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Addressing Primary Care Needs in People Living With Sickle Cell Disease

A Narrative Review

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Adults with sickle cell disease (SCD) are living longer due to advances in care but face a growing burden of chronic comorbid conditions that fall within the scope of primary care. However, primary care providers often lack structured guidance because literature on managing these conditions in the context of SCD is limited. This article outlines clinical approaches to hypertension, diabetes, obesity, chronic constipation, reproductive health, cognitive impairments, depression, and anxiety in people living with SCD. The authors highlight relevant epidemiology, screening recommendations,

and treatment considerations that differ from those in the general population. Primary care providers play a crucial role in delivering comprehensive and preventive care to people living with SCD. Specific management of common chronic conditions in this population is necessary to reduce morbidity and improve quality of life.

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Sickle cell disease (SCD) is a rare blood disorder that affects an underserved population in the United States, primarily African Americans, who face significant health care disparities. Historically a disease of childhood, SCD is now a lifelong chronic disease that can cause irreversible organ damage over time (1). Organ dysfunction in SCD is often gradual, cumulative, and irreversible, driven by chronic hemolysis, vaso-occlusion, and inflammation (1).

As people living with SCD live into adulthood, primary care providers (PCPs) are increasingly tasked with managing the complex, chronic health needs of this aging population (2, 3). Because providers specializing in adult SCD are limited, most existing primers for PCPs focus primarily on the hematologic management of SCD, including pathophysiology, disease-modifying therapies, clinical research advances, and complications (2, 4, 5). Although the hematologic complications of SCD have historically dominated clinical focus, nonhematologic comorbid conditions that PCPs typically manage, such as hypertension, diabetes, obesity, and mental health disorders, are major contributors to morbidity and health care use in the SCD population (6). However, guidance is limited on routine primary care concerns for chronic disease prevention, mental health, and reproductive health, which can be nuanced for people living with SCD because of the complex nature of the disease.

This narrative review presents evidence-based, SCD-informed guidance on the identification and management of key chronic conditions relevant to adult primary care: hypertension; type 2 diabetes mellitus (DM); obesity; skeletal complications; chronic constipation; reproductive health; neurocognitive conditions, including attention deficit-hyperactivity disorder (ADHD); and mental health conditions, such as depression and

anxiety. Roles and responsibilities in SCD care vary substantially by institution because few comprehensive programs exist. Published standards defining which provider manages specific conditions are limited to guidelines for a comprehensive SCD center (3). Accordingly, this review focuses on the issues typically addressed in primary care and outlines how these considerations require SCD-specific adaptation. This information will equip PCPs with actionable tools to optimize longitudinal care for people living with SCD.

METABOLIC SYNDROME

Hypertension

Hypertension in people living with SCD is an increasingly recognized comorbidity, although its reported prevalence varies widely among cohorts, ranging from 2.3% to 19%, in part due to evolving definitions of hypertension (7, 8). Although blood pressures (BPs) tend to be lower (with lower rates of hypertension) in people with hemoglobin SS disease, and in those with hemoglobin SC disease to a lesser extent, systemic hypertension is associated with adverse outcomes (9). In adults living with SCD, hypertension is still associated with the development of renal dysfunction and pulmonary hypertension (10). As in the general population, hypertension has a clear role in stroke risk in SCD. Systolic hypertension, but not diastolic hypertension, was found to be associated with occlusive stroke in the CSSCD (Cooperative Study of Sickle Cell Disease) (9). Hypertension has been identified as a risk factor for silent cerebral infarctions (SCIs) in SCD, with systolic hypertension linked to increased odds of SCIs in children (11). In young adults living with SCD, hypertension has been identified as a risk factor for both new SCIs and infarction progression (12). Last,

the CSSCD showed an association between hypertension and all-cause mortality (9).

The National Alliance of Sickle Cell Centers recommends office visits every 3 to 6 months, depending on age and disease severity, with monitoring of vital signs (13). A diagnosis of hypertension may be based on multiple elevated BP readings, although many guidelines stress the importance of using proper technique and confirming the diagnosis with home or ambulatory monitoring. The American Society of Hematology recommends targeting a BP of less than or equal to 130/80 mm Hg, based on evidence for intensive BP management in the general population (14). Despite the multiple adverse outcomes associated with hypertension in SCD and evidence for overall lower BPs, no prospective trials have evaluated BP targets in SCD and their effect on outcomes. In addition, current guidelines incorporate cardiovascular disease risk into treatment decision making, which does not consider the lower risk for atherosclerotic cardiovascular disease in SCD.

