



2019-2021 ASH Clinical Practice Guidelines on Sickle Cell Disease (SCD):

What You Should Know

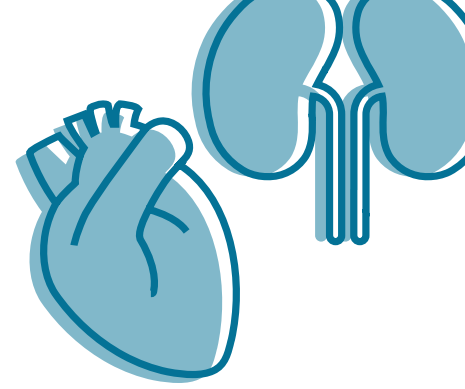
The American Society of Hematology (ASH) believes it is essential to provide updated treatment guidelines that reflect the newest evidence about the disease, ensuring the medical community can better treat SCD and people living with SCD can make the best decisions for their care.

In partnership with the Evidence-Based Practice Research Program at Mayo Clinic, the 2019-2021 ASH Clinical Practice Guidelines on Sickle Cell Disease (SCD) were developed using the GRADE methodology to ensure the highest standards for trustworthiness. ASH brought together more than 70 experts, including hematologists, clinicians from other specialties, and patient and caregiver representatives to identify best practices for the management of acute and chronic complications of SCD and ways to improve the quality of care for people living with SCD.

What follows are the five 2019-2021 ASH Clinical Practice Guidelines on Sickle Cell Disease.

For more information on the 2019-2021 ASH Clinical Practice Guidelines on Sickle Cell Disease, www.hematology.org/SCDguidelines





SCD-Related Cardiopulmonary and Kidney Disease



What it covers

- Evidence-based treatment guidelines for sickle cell disease complications that affect the heart, lungs, and kidneys.



Why it matters

- SCD affects multiple organs that require patients to seek care from doctors that specialize in treating complications of the heart, lungs, and kidneys. It is important for these specialists to work closely with hematologists or SCD doctors to provide coordinated care for patients with SCD.

Doctors treating patients with SCD need to know the landscape of scientific evidence that exists for screening and treating complications of the heart, lungs, and kidneys and involve patients in the shared decision-making process.

Developing treatment guidelines based on current scientific evidence and identifying the gaps helps the community determine what additional research needs to be done to improve the lives of patients with SCD.



Who it affects

- **Hematologists and other specialists:** Doctors will have access to guidelines that are based on the best available scientific evidence to improve their understanding of how to look for and treat complications of the heart, lungs, and kidneys, and make shared-decisions with patients.
- **SCD patients:** Their physicians will have more information and evidence-based guidance so that they can have informed discussions with patients to make the best testing and treatment decisions.
- **Policymakers:** Policymakers will be informed of the knowledge gaps that exist in SCD evidence so they can direct research funding to fill in the gaps. In this regard, these guidelines may help shape policy.



What are the highlights

- **Hypertension:** The negative impact of hypertension on patient outcomes, particularly for African American individuals, means that a blood pressure goal of $\leq 130/80$ mm Hg is the appropriate target to achieve in adults with sickle cell disease.
- **Screening:** Patients with SCD who do not show any symptoms should not be routinely screened for pulmonary hypertension, abnormal lung function or sleep disorders. However, providers should carefully evaluate patients with SCD for signs and symptoms of cardiopulmonary disease that could suggest the need for diagnostic testing.
- **Kidney Transplant:** Patients with SCD experiencing End-Stage Renal Disease or advanced chronic kidney disease requiring dialysis should not be excluded from consideration for kidney transplantation.

Total number of panel recommendations: 13

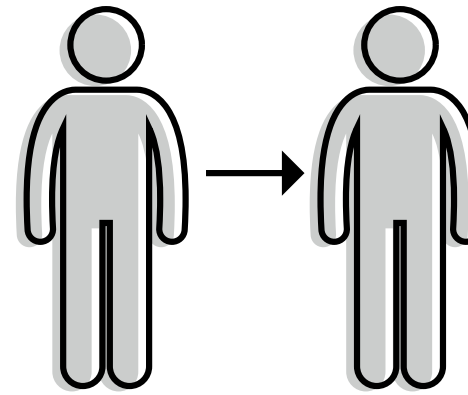
REFERENCE

Liem RI, Lanzkron S, Coates TD, et al. [American Society of Hematology 2019 guidelines for sickle cell disease: cardiopulmonary and kidney disease](#). Blood Adv. 2019; 3(23):3867-3897.

