

**Pre-Genetic Therapy Assessments of Patient Readiness and Resilience:  
Best Practices and Recommendations for Implementation in Sickle Cell Disease**

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## **Pre-Genetic Therapy Assessment of Patient Readiness and Resilience: Overview**

The following best practice recommendations were developed by the NHLBI Cure Sickle Cell Initiative's (CureSCi) Patient Readiness and Resilience Working Group (PRRWG) based on scientific evidence, expert clinical guidance, and review of strategic planning documents, and in consultation with other CureSCi subcommittees and working groups representative of patient, advocate, and researcher perspectives.

This set of PRRWG best practice recommendations is focused on pre-genetic therapy education delivery and assessment of knowledge, readiness, and psychosocial risk and resilience factors.

*The basis for these recommendations is founded upon the following observations:*

1. Invasive and life-altering procedures can introduce stress and influence psychosocial well-being.
2. Premorbid psychosocial factors can influence peri- and post-treatment mental health outcomes.
3. Premorbid psychosocial factors can influence peri- and post-treatment physical health outcomes.
4. Assessing psychosocial factors related to the anticipated experience of undergoing genetic therapy for sickle cell disease can produce useful information for determining readiness and optimizing mental and physical health.

The recommended progression of the Pre-Genetic Therapy Patient Readiness and Resilience Assessment is outlined in Figure 1. An essential first step of implementing this assessment involves an institutional self-evaluation of available psychosocial supports and resources. Institutions should ensure the availability of qualified and accessible clinicians to conduct the Pre-Genetic Therapy Patient Readiness and Resilience Assessment and provide ongoing psychotherapeutic services as determined to be necessary following the assessment. Institutional and community resources (e.g., transportation assistance, temporary housing options, letters for work or school) should also be reviewed to ensure they are sufficient and that processes are in place to connect patients with resources. Identified gaps in supports and resources should be addressed before providing patient education about genetic therapy.

Once a program is adequately prepared to assess and support patients' psychosocial health, most investigative and clinical teams will begin providing patients information about genetic therapy at least 6-12 months prior to anticipated consent. Recommendations are provided below regarding evidence-based strategies to support effective delivery of education about gene therapy (Table I). Although the PRRWG favors providing comprehensive education and assessing readiness and resilience prior to informed consent, it recognizes that it may be necessary for some trials to obtain consent earlier in the process. However, the PRRWG views data obtained from the Pre-Genetic Therapy Patient Readiness and Resilience Assessment as key to informing decisions about: 1) how to carry out informed consent; and 2) the presence of undue pressures to participate or psychosocial risks that should be addressed before enrolling on the trial.