Recommended first-line BP-lowering agents include angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers, dihydropyridine calcium-channel blockers, and thiazide diuretics, with an emphasis on combination therapy. No data are available to guide medication selection in SCD, beyond the treatment of concurrent albuminuria with an angiotensin-converting enzyme inhibitor or angiotensin-receptor blocker (15). Despite limited SCD-specific evidence, given the strong associations between hypertension and adverse outcomes, providers should approach BP management with heightened vigilance and prioritize individualized care to mitigate risks, such as stroke, renal dysfunction, and mortality.

Type 2 DM

The prevalence and incidence of DM in people living with SCD are not well studied. However, DM has been increasingly recognized as a comorbidity in SCD, and some studies show a similar prevalence of DM between people living with SCD (16.5%) and African Americans from NHANES (National Health and Nutrition Examination Survey) (18.2%) (16). At a single institution, 5.6% of the adult SCD cohort had diabetes, and patients with obesity were more likely to have comorbid DM (17). Chronic inflammation, oxidative stress, and iron overload from repetitive transfusions in SCD may contribute to increased rates of DM (18, 19).

In alignment with guidelines from the U.S. Preventive Services Task Force, routine screening for DM is recommended for people living with SCD at age 35 to 70 years, or earlier if other risk factors are present (20).

A unique and often overlooked concern is the wide adoption of hemoglobin A_{1c} as the screening method for DM. In fact, the International Expert Committee does not recommend this method for individuals with hemoglobinopathies (21). Hemoglobin A_{1c} relies on a normal functioning erythrocyte count, a normal lifespan, and

hemoglobin A. People living with SCD have none of these, making hemoglobin A_{1c} unsuitable for screening, diagnosis, or management. The use of random plasma glucose or fasting plasma glucose has been suggested as a reliable alternative to screen for diabetes, although no guideline exists (22). Table 1 shows the proposed algorithm for DM screening in SCD. The use of fructosamine is not recommended to screen for or diagnose diabetes in people living with SCD, in line with the guidance of the 2022 Standards of Medical Care in Diabetes from the American Diabetes Association (23).

In people living with SCD with newly diagnosed DM, an individualized treatment plan must be created to manage comorbid conditions (19). A combination of education, nutritional and lifestyle changes, and medication may be needed to achieve glycemic control. Pharmacotherapy choices for DM in people living with SCD should be guided by the American Diabetes Association guideline, accounting for monitoring of potential interactions with medications for SCD and other chronic conditions (24). Metformin was found to increase fetal hemoglobin, which is known to be protective in SCD (25). Monitoring of glycemic control should be done through a combination of at-home and in-office checks of fasting plasma glucose and random plasma glucose. Fructosamine may be more useful for monitoring glycemic control than screening, although supporting data remain limited. If fructosamine is used, it should still be combined with fasting plasma glucose and random plasma glucose checks (19). As DM becomes an increasingly recognized comorbidity in adults with SCD, a disease-specific approach to screening, diagnosis, and management is vital to improve overall outcomes.

Obesity

Historically, people living with SCD had lower prevalence rates of obesity than their peers of the same race or ethnicity (17). Reasons for this were not clear but may include reduced calorie intake, increased calorie use due to hypermetabolism, reduced intestinal absorption, or intestinal microbiome imbalance. Concern about obesity has been growing recently because 17% to 43% of adults with SCD now have a body mass index above 25 kg/m², associated with older age, less severe disease, and female gender (26).

However, among people with SCD and obesity, the prevalence of DM is significantly higher than among those with SCD alone. Acute and chronic organ damage are key drivers of early mortality in adults with SCD. Similar to recommendations for the general population, people living with SCD should be encouraged to have a healthy lifestyle, including improved nutrition, exercise, and sleep (27). The beneficial effects of glucagon-like peptide-1 (GLP-1) receptor agonists and sodium-glucose cotransporter-2 (SGLT-2) inhibitors on kidney function are independent of their blood glucose-lowering effects in people with DM and chronic kidney

