or SickKids secure file transfer.

At Seattle and all other sites: Child participants will be receiving care from one of our study sites. Potential participants will be introduced to the study and given a flyer about the study by their provider. If interested in being contacted, their provider will send the potential participant's contact information to the study team at Seattle Children's. The potential participant will be contacted over the phone by Seattle Children's to screen for eligibility. If eligible, consent forms will be emailed to participants and a consent call will be set up for a future time.

Additional participants will be identified via the websites and social media outlets (Facebook and Instagram) of sickle cell disease community organizations such as [redacted] These participants will be able to view a study flyer, and if they are interested in participating, they may fill out the referral form through REDCap with their contact information and a few preliminary eligibility questions. They may also contact SCRI staff directly if they have questions about the study. SCRI staff will then contact these potential participants and screen them for eligibility over the phone. If eligible, consent forms will be emailed to participants and a consent call will be set up for a future time.

19.2. Steps that will be taken to protect potential subjects' privacy interests:[40]

Participants will be asked by someone known to them if interested in participating before contact information is shared with the coordinating center for approach.
Participants recruited from the community will have information stored and transmitted securely through REDCap.

19.3. Sources of subjects:[41]

Potential subjects will be identified by their clinic provider at participating sites. Additional participants will be recruited from sickle cell disease community organizations.

19.4. Methods that will be used to identify potential subjects:

Potential participants will be introduced to the study and given a flyer about the study by their provider at the clinic. If interested in being contacted, their provider will send the potential participant's contact information to the Seattle Children's Research Institute study team using either a secure and direct fax line to the study staff or submitting a REDCap form online The contact information will be sent to Seattle Children's using the referral form (see attached Referral Form document). Providers will only need to check Yes or No to the following eligibility criteria: age 12-18 years, has pain from sickle cell disease, able to speak and read English, and has access to the Internet. Study staff at SCRI will then screen for further eligibility during a phone call with the potential participants. Identifying potential subjects will rely on the identification by the patients' care providers.

Potential participants will also be able to contact the SCRI study team through the social media advertisement.

19.5. Materials that will be used to recruit subjects:[42]

Participants will receive a study flyer from their provider or see the flyer through social media. If the participant is interested in hearing more, the provider will use a referral form to send participant contact information. The participant may also contact the study team directly. The referral form will be submitted using a secure and direct fax line, secure email or as a REDCap survey online.

19.6. Recruitment methods not controlled by Seattle Children's:

Emory/CHOA, The Hospital for Sick Children, and Connecticut Children's Medical Center have their local IRB approval to screen for eligibility and enroll participants. Local study investigators (Zempsky, Dampier/Bakshi, or Odame) will be contacted to review eligibility if research staff have questions or concerns. Initial patient contact will be made either (1) through a mailed letter signed by a clinic staff, followed up by a telephone call from study staff, or (2) in-person during scheduled clinic visits. If parent/youths are interested in learning more, study staff will explain the study and go over the Sickle Cell Pain Burden Interview (in person or over the telephone), as this is not currently a standard of care clinical measure. If they patient is not eligible, the results from the Sickle Cell Pain Burden Interview will not be used for the research study. We will only track how many patients did not meet the criteria, we will not store any data from the SCPBI. See section 19.1 for further recruitment information for these sites. These recruitment methods will only be used at the sites listed in the beginning and not Seattle or any other sites.

20. Consent/Assent Process

20.1. Where the consent process will take place:

At Emory/CHOA, The Hospital for Sick Children, and Connecticut Children's Medical Center: Consent/assent will be obtained by a trained member of the research team. Consent/assent will preferably be obtained in person, or by telephone if the patient is not able to come to the hospital. If the patient is not able to come to the hospital in person to sign the consent forms, the research staff will review the forms over the phone with the patient and provide instructions to send the signed consent form back either by mail, fax, or SickKids secure file transfer.

