The NEW ENGLAND JOURNAL of MEDICINE

Perspective

OCTOBER 23, 2025

Involving Palliative Care to Improve Outcomes in Sickle Cell Disease

Eberechi Nwogu-Onyemkpa, M.D.,[1] Griffin Collins, M.D.,[2] Mgbechi Erondu, M.D.,[3] and Erica C. Kaye, M.D., M.P.H.[2]

Abiku, in Yoruba, means *born to die.*

Ogbanje, in Igbo, refers to *a child who dies young and is reborn again.*

Chwechweechwe, in Ga, is *the relentless, repetitive sound of chewing or gnawing pain.*

For generations, the Indigenous peoples of Africa have depicted sickle cell disease (SCD) using language evoking the agony that remains a hallmark of this debilitating condition. The result of an aberrant hemoglobin molecule that polymerizes to deform erythrocytes, SCD can cause excruciating pain, life-threatening complications, multiorgan dysfunction, and premature death. More than 7 million people have SCD worldwide, including more than 100,000 people in the United States, where the burden of disease falls disproportionately on marginalized Black and Brown communities that are already at risk for adverse outcomes owing to systemic racism and socioeconomic disparities.

Despite recent advances in therapy, mortality among people with SCD remains strikingly high. In 2021, an estimated 376,000 deaths from any cause were reported in this population worldwide, and SCD became the 12th-leading cause of death among children younger than 5 years of age.[1] Even in high-income countries such as the United States, the average life expectancy is more than 20 years shorter for people with SCD than for people without SCD.[2] Although recent therapeutic advances offer hope for narrowing these gaps, additional efforts are needed to improve quality of life and mitigate suffering in these patients and their families.

In 2007, McClain and Kain called for the early introduction of palliative care in the treatment of children with SCD, arguing that holistic palliative care services and resources could improve outcomes for patients, communities, and health care systems.[3] Since then, supportive care for people with SCD has markedly improved, thanks to enhanced integration of psychosocial support, use of individualized pain plans, and the development of multidisciplinary clinics and transition programs in partnership with pain and palliative care clinicians. Today, a growing number of centers of excel-

lence are focused on improving quality of life in patients with SCD by incorporating biopsychosocial and palliative care principles in SCD care models.

Beyond these centers of excellence, however, integration of palliative care into SCD management remains insufficient and inconsistent, and considerable challenges persist in improving quality of life and other outcomes in this population. An analysis of nearly 1 million SCD-related hospitalizations in the United States between 2008 and 2017 revealed that less than 0.5% of patients received palliative care services.[4] Meanwhile, most hospitalized patients with SCD continue to report immense suffering. In a survey of more than 2000 patients with SCD in the United States and 15 other countries, many reported severe pain, fatigue, depression, anxiety, and emotional distress. The most commonly reported treatment goal, cited by the majority of patients, was improving quality of life.[5]

The field of palliative care is well positioned to help address this need. Palliative care encompasses interdisciplinary supportive care, often provided concurrently with disease-directed therapy to improve quality of life in patients with serious illness and their caregivers. Palliative care clinicians accompany patients and families throughout the illness course, providing whole-person care to assess and address physical, psychological, sociocultural, spiritual, and existential needs.

Over the past two decades, research has detailed the benefits of palliative care integration in the treatment of patients with cancer, heart failure, chronic lung disease, end-stage kidney disease, cirrhosis, and other serious illnesses. Across populations, palliative care involvement has been associated with increased longevity, improved quality of life, and reduced symptom burden. Palliative care also strengthens health care communication, facilitates shared decision making, encourages goals-of-care conversations and advance care planning, enhances care coordination, and bolsters caregiver support and bereavement care.

Multidisciplinary palliative care teams are particularly well suited in supporting the care of patients with complex or refractory suffering. Palliative care clinicians are trained to collaborate on the development of individualized care plans that leverage therapeutic agents alongside nonpharmacologic and integrative interventions. With a focus on person-centered, total pain management, palliative care teams also can challenge the use of stereotyping or dehumanizing labels and advocate for culture change to subvert implicit bias at the bedside.