Table 1. Criteria for Diagnosing DM in People Living With SCD*

Finding	Next Steps
RPG monitoring	
All RPG test results <7.8 mmol/L (<140 mg/dL)	No additional testing indicated
One RPG test result 7.8–11.0 mmol/L (140–199 mg/dL)	Recommend FPG test
One RPG test result ≥11.1 mmol/L (≥200 mg/dL)	Recommend repeated RPG and/or FPG test Possible indicator for type 2 DM
Result of repeated RPG test >11.1 mmol/L (>200 mg/dL) and patient having symptoms of hyperglycemia (i.e., polyuria and polydipsia)	Confirms diagnosis of type 2 DM
FPG monitoring	
All FPG test results <5.6 mmol/L (<100 mg/dL)	Normal screening Return to routine USPSTF other than use of hemoglobin A _{1c} guidelines
One FPG test result 5.6–6.9 mmol/L (100–125 mg/dL)	Patient has prediabetes Recommend initiation of diet/lifestyle recommendations
One FPG test result ≥7.0 mmol/L (≥126 mg/dL)	Repeat FPG test Patient may have type 2 DM
Result of repeated FPG test ≥7.0 mmol/L (≥126 mg/dL)	Confirms diagnosis of type 2 DM

DM = diabetes mellitus; FPG = fasting plasma glucose; RPG = random plasma glucose; SCD = sickle cell disease; USPSTF = U.S. Preventive Services Task Force.

* Data from Carrithers and colleagues (22).

disease, suggesting alternative renoprotective mechanisms for these therapies. The frequency of acute pain from vaso-occlusive episodes (VOEs), however, may increase with these medications if attention is not paid to risk for dehydration from reduced water intake with GLP-1 receptor agonists and from natriuresis and glucosuria with SGLT-2 inhibitors. In 1 small study of 7 patients receiving these medications, other clinical event rates (VOEs, strokes, acute chest syndrome, avascular necrosis [AVN], and gallstones) did not change (28). Clinicians should discuss the risks and benefits of GLP-1 receptor agonists and SGLT-2 inhibitors in appropriate populations with SCD; for those who have significant metabolic illness or warrant additional renoprotection, clinicians should avoid concurrent use of diuretics while prescribing.

SKELETAL COMPLICATIONS

Significant bone morbidity, including osteoporosis, osteopenia, AVN, and chronic bone pain, is prevalent in people living with SCD. Studies report that 80% of young patients with SCD have bone pain, low bone mineral density (BMD), osteopenia, osteoporosis, vertebral collapse, and increased risk for fracture (29). In addition, 30% to 50% of adults with SCD develop osteoporosis (29). Similarly, AVN affects up to one third of adults with SCD, primarily in the femoral head but possibly in any skeletal region (30).

These skeletal issues have multiple causes. They can arise due to chronic hemolysis, bone marrow expansion, vaso-occlusion, and systemic inflammation, all of which contribute to skeletal fragility and progressive bone damage. Long-term use of opioids, a mainstay in SCD pain management, is increasingly recognized as a significant contributor to osteoporosis. Opioids promote bone loss by suppressing gonadal hormones (leading to hypogonadism), impairing osteoblast activity, reducing

mobility, and exacerbating vitamin D and calcium deficiencies (31). Existing evidence shows a strong association between long-term opioid use and fractures, raising the importance of pain management strategies that minimize such use (32). Buprenorphine is well tolerated in people living with chronic pain in SCD and shows promise to reduce total daily morphine milligram equivalents; it may also reduce acute care use (ACU) (33, 34). Compared with other opioid agonists, buprenorphine has the lowest risk for fractures and decreased suppression of testosterone (32). Of note, systemic corticosteroid use in SCD may increase the risk for hospitalization from VOEs (35).

The National Heart, Lung, and Blood Institute recommends evaluating all adults with SCD and intermittent or chronic hip pain for AVN by history, physical examination, radiography, and magnetic resonance imaging as needed. It also recommends treating AVN with physical therapy, analgesics, and orthopedics for assessment and follow-up (36). No high-quality prospective studies or randomized controlled trials have evaluated strategies for preserving or improving bone health in SCD. Vitamin D and calcium supplementation remain essential to lower osteoporosis risk and may improve chronic pain (37, 38). Hematopoietic stem cell transplantation may also reduce bone morbidity: Children with AVN before transplantation showed some improvement afterward, although they remain at high risk for osteoporosis (39). In addition, in small studies, bisphosphonates have been shown to reduce bone pain, preserve BMD, and improve AVN, but additional prospective data evaluating risks, benefits, and treatment duration are needed before routine use is recommended (40, 41).

Given the effect of bone morbidity on SCD-related disability, early detection of mitigable morbidity, opioid alternatives for chronic pain, and appropriate therapy are key to improving outcomes. Future research should

randomize screening and treatment strategies to address bone deterioration and chronic pain while promoting early strategies to reduce long-term skeletal complications in SCD.