At Seattle Children's and other participating sites: Consent will take place over the phone, after the family has had sufficient time to decide whether they would like to participate. We will go through the consent script with the parent and then the child and their electronic consent will be obtained on REDCap.

20.2. Steps that will be taken to protect prospective subjects' privacy interests:[43]
Consent will be done over the phone while the participant is in the privacy of their own home.

20.3. Waiting period available between approaching a prospective subject and obtaining consent:
Each participant will be given sufficient time to read, review and ask questions before obtaining consent.

20.4. Process to ensure ongoing consent:
We will ask youth and parents questions about the study, so they fully understand their involvement over the course of the study. We will be touching base with them at each time point to answer questions and let them know next steps.

20.5. If this box is checked, "SOP: Informed Consent Process for Research (HRP-090)" will be followed: ☒

20.6. If "SOP: Informed Consent Process for Research (HRP-090)" will not be followed, address the following:[44]

20.6.1. Role of the individuals listed in the application as being involved in the consent process:
N/A

20.6.2. Time that will be devoted to the consent discussion:
N/A

20.6.3. Steps that will be taken to minimize the possibility of coercion or undue influence:
N/A

20.6.4. Steps that will be taken to ensure the subject's understanding:
N/A

20.7. Non-English Speaking Subjects[45]

20.7.1. Anticipated preferred language(s) for subjects or their representatives:
N/A

20.7.2. Presentation of Research Information and Documentation:

☐ Appendix A-10 of the Investigator Manual will be followed[46]

☐ Short form procedures may be used per HRP-091. If so, choose applicable box(es):

☐ Per section 5.5.1

☐ Per section 5.5.2

☐ Appendix A-10 of the Investigator Manual will not be followed. Explanation of procedures not following Appendix A-10:
✍Click here to enter text.

20.7.3. Justification if non-English speaking subjects will be excluded from the research:[47]
The *iCanCope with Sickle Cell Pain* Program is only available in English.

20.8. Subjects Who Are Not Yet Adults (Infants, Children, Teenagers)

20.8.1. Process used to determine whether an individual has not attained the legal age of consent under the applicable law of the jurisdiction in which the research will be conducted (e.g., individuals under the age of 18 years):[48]

We will be enrolling individuals under the age of 18, we will be collecting date of birth to determine age. Parent consent for their participation will be obtained.

20.8.2. Parental permission will be obtained from:[49]

☐ Both parents unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

☒ One parent even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child.

☐ Neither parent.[50]

20.8.3. Process used to determine an individual's authority to consent to each child's general medical care if permission will be obtained from someone other than parents:[51]

N/A

20.8.4. Assent will be obtained from:[52]

☒ All children.

☐ Some children. Specify: ✍Click here to enter text.

☐ None of the children. Explain: ✍Click here to enter text.

20.8.5. Procedures for obtaining and documenting assent:

Consent forms will be read and completed at the participants' home, while speaking to a SCRI study coordinator on the phone. This phone conference will be used to answer additional questions, further explain the study, and obtain consent. After going through the consent script, participants will be asked to indicate their consent and authorization on an electronic form.

During the consent script, the study coordinator will discuss information about study procedures, study risks, potential benefits, and the voluntary nature of the study. In addition, the study coordinator will assess how well potential participants understand the study through the types of questions raised during the discussion of the protocol. The study coordinator will use lay language when speaking with the participant (and parent). For participants under 18, the study coordinator will obtain consent of the parent first. The study coordinator will document the day and time of consent in the participant database. The participant will then be asked to document their consent on a secure electronic form via REDCap. The process will take about 15 minutes.

If a phone conference cannot be arranged at the same time for the parent and child participants, the study coordinator will speak with the parent and child separately over the phone. The study coordinator will only speak with the child after speaking with the parent.