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SCD-Related Transfusion Support



What it covers

- Clinical situations when transfusion should be used to care for people with sickle cell disease (SCD).



Why it matters

- People with SCD often require blood transfusions to prevent or treat organ damage associated with the disease. Additional clinical guidance may help physicians standardize and advance their patients' care and decrease side effects.



Who it affects

- **Patients with SCD:** To inform conversations with their physicians, particularly around when, where, how and why a transfusion should be provided.
- **Blood banks:** To create an understanding of the more nuanced recommendations that affect how transfusions are administered.
- **Hematologists:** To provide a basis for guiding decisions for specific types of blood testing and circumstances for transfusion.
- **Policymakers:** Policymakers will be informed of the knowledge gaps that exist in SCD evidence so they can direct research funding to fill in the gaps. In this regard, these guidelines may help shape policy.



What are the highlights

- Patients with SCD who require transfusions should receive red blood cells that have undergone more extensive profiling that goes beyond traditional blood-type testing techniques.
- Therapies to suppress the immune system should be used under certain circumstances such as in patients with a sudden and pressing need for transfusion if they are at high risk of an immune response to the transfusion, a serious complication that can occur after a blood transfusion.
- The guidelines make additional recommendations on transfusion and SCD, including in:

Circumstances where physicians should consider a procedure to exchange red blood cells from the patient rather than a traditional blood transfusion, including in patients with SCD and severe acute chest syndrome.

Patients who receive transfusions on a chronic, regular basis.

Pre-operative scenarios, where providing transfusions prior to operations is suggested.

Total number of panel recommendations: 12

REFERENCE

Chou ST, Alsawas M, Fasano RM, et al. [American Society of Hematology 2020 guidelines for sickle cell disease: transfusion support](https://www.bloodjournal.org/lookup/suppl/doi:10.1182/blood-2020-04-327355/-/DC1). Blood Adv. 2020;4(2):327-355.

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SCD-Related Cerebrovascular Disease



What it covers

- Screening and treatment guidelines for SCD complications affecting the brain, including risk of strokes and other neurological complications for both children and adults.



Why it matters

- Neurologic complications such as stroke and silent stroke are a major cause of disability and death for children and adults living with SCD.
- Effective screening for stroke risk in SCD may help prevent or reduce the risks associated with these types of complications.
- “Silent strokes” – those without obvious neurological symptoms – affect 1 in 3 children and at least 1 in 2 adults with SCD, and often go undetected. They are linked to cognitive impairment potentially impacting school performance, and are risk factors for future strokes, which can be life-threatening. Silent strokes occur in a region of the brain that does not affect motor skills, which is why they are often not detected without a brain scan.
- Clear, updated guidelines can help emergency room physicians quickly manage and treat children who may have had a stroke. In these settings, the faster a child or adult with SCD is treated, the better the outcome.
- Most children born with SCD live in low-to-middle income countries, which have the largest global population of SCD, but are frequently without access to stroke-prevention practices.



Who it affects

- **Hematologists:** Hematologists are looked to as experts on SCD and therefore have a role to play in ensuring neurologists and other specialists are implementing the most current clinical practice guidelines.
- **Primary care providers:** Many primary care providers have limited experience managing SCD, but are often caring for people living with SCD. The guidelines will serve as an easy, accessible reference to support them in preventing and treating neurological complications of the disease.
- **Neurologists:** Neurologists are the experts in acute and long-term management of strokes; however, they have not been traditionally part of the care team of children and adults who have had a stroke. The guidelines will integrate the known management of strokes in the general population with the management of strokes in those with SCD.
- **Emergency room physicians:** In the emergency room setting, caregivers need to act quickly and navigate complex issues to prevent further brain damage for a patient experiencing stroke. This includes knowing when to call a hematologist and neurologist, order an image of the brain, and give a patient a transfusion.
- **Parents:** Parents can seek professional help in assessing whether their child has had or is at risk for strokes or silent strokes. Knowing this information will help their child get needed support.
- **Educators, employers, and family members:** Educators, employers, and family members should understand that children and adults with SCD may have experienced silent strokes and not know it. They may need or require additional educational, employment, or family support to maximize their potential.
- **Policymakers:** Policymakers will be informed of the knowledge gaps that exist in SCD evidence so they can direct research funding to fill in the gaps. In this regard, these guidelines may help shape policy.

