Consensus definition of essential, optimal, and suggested components of a pediatric Sickle Cell Disease Center

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Abstract

Sickle cell disease (SCD) requires coordinated, specialized medical care for optimal outcomes. There are no United States (US) guidelines that define a pediatric comprehensive SCD program. We report a modified Delphi consensus-seeking process to determine essential, optimal, and suggested elements of a comprehensive pediatric SCD center. Nineteen pediatric SCD specialists participated from the US. Consensus was predefined as 2/3 agreement on each element's categorization. Twenty-six elements were considered essential (required for guideline-based SCD care), ten were optimal (recommended but not required), and five were suggested. This work lays the foundation for a formal recognition process of pediatric comprehensive SCD centers.

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Abbreviations:

SCD	Sickle cell disease
US	United States
CF	Cystic fibrosis
NHLBI	National Heart, Lung, and Blood Institute
ASH	American Society of Hematology
NIH	National Institutes of Health
ED	Emergency Department
Hb	Hemoglobin
HU	Hydroxyurea
HSCT	Hematopoietic stem cell transplant

Keywords:

Sickle cell disease, comprehensive care, comprehensive center, guideline-based care, implementation

Abstract

Sickle cell disease (SCD) requires coordinated, specialized medical care for optimal outcomes. There are no United States (US) guidelines that define a pediatric comprehensive SCD program. We report a modified Delphi consensus-seeking process to determine essential, optimal, and suggested elements of a comprehensive pediatric SCD center. Nineteen pediatric SCD specialists participated from the US. Consensus was predefined as 2/3 agreement on each element's categorization. Twenty-six elements were considered essential (required for guideline-based SCD care), ten were optimal (recommended but not required), and five were suggested. This work lays the foundation for a formal recognition process of pediatric comprehensive SCD centers.

Introduction:

Sickle cell disease (SCD) affects approximately 100,000 Americans, though exact numbers are not known due to lack of formal tracking.[1] Infants with SCD are identified through newborn screening, but follow-up processes vary between states, affecting care access. Unlike other childhood genetic diseases, namely cystic fibrosis (CF) and hemophilia, there are no defined standards of SCD care within the United States (US).[2] While the National Heart, Lung, and Blood Institute (NHLBI)'s 2014 "Evidence Based Care for Sickle Cell Disease" guideline stipulates some pediatric care elements, and the American Society of Hematology (ASH)'s care guidelines fill some clinical gaps in the NHLBI document, implementation is not monitored.[3] Evidence

from Medicaid claims and a recent National Institutes of Health (NIH)-funded multicenter implementation study show that many children do not receive indicated penicillin prophylaxis[4] or annual transcranial Doppler ultrasound screening.[5]

Individuals with SCD require highly-knowledgeable, coordinated care throughout their lifespan. Initiation of preventive therapies early in life can minimize irreversible organ damage.[6,7]Pre-symptomatic hydroxyurea initiation, novel therapies, shared decision-making, and comprehensive preventive care require expertise, support staff, and time investment. Without mechanisms to monitor outcomes throughout childhood, there is a lost opportunity to minimize the lifelong burden of SCD. While >98% of children with SCD survive into adulthood, the estimated median survival is in the mid-40s and has not improved over the past 20 years due to limited care access, few disease-specific therapies, and underinvestment in SCD.[8] The need for comprehensive care was recognized in the National Sickle Cell Disease Control Act in 1972.[9] However, the NIH-funded comprehensive sickle cell centers were disbanded, and there is no current federal mechanism supporting comprehensive SCD centers.

In 2019, SCD physicians identified essential, optimal, and suggested elements of comprehensive SCD care for adults.[10] Here, we report a similar process in which pediatric SCD physicians reached consensus on essential, optimal, and suggested elements of comprehensive SCD care. This is the first step towards defining an accreditation process for comprehensive pediatric SCD centers.