CHRONIC OPIOID-INDUCED CONSTIPATION

Opioids are a mainstay of treatment of acute VOs and are often used for chronic pain in SCD; constipation is a frequent adverse drug event seen with opioid use. Proactive use of laxatives and stool softeners is recommended when opioids are prescribed (42). In addition, SCD can cause abdominal crisis due to small infarcts of the mesentery and abdominal viscera. Such a crisis often causes severe abdominal pain, signs of peritoneal irritation, and a generalized ileus from decreased motility on plain film. The risks for constipation are affected by the multifactorial effect of abdominal crises, front-line opioid treatments of chronic and acute pain, fiber intake, exercise capacity, and dietary fluid (43). The clinical picture might be indistinguishable from other acute abdominal diseases (44). The goal of the outpatient care team should be both prevention at baseline and reaction when a crisis may be present.

A small study found unexpected variability in the use of laxatives and stool softeners among people living with SCD, especially among younger and postsurgical patients. Increased attention needs to be paid to including all 3 of the following groups of laxatives when preventing and treating constipation: stimulant laxatives for increased performance of the bowel wall musculature (for example, senna and bisacodyl), bulk-forming laxatives for improved bulk and passage (for example, psyllium and methylcellulose), and osmotic laxatives for improved stool softening with water recruitment by osmosis (for example, lactulose and polyethylene glycol).

Besides the liberal use of these laxatives, methyl-naltrexone can be considered and is approved to treat opioid-induced constipation in adults with advanced illness or chronic noncancer pain, although no literature addresses its use in SCD (45, 46). Managing constipation in SCD requires a comprehensive treatment approach to address the compounded risks posed by opioid and abdominal crises.

REPRODUCTIVE HEALTH

People living with SCD face significant reproductive health challenges, including pregnancy complications, menstrual cycle-triggered VOs, and contraceptive-related risks. Effective reproductive health care is essential to mitigate these issues.

Menstruation frequently exacerbates VOs, increasing pain and ACU. Many women with SCD report more severe pain around their cycles, distinct from dysmenorrhea, and heavier, prolonged bleeding has been linked to higher VO risk (47). Hormonal fluctuations likely contribute to these crises.

Contraceptive management plays a critical role in reducing unintended pregnancies and stabilizing hormonal fluctuations. Combined hormonal contraceptives can increase thromboembolic risk, so progestin-only contraceptives are preferred (48, 49). Vaginal rings provide half the systemic estrogen of other combined hormonal contraceptives (50). Progestogen-only pills, depot medroxyprogesterone acetate (DMPA), and etonogestrel implants can reduce VO frequency and menstrual pain (48). However, prolonged DMPA use raises concerns about weight gain, BMD loss, and higher thromboembolic risk (48, 49). Levonorgestrel-releasing intrauterine devices offer long-term contraception with minimal systemic effects and are often a preferred option (48). Etonogestrel-releasing contraceptive implants cause less pain with insertion than intrauterine devices and provide similar VO reduction (51). However, use of DMPA has been higher than that of other contraceptive choices (52, 53).

Pregnant people living with SCD are at increased risk for complications, including preeclampsia, preterm birth, and worsening VOs. Therefore, they require early involvement of maternal-fetal medicine specialists and a sickle cell specialist to discuss transfusion support and the risks and benefits of resuming treatment with disease-modifying agents (54).

Early menopause and infertility are other concerns, stemming from chronic illness, iron overload, medications, and gonadal dysfunction (55). Managing fertility in both men and women may require adjustments to hydroxyurea (that is, holding treatment) and timely referral to reproductive specialists because it can affect sperm count and ovarian reserve (55–57). If considering adjustments to disease-modifying agents, people living with SCD should be referred to a sickle cell specialist. Fertility preservation is exceedingly important in the new era of transplant and gene therapy, with preconditioning regimens typically leading to infertility.

Given the complex interactions among menstruation, VOs, fertility, and contraception, reproductive health care in SCD must be individualized. Getting specialists involved early and choosing contraception carefully can improve both outcomes and quality of life.

MENTAL HEALTH

Cognitive Impairment and ADHD

Cognitive impairment and neurodevelopmental disorders, including ADHD, are increasingly recognized as significant comorbid conditions in both pediatric and adult SCD populations (58).