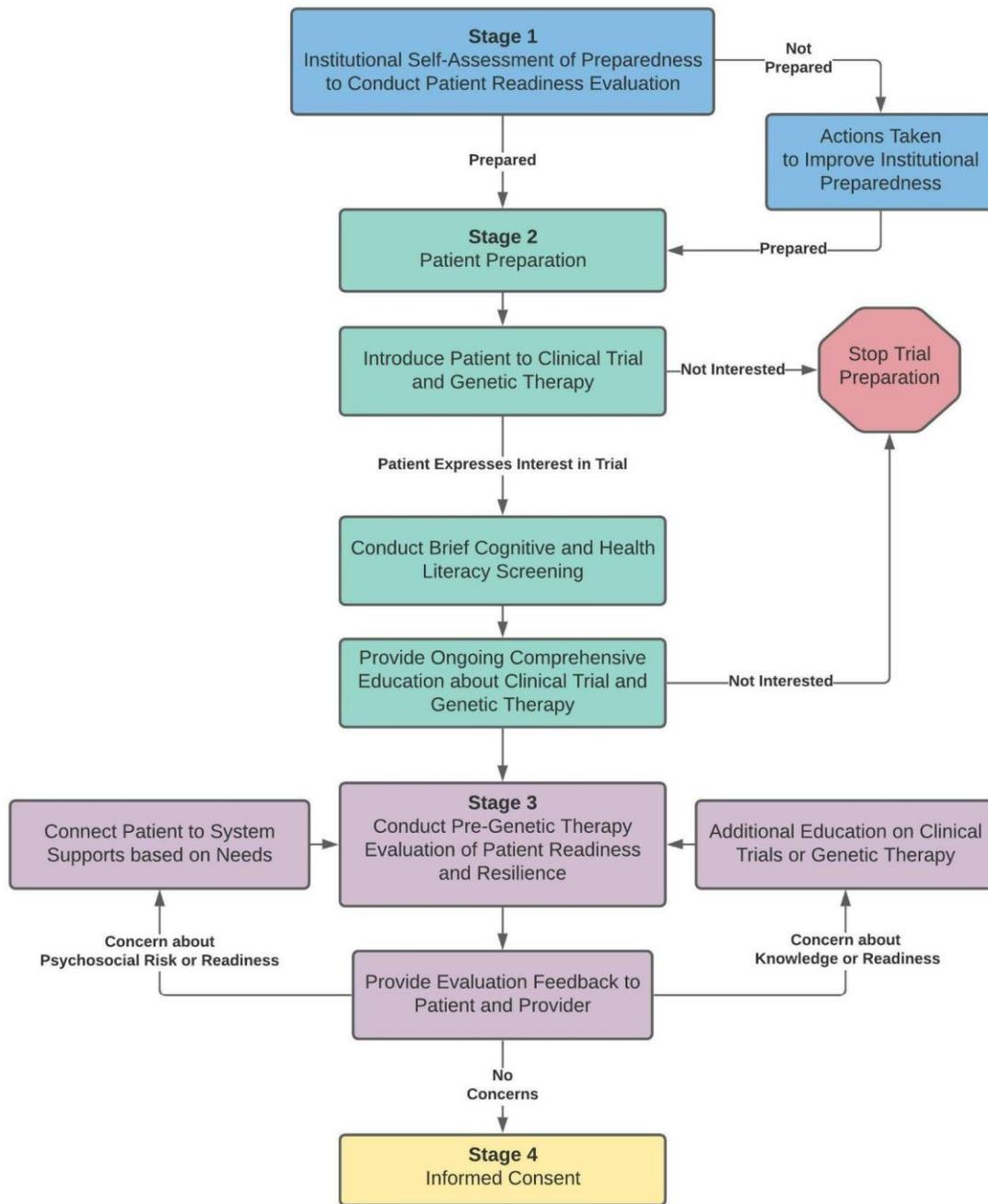
*After education where patients learn about genetic therapy and what to expect during the clinical trial, the PRRWG recommends conducting a comprehensive assessment of patient knowledge about genetic therapy and clinical trials (Table II), readiness and motivation (Table III), and psychosocial risk and protective factors (Table IV). This assessment should be conducted by a reasonably impartial or independent member of the psychosocial team with training and expertise in psychosocial assessment as well as adequate knowledge of sickle cell disease, genetic therapies, medical ethics, and clinical trials. This clinician should also be familiar with details of trial-related education being provided to the patient. Importantly, the PRRWG views attention to these considerations as the responsibility of not only the psychosocial clinician and study PI, but also that of all members of the clinical, research, and sponsor teams. The assessment should primarily take the form of a clinical interview, though cognitive testing and standardized questionnaires may be used to supplement the assessment.*

*The goals of the Pre-Genetic Therapy Patient Readiness and Resilience Assessment are to:*

1. Gather information about a patient's understanding of and perceived readiness for a genetic therapy clinical trial.
2. Encourage open dialogue regarding any concerns about genetic therapy.
3. Provide a conceptualization of psychosocial factors likely to influence the conduct of the genetic therapy clinical trial and affect relevant outcomes.
4. Identify patient strengths to be leveraged to promote psychosocial well-being before, during, and after the genetic therapy clinical trial.
5. Identify psychosocial risks to be considered and addressed through tailored education, psychosocial support, and community resources.

This assessment is not in any way intended to pressure or persuade a patient to participate in a genetic therapy clinical trial nor should its findings be used to permanently exclude a patient from receiving a potentially therapeutic treatment. In cases where concerns are noted, the PRRWG recommends a collaborative approach to developing resolutions that may involve actions or commitments from both investigative teams and patients or families.

**Figure 1. Patient Readiness and Resilience Pre-Trial Process**



\*In some circumstances, it may be necessary and appropriate to bypass much of the Pre-Genetic Therapy Patient Readiness and Resilience Assessment. Examples of such cases include a very young patient, a patient with severe cognitive limitations, or a patient presenting with a medical indication that raises the urgency for treatment or clearly shifts the risk/benefit balance. However, in these cases, consideration should be given to whether portions of the evaluation can still be completed in some form, whether an evaluation needs to be completed with a guardian or advocate, and whether an ethics consultation is warranted.

## **Best Practices for Assessing Patient Readiness and Resilience**

A set of best practice recommendations spanning four broad activities are identified: 1) supporting the effective delivery of initial education about genetic therapy and clinical trials; 2) assessing an individual's knowledge of the proposed treatment and trial; 3) assessing an individual's readiness and motivation for genetic therapy; and 4) assessing an individual's risk and protective factors that could influence psychosocial well-being, self-care, and health before, during, and after genetic therapy. Additional guidance for implementing these best practices is provided in a later section of this document (Tables I - IV). Of note, clinicians should be mindful of developmental and cognitive considerations and tailor questions to optimize effective communication. Providers will also need to rely on their clinical judgment to navigate other situational issues, such as those that accompany work with younger patients. For example, when assessing a child, consideration must be given to determining when it is important to meet privately with the child, how to adapt questions that are directed to a child's caregiver, and which tasks would be necessary for a child to master vs. tasks for which a caregiver would be responsible, and tasks for which there is shared responsibility. Institutions and programs may need to further adopt a flexible approach in adhering to the following guidance based on patient needs, situational and cultural context, and available resources.