Methods:

We employed a modified Delphi process to establish consensus on SCD care elements.[11] The study initiators (MLH, DM, ERM, JK) compiled center elements from guidelines, medical literature, and clinical experience. Consensus was pre-specified as 66% agreement for each element. Elements clustered in categories: center personnel, treatments, screening/diagnostic tests, center processes, physical spaces, and collaborations.

Twenty-one pediatric SCD specialists were invited to participate in the process during 2021. All invitees were pediatric hematologists at academic SCD centers, active in research, public health, and/or state newborn screening programs. Participants of diverse ages, gender, location, and ethnicity were invited. During the process, three participants moved from academic practice to industry but continued on the panel.

In the first questionnaire, participants rated each element as essential, optimal, or suggested. Essential was defined as required for comprehensive care, either embedded within the SCD team or via a defined referral process. Essential elements have evidence-based support in NHLBI, ASH, or other published guidelines. Optimal elements were defined as beneficial but not required for guideline-based care.[10] Suggested elements were defined as likely to enhance treatment but not required for guideline-based care.

Elements that did not reach consensus initially were re-queried in a second email questionnaire. If one category received [?]3 votes, only the remaining two options were provided (example: if an element had 7 essential votes, 9 optimal votes, and 3 suggested votes, the "suggested" choice was removed). Finally, a virtual meeting was held to categorize elements that had not yet reached consensus. During the virtual meeting, panel participants nominated four additional elements.

Results:

Of 21 pediatric hematologists invited, 19 participated. The participants' SCD programs care for 150 to 1600 patients and are located in all regions of the United States (Northeast: 2, Mid-Atlantic: 3, Southeast/South: 6, Midwest: 6, West Coast: 2).

Initially, 37 elements were included. Twenty-four elements reached consensus via email questionnaires. Fifteen participants attended the virtual meeting to attain consensus on 13 remaining elements. Four new elements (nutritionist, timely access to subspecialists, formal quality improvement process, and formal mechanism for parent/family input) were added and categorized during the virtual meeting.

Twenty-six elements were considered essential, encompassing center staff, processes, diagnostic and treatment modalities, and necessary collaborations outside the core SCD team (Table 1). Ten elements were considered

optimal, including staff, physical spaces, treatments, and collaborations (Table 2). Five elements were considered suggested, comprising staff and process elements (Table 2).

Essential elements:

A multidisciplinary team forms the core of the comprehensive pediatric SCD center. The team must be directed by a physician expert in SCD who oversees medical care and staff. This physician should have post-residency training and experience in hydroxyurea, transfusion therapy, and other SCD-modifying treatments. The multidisciplinary team includes outpatient nursing staff with SCD experience and a care coordinator/manager. A social worker dedicated to SCD helps patients/families navigate the insurance environment and address social determinants of health.[12] Children with SCD experience cognitive deficits and lower academic attainment, so an education liaison (a social worker, neuropsychologist, teacher, or nurse) is essential to support educational attainment.[13] A pediatric hematology team (attending physician, supervising advance practice providers or residents/trainees, and nurses with hematology experience) is essential for inpatient care (either by admission to a pediatric hematology inpatient service or a pediatric hospitalist service with a consulting pediatric hematologist).

Standardized processes are essential to uniform, guideline-based care. Newborn screening follow-up ensures affected infants are immediately engaged in SCD care to initiate penicillin prophylaxis and preventive care.[3,14] Standardized order sets and written protocols for acute and chronic management, including in the ED, promote adherence to care guidelines.[15] A defined transition process between pediatric and adult centers (or within a lifespan center) prevents loss of hematology access, which is associated with increased morbidity, greater acute care utilization, and early mortality in young adulthood.[16-18] A formal quality improvement process is essential to evaluate and improve care delivery. Finally, a formal patient/family input process is essential to ensure SCD care meets families' needs and is delivered with cultural sensitivity.