In addition, palliative care involvement can mitigate health disparities affecting patients with serious illness. The population of people with SCD in the United States, which is predominantly Black and Brown, faces structural barriers undermining access to equitable health care, stable housing, nutritious food, education, and employment. Simultaneous dependence on and mistreatment by existing systems can engender mistrust and compound suffering. Suspicion of experimental agents and clinical trials, potentially exacerbated by the recent withdrawal of voxelotor from the market because of safety concerns, risks further fracturing of trust related to the use of new therapeutics. Palliative care teams are trained to recognize and address mistrust within historical contexts, to practice and model trauma-informed care, and to strengthen therapeutic alliance by building longitudinal relationships and advocating for patients and families throughout the illness course.

Although new experimental therapies for SCD offer the possibility of cure, they also introduce prognostic uncertainty and carry substantial risks of death, disability, and disruption of school, work, and home life. Within this high-risk, high-reward paradigm, palliative care clinicians can support complex discussions about goals of care, shared decision making, and advance care planning. Moreover, people with SCD are at high risk for multiorgan dysfunction, which requires patients to receive care from multiple specialists within a complex health care system. Palliative care teams can help patients and families navigate appointments across care locations, coordinate resources to facilitate continuity of care, and streamline information exchange among clinicians. They also can provide support during critical periods, such as the transition from pediatric to adult care, when patients are at high risk for care discontinuity.

As with cancer and other chronic illnesses, not every patient with SCD needs palliative care. Inclusion of palliative care may be particularly helpful for people with SCD who face debilitating symptoms, frequent hospitalizations, complications with long-term effects, complex care coordination, and prognostic uncertainty and in the context of therapies associated with high morbidity and mortality. Many patients with complex or severe SCD and their families may benefit from palliative care, and purposeful approaches are needed to integrate these services and

Challenges and Action Items for Supporting Integration of Palliative Care into SCD Treatment.*

Challenges	Action Items
Limited palliative care staffing and resources	Define consult parameters (e.g., eligibility, timing, scope) to maintain bandwidth Track quality metrics to assess value and advocate for more resources Embed palliative care clinicians in SCD teams to support palliative care principles without needing 1:1 coverage Create a combined palliative care–SCD fellowship to expand the workforce Build capacity by implementing global training in palliative care for SCD
Lack of standardized care models and guidelines	Codesign best-practice standards (e.g., referral criteria, care models) with stakeholders, including patients, caregivers, clinicians in various disciplines, administrators, and policymakers Develop and disseminate clinical guidelines and benchmarks
Misconception that patients with SCD don't need palliative care	Provide didactics on the benefits of palliative care in SCD management and indicators for palliative care consultation Integrate palliative care into SCD clinics and inpatient settings gradually to enable longitudinal relationships and reframe palliative care as concurrent care
Equation of palliative care with end-of-life care	Embed palliative care teams early to promote trust and person-centered care throughout the illness course In partnership with SCD clinicians, cocreate criteria to prompt consideration of palliative care at earlier disease stages
Fear that palliative care may deter use of new therapeutics	Reinforce palliative care as an added layer of support alongside curative efforts Demonstrate the ways in which palliative care teams advocate for access to new therapies while supporting quality of life
Concern that adding new team members may complicate care	Emphasize specific ways in which palliative care has improved care coordination in other fields Define clear roles and procedures to enhance teamwork, particularly during critical periods, such as the transition to adult care
Worry that SCD-related pain management will overwhelm palliative care staff	Address implicit biases in assumptions about time burdens associated with SCD care Educate and empower SCD clinicians to leverage primary palliative care skills Encourage comanagement of SCD symptoms across disciplines
Perception that employing both palliative care and pain teams is redundant	Emphasize that, in settings without pain services, palliative care can help mitigate suffering In facilities with pain teams, collaborate on the design of comanagement protocols
Disparities in palliative care access caused by bias, discrimination, and systemic racism	Propose ways in which palliative care can help counteract clinical bias and promote equity Partner with teams providing psychosocial services to address social determinants of health and structural barriers Promote pipeline programs to diversify the palliative care workforce Engage SCD communities in the design of palliative care programs and scholarship
Underuse of telehealth and mobile monitoring	Emphasize the ways in which palliative care teams can leverage telehealth for symptom management and care coordination Collaborate with care teams to respond to patient-reported outcomes in real time
Lack of professional forums for collaboration	Support the creation of national and international special interest groups and collaboratives focused on palliative care and SCD Promote networking and mentorship at the intersection of palliative care and SCD for trainees and early-career professionals
Lack of research on palliative care in SCD management	Partner with community groups to advocate for increased funding to support scholarly activities Build collaborative networks to propose and achieve research goals
Lack of palliative care in high-burden regions globally	Support global palliative care capacity building by means of training, education, and research programs Use global research to inform advocacy As curative treatments become available globally, develop palliative care services in tandem to improve outcomes in cost-effective ways

* SCD denotes sickle cell disease.

resources into SCD treatment and to assess their effects.

Efforts to involve palliative care teams in the treatment of people with SCD will need to overcome challenges similar to those that previously hindered the integration of palliative care in the management of other serious illnesses. The table shows common misperceptions about and barriers to palliative care integration in SCD treatment alongside steps to overcome these challenges. As one example, clinicians may worry that management of SCD-related pain will overwhelm limited palliative care staff and resources. To mitigate this concern, palliative care teams can partner with SCD and pain clinicians to define the parameters (e.g., eligibility, timing, and scope) of palliative care consults, develop systems that encourage comanagement of symptoms, educate and empower SCD teams to leverage primary palliative care skills, track quality metrics to assess the value added by palliative care involvement and advocate for additional resources as needed, and address implicit biases regarding assumptions about the amount of time involved in caring for people with SCD.

An audio interview with Eberechi Nwogu-Onyemkpa is available at NEJM.org

Over the past decade, a growing body of literature has examined strategies for reducing pain, improving quality of life, and supporting psychosocial needs in patients with SCD. Yet research on the effects of palliative care integration into SCD treatment is still lacking. Collaboration between health care professionals and the SCD community is needed to increase dialogue, funding, and scholarship to further advance care.

People with SCD deserve access to compassionate, person-centered, goal-concordant care throughout their lives. Palliative care clinicians can help provide this care. Opportunities exist for clinicians, educators, and researchers to partner with and learn from people with SCD, caregivers, and existing centers of excellence to expand access to palliative care and improve outcomes for patients and families affected by this debilitating disease.

Disclosure forms provided by the authors are available at NEJM.org.

[1]Department of Medicine, Washington University, St. Louis; [2]Department of Oncology, St. Jude Children's Research Hospital, Memphis, TN; [3]Department of Anesthesia, Pain, and Perioperative Medicine, Stanford University, Palo Alto, CA.

This article was published on October 18, 2025, at NEJM.org.

1. GBD 2021 Sickle Cell Disease Collaborators. Global, regional, and national prevalence and mortality burden of sickle cell disease, 2000-2021: a systematic analysis from the Global Burden of Disease Study 2021. Lancet Haematol 2023;10(8):e585-e599.
2. Lubeck D, Agodoa I, Bhakta N, et al. Estimated life expectancy and income of patients with sickle cell disease compared with those without sickle cell disease. JAMA Netw Open 2019;2(11):e1915374.
3. McClain BC, Kain ZN. Pediatric palliative care: a novel approach to children with sickle cell disease. Pediatrics 2007;119:612-4.
4. Nwogu-Onyemkpa E, Dongarwar D, Salihu HM, et al. Inpatient palliative care use by patients with sickle cell disease: a retrospective cross-sectional study. BMJ Open 2022;12(8):e057361.
5. Osunkwo I, Andemariam B, Minniti CP, et al. Impact of sickle cell disease on patients' daily lives, symptoms reported, and disease management strategies: results from the international Sickle Cell World Assessment Survey (SWAY). Am J Hematol 2021;96:404-17.

DOI: 10.1056/NEJMp2505493

Thirty Years of Hydroxyurea for Sickle Cell Anemia — Scientific Progress, Global Health Gaps

Enrico Costa, Ph.D.,[1] Russell Ware, M.D.,[2] Leon Tshilolo, M.D.,[3] and Lucio Luzzatto, M.D.[4]

Medical students learn that a disease can be most effectively treated with an approach that is based on an understanding of the condition's causes and pathogenesis. Sickle cell anemia (SCA) was the first identified "molecular disease" and the condition for which the term was coined. As early as the 1960s, it had become evident that the primary pathogenetic mechanism in SCA was polymerization of deoxyhemoglobin S, which causes sickling of red cells. But for decades, no treatment other than supportive care was available. Even early on, it was clear that it would be important to develop a therapy that would be accessible to patients in under-resourced areas that have a high prevalence of SCA.

In the 1960s, investigators attempted to inhibit polymerization of deoxyhemoglobin S by using urea as a denaturing agent. But this effort proved to be misguided, since the required concentration of urea couldn't be reached in vivo, and even much lower con-