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SCD-Related Cerebrovascular Disease



What are the highlights

- Adults and children should be screened via brain scans to assess their risk for a silent stroke. Based on the screening:
 - Children can receive regular blood transfusions to reduce the risk of a new stroke, another silent stroke, or both. In addition, screening can identify children who have already had a silent stroke and are therefore eligible for school-based resources and other types of educational support.
- *In children age 2-16 years with the most common type of SCD who have abnormal brain scan measurements:* receiving monthly blood transfusion therapy - over no transfusion - is recommended in order to decrease the 1 in 10 risk of having a stroke in the next 12 months.
- *In children age 2-16 years with SCD, living in low-resource settings with abnormal ultrasound brain scan measurements, and unable to receive regular blood transfusion therapy:* hydroxyurea therapy - over no therapy - is recommended to decrease the 1 in 10 risk of having a stroke in the next 12 months.
- *In children and adults presenting with acute strokes:* physicians should consider performing a simple red blood cell transfusion without delaying for sub-specialty consults or a definitive diagnosis of stroke via brain scan.

Total number of panel recommendations: 18

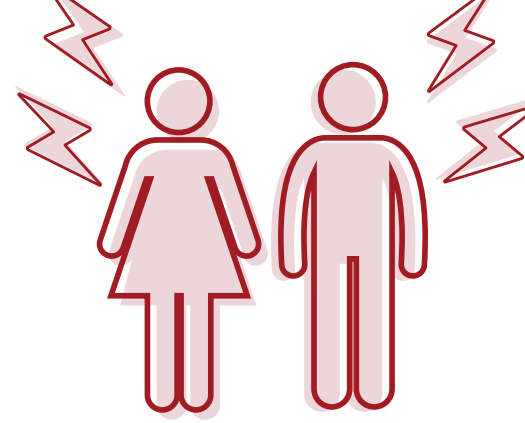
REFERENCE

DeBaun MR, Jordan LC, King AA, et al. [American Society of Hematology 2020 guidelines for sickle cell disease: prevention, diagnosis, and treatment of cerebrovascular disease in children and adults.](#) *Blood Adv.* 2020;4(6):1554-1588.

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SCD-Related Acute and Chronic Pain



What it covers

- Evidence-based guidelines for the management of sickle cell disease (SCD)-related acute and chronic pain in children and adults.



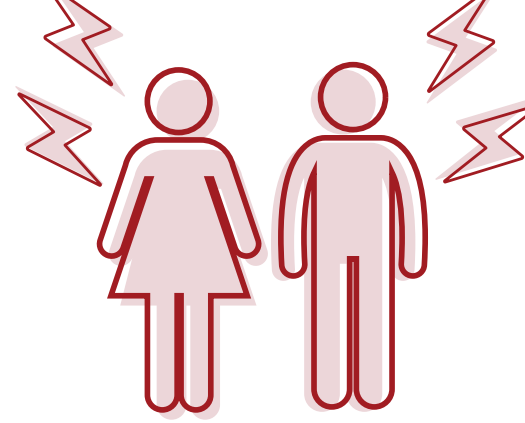
Why it matters

- Severe pain is the most common complication of SCD and affects individuals' quality of life. Acute pain episodes are the leading cause of emergency department visits and hospitalizations for individuals living with SCD. Further, chronic pain develops as individuals age and affects them daily.
- Acute and chronic pain management is a common clinical challenge for health care providers. This is in part due to the lack of strong evidence to support clinical decision-making.
- Health care providers may be unaware of all the available tools that can be used to manage acute and chronic SCD pain. These tools include both medications and treatments that are not medications.



Who it affects

- **Hematologists and other clinicians providing pain management care:** Clinicians will have access to guidelines based on the best available scientific evidence to improve their understanding of how to look for, treat, and manage acute and chronic SCD pain.
- **Emergency room physicians:** The guidelines make important recommendations for how quickly individuals living with SCD experiencing acute pain should receive medical attention.
- **Primary Care and Family Physicians:** Care of individuals living with SCD is often the responsibility of primary care and family physicians. This physician community has expressed a strong need for guidance and tools to help inform their care.
- **Individuals living with SCD and their family members:** These guidelines provide an opportunity to make shared decisions with their health care providers regarding the management of their pain.
- **Policymakers:** Policymakers will be informed of the knowledge gaps that exist in SCD evidence so they can direct research funding to fill in the gaps. In this regard, these guidelines may help shape policy.



SCD-Related Acute and Chronic Pain



What are the highlights

- **Acute pain:** Individuals seeking care for the treatment of acute pain should have their pain assessed and medication administered within one hour of their arrival at the acute care facility. Individuals should then be frequently reassessed every 30-60 minutes for consideration of additional doses of pain medication to optimize their pain control.
- **Chronic pain:** Individuals who experience chronic pain may benefit from a tailored treatment plan when starting or ending chronic opioid therapy. Treatment decisions should balance the risks and benefits of opioids and consider the individual's function, goals, and durability of benefit over time.
- **Chronic pain:** Medications that treat pain that are not opioids can be considered for individuals who experience chronic pain as part of a comprehensive pain treatment plan.
- **Pain management approaches beyond and in addition to prescription medicines:**
 - Clinicians treating individuals with SCD and acute pain can consider approaches including massage, yoga, virtual reality, and guided audiovisual relaxation in addition to medications (e.g., opioids, NSAIDs).
 - Clinicians treating individuals living with SCD and chronic pain can consider Cognitive Behavioral Therapy and other integrative approaches (e.g., acupuncture, massage therapy) in addition to medications as part of a comprehensive disease and pain management plan.
- **Transfusion:** Individuals living with SCD who have recurrent acute pain may not benefit from chronic monthly transfusions as a first-line strategy to prevent or reduce future acute pain episodes.

Total number of panel recommendations: 18

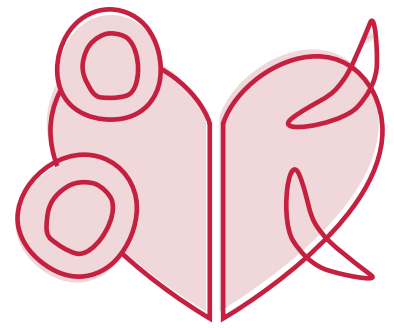
REFERENCE

Brandow AM, Carroll CP, Creary S, et al. [American Society of Hematology 2020 guidelines for sickle cell disease: management of acute and chronic pain](#). Blood Adv. 2020;4(12):2656-2701.

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ASH Guideline Recommendations for Sickle Cell Disease: Stem Cell Transplantation



What it covers

- Evidence-based guidelines to support individuals with sickle cell disease and their clinicians considering allogeneic stem cell transplants.



Why it matters

- SCD is a common inherited blood disorder in the United States. SCD results in significant health complications and affects quality of life.
- Allogeneic Hematopoietic stem cell transplant (HSCT), a process in which the individual's blood-forming stem cells are replaced with healthy cells from a donor (allogeneic), is currently the only potentially curative therapy for SCD.
- Guidelines are needed to inform how to apply HSCT in clinical practice, particularly to weigh the risks and benefits versus disease modifying/supportive therapies or potential curative therapies under development, such as gene therapy.



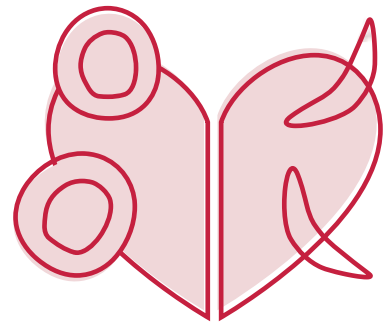
Who it affects

- **Hematologists, internists, general practitioners, pediatricians, and other clinicians:** Health care providers seeking clinical decision support to help identify which individuals with SCD should be considered for HSCT.
- **Individuals with SCD:** Individuals who may be discussing therapy options with their families and health care providers.
- **Researchers:** Those seeking to address potential gaps in evidence supporting treatment decisions.

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ASH Guideline Recommendations for Sickle Cell Disease: Stem Cell Transplantation



What are the highlights

- HSCT should be considered over standard of care (transfusion) in individuals with SCD who have experienced a stroke or are at very high risk of stroke. Further, transplantation should be considered for all patients with neurologic injury who have a matched, related sibling donor. Recommendations point to evidence suggesting that children under age 13 who receive HSCT from a matched sibling donor have better outcomes than those older than age 13.
- For patients with frequent pain, as well as those with recurrent episodes of acute chest syndrome, the ASH guidelines suggest transplantation from a matched sibling donor over the standard of care.
- For individuals with an indication for HSCT who lack a matched sibling donor, the ASH guideline panel suggests transplantation from alternate donors only in the context of a clinical trial.
- In patients with an indication for transplant, the ASH guideline panel suggests transplantation with cells from a matched donor earlier in life due to the risk of irreversible SCD-related damage to the body that increases with age.

Total number of panel recommendations: 8 recommendations

REFERENCE

Kanter J, Liem RI, Bernaudin F, et al. [American Society of Hematology 2021 guidelines for sickle cell disease: stem cell transplantation](#). *Blood Adv*. 2021;5(18):3668-3689.

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