There are essential diagnostic tests and treatments supported by SCD literature and guidelines. Transcranial Doppler ultrasonography screening (also known as sickle stroke screening) for primary stroke prevention in children with hemoglobin (Hb) SS/S-β^0thalassemia should be performed in the SCD clinic or in the same hospital to reduce barriers to care.[13] Hydroxyurea (HU) is recommended for all children with Hb SS/S-β^0thalassemia starting at 9-12 months to prevent pain, acute chest syndrome (ACS), strokes, transfusion needs, and hospitalizations.[3] HU is commercially available as capsules or tablets, so a compounded liquid form is essential for young children. Erythrocytapheresis for acute and chronic management is essential; ASH's transfusion management guidelines suggest erythrocytapheresis when long-term transfusion therapy is employed, including for stroke prevention, and for acute complications such as severe ACS.[19] Magnetic resonance imaging quantitation of liver iron to assess transfusion-related iron overload is essential for effective iron chelation.[19] Finally, while most children experience infrequent vaso-occlusive pain that is adequately managed with standard weight-based dosing of opioids and non-opioid medications, some benefit from specific pain medications or medication combinations.[15] Therefore, an annual review of each patient's pain management, with consideration of an individualized pain plan, is essential.

Comprehensive care for SCD is multidisciplinary, and collaboration with other medical teams is essential. Collaboration was defined as regular communication and availability. Collaboration with a hematopoietic stem cell transplant (HSCT) team is essential to offer curative therapy, especially since early consideration of HSCT for children with Hb SS and S-β^0 thalassemia who have an unaffected human leukocyte antigen-identical sibling was suggested by ASH in 2021.[20] Since the goal of pediatric SCD care is survival into adulthood and continued lifespan care, a partnership with an adult SCD program is essential.[16] Transition requires not only a referral to an adult hematologist/center, but also communication with the receiving team to convey essential knowledge about the patient's prior care and complications. Additional essential collaborations included a transfusion medicine specialist to manage erythrocyte alloimmunization; timely access to medical subspecialists including surgeons, neurologists, pulmonologists, and nephrologists; a pediatric neuropsychologist to perform educational and cognitive assessments; a mental health care provider for children and young adults with SCD; a gynecologist or other contraception prescriber; and reproductive care for parents of children with SCD who wish to minimize the risk of having another affected child.

Optimal elements:

Optimal elements are specific to SCD and likely to be beneficial but are not required for guideline-based care. Optimal members of the multidisciplinary team include advanced practice providers who expand the SCD team's capacity; dedicated inpatient nursing staff; and physical therapy and expressive therapies (art, music, child life). A pain management specialist is optimal; while opioid and non-opioid pain medications are the mainstay of SCD pain management and can typically be managed by a hematologist, newer treatments, such as ketamine and regional anesthesia, are gaining support.[15,21] Optimal physical spaces include a dedicated outpatient clinic, dedicated inpatient unit, and day hospital/infusion center. Children and adults benefit from care for vaso-occlusive pain in an infusion center compared to the ED, with more rapid analgesia administration and lower likelihood of hospitalization.[22,23] Clinical trial availability is optimal, since enrollment may provide early access to new treatments; in other diseases, patients receiving care at centers with active clinical trials may have better outcomes, regardless of enrollment.[24] Partnership with a community-based organization is optimal. Although some communities lack a local organization, a community-based organization provides support for the child, family, and SCD community.

Suggested elements:

Suggested elements are not required for guideline-based care and can be provided outside the comprehensive SCD program. Suggested personnel include a clinical pharmacist, primary care physician, genetic counselor, and nutritionist/dietician. A written business plan detailing center funding sources, financial impact, and organizational support is a suggested process.

Discussion:

Although SCD is the most prevalent genetic disease of childhood in the US, SCD treatment, care infrastructure, and research have been underfunded compared to CF and hemophilia.[22] The funding disparity has produced limited treatments, few care guidelines or standards, and inadequate reimbursement compared with other complex pediatric diseases. Currently, there is no definition of a "pediatric SCD center" or "SCD comprehensive care". The components of an adult SCD center were recently defined in a similar study identifying 19 elements, of which 8 were classified as essential.[10]Here we report a consensus set of elements required for recognition as a comprehensive pediatric SCD center in the US.