A systematic review reported a prevalence of 38% (95% CI, 14% to 62%) for suspected cognitive impairment in adults with SCD (59). These deficits often include impairments in working memory, verbal learning, executive functions, and attention and lead to poor functional results, including nonadherence to treatment and unemployment (60). The pathophysiology underlying these neurocognitive issues is multifactorial. Cerebral vasculopathy, including SCIs and overt strokes, plays a

central role. Up to 39% of children with SCD have SCIs by age 18 years, and SCIs are strongly associated with decreased IQ and academic achievement (61). They become even more common in adulthood, with a lifetime prevalence of about 50% (12). Chronic anemia and hypoxemia also contribute to neurocognitive dysfunction through reduced oxygen delivery to the brain (60).

Internal medicine physicians should have a high index of suspicion for ADHD in people living with SCD who report difficulty with executive functioning (that is, task initiation, planning and organization, and emotional regulation), trouble focusing on an activity, easy distractibility, or difficulty following through with a plan. Early screening is essential for identifying neurocognitive deficits and ADHD in this high-risk population. Although no cognitive screening tool has been formally validated in adults with SCD, clinicians should weigh the relative benefits and limitations of different screening tools to select an adapted approach tailored to their specific needs (59). Diagnosis of ADHD in SCD should involve a multidisciplinary approach, integrating findings from neurocognitive testing, behavioral assessments, school reports, and caregiver input. Of note, clinicians must differentiate between symptoms due to neurologic injury, obstructive sleep apnea (present in 18% to 51% of children and 43% of adults), and primary ADHD because overlapping presentations are common (62, 63).

Management strategies include both pharmacologic and nonpharmacologic interventions. Stimulant medications, such as methylphenidate, are safe and effective in people living with SCD and ADHD but require close monitoring given potential cardiovascular risks (64). Cognitive behavioral therapy and socioemotional supports are crucial adjuncts (65). Improved screening, early diagnosis, and tailored management strategies are essential to mitigate the lifelong neurodevelopmental burden in people living with SCD, ultimately improving quality of life and health outcomes.

Depression and Anxiety

Depression and anxiety are common yet often underrecognized complications in people living with SCD. Depression prevalence rates in this population are 20% to 57%, consistently higher than in the general population (66). Anxiety is also prevalent (6.5% to 29%) (67). Contributing factors include demographics, education, social support, transfusions, ACU, and the frequency of acute VOs and chronic pain episodes. Depression and anxiety in SCD are associated with increased health care use, greater pain burden, poorer quality of life, and mortality (68, 69).

Regular mental health screening is critical for people living with SCD, yet implementation remains inconsistent (70). Many people living with SCD rely on hematologists for sole care, who may not routinely conduct preventive screenings. One study found that only 20% of adolescents with SCD saw a PCP before transitioning to adult

care, and even fewer were screened for depression (71). Screening is complicated by stigma, underreporting, and symptom overlap between SCD and depression or anxiety. Validated tools for depression and anxiety screening are commonly used, but interpretation can be challenging. Diagnosis of depression and anxiety requires careful evaluation using criteria from the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, to distinguish mental health symptoms from those of SCD.

Although evidence-based treatments of mental health conditions are well established in the general population, there is limited research specifically guiding optimal treatment approaches for people living with SCD. However, optimal treatment typically includes a comprehensive approach to mental health, including psychotherapy, pharmacotherapy (for example, selective serotonin reuptake inhibitors [SSRIs] or serotonin-norepinephrine reuptake inhibitors), symptom management, social support, lifestyle changes, effective pain management, and education. Careful monitoring is needed due to risks, such as increased bleeding with SSRIs and the potential for serotonin syndrome when SSRIs are combined with opioids. Peer support, family involvement, and healthy habits, including exercise, mindfulness, and sleep, promote well-being. A personalized, multidisciplinary approach with shared decision making is essential for safely and effectively managing mental health in people with SCD.

DISCUSSION

As more people living with SCD survive into adulthood, PCPs must play a central role in managing the long-term health of this population: PCPs are uniquely positioned to address nonhematologic health needs that strongly influence morbidity and quality of life. This narrative fills a critical gap by translating existing evidence and expert consensus into a practical review for PCPs. Although some comorbid conditions, such as hypertension and diabetes, are common across populations, their risk profiles, presentation, and treatment response in SCD are distinct; Table 2 provides

Table 2. Take-Home Points

PCPs should be aware of SCD-specific considerations when evaluating common conditions.
Diagnostic criteria for diabetes and hypertension may differ in people living with SCD and require careful interpretation.
Osteoporosis occurs at higher rates and at younger ages in this population, making early screening essential.
Contraception counseling should be individualized to assist with menstrual-related vaso-occlusive episodes, with attention to possible thrombotic risks with combined hormonal contraceptives.
Cognitive impairments are more common in people living with SCD and may warrant early screening and support.
As with many chronic illnesses, depression and anxiety are prevalent and should be proactively addressed.