20.8.6. Plan for re-approaching children who have reached the age of majority to obtain consent:[53]

It is possible that some child participants will turn 18 between the time they are enrolled in the study and the time they complete follow-up assessments. If this occurs, these participants will be re-approached when they are scheduled to complete a follow-up. The study staff will attempt to call until they reach the child participant and obtain verbal consent. If they completed all study timepoints including the last follow up, they will not be contacted since their participation in the study is complete. After the completion of the study, they are free to use the website and app as a user, not a participant of the research study. If they are still interested in participating in the study, we will obtain verbal consent using the procedures listed above before conducting further study procedures.

20.9. Cognitively Impaired Adults/Adults Unable to Consent[54]

20.9.1. Process used to determine whether an individual is capable of consent:

Cognitively impaired adults/adults unable to consent will not be enrolled in the study.

20.9.2. Individuals from whom permission will be obtained in order of priority:[55]

N/A

20.9.3. Assent will be obtained from:

☐ All of these subjects.

☐ Some of these subjects. Specify: ✍Click here to enter text.

☐ None of these subjects. Explain: ✍Click here to enter text.

20.9.4. Process for obtaining and documenting assent:[56]

N/A

20.10. Waiver or Alteration of Consent Process

20.10.1. Reasons for requesting a waiver or alteration of informed consent:[57]

We are requesting a waiver of consent for subjects who turn 18 whose private identifiable information is still being used (but are not actively participating). This study is minimal risk and without the waiver, the study could not be practicably conducted.

20.10.2. Consent Waiver/Alteration Criteria justifications:[58]

20.10.2.1. The research involves no more than minimal risk to the subjects because:

The study procedures only include surveys and a web program. The anticipated risks in this research are less than those our participants would ordinarily encounter in daily life.

20.10.2.2. The waiver or alteration will not adversely affect the rights or welfare of the subjects because:[59]

The study will not be collecting information that could put subjects or their families at harm, e.g., affect eligibility for insurance, employability, stigmatization; Their participation in the study would not alter or affect the subject's care; Any publication or presentation of research results would be done in a manner that would never reveal an individual's identity either directly or indirectly. These participants would have already been assented to participate in the study and

would have used the website and/or app for purposes of the research. The continued use of their data for research analysis would not impact their rights or welfare. Participants always have the option to contact the research team and request to withdraw from the study.

20.10.2.3. The research could not practicably be carried out without the waiver or alteration because:[60]

Since the study time frame is about 5 years, most participants would turn 18 before data is finished being collected, analyzed and/or de-identified. Once subjects turn 18, the study team may be unable to get in contact with participants who have already completed all active research participation. Due to the small scope of this project, it is important to retain all the data collected from all eligible patients for the results of the study to be meaningful.

20.10.2.4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation:

N/A

20.10.3. If the research involves a waiver of the consent process for emergency research, provide sufficient information for the IRB to make it determinations:[61]

N/A

21. Process to Document Consent in Writing

21.1. If consent will be documented in writing (check one):

☐ "SOP: Written Documentation of Consent (HRP-091)" will be followed.

☒ "SOP: Written Documentation of Consent (HRP-091)" will not be followed.

Process of documenting consent:[62]

The study coordinator will document the day and time of consent in the participant database. The participant will then be asked to document their consent on an electronic form via REDCap. For this reason, we request a waiver of documentation of informed consent because the project would present no more than minimal risk to the research subjects and involves no procedures for which written consent is required outside of the research context.

21.2. If consent will not be documented in writing (check all boxes that apply):[63]

☒ A written statement/information sheet describing the research will be provided to subjects.[64]

☐ A written statement/information sheet describing the research will not be provided to subjects. Explain: ✍Click here to enter text.

☐ A consent script will be used.[65]

22. HIPAA Authorization and RCW Criteria

22.1. HIPAA Authorization (check all boxes that apply):

☐ The study does not involve the receipt, creation, use and/or disclosure of protected health information (PHI).[66]

☐ HIPAA authorization will be obtained as part of a signed consent form.