Literature and guideline review identified most of the included elements. SCD was historically a childhood condition due to early mortality, so there are more guidelines for children than for adults, resulting in a greater number of essential elements for pediatric comprehensive care. Developmental stages of childhood from infancy through young adulthood require age-specific elements that are not needed for adults, such as newborn screening follow-up and transition education plans. Importantly, as with the adult center study, the Delphi method was used to identify *elements of care* as opposed to defining actual quality outcome measures. The presence of necessary elements does not guarantee appropriate utilization, so additional quality improvement, implementation research, and outcomes monitoring are necessary. Identifying the elements needed for quality care is a crucial first step to ensuring guideline-based care.

Comprehensive care centers for other pediatric conditions are accredited by disease-specific not-for-profit organizations, such as the Cystic Fibrosis Foundation, or designated by public-private collaborations, such as the partnership between the Centers for Disease Control and Prevention, Health Resources and Services Administration, and the National Hemophilia Foundation.[2] The accreditation/designation processes include private or federal funding for centers and, for hemophilia, participation in the federal 340B drug reimbursement program. In turn, participating centers have required oversight and outcome tracking. The opportunity for accreditation of comprehensive SCD centers, with accompanying funding, would incentivize hospitals to provide resources necessary for high-quality, guideline-based care. Center accreditation and tracking of center-specific outcomes would allow patients and families to compare care options and pursue the best available care in their region. In the hemophilia and CF models, accreditation requires center engagement in quality improvement. As evidence of the success of this approach, individuals with hemophilia have lower mortality if their care is managed in an HTC.[25] In the Cystic Fibrosis Care Center Network,

collaborative quality improvement initiatives across centers improve patient outcomes.[26,27]

Before SCD center accreditation can be implemented, the elements needed for comprehensive care must be defined. Once pediatric SCD centers are recognized for having the necessary elements, specific outcome targets will be developed. Unfortunately, in 2019, the Centers for Medicare and Medicaid Services declined to add any SCD-related outcomes to the pediatric parameters reported by state Medicaid programs despite the Pediatric Measure Application Partnership committee recommendation, perpetuating a history of excluding SCD from specific oversight.[28] A recent publication urging inclusion of SCD metrics in the US News and World Report's "Best Hospitals" program underscores the benefits of an accreditation process in securing resources and improving care.[29] The care disparities between SCD and other childhood diseases have been driven by lack of federal funding and heightened by structural racism, and a standardized definition of comprehensive SCD care and center accreditation would be a step towards mitigating these disparities.[30]

Many children with SCD live far from academic children's hospitals. Similar to proposed adult comprehensive care, a "hub and spoke" model may be feasible, in which a larger accredited center serves as a hub for smaller, often rural, programs.[10] Additional opportunities include expanding outreach clinics, tele-medicine, and primary care-SCD partnerships, facilitating comprehensive care close to home with referrals for complex management such as severe complications, alloimmunization, or HSCT or gene therapy treatments.[31]

The National Alliance of Sickle Cell Centers (NASCC) was founded in 2020 to address the need for SCD center recognition. The NASCC goals are to support SCD center development, share improvement processes, and increase access to guideline-based care. It is hoped that the NASCC will have funding to support essential care implementation and quality improvement. Currently, NASCC identifies SCD centers through a recognition process. Eventually, NASCC plans to initiate an accreditation process for centers meeting care standards. Process improvement and quality assessment will be embedded in all NASCC centers to ensure that all individuals receive consistent, equitable medical treatment regardless of location or socio-economic status.

Limitations of this work are inherent in the Delphi process. This sample of 19 leaders in pediatric SCD is biased toward urban tertiary-care centers. A multidisciplinary team is critically important, but non-physician SCD team members did not participate (e.g. nursing, social worker, behavioral health). Primary care providers and patient stakeholders were not involved in this stage. Elements of care will need regular updates as the field adds new preventive strategies, treatments, and curative approaches. Future studies will address these limitations, but this consensus provides a significant foundation for further development within NASCC.

A critical first step in ensuring high-quality SCD care is to define the essential, optimal, and suggested components of a comprehensive pediatric SCD center. With these necessary definitions, accreditation and federal funding for recognized SCD centers should be pursued to ensure access to care and quality of care for children living with SCD.

Disclosures:

MLH: consulting: bluebird bio; research funding to institution: Global Blood Therapeutics, Forma Therapeutics; spouse employment: Pfizer, Inc.; Scientific Executive Committee co-chair: Sickle Cell Transplant Advocacy and Research Alliance

DM: consulting: Global Blood Therapeutics, Novartis, Pfizer

ERM: employment: Global Blood Therapeutics

OAA: Advisory board member: Global Blood Therapeutics, Novartis

RCB: Consulting: Global Blood Therapeutics, Imara, Novartis, and Novo Nordisk; Research funding: Global Blood Therapeutics, Imara, Novartis, FORMA Therapeutics, Pfizer

MUC: employment: Agios Pharmaceuticals

ADC: consulting: Agios Pharmaceuticals, Forma Therapeutics, Global Blood Therapeutics, Novartis

TDC: Consulting: Vifor, Forma Therapeutics, Chiesi, Novartis, bluebird bio, Agios Pharmaceuticals

MJF: none

MMH: Consulting: Vertex/CRISPR Therapeutics, Novartis, AstraZeneca, FORMA Therapeutics, Pharmacosmos, ORIC Pharmaceuticals, bluebird bio

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JSH: Consulting: Global Blood Therapeutics, FORMA Therapeutics, CVS Health

JDL: Consulting: Agios, Forma Therapeutics, Novartis, Bioproducts Laboratory

CTQ: Research funding: Emmaus Medical, Merck, Aruvant

NS: Consulting: Global Blood Therapeutics, Novartis, FORMA Therapeutics, Agios Pharmaceuticals, Emmaus; speaker: Global Blood Therapeutics, Novartis, Emmaus, Alexion; Research: Global Blood Therapeutics

KSW: employment: Global Blood Therapeutics

CT: Data Safety Monitoring Board: bluebird bio

JK: Consulting: Novartis, Fulcrum Therapeutics, Graphite Bio, ORIC Pharmaceuticals; Data Safety Monitoring Board: NovoNordisk, Magneta

References

1. Kanter J, Meier ER, Hankins JS, Paulukonis ST, Snyder AB. Improving outcomes for patients with sickle cell disease in the United States: Making the case for more resources, surveillance, and longitudinal data.*JAMA Health Forum* . 2021;2(10):e213467. doi:doi:10.1001/jamahealthforum.2021.3467

2. Skinner MW, Soucie JM, McLaughlin K. The national haemophilia program standards, evaluation and oversight systems in the United States of America. *Blood Transfus* . Apr 2014;12 Suppl 3:e542-8. doi:10.2450/2014.0019-14s

3. Yawn BP, Buchanan GR, Afenyi-Annan AN, et al. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members. *JAMA* . Sep 10 2014;312(10):1033-48. doi:10.1001/jama.2014.10517

4. Reeves SL, Tribble AC, Madden B, Freed GL, Dombkowski KJ. Antibiotic Prophylaxis for Children With Sickle Cell Anemia. *Pediatrics* . Mar 2018;141(3)doi:10.1542/peds.2017-2182

5. Kanter J, Phillips S, Schlenz AM, et al. Transcranial Doppler Screening in a Current Cohort of Children With Sickle Cell Anemia: Results From the DISPLACE Study. *J Pediatr Hematol Oncol* . Nov 1 2021;43(8):e1062-e1068. doi:10.1097/MPH.0000000000002103

6. Heitzer AM, Longoria J, Okhomina V, et al. Hydroxyurea treatment and neurocognitive functioning in sickle cell disease from school age to young adulthood. *Br J Haematol* . Oct 2021;195(2):256-266. doi:10.1111/bjh.17687

7. Adams RJ, McKie VC, Hsu L, et al. Prevention of a first stroke by transfusions in children with sickle cell anemia and abnormal results on transcranial Doppler ultrasonography. *New England Journal of Medicine* . 1998;339(1):5-11.