PCP = primary care provider; SCD = sickle cell disease.

take-home points. In SCD, commonly accepted clinical cutoffs do not fully apply. The standard marker for diabetes diagnosis, hemoglobin A_{1c}, is unreliable in SCD due to chronic hemolysis and frequent blood transfusions (22). Hypertension goals are also more stringent than in the general population (14, 15). Reduced BMD in people living with SCD warrants earlier awareness to ensure timely diagnosis and intervention to prevent downstream complications (29).

Moreover, addressing cognitive impairment, ADHD, and mood disorders is essential to improve outcomes, treatment adherence, and participation in daily life (61, 68). Reproductive health counseling should include guidance on increased infertility and contraceptive options in the setting of menses associated with VOs and possible thrombotic risk associated with estrogen-containing contraceptives (48).

Research on SCD-specific guidelines for best management is still limited. Because SCD affects every organ, further research is needed to determine best practices in disease-specific diagnosis and treatment guidelines. As long as disease-specific research on common conditions remains limited, SCD management should focus on comprehensive care using the research and guidelines that are currently published.

Care for SCD is best delivered through a multidisciplinary model, where PCPs coordinate with hematologists, mental health professionals, pain specialists, social workers, and other subspecialists (3). This approach can help decrease ACU and improve preventive outpatient care. Therefore, with longer life expectancy for patients with SCD, PCPs should be aware of SCD-specific differences in clinical guidelines and play an active role in patient care.

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References

- Vichinsky E. Chronic organ failure in adult sickle cell disease. *Hematology Am Soc Hematol Educ Program*. 2017;2017:435-439. [PMID: 29222290] doi:10.1182/asheducation-2017.1.435
- Humphreys JVA. The management of sickle cell disease in a primary care setting. *J Family Med Prim Care*. 2012;1:56-58. [PMID: 24479003] doi:10.4103/2249-4863.94454
- 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*. 2020;4:3804-3813. [PMID: 32785684] doi:10.1182/bloodadvances.2020001743
- Hehre RJ. Managing patients with sickle cell disease in primary care. *JAAPA*. 2020;33:21-28. [PMID: 32941305] doi:10.1097/01.JAA.0000697232.25913.b1
- Pecker LH, Lanzkron S. Sickle cell disease. *Ann Intern Med*. 2021;174:ITC1-ITC16. [PMID: 33428443] doi:10.7326/AITC202101190
- Complications of sickle cell disease and current management approaches. In: McCormick M, Osei-Anto HA, Martinez RM, eds; National Academies of Sciences, Engineering, and Medicine. *Addressing Sickle Cell Disease: A Strategic Plan and Blueprint for Action*. National Academies Pr; 2020. Accessed at www.ncbi.nlm.nih.gov/books/NBK566466 on 19 November 2025.
- Nguweneza A, Ngo Bitoungui VJ, Mnika K, et al. Clinical characteristics and risk factors of relative systemic hypertension and hypertension among sickle cell patients in Cameroon. *Front Med (Lausanne)*. 2022;9:924722. [PMID: 35928290] doi:10.3389/fmed.2022.924722
- Benneh-Akwasi Kuma A, Owusu-Ansah AT, Ampomah MA, et al. Prevalence of relative systemic hypertension in adults with sickle cell disease in Ghana. *PLoS One*. 2018;13:e0190347. [PMID: 29300776] doi:10.1371/journal.pone.0190347
- Pegelow CH, Colangelo L, Steinberg M, et al. Natural history of blood pressure in sickle cell disease: risks for stroke and death associated with relative hypertension in sickle cell anemia. *Am J Med*. 1997;102:171-177. [PMID: 9217567] doi:10.1016/s0002-9343(96)00407-x
- Gordeuk VR, Sachdev V, Taylor JG, et al. Relative systemic hypertension in patients with sickle cell disease is associated with risk of pulmonary hypertension and renal insufficiency. *Am J Hematol*. 2008;83:15-18. [PMID: 17696198] doi:10.1002/ajh.21016
- DeBaun MