CURE SICKLE CELL.

National Heart, Lung, and Blood Institute

Guidelines for Assessing, Monitoring, and Supporting Psychosocial Health During and After Gene Therapy for Sickle Cell Disease (SCD)

PATIENT READINESS AND RESILIENCE WORKING GROUP

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Table of Contents

Introduction

The Cure Sickle Cell Initiative (CureSCi) Patient Readiness and Resilience Working Group (PRRWG) was formed by the National Heart, Lung, and Blood Institute (NHLBI) in 2020 to provide guidance on how best to support psychosocial health for people living with sickle cell disease (SCD) undergoing gene therapy. Phase 1 focused on developing recommendations for assessing and optimizing readiness for the gene therapy process. These guidelines were released as a White Paper in 2023, and an associated article published in JAMA Network Open in August of 2024 (https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2822554). Building on these earlier recommendations, Phase 2 focused on developing recommendations to guide assessing, monitoring, and supporting psychosocial health during and after gene therapy.

INTENDED USE

This guide outlines key considerations and recommendations for psychosocial health assessment and support during and after gene therapy for individuals with sickle cell disease (SCD). Of note, these guidelines are intended for use with people with SCD aged 12 years and above; however, these guidelines can also guide practices for younger children who are developmentally and cognitively able to participate in clinical interviews. It assumes that a thorough psychosocial assessment has been conducted prior to treatment, as outlined in the previously published white paper on pre-gene therapy psychosocial assessment (available at https://curesickle.org/research-resources). Building on that assessment, the current guidelines promote brief, ongoing assessments of psychosocial health to direct personalized support strategies. The intended audience includes healthcare systems, medical and psychosocial care providers, clinical research administrators, and support staff. In addition, content presented here may be of interest to community-based organizations, advocacy groups, managed care organizations and payors, policymakers, and other parties.

PROCESS FOR DEVELOPMENT

The PRR working group is composed of experts in psychosocial health and related disease symptoms among people living with SCD. It includes clinicians, researchers, patient advocates, and individuals with lived experience of SCD. The working group had monthly virtual meetings from July 2024 to December of 2025 to develop the current recommendations.

The guidelines were developed using a modified Delphi method, a structured process for achieving expert consensus through a series of iterative discussions and feedback loops. During a series of structured virtual meetings, working group members responded to open-ended questions. Some foundational questions that shaped the discussion and subsequent recommendations included: "When and by whom should psychosocial assessments be performed?", "What is the role of referring versus treating centers in the gene therapy process?", and "What psychosocial areas should be evaluated and prioritized during the gene therapy process?". The working group's written and verbal feedback was collected, organized, and circulated for review. Subsequent meetings focused on refining themes and achieving consensus around the most critical areas and recommendations for promoting optimal psychosocial health assessment, monitoring, and intervention.

Discussions were informed by a number of sources. This included ongoing feedback throughout the process from the CureSCi Community Input Panel (CIP), a working group composed of people with lived experience of SCD. Information was also sought from people with lived experience of the SCD gene therapy process, and clinicians and researchers with expertise in aspects of the SCD gene therapy process. The empirical literature was reviewed to identify psychosocial challenges and strengths relevant to individuals with SCD undergoing gene therapy. Given the limited literature in individuals with SCD who have undergone gene therapy, the working group also reviewed literature on individuals with SCD who underwent hematopoietic cell transplantation (HCT) as well as from comparable populations, including individuals undergoing gene therapy for non-SCD conditions, patients with histories of prolonged hospitalization, and survivors of childhood and adult cancers. Lastly, feedback was solicited on an earlier draft of the guidelines via online survey from clinical providers who work with individuals with SCD as well as the CureSCi CIP.

The evidence gathered from these sources supported that the psychosocial challenges related to gene therapy are multi-faceted and often extend well beyond the recovery period of gene therapy-related hospitalization. Feedback from people with lived experience of SCD and clinicians highlighted the emotional and psychological demands of the treatment and post-treatment process; particularly as it relates to identity, relational, and life transitions patients often experience as a result of gene therapy. However, they also highlighted the potential for positive outcomes, including increased energy, focus, excitement, growth, and opportunities for new experiences. Of note, the need for psychosocial support and education for people with SCD prior to gene therapy was emphasized. Literature review findings indicated that after gene therapy, while many patients report improved psychosocial health, psychosocial challenges may persist even after physical symptoms have been reduced; thus, mental health assessment support must extend beyond the treatment itself. Also, prolonged hospitalizations (e.g., those lasting 100 days or more) are associated with recurring psychosocial issues, including anxiety, depression, and general emotional distress.

Overall, this process combined empirical evidence, clinical expertise, and community input to shape a comprehensive and patient-centered set of recommendations. A draft consensus document was released for public comment in October of 2025, and final revisions were completed by December of 2025. The summary of recommendations is below.

Summary of Recommendations

I. PRE-GENE THERAPY PLANNING FOR POST-THERAPY PSYCHOSOCIAL HEALTH

Develop a comprehensive plan for psychosocial health monitoring and support throughout and beyond the gene therapy process. Clarify roles and responsibilities for psychosocial follow-up, including transitions between Treating and Referring Centers. Communicate the long-term follow-up timeline and expectations to the patient and family from the outset.

II. RECOMMENDED SCHEDULE AND STRATEGIES FOR PSYCHOSOCIAL HEALTH CHECK-INS

Table 1 details the recommended schedule for psychosocial health check-ins during and after the gene therapy process. While the guideline focuses on the first 5 years post-gene therapy, psychosocial monitoring and support should continue past this milestone as needed. Also, when an investigational gene therapy product is used, the timeline for assessment and support should be expanded to be consistent with FDA recommendations. The 2020 FDA recommendations support a minimum of 15 years of follow-up post-exposure to investigational gene therapy products to monitor for long-term safety and effectiveness consisting of annual visits during the first 5 years, and in-person or survey queries during the following 10 years. These long-term follow-ups should include psychosocial assessments. To reduce patient burden, it is recommended to coordinate assessments with other clinic visits and/or offer telehealth options as possible.

TABLE 1. **Recommended Frequency of Psychosocial Assessments During and up to 5 years Post-Therapy**

PHASE	CHECK-IN FREQUENCY	NOTES
During therapy	At least 1 a week	Begin at the time of hospitalization and continue throughout the therapy process; may adjust based on patient status
Years 1-2 post-therapy	Every 3–6 months	Begin shortly after hospital discharge. Increase frequency if problems are detected.
Years 3–5 post-therapy	Annually	Continue regular monitoring; may adjust based on patient status.

Recommended strategies for ongoing monitoring of psychosocial health during and after gene therapy are detailed in Appendix Table A. Prior to each assessment, the patient's pre-gene therapy and previous psychosocial health assessments should be reviewed. The assessment should primarily take the form of a clinical interview, though validated questionnaires may be used to supplement the assessment.

IMPORTANT CONSIDERATIONS

Developmental, emotional, cognitive, and relational considerations should be taken into account when planning the assessment. For example, as the assessment itself may lead to emotional distress, it is

important to consider the patient's emotional state throughout and immediately after the assessment. Also, considerations should be given to the evolving role of caregivers during the gene therapy process, and their possible need for psychosocial assessment and support.

Appendix Table A presents recommendations for assessing a core set of domains, and then, based on individual patient's circumstances, secondary domains that can also be assessed. Sample questions are provided for assessing each domain, understanding that the interviewers may modify questions to tailor to the patient's needs and characteristics. Below is the list of primary and secondary assessment domains.

PRIMARY ASSESMENT DOMAINS

- Emotional and Physical Issues
- Current Health and health Challenges
- Coping
- Adequacy of Emotional Support
- Expectations

SECONDARY ASSESMENT DOMAINS

- Pain Management
- Problems with Life Activities
- Optimism
- SCD Identity
- Relationship with Primary Support
- Health Care Team Support
- Life Goals
- Gene Therapy Challenges and Benefits

III. RESPONSIBILITIES: WHO CONDUCTS THE ASSESSMENTS?

Decisions about who will conduct psychosocial assessments at different phases of care should be made before treatment begins. Table 2 provides recommendations concerning which center (i.e., treating or referring) should be responsible for monitoring psychosocial health. Consistent with pre-gene therapy guidelines, it is recommended that a mental health provider with SCD knowledge and experience conduct the assessments. Continuity of care and communication between centers should be prioritized.

TABLE 2. **Recommendations for Responsibility for Psychosocial Assessments during Gene Therapy Phases**

PHASE	RESPONSIBLE PARTY	NOTES
Pre-gene therapy	Treating Center	Full psychosocial assessment should already be completed.
During therapy	Treating Center	Includes hospitalization and immediate post-treatment monitoring.
Post-gene therapy	Referring Center or Treating Center	Decision depends on patient location, care model, and funding. Aim for at least one follow-up every 6 months in years 1-2, and annually in ≥ year 3.

IMPORTANT CONSIDERATIONS

Ideally, the same center or team should oversee assessments across all phases. If patients are traveling between centers, a transition plan must be established to ensure continuity and coordination. Clinical trials may have separate timelines and funding (e.g., 2 years of follow-up); align expectations accordingly.

Consider long-term care models, particularly given that patients may no longer be designated as having SCD post-treatment; thus, their eligibility for access to specific services may change. Lastly, be mindful of the learning curve at the Referring Center if less familiar with gene therapy needs.