### **1. Supporting effective education delivery (see [Table I](#))**

- a. Assess receptive language, working memory, literacy, and health literacy.
- b. Provide written and audio information that can be easily understood and referenced outside of clinic visits.
- c. Plan to provide education in small chunks starting early in the process.
- d. Use evidence-based communication strategies to enhance knowledge transfer.
- e. Consider and address concerns about trust and bias that could interfere with education delivery.
- f. Monitor comprehension during education delivery.

### **2. Evaluating knowledge of genetic therapy and clinical trials (see [Table II](#))**

- a. Assess knowledge of sickle cell disease and sickle cell disease treatment.
- b. Assess understanding of the clinical trial and genetic therapy process.
- c. Assess understanding of possible outcomes of genetic therapy.
- d. Assess prior knowledge and exposure to information about genetic therapy that could impact an individual's perspective.

- e. Assess awareness of and connectedness with supportive resources and organizations.

### **3. Evaluating patient readiness for genetic therapy (see [Table III](#))**

- a. Assess values and adopt a non-judgmental approach to assess how genetic therapy fits with values.
- b. Assess overall readiness and current position on continuum of readiness for genetic therapy.
- c. Assess confidence in different components of the genetic therapy process.
- d. Assess potential for pressure or influence from others.
- e. Assess past experiences of adversity and link to perceived readiness.

### **4. Evaluating psychosocial risk and resilience factors (see [Table IV](#))**

- a. Assess Individual Factors (Screening Instruments)
  - 1. Pre-existing emotional and physical issues.
- b. Assess Individual Factors (Clinical Interview)
  - 1. Pre-existing emotional and physical issues.
  - 2. Schedule of life activities and events.
  - 3. Current challenges and stressors.
  - 4. Coping style.
  - 5. Optimism.
  - 6. Self-identity.
  - 7. Expectations.
- c. Assess Family/Close Social Network Factors
  - 1. Social networks of support.
  - 2. Primary support person or people.

3. Family composition.
  4. Family structure.
  5. Quality of family relations.
- d. Assess Environmental/Community Factors
1. Past relationships with healthcare providers.
  2. Access to the treating center.
  3. Connections with community-based resources and comfort with seeking support.
  4. Professional support for pre-existing issues/conditions.
- e. Assess Cultural and Societal Factors
1. Family and cultural traditions.
  2. Acculturation (to the U.S., society, medical system, other systems and cultures).
  3. Immigration.
  4. Medical mistrust and suspicion.
  5. Experiences of racism, with a focus on the healthcare setting, and associated impact.

**Table I. Strategies recommended to support implementation of best practices for initial education delivery**

**ASSESS RELEVANT COGNITIVE/LEARNING ABILITIES (PRIOR TO COMPREHENSIVE EDUCATION)**

<b>Best Practice</b>	<b>Suggestions for Implementation</b>
<p>1. Assess receptive language, working memory, literacy, and health literacy</p>	<p><i>Review any records of past cognitive or academic testing. Discuss previous treating team’s observations of literacy, health literacy, and cognitive functioning.</i></p> <ul style="list-style-type: none"> <li>● NIH Toolbox Cognition Battery                             <ul style="list-style-type: none"> <li>○ Picture Vocabulary Test (Ages 3-85)</li> <li>○ Oral Reading Recognition Test (Ages 7-85)</li> <li>○ List Sorting Working Memory Test (Ages 3-85)</li> </ul> </li> <li>● Health Literacy (for adolescent and adult patients) *choose one from options below                             <ul style="list-style-type: none"> <li>○ Brief Health Literacy Screen (BHLS)</li> <li>○ Medical Term Recognition Test (METER)</li> <li>○ Newest Vital Sign (NVS)</li> </ul> </li> </ul>

**EDUCATION DELIVERY**

<b>Best Practice</b>	<b>Suggestions for Implementation</b>
<p>1. Provide written and audio information that can be easily understood and referenced outside of clinic visits</p>	<ul style="list-style-type: none"> <li>● Create a glossary of terms and plain language summary of study procedures, risks, and benefits.</li> <li>● Include supplemental visual and audio aids to explain complex processes and timelines.</li> <li>● Consider making study materials available electronically so they can be easily accessed by potential participants.</li> </ul>

<p>2. Plan to provide education in small chunks starting early in the process</p>	<ul style="list-style-type: none"> <li>● Education should occur well enough in advance of consent to allow for varied rates of information acquisition.</li> <li>● Education should occur over multiple short sessions rather than 1-2 long sessions.</li> </ul>
<p>3. Use evidence-based communication strategies to enhance knowledge transfer</p>	<ul style="list-style-type: none"> <li>● Information should be grouped into small but related sections.</li> <li>● Key information should be repeated multiple times and not assumed that discussing a topic on a single occasion will lead to adequate comprehension.</li> <li>● Use engaging methods (e.g., images, videos) to deliver information and increase discussion, reflection, and bidirectional conversation.</li> <li>● Use relatable terms and analogies when possible to explain complex processes.</li> <li>● Use vignettes to assist in describing possible outcomes.</li> </ul>
<p>4. Consider and address concerns about trust and bias that could interfere with education delivery</p>	<ul style="list-style-type: none"> <li>● Include familiar medical and psychosocial providers to assist with providing education.</li> <li>● Invite a patient advocate to join early discussions to address potential for a power differential (i.e., an impartial party, someone to help ask questions).</li> <li>● Provide opportunities to hear other patients' stories (e.g., about decision-making, what questions they asked, what knowledge they felt they needed to be prepared, about outcomes).</li> <li>● Provide print educational materials not funded or created by industry, individuals, or groups who could be viewed as having conflicts of interest.</li> </ul>
<p>5. Monitor comprehension during education delivery</p>	<ul style="list-style-type: none"> <li>● Incorporate and normalize frequent pauses to allow patients to teach back new information (e.g., benefits, risks, side effects, management of regular medical care within and outside of the study).</li> </ul>

**Table II. Strategies recommended to support implementation of best practices for evaluating knowledge and understanding**

<b>Best Practice</b>	<b>Suggestions for Implementation</b>
<p>1. Assess knowledge of sickle cell disease and sickle cell disease treatment</p>	<ul style="list-style-type: none"> <li>● Sickle cell disease is a complicated illness. I'm interested to know more about what parts of sickle cell disease you feel like you have a good grasp on and which parts are more unclear. Tell me what you know about how sickle cell disease is passed from parents to children. What do you know about how sickle cell disease causes problems like pain, fatigue, and stroke? In the short-term, what are some of the complications of sickle cell disease? What are the longer-term risks?</li> <li>● The causes of sickle cell problems are complicated, but treatments can be complicated too. There are also new treatments being developed all the time and it can be hard to keep up with all of them. What sickle cell treatments are you familiar with? What do you know about how they work? What specific sickle cell problems do they help treat? What do you see as the pros and cons to each treatment?</li> <li>● What sickle cell treatments have you tried in the past? What treatments are you currently taking or receiving? Which treatments have you found most helpful? What hasn't worked? Have you ever made the decision to stop a treatment? If so, why? What has kept you from trying other treatments?</li> </ul>
<p>2. Assess understanding of the clinical trial and genetic therapy process</p>	<ul style="list-style-type: none"> <li>● Tell me what you understand about what will happen if you decide to go forward with the genetic therapy treatment?</li> <li>● What have you heard about the treatment or clinical trial schedule? What all needs to happen before the treatment begins? Once you are admitted to the hospital for treatment, what happens and when?</li> <li>● What do you know about the prep regimen—the treatments you would need to get before the genetic therapy starts? For example, what are the names of the treatments, how are they given to you, and when would you receive them? Why is that prep treatment needed? What side effects do you think you might experience as a result?</li> </ul>

	<ul style="list-style-type: none"> <li>Let's imagine that you decide to proceed with the genetic therapy treatment. After the treatment is over, what do you think your life would be like in terms of ongoing doctors' appointments, treatments, and medications? How does your life look the same or different after treatment?</li> </ul>
<p>3. Assess understanding of possible outcomes of genetic therapy</p>	<ul style="list-style-type: none"> <li>Based on what you know about the genetic therapy treatment, what do you think are the possible outcomes, ranging from worst case to best case scenario?</li> <li>What does a successful treatment outcome look like to you? How likely do you think it is that you will experience this kind of outcome? What does an unsuccessful outcome look like? How likely do they think it is that you will experience this kind of outcome?</li> <li>Is it possible that the outcome of your genetic therapy treatment could be somewhere in between—something that doesn't feel totally unsuccessful but also doesn't feel totally successful? What would that look like?</li> <li>What new problems, if any, do you think are possible after the genetic therapy treatment? Do you think these would be short-term or long-term problems? Do these seem like major or minor problems to you?</li> </ul>
<p>4. Assess prior knowledge and exposure to information about genetic therapy that could impact an individual's perspective</p>	<ul style="list-style-type: none"> <li>Before you started talking seriously to the doctors in charge of the genetic therapy clinical trial, what had you heard about gene therapy in general or specifically for sickle cell disease?</li> <li>People get information about new treatments from lots of different places—family or friends, doctors, social media. Where do you see or hear people talking about genetic therapy for sickle cell disease? Who do you go to or where do you look for information about new treatments like genetic therapy?</li> </ul>
<p>5. Assess awareness of and connectedness with</p>	<ul style="list-style-type: none"> <li>Are you familiar with any sickle cell community organizations or resource or advocate groups? Have you been involved with any of them in the past (e.g., SCDA, Sickle Cell Consortium, CBOs, CureSCi, SC RED)?</li> </ul>

supportive resources and organizations

*If needed, provide information about resources (within treating institutions, SCD advocacy groups, insurance-specific resources) to support patient knowledge and readiness.*

**Table III. Strategies recommended to support implementation of best practices for evaluating patient readiness**

<b>Best Practice</b>	<b>Possible Questions</b>
<p>1. Assess values and adopt a non-judgmental approach to assess how genetic therapy fits with values</p>	<ul style="list-style-type: none"> <li>● Everyone finds meaning in life in different ways. We all have different values and life priorities. For some people, their family is the thing they value most. For others, it's their religion or spirituality, their health, friendships, having fun, making art or music, learning, or other things. What are the things in life that are most important to you?</li> <li>● Would treating your sickle cell disease with genetic therapy align with your values? In what way?</li> <li>● How might treating sickle cell disease with genetic therapy interfere with or get in the way of your values?</li> <li>● What are some reasons you are interested in genetic therapy? If you moved forward with genetic therapy, what would change? What are some of your concerns about genetic therapy?</li> </ul>
<p>2. Assess overall readiness and current position on continuum of readiness for genetic therapy</p>	<ul style="list-style-type: none"> <li>● How long have you been seriously considering a cure for your sickle cell disease? How long have you been thinking about genetic therapy, specifically?</li> <li>● Obviously, coming here and talking to me is a big step towards seriously considering genetic therapy. What other steps, either in the hospital or at home, school/work, or in your community, have you taken to prepare for genetic therapy?</li> <li>● Outside of your doctors or other medical staff, who all have you talked to about your interest in genetic therapy, if anyone? How have they reacted?</li> </ul>

	<ul style="list-style-type: none"> <li>● Getting to this point in exploring a curative treatment for sickle cell disease can be like a roller coaster where there are frequent ups and downs. Sometimes you might feel very ready for or confident in a curative therapy, but sometimes you might feel really uncertain about that same treatment. Imagine a scale that ranges from 0 to 10 where 0 is “Not ready at all for genetic therapy” and 10 is “I’m extremely ready for genetic therapy.” Where do you think you fall on that continuum? Talk to me about how you reached that estimate and what things keep you from being higher or lower.</li> <li>● Tell me about a time when you felt uncertain about or less confident in genetic therapy. What moved you towards greater certainty or more confidence in genetic therapy?</li> <li>● What alternatives to genetic therapy are you considering or have you considered?</li> </ul>
<p>3. Assess confidence in different components of the genetic therapy process</p>	<ul style="list-style-type: none"> <li>● Describe your level of readiness for the <i>pre-procedural process</i> (e.g., How prepared do you feel to participate in a genetic therapy clinical trial? Are you prepared to be separated from your support system? How confident are you that you know the treatment process? How prepared are you to be disconnected from responsibilities and important life activities? Are you ready to devote significant time to medical appointments before treatment? Have you thought about fertility preservation?).</li> <li>● How confident are you feeling about how you will handle the <i>procedural components</i> (e.g., receiving chemotherapy, not feeling well, possibly feeling depressed or anxious)?</li> <li>● Describe your level of readiness for the <i>post-procedural process</i> (e.g., frequent follow-up medical appointments, adherence to medications, possibly feeling depressed or anxious, activity limitations, potential infertility, changes in family, peer, and community relationships).</li> </ul>

<p>4. Assess potential for pressure or influence from others</p>	<ul style="list-style-type: none"> <li>● What do the important people in your life think about the possibility of you undergoing genetic therapy for your sickle cell disease?</li> <li>● It's common for people considering serious treatments like genetic therapy to ask for thoughts or advice from people they trust—like their family or friends. Sometimes those people have strong feelings one way or another about the treatment. To what extent are others' feelings influencing your decision about pursuing or not pursuing treatment?</li> <li>● Other than yourself, who else in your family, friend, or community group has the loudest voice or strongest opinion about your option to undergo genetic therapy?</li> <li>● Do you feel pressured by anyone to make a decision that you aren't comfortable with?</li> </ul>
<p>5. Assess past experiences of adversity and link to perceived readiness</p>	<ul style="list-style-type: none"> <li>● Can you tell me about a time when you experienced adversity or something really difficult? How did you handle or cope with that situation?</li> <li>● In what ways, if at all, have your past experiences of adversity moved you toward genetic therapy or prepared you for what you think your genetic therapy experience will be like?</li> <li>● Tell me about some of the challenges you have experienced living with sickle cell disease. How have you coped with those challenges and how have those experiences led you to this point—considering genetic therapy?</li> </ul>

**Table IV. Strategies recommended to support implementation of best practices for evaluating psychosocial risk and resilience factors**

**ASSESS INDIVIDUAL FACTORS (SCREENING INSTRUMENTS)**

<b>Assessment Area</b>	<b>Suggestions for Implementation</b>
1. Pre-existing emotional and physical issues	<ul style="list-style-type: none"> <li>● Assess for comorbid psychiatric or medical conditions (measures can be identified from the CureSCi Common Data Elements or PhenX Toolkit)                             <ul style="list-style-type: none"> <li>○ Depression</li> <li>○ Anxiety</li> <li>○ Stress</li> <li>○ Sleep/fatigue problems</li> <li>○ Poor health-related quality of life</li> <li>○ Other medical/pain conditions</li> </ul> </li> </ul>

**ASSESS INDIVIDUAL FACTORS (CLINICAL INTERVIEW)**

<b>Assessment Area</b>	<b>Possible Questions</b>
1. Pre-existing emotional and physical issues.	<ul style="list-style-type: none"> <li>● What challenges, if any, have you dealt with in managing sickle cell disease symptoms or other aspects of your health?</li> <li>● In what ways has it been difficult emotionally to cope with sickle cell disease or other health issues?</li> <li>● How would you describe your health currently?</li> <li>● How do you feel you are doing now from an emotional standpoint in terms of coping with sickle cell disease or other health issues?</li> <li>● Unfortunately, many people say they have experienced traumas or other significant life events that are distressing. Have you ever experienced any traumas or other distressing</li> </ul>

	<p>life events? This could include medical traumas, but it could also include traumas unrelated to sickle cell disease or your health.</p> <ul style="list-style-type: none"> <li>● If so, when was the last time you experienced a trauma or other stressful life event?</li> </ul> <p><i>Review medical charts and then follow-up with patients concerning any issues not discussed based on previous questions.</i></p>
<p>2. Schedule of life activities and events</p>	<ul style="list-style-type: none"> <li>● Are you working? What type of work do you do? Do you have a regular work schedule? What hours do you typically work per week? Is your job flexible? Can you do your job remotely or do you have to be in-person?</li> <li>● Are you currently in school? What days/hours do you typically attend school? Is your school flexible? Can you continue your school remotely or do you have to be in-person?</li> <li>● Are there any additional activities that you participate in regularly? When do you usually do those activities?</li> <li>● What important activities, events, or commitments do you have coming up over the next year or two?</li> </ul>
<p>3. Current challenges and stressors</p>	<ul style="list-style-type: none"> <li>● Stress is a normal part of life. What's the most stressful thing you are dealing with right now?</li> <li>● What are some things that commonly get in your way when you are trying to achieve goals or get things done?</li> <li>● What is going on in your life right now that could make it challenging for you to participate in this trial?</li> <li>● A lot of people tell us that finances are a source of stress. How often do you worry about having enough money for things like food, gas, the power bill, or rent or the mortgage? What would you do if there were significant unexpected costs that came up during the trial (e.g., gas or travel costs, extra meals)</li> </ul>

<p>4. Coping style</p>	<ul style="list-style-type: none"> <li>● How do you usually cope with stressful situations, such as unexpected life events, escalating symptoms, or fear?</li> <li>● What do you currently do to manage the stress that often comes along with SCD symptoms or other health issues?</li> <li>● What strategies are you using to manage COVID-19?</li> <li>● Do you ever use your religious or spiritual beliefs or practices to manage stress or SCD? What does this usually include? Has that worked for you?</li> <li>● Do you think how you are coping helps you manage your stress (i.e., do your strategies work)? Which strategies are more or less effective than others?</li> </ul>
<p>5. Optimism</p>	<ul style="list-style-type: none"> <li>● How would you rate your level of hope that things will work out positively on a 0 to 10 scale where 0 is “No hope at all that things will work out positively” and 10 is “Total confidence that things will work out positively”?</li> <li>● If you think of yourself as a generally optimistic person, how would you handle a situation where there is overwhelming evidence that things are not going to work out ?</li> </ul>
<p>6. Self-identity</p>	<ul style="list-style-type: none"> <li>● To what degree do you view having sickle cell and being a sickle cell warrior as being an essential part of who you are?</li> <li>● Have you considered whether participating in this trial will change that? If so, in what way?</li> </ul>
<p>7. Expectations</p>	<ul style="list-style-type: none"> <li>● What do you think life will be like after the trial? What about during the trial?</li> <li>● What are your goals for going through genetic therapy?</li> </ul>

	<ul style="list-style-type: none"> <li>• What are your life goals? Do you think participating in this trial will help, have no impact, or get in the way of you meeting those goals?</li> <li>• Are you concerned you could lose your job/get demoted or that your schoolwork will be disrupted?</li> <li>• Does this change who you are? In what ways?</li> <li>• Do you think participating in this trial will change your everyday life? In what ways?</li> <li>• Have you thought about if this does not work out the way you expect it to? What do you think will happen to you if it does not work out?</li> </ul>
<b>ASSESS FAMILY/CLOSE SOCIAL NETWORK FACTORS</b>	
<b>Assessment Area</b>	<b>Possible Questions</b>
1. Social networks of support	<ul style="list-style-type: none"> <li>• Everyone needs help at one point or another. Usually, people can find support from a wide range of people like family members, partners, friends, neighbors, and people in their religious or community organizations. Who are the important people in your life that you feel like you can turn to when you need help?</li> <li>• Some people are really good at helping by providing emotional support, some people provide helpful information, and others provide tangible or practical support like taking you to the doctor if you can't find another way. Who would you go to for each of these things - someone for emotional support, someone to get information, and someone to help you do something or handle a problem?</li> <li>• Do you feel comfortable asking for support from these people? Do you feel confident that they would help you if you needed help? When was the last time you asked someone for help?</li> <li>• What resources are available to help with home/family responsibilities like childcare? Do you have people beyond your primary caregiver who can help with these obligations?</li> </ul>

2. Primary support person or people	<ul style="list-style-type: none"> <li>• Other than your doctor, who would be the first person or first people you called if you needed help with something related to your health?</li> <li>• Why did you choose that person (or those people)?</li> <li>• Have they helped you in the past with your health?</li> <li>• Is there anything that might get in the way of them helping you (e.g., responsibilities or commitments, limited familiarity with medical topics, mental/physical health challenges)?</li> <li>• What does that person think about you participating in a genetic therapy clinical trial?</li> </ul>
3. Family composition	<ul style="list-style-type: none"> <li>• Who lives at home with you (e.g., parents, caregivers, significant others, children, extended family, friends)?</li> <li>• Does anyone else in the family have sickle cell disease or other special healthcare needs (either developmental, psychological, or physical health issues)?</li> <li>• Who in the home is working (working at home vs. outside of the home)?</li> <li>• Do you feel like your family has mostly everything it needs to get by (e.g., transportation, money, food, housing, etc.)?</li> </ul>
4. Family structure	<ul style="list-style-type: none"> <li>• In some families, one person is clearly in charge and makes most decisions for the family but in other families, multiple people share that responsibility. How do decisions get made or problems get solved in your family?</li> <li>• How would you describe each person's role in your family?</li> </ul>
5. Quality of family relations	<ul style="list-style-type: none"> <li>• How do people get along in your family?</li> </ul>

	<ul style="list-style-type: none"> <li>• Who gets along well?</li> <li>• Are there any strained or challenging relationships?</li> <li>• Do people in your family feel comfortable and safe expressing their honest feelings?</li> </ul>
<b>ASSESS ENVIRONMENTAL/COMMUNITY FACTORS</b>	
<b>Assessment Area</b>	<b>Possible Questions</b>
<p>1. Past relationships with healthcare providers</p>	<ul style="list-style-type: none"> <li>• How would you describe the quality of communications with your current medical team? How about with other doctors that have treated you?</li> <li>• What is your communication style like? What tends to be the communication style of your doctors or the medical team?</li> <li>• Do you feel you can communicate well with your doctor? If not, what gets in the way? How would you describe your relationship, in general, with doctors, medical teams, hospitals, etc.?</li> <li>• To what extent do you feel that your doctors and treatment team respect and trust you?</li> <li>• To what extent do you feel able to respect and trust your doctors and treatment team?</li> <li>• Tell me about some challenging experiences you have had with a medical provider or the larger medical system.</li> <li>• Tell me about a positive relationship you have had with a medical provider or team. What made that relationship positive?</li> <li>• Do you feel like your doctor or medical team spends enough time when providing information? Do they give you enough time to process information before making a decision?</li> </ul>

	<ul style="list-style-type: none"> <li>• How confident do you feel about your doctors' knowledge of sickle cell disease?</li> <li>• How involved in treatment decisions do you like to be? To what extent do you feel like your medical team(s) ask for, value, and honor your opinions/preferences?</li> </ul>
2. Access to the treating center	<ul style="list-style-type: none"> <li>• How far away is the center from where you live? How long does it take to get there?</li> <li>• How do you typically get to the center? Do you have reliable access to transportation?</li> <li>• How much does it cost for you to get back and forth from the hospital? Is that cost manageable for the duration of treatment and follow-up care?</li> <li>• Do you know of any resources that are available to help with access and/or transportation to the treatment center (e.g., staying overnight, travel, parking, modes of transportation available, ambassador programs, available partners)?</li> </ul>
3. Connections with community-based resources and comfort with seeking support	<ul style="list-style-type: none"> <li>• Are you involved in any religious or spiritual groups/organizations? Do you feel like you can get support from them before, during, and after the trial?</li> <li>• Are you involved in any community organizations that support or advocate for people with sickle cell disease?</li> <li>• Have you ever been involved in advocacy efforts to change things for people with sickle cell disease?</li> <li>• Are you familiar with the Sickle Cell Disease Association of American (SCDAA) and any of their local chapters or other advocacy groups/organizations (e.g., the Sickle Cell Reproductive Health Education Directive–SC RED)?</li> </ul>
4. Professional support for pre-existing issues/conditions	<ul style="list-style-type: none"> <li>• What existing supports or relationships do you already have in place for existing medical, psychological, social, or academic/work issues? Who would you go to for various medical concerns, mental health or social issues, academic/work issues?</li> </ul>

	<ul style="list-style-type: none"> <li>• Do you have a primary care provider? Are they aware that you are considering genetic therapy? Do they ever communicate with your medical specialist teams?</li> </ul>
<b>ASSESS CULTURAL AND SOCIETAL FACTORS</b>	
<b>Assessment Area</b>	<b>Possible Questions</b>
1. Family and cultural traditions	<ul style="list-style-type: none"> <li>• I want to understand more about the family and/or cultural beliefs, values, and structures that are important to you. How would you describe your culture? What family or cultural traditions are central to your life?</li> <li>• Different families and cultures often have different expectations for how various family members should be involved in each other's life. This can include biological family members, spouses, legal caregivers, chosen or adopted family, other extended family members, and close family friends or community members (e.g., religious leader). Who are the people that play an important role in your life? Are there cultural issues and expectations for involving certain people (e.g., roles of gender, seniority, or authority) in your important life decisions? If so, have they been involved in discussions about the genetic therapy clinical trial?</li> <li>• What family or cultural traditions bring you resilience or strength that can be called upon during times of challenge (e.g., prayer, affirmations)?</li> </ul>

<p>2. Acculturation (to the U.S., society, medical system, other systems and cultures)</p>	<ul style="list-style-type: none"> <li>● What are your/your family's preferred ways of communicating with the healthcare team? Are there established family expectations or norms for who communicates with the healthcare team?</li> <li>● Sometimes people notice generational differences in beliefs and perspectives that can cause stress or conflicts in their family. For example, an older family member might have certain cultural values that differ from family members from a younger generation. What generational issues affect you and your family?</li> <li>● Although the sickle cell disease care team and the genetic therapy clinical trial team are both made up of healthcare professionals, our teams may act and communicate in different ways. Sometimes, that takes some time for people to get used to. What have you found to be helpful ways of working and communicating with your sickle cell team?</li> </ul>
<p>3. Immigration</p>	<ul style="list-style-type: none"> <li>● Are there any current or past immigration issues that would be helpful to discuss related to you or other family members?</li> </ul> <p style="text-align: center;"><i>If care has been primarily provided outside of the U.S., consider potential differences (both positive and negative) between care and experiences in the U.S. and previous place of living/origin.</i></p>
<p>4. Medical mistrust and suspicion</p>	<ul style="list-style-type: none"> <li>● Do you feel your healthcare team has your best interests at heart?</li> <li>● Have there been times when you have felt that your healthcare team has seemed to actively work against you?</li> <li>● Who are the healthcare team members you trust the most? Who are the healthcare team members that you have difficulty trusting?</li> </ul>

5. Experiences of racism, with a focus on the healthcare setting, and associated impact

- Can you tell me about any times when you felt that you were treated with less courtesy than other patients? How often do you have negative experiences like this?
- In what ways have you been treated differently in healthcare settings because you have sickle cell disease? Does this seem to vary depending on the settings (e.g., emergency department vs. inpatient setting vs. sickle cell care clinic)?
- To what extent do you feel you have been denied care or provided inferior medical care because of your race? Does this seem to vary depending on the settings (e.g., emergency department vs. inpatient setting vs. sickle cell care clinic)?
- Have you heard of other people having negative experiences with the healthcare system because of their race or having sickle cell disease?
- How do these experiences affect the trust that you are able to develop with doctors, healthcare teams, hospitals, and/or researchers?