8. Lanzkron S, Carroll CP, Haywood C, Jr. Mortality rates and age at death from sickle cell disease: U.S., 1979-2005. *Public Health Rep* . Mar-Apr 2013;128(2):110-6. doi:10.1177/003335491312800206

9. Manley AF. Legislation and funding for sickle cell services, 1972-1982. *Am J Pediatr Hematol Oncol* . Spring 1984;6(1):67-71.

10. Kanter J, Smith WR, Desai PC, et al. Building access to care in adult sickle cell disease: defining models of care, essential components, and economic aspects. *Blood Adv* . Aug 25 2020;4(16):3804-3813. doi:10.1182/bloodadvances.2020001743

11. Dalkey N, Helmer O. An experimental application of the Delphi method to the use of experts. *Management Science* . April 1963 1963;9(3):458-467.

12. Power-Hays A, Li S, Mensah A, Sobota A. Universal screening for social determinants of health in pediatric sickle cell disease: A quality-improvement initiative. *Pediatr Blood Cancer* . Jan 2020;67(1):e28006. doi:10.1002/pbc.28006

13. 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* . Apr 28 2020;4(8):1554-1588. doi:10.1182/bloodadvances.2019001142

14. Meier ER, Janson IA, Hampton K, et al. Adherence to Quality of Care Indicators and Location of Sickle Cell Care Within Indiana. *J Community Health* . Feb 2020;45(1):81-87. doi:10.1007/s10900-019-00721-x

15. 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* . Jun 23 2020;4(12):2656-2701. doi:10.1182/bloodadvances.2020001851

16. Bryant R, Porter JS, Sobota A, Association of Pediatric Hematology/Oncology N, American Society of Pediatri Hematology O. APHON/ASPHO Policy Statement for the Transition of Patients With Sickle Cell Disease From Pediatric to Adult Health Care. *J Pediatr Oncol Nurs* . Nov-Dec 2015;32(6):355-9. doi:10.1177/1043454215591954

17. Brousseau DC, Owens PL, Mosso AL, Panepinto JA, Steiner CA. Acute care utilization and rehospitalizations for sickle cell disease.*JAMA* . Apr 7 2010;303(13):1288-94. doi:10.1001/jama.2010.378

18. Kayle M, Docherty SL, Sloane R, et al. Transition to adult care in sickle cell disease: A longitudinal study of clinical characteristics and disease severity. *Pediatr Blood Cancer* . Jan 2019;66(1):e27463. doi:10.1002/pbc.27463

19. Chou ST, Alsawas M, Fasano RM, et al. American Society of Hematology 2020 guidelines for sickle cell disease: transfusion support.*Blood Adv* . Jan 28 2020;4(2):327-355. doi:10.1182/bloodadvances.2019001143

20. Kanter J, Liem RI, Bernaudin F, et al. American Society of Hematology 2021 guidelines for sickle cell disease: stem cell transplantation. *Blood Adv* . Sep 28 2021;5(18):3668-3689. doi:10.1182/bloodadvances.2021004394C

21. Karsenty C, Tubman VN, Liu CJ, Fasipe T, Wyatt KEK. Regional anesthesia for sickle cell disease vaso-occlusive crisis: a single-center case series. *Pediatr Blood Cancer* . 2022;

22. Farooq F, Mogayzel PJ, Lanzkron S, Haywood C, Strouse JJ. Comparison of US Federal and Foundation Funding of Research for Sickle Cell Disease and Cystic Fibrosis and Factors Associated With Research Productivity.*JAMA Netw Open* . Mar 2 2020;3(3):e201737. doi:10.1001/jamanetworkopen.2020.1737

23. Karkoska K, Appiah-Kubi A, Rocker J, Stoffels G, Aygun B. Management of vaso-occlusive episodes in the day hospital decreases admissions in children with sickle cell disease. *Br J Haematol* . Sep 2019;186(6):855-860. doi:10.1111/bjh.16002

24. Majumdar SR, Roe MT, Peterson ED, Chen AY, Gibler WB, Armstrong PW. Better outcomes for patients treated at hospitals that participate in clinical trials. *Arch Intern Med* . Mar 24 2008;168(6):657-62. doi:10.1001/archinternmed.2007.124

25. Soucie JM, Nuss R, Evatt B, et al. Mortality among males with hemophilia: relations with source of medical care. The Hemophilia Surveillance System Project Investigators. *Blood* . Jul 15 2000;96(2):437-42.

26. Marshall BC, Nelson EC. Accelerating implementation of biomedical research advances: critical elements of a successful 10 year Cystic Fibrosis Foundation healthcare delivery improvement initiative.*BMJ Qual Saf* . Apr 2014;23 Suppl 1:i95-i103. doi:10.1136/bmjqs-2013-002790

27. Mogayzel PJ, Jr., Dunitz J, Marrow LC, Hazle LA. Improving chronic care delivery and outcomes: the impact of the cystic fibrosis Care Center Network. *BMJ Qual Saf* . Apr 2014;23 Suppl 1:i3-8. doi:10.1136/bmjqs-2013-002363

28. Freed GL. A Missed Opportunity to Address a National Shame: The Case of Sickle Cell Disease in the United States. *JAMA Pediatr* . Aug 1 2019;173(8):715-716. doi:10.1001/jamapediatrics.2019.1536

29. Power-Hays A, Dandoy CE, Lorts A, et al. US News & World Report and quality metrics: Inclusion of sickle cell disease is a matter of equity.*Pediatr Blood Cancer* . Apr 20 2022:e29679. doi:10.1002/pbc.29679

30. Power-Hays A, McGann PT. When Actions Speak Louder Than Words - Racism and Sickle Cell Disease. *N Engl J Med* . Nov 12 2020;383(20):1902-1903. doi:10.1056/NEJMp2022125

31. Brown LC, Hampton KC, Bloom EM, Lawson D, Cooper SH, Meier ER. No child left behind: Building a comprehensive sickle cell disease care oasis in the Lake County, Indiana care desert. *Pediatr Blood Cancer* . Aug 2022;69(8):e29619. doi:10.1002/pbc.29619

TABLE 1 Essential elements of pediatric SCD centers

Staff/team members	**Processes**
SCD physician expert*	Procedure for newborn screen follow-up
Pediatric hematology (or pediatric hem/onc) team providing inpatient care	Written guidelines for acute & chronic care
Outpatient nursing staff with SCD expertise*	Protocols for Emergency Dept care
Case manager/care coordinator*	Defined program for transition from pediatric
Social worker*	Standardized order sets in electronic medical
Education liaison	Quality management and improvement proces
	Formal process for patient/family input**

*also identified as essential for adult SCD centers

**added during the virtual consensus meeting

SCD: Sickle cell disease; HSCT: hematopoietic stem cell transplant; MRI: magnetic resonance imaging

TABLE 2 Optimal and suggested elements of pediatric SCD centers

Staff/team members	**Physical space**	**Treatments**
Optimal	**Optimal**	**Optimal**
Advanced practice provider (nurse practitioner/physician assistant)	Dedicated inpatient unit	Clinical trial enrollmen
Pain management specialist	Dedicated outpatient space	
Dedicated inpatient nursing staff	Infusion center/day hospital	
Physical therapist		
Child life specialist/expressive therapist (ex: music, dance)		
Suggested	**Suggested**	**Suggested**
Clinical pharmacist		
Primary care physician		
Genetic counselor		

Staff/team members	Physical space	Treatments
Nutritionist		

*added during the virtual consensus meeting