IV. LOGISTICS AND COMMUNICATION

1. COMMUNICATION OF EXPECTATIONS
   Clearly communicate the timeline and purpose of follow-up assessments at the outset. Discuss potential changes in psychosocial needs and support availability over time. Take into account developmental and cognitive considerations and adapt questions/strategies to optimize comprehension.

2. DESIGNATE A POINT PERSON
   Assign a provider or coordinator at the center providing care who is built into the structure of the organization. That person will be responsible for the following: scheduling psychosocial appointments, facilitating check-ins and referrals between formal assessments, and acting as a bridge between the Treating and Referring Centers.

V. SUMMARY OF KEY STRATEGIES

- Start with a strong pre-treatment psychosocial foundation.
- Plan proactively for continuity of care post-treatment.
- Maintain structured, regular check-ins aligned with patient recovery and adaptation.
- Ensure clear role delineation and communication among clinical teams.
- Tailor monitoring and implementation of support to address evolving psychosocial needs of the patient and their support systems, including their primary caregiver(s).

Appendix

TABLE A. **Recommended Strategies for Ongoing Monitoring of Psychosocial Health during and after Gene Therapy.**

ASSESS INDIVIDUAL FACTORS USING SCREENING INSTRUMENTS AND CLINICAL INTERVIEW QUESTION GUIDE (DOMAINS BEING ASSESSED ARE UNDERLINED)

ASSESSMENT FORMAT	ASSESSMENT DOMAIN AND SUGGESTED TOPICS
1. Areas of Monitoring for Validated Screening Questionnaires - Measures can be identified from the CureSCi Common Data Elements or PhenX Toolkit	EMOTIONAL AND PHYSICAL ISSUES Are you experiencing issues in any of the following areas? - Depression, including suicidal ideation - Anxiety - Post-traumatic stress disorder - Acute and chronic pain - Pain interference - Sleep - Fatigue - Social support - Quality of Life Recommended to be consistent with pre-gene therapy questionnaires so that changes can be assessed. May be paired with an executive functioning/neurocognitive monitoring assessment. Also, for pediatric patients, self-report and parent proxy reports are recommended.
2. Core List of Clinical Interview Questions - Interview should be done after screening questionnaires, and should be informed by questionnaire scores	CURRENT HEALTH AND HEALTH CHALLENGES - How would you describe your current health? What challenges, if any, are you CURRENTLY experiencing in managing the following? - The gene therapy process? - Any lingering symptoms or problems related to sickle cell disease, including pain? - Other medical concerns (e.g., fertility preservation)? - Mental health issues? - Other aspects of your health? COPING - How do you feel you are doing now from an emotional standpoint in terms of coping with sickle cell disease and the gene therapy process? - What things are you doing currently to manage stress? Do you still feel like you have the support you need to move forward? - What strengths have you drawn on or do you continue to draw on during this process? How have things changed for the better as a part of this process? ADEQUACY OF EMOTIONAL SUPPORT - Are you receiving any professional support for your mental health from a counselor, social worker, psychologist, or psychiatrist, for example?

	EXPECTATIONS - Do you feel that your expectations for yourself and your life have changed? Do you feel like things about you and your life have changed? Do you feel like other people's expectations for you or your life have changed? - Is there anything that happened during the gene therapy process that you wish you had known or understood more clearly beforehand? *Also, review the medical chart and then follow-up with the patient concerning any issues not discussed based on previous questions.*
3. Additional List of Clinical Interview Questions - To be used to augment the Core List of Questions above, as needed for specific patients	PAIN MANAGEMENT - How has your management of pain changed, including how much you use pain medications? How about how you manage your other sickle cell symptoms? PROBLEMS WITH LIFE ACTIVITIES - Are you experiencing any problems with school/work? Do you have any worries about having enough money for things like food, transportation, bills, or housing? OPTIMISM - How would you rate your level of confidence that things will work out, 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?" SCD IDENTITY - How much do you think SCD is impacting your life right now? How central is SCD to your identity these days? How are changes to your identity impacting your life? RELATIONSHIP WITH PRIMARY SUPPORT - Have there been any changes to who is your primary support person (or people)? How has your relationship with your primary support person (or people) changed as a part of this process? HEALTH CARE TEAM SUPPORT - Have there been any significant changes in your primary health care team? Do you have any concerns with how you and your healthcare team are communicating or working together? LIFE GOALS - Have your life goals changed? Do you feel like your gene therapy treatment is helping you move closer to your life goals or getting in the way? GENE THERAPY CHALLENGES AND BENEFITS - What are/were the main challenges or drawbacks you experienced during the gene therapy process? - What are/were the most beneficial or positive aspects of the gene therapy process for you?

Note: As the assessment may lead to emotional distress, be mindful of the ordering of the surveys and questions during the assessment, as well as the emotional state of the patient throughout the assessment process.