☒ The study will access PHI without prior authorization from subjects (including for recruitment purposes – e.g., reviewing the medical record to determine eligibility). *See 21.2 below for required HIPAA waiver/alteration criteria*.

☒ Subjects will review a written statement/information sheet with the appropriate HIPAA language but will not provide a written signature. See 21.2 below for required *HIPAA alteration criteria*.[67]

☐ Other. Explain:[68]
✍Click here to enter text.

22.2. HIPAA Waiver/Alteration Criteria: Explain why:

22.2.1. The use or disclosure of PHI involves no more than a minimal risk to privacy of individuals, based on, at least the presence of the following elements:

22.2.1.1. An adequate plan to protect the identifiers from improper use and disclosure:

We will protect all identifiers by using unique study ID numbers on all PHI and only study team members will have access to a subject's PHI and ID number. All identifying information will be stored in a secure database in a protected folder including the information of patients who were referred, but not enrolled in the study. These patients who were referred but did not enroll in the study will have a different ID so they are not approached after recruitment.

22.2.1.2. An adequate plan to destroy identifiers at earliest opportunity consistent with conduct of research:

All identifiers will be destroyed at the earliest opportunity consistent with conduct of this research This means that once all analysis of identifiable data for the study is complete, all identifiers will be destroyed.

22.2.1.3. Assurances that PHI will not be reused or disclosed to any other party or entity, except as required by law or for authorized oversight of the research:

PHI will not be reused or disclosed to any other person or entity.

22.2.2. The research could not practicably be conducted without the waiver or alteration of authorization:

Without the waiver of authorization, study sites would not be able to obtain patient contact and eligibility information. The study would have limited eligible patients if patients were given the option to contact the study staff first. Study staff would not be able to contact potentially eligible participants for screening purposes without access or use of their PHI. Obtaining PHI is necessary for the characterization of the groups of the individuals who screen out of the study.
Because we will not be seeing the participants in person, we are asking for an alteration for online authorization. Without it, study time lines would be delayed and participant interest would decrease waiting for mailed consent forms. The participant will document their consent authorization on a secure electronic form via REDCap. The study staff at SCRI will not have any in-person contact with any participants in this study.

22.2.3. The research could not practicably be conducted without access to and use of the PHI:[69]

The nature of this research is specific to the participant's health.

23. Payments/Costs to Subjects[70]

23.1. Amount, method, and timing of payments to subjects:[71]

Each parent/child dyad will receive a $40 electronic gift card for each timepoint assessment they complete.

23.2. Reimbursement provided to subjects:[72]

N/A

23.3. Additional costs that subjects may be responsible for because of participation in the research:[73]

Subjects will be given the option to receive text message communications from the study team. If the subject opts in, there may be a cost associated with the text messages. Subjects will be informed of this possible cost.

24. Setting

24.1. Site(s) or location(s) where the research team will conduct the research:

Patients from the following hospitals will have the opportunity to participate in the research: Emory/CHOA, The Hospital for Sick Children (SickKids), and Connecticut Children's Medical Center (CCMC), University of Mississippi, University of Florida, Boston Medical Center, Ann & Robert H. Lurie Children's Hospital of Chicago, Nationwide Children's Hospital, C.S. Mott Children's Hospital and Seattle Children's Hospital. SCRI, CHOA, SickKids, and CCMC are the only locations where research will be conducted. All participating sites will approach their IRB for review of their engagement on this research study. At SCRI, study staff will receive referrals from the participating clinics through email, fax, or REDCap. For participants, all survey assessments/diaries will be sent via REDCap for participants to complete in their home. All research activities conducted by SCH agents will be done at Dr. Palermo's lab space.

24.2. Composition and involvement of any community advisory board:

N/A

24.3. For research conducted outside of the organization and its affiliates:[74]

24.3.1. Site-specific regulations or customs affecting the research:

All other participating sites will be conducting the own IRB review and if there are any regulations, customs, etc. that might impact the research or this Protocol. CHOA, SickKids, and CCMC have already obtained IRB approval to conduct the research and we are aware of their site-specific regulations and customs. This study has been modified accordingly and SCH IRB will be consulted if any additional modifications are needed.

24.3.2. Local scientific and ethical review structure:

N/A

25. Resources Available

25.1. Qualifications (e.g., training, education, experience, oversight) of investigator(s) to conduct and supervise the research:[75]

The PI and study staff of SCRI have years of experience in the recruitment methods used in this study and skills needed to organize, track, and follow this many participants through the completion of the study. All study procedures will be done under the supervision of the PI who assumes responsibility for all study related actions and events. The PI will be available to clarify recruitment eligibility, answer questions, etc. throughout the course of the study.

25.2. Other resources available to conduct the research:[76]

Each local site PI will be responsible for local study oversight, and review/management of any local adverse events, and reporting to their local IRB per their local requirements. Dr. Dampier, the PI at CHOA will serve as the study medical monitor and will provide each site with a yearly study-wide summary of safety events for continuing reviews by local IRBs. A Steering Committee consisting of the study and site PIs will meet monthly by teleconference and be responsible for overall study management. The progress of the study in terms of recruitment will be monitored via a data tracking system that will allow the PIs to review subject enrollment by age, gender and race. If requested by the NIH or by one of the local institutional IRBs, the AFLAC DSMB is available to review for the local site or all study sites on a quarterly schedule (as per their SOPs).

26. Coordinating Center Procedures

26.1. Coordinating center institution:

Seattle Children's

26.2. If Seattle Children's is the coordinating center:

26.2.1. Process to ensure communication among sites:[77]

Seattle Children's will coordinate monthly research coordinator and investigator teleconference meetings. An agenda and any additional documents will be sent via email to members of the study team.

26.2.2. Process to ensure all site investigators conduct the study according to the IRB approved protocol and report all non-compliance:

Our monthly calls will be to discuss study progress, answer questions, and ensure proper study conduct.

26.2.3. Process to ensure all required approvals are obtained at each site:

Before beginning the research, we will ensure that required approvals have been obtained at all sites, and we will maintain a record of their approvals including all modifications.

26.2.4. Process to ensure all sites are informed of any problems and/or interim results:

These will be discussed at monthly phone meetings.

27. Good Clinical Practice

27.1. If you have committed to conducting the described study per International Center for Harmonization of Good Clinical Practice (ICH-GCP), check this box: ☐[78]

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[1] Include information if this protocol is associated with other IRB-approved studies (e.g. is this application the next part/phase of a previously approved application.
[2] In clinical trials, an endpoint is an event or outcome that can be measured objectively to determine whether the intervention being studied is beneficial. Some examples of endpoints are survival, improvements in quality of life, relief of symptoms, and disappearance of the tumor.
[3] Include information on a drug or biologic in this section if: (1) the study specifies the use of an approved drug or biologic; (2) the study uses an unapproved drug or biologic; (3) the study uses a food or dietary supplement to diagnose, cure, treat, or mitigate a disease or condition; or (4) data regarding subjects will be submitted to or held for inspection by the Food and Drug Administration (FDA). Only include information on a device in this section if: (1) the study evaluates the safety or effectiveness of a device; (2) the study uses a humanitarian use device (HUD) for research purposes; or (3) data regarding subjects will be submitted to or held for inspection by the FDA. Please note that mobile medical applications may meet the definition of a device – see FDA Guidance.
[4] See the Investigator Manual HRP-103 for sponsor requirements for FDA-regulated research.
[5] Explain what IND exemption category applies to the drug and why. Note that a drug is not exempt from an IND unless all criteria for one category are met. See "HRP-306: Drugs" for more information.
[6] Explain what IDE exemption category applies to the device and why. Note that a device is not exempt from an IDE unless all criteria for one category are met. See "HRP-307: Devices" for more information.
[7] Explain why the device is NOT a significant risk device. A significant risk device means an investigational device that: (a) is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject; (b) is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject; (c) is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or (d) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.
[8] Be sure to indicate if controls will be included and include information about why control arms are ethically acceptable.
[9] Describe all of the research procedures being performed. Be sure to make it clear which procedures apply to each subject population. When applicable, describe how research procedures differ from standard of care and/or affect standard of care. Describe any audio/video recording that will be involved.
[10] Attach all surveys, scripts, and data collection forms to the "Supporting Documents" page.
[11] Include information about the frequency of data collection.
[12] See HRP-001 - SOP – Definitions for definition of banking. Type N/A if not applicable. If the data is subject to NIH Genomic Data Sharing Policies (e.g. you will submit data to dbGaP, NDAR, FITBIR), indicate here.
[13] If applicable, include a list of identifiers that will be banked.
[14] Be general (e.g., researchers' lab, clinic, etc.)
[15] Generally, data and/or specimens should be released in a coded, non – identifiable manner.
[16] Include a description of the process used to verify and document that any required approvals have been obtained prior to release of data/specimens from the bank.
[17] You can allow for use for broad purposes

[18] This includes putting results and/or data in the subject medical records.
[19] If your population will differ from the representative population where the study will take place (e.g., race, ethnic group, or gender), provide a rationale for the differences.
[20] If you check a box below, be sure to include the additional safeguards associated with the population.
[21] Refer to HRP-416 CHECKLIST: Children.
[22] If the study is minimal risk, explain why. Must also include, as applicable: (1) why direct benefits are anticipated, (2) why risks are justified by anticipated benefit and/or the relationship between risk and prospective benefit compared to available alternatives, (3) why risk represents only minor increase over minimal risk, (4) how study procedures are reasonably commensurate with those inherent to the child's actual or expected conditions, (5) whether the interventions/procedures are likely to yield generalizable knowledge about the participant's condition and why it is of "vital importance" to understanding or amelioration of the participant's underlying disorder or condition, and (6) an explanation of what alternative methods/approaches were considered to make the above assessments (as applicable).
[23] This population may be wards of the state or any other agency, institution, or entity. Refer to HRP-416 CHECKLIST: Children, Section 6, for additional guidance on required considerations for this population.
[24] This refers to both cognitive impairments and adults who are incapacitated for any other reason. As applicable, refer to HRP-417 CHECKLIST: Cognitively Impaired Adults.
[25] Refer to HRP-413 CHECKLIST: Neonates and HRP-414 CHECKLIST: Neonates of Uncertain Viability.
[26] Refer to HRP-412 CHECKLIST: Pregnant Women.
[27] Refer to HRP-415 CHECKLIST: Prisoners
[28] A subject is considered "enrolled" when they consent to be in the study.
[29] Only applicable for multisite studies.
[30] i.e., numbers of subjects excluding screen failures.
[31] Payment for participation is not considered a benefit.
[32] For example, data will be double entered, data will be reviewed by another study team member to ensure accuracy, etc.
[33] If your study is multisite and there are differences in how confidentiality will be maintained by the coordination center and our local site, this should be explained in this section (e.g. local site will have samples that are linked to a person's name, but the coordination center will only receive coded samples without any links). Confidentiality regarding use of Social Media will be explained in a protocol section below.
[34] Applicable for studies that present more than minimal risk.
[35] Include information about who (describe in terms of role or group) will review the data.
[36] This should be specific to the social media you are using for the research.
[37] All communications that are directed towards subjects and specific to a particular study will require prior IRB review and approval. All non-IRB reviewable communications can be described in general terms by category – news stories, relevant publications – and representative examples of each can be provided.
[38] Applicable if the research involves more than minimal risk to subjects. If minimal risk, this section is N/A.
[39] If this is a multicenter study and subjects will be recruited by methods not under the control of the local site (e.g., call centers, national advertisements) those methods should also be described here.
[40] "Privacy interest" refers to a person's desire to place limits on whom they interact or whom they provide personal information.
[41] For example: medical records, CIS, clinical databases, other study records. If the study will access PHI for recruitment purposes without prior authorization from subjects, please address this in the HIPAA Authorization section below.
[42] Attach copies of these documents to the Recruitment Materials section of the study SmartForm. For printed advertisements, attach the final copy. For online advertisements, attach the final screen shots (including any images). When advertisements are taped for broadcast, send the final audio/video tape to IRB@seattlechildrens.org. You may attach the wording of the advertisement to the SmartForm prior to taping to preclude re-taping because of inappropriate wording, provided the IRB reviews the final audio/video tape.
[43] "Privacy interest" refers to a person's desire to place limits on whom they interact or whom they provide personal information.
[44] This section describes the way(s) in which the processes for this study will not follow Seattle Children's SOP.
[45] See HRP-090, HRP-091, and Investigator Manual HRP-103 for more information.
[46] Note the Short Form Consent may only be used when certain conditions are met. See HRP-091 for requirements for Short Form consent form use.
[47] Seattle Children's IRB prohibits the exclusion of non-English speaking populations from research unless there is sufficient justification for the exclusion. See Investigator Manual HRP-103 for more information.
[48] For research conducted in the state, review "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" to be aware of which individuals in the state meet the definition of "children." The age of majority in Washington is 18; however, sometimes younger children have ability to consent for certain types of care (e.g. sexual reproduction/health; mental health; drug/alcohol treatment). For research conducted outside of the state, provide information that describes which persons have not attained the legal age for consent to treatments or procedures involved the research, under the applicable law of the jurisdiction in which research will be conducted. One method of obtaining this information is to have a legal counsel or authority review your protocol along the definition of "children" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)." If the sites in other states in the study are conducting their own IRB review, you do not need to worry about this--type N/A. If you are conducting research and are actively recruiting participants outside of Washington who are NOT coming to SCH to give consent and who will be covered under SCH IRB approval, this section should be addressed in your protocol.
[49] For minimal risk studies and greater than minimal risk studies that offer a prospect of benefit, the IRB generally requires one parent to provide permission for the child to participate.
[50] If parental permission will not be obtained, please address this in the Waiver or Alteration of Consent Process below.
[51] See HRP-013 for more information.
[52] The IRB generally follows the following guidelines for written assent: children 7-12 should provide written assent on the "simple" assent form (HRP-502G); children 13-17 should provide written assent by co-signing the parental permission form (HRP-502A). The IRB will consider other assent scenarios (e.g. verbal assent for some or all children; not requiring assent for some or all children; or waiving assent): please provide details about the plan for your study. See HRP-090 and HRP-416 for more information on waiving assent and when assent is not necessary.
[53] See Appendix A-13 of the Investigator Manual HRP-103 for requirements for re-consent at age 18. If you think you meet the conditions for a waiver at 18, please address this in the Waiver or Alteration of Consent Process below.
[54] See "HRP-417 Cognitively Impaired Adults" for further information.
[55] For example: durable power of attorney for health care, court appointed guardian for health care decisions, spouse, and adult child. If you are following HRP-013 in order to make this determination, simply state that in this section. For research conducted in the state, review "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)" to be aware of which individuals in the state meet the definition of "legally authorized representative." For research conducted outside of the state, provide information that describes which individuals are authorized under applicable law to consent on behalf of a prospective subject to their participation in the procedure(s) involved in this research. One method of obtaining this

information is to have a legal counsel or authority review your protocol along the definition of "legally authorized representative" in "SOP: Legally Authorized Representatives, Children, and Guardians (HRP-013)." If the sites in other states in the study are conducting their own IRB review, you do not need to worry about this--type N/A. If you are conducting research and are actively recruiting participants outside of Washington who are NOT coming to Washington to give consent and who will be covered under SCH IRB approval, this section should be addressed in your protocol.

[56] The IRB may allow the person obtaining assent to document assent on the consent document.

[57] For example: consent/parental permission will not be obtained, required information will not be disclosed, the research involves deception, waiver for participants who turn 18, waiver for information collected about a non-present parent, or other waivers as necessary.

[58] The IRB needs to make all the waiver findings and key to this determination is that the IRB understand why it is not practicable to do the research without a waiver of consent. You need to provide a rationale in order for the IRB to consider whether the waiver criteria are met. See "HRP-410: Waiver or Alteration of the Consent Process" for further information.

[59] Possible reasons might include: a) you are not collecting information that could put subjects or their families at harm, e.g., affect eligibility for insurance, employability, stigmatization; b) you are not collecting information that would alter or affect the subject's care; c) any publication or presentation of research results would be done in a manner that would never reveal an individual's identity either directly or indirectly.

[60] Possible reasons could be: a) inability to locate families because of the lengthy time period over which the records/samples were created; b) many of the subjects whose records, data, or specimens will be used may have died and contacting the families about the research could cause harm and anguish to families; c) all eligible patients must be included in the study for the results to be meaningful.

[61] See "HRP 419: Waiver of Consent for Emergency Research" for further information.

[62] This section describes the ways in which the procedures will not be following Seattle Children's SOP.

[63] See "HRP-411: Waiver or Written Documentation of Informed Consent" for further information.

[64] An information sheet template can be found in the Click IRB Library and should be attached to the consent form of the study SmartForm. For internet research, the information sheet can be translated to an on-line format, if desired.

[65] The IRB sometimes requires a script if you are having the consent conversation over the phone rather than in person. Templates for a consent script are available on the IRB website on the Participant Recruitment page and should be attached to the study SmartForm.

[66] PHI is health information that is also identifiable because it includes one or more of the 18 HIPAA identifiers. See Investigator Manual HRP-103 for the list of HIPAA identifiers.

[67] If your study involves using or creating PHI and your only contact with participants is online, you can request an alteration of HIPAA authorization to remove the signature requirement. As an alternative to a waiver of documentation of consent and an alteration of HIPAA authorization, you must demonstrate that the electronic consent signatures are compliant with applicable state/international law (in Washington, see RCW 19.34.300).

[68] For example: altering HIPAA elements for international research.

[69] Possible reason could be: the nature of the research is specific to individuals' health and requires access to individuals' health records.

[70] See "HRP-316: Payments" for further information.

[71] Methods of payment include check, ClinCard, gift cards, etc. Provide details on who will be the recipient of the payment (parent or child).

[72] Reimbursement is used when the subject is paid back for travel expenses such as transportation, food, childcare, or lodging. Reimbursement is generally distributed to person who incurred cost (usually parent) and requires receipts to be submitted.

[73] This could include things like fuel/transportation costs, parking, and/or childcare.

[74] Type N/A if this section does not apply.

[75] Provide enough information to convince the IRB that the principal and/or co-investigator(s) are appropriately qualified to conduct and supervise the proposed research. When applicable, describe their prior clinical experience with the test article or study-related procedures, or describe their knowledge of the local study sites, culture, and society.

[76] For example, as appropriate: (1) Justify the feasibility of recruiting the required number of suitable subjects within the agreed recruitment period. For example, how many potential subjects do you have access to? What percentage of those potential subjects do you need to recruit? (2) Describe the time that you will devote to conducting and completing the research. (3) Describe the facilities in which the research will be conducted. (4) Describe the availability of medical or psychological resources that subjects might need as a result of an anticipated consequences of the human research. (5) Describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions.

[77] Including communication between sites of current study document versions and modifications.

[78] See your contract/agreement or Sponsor Documentation if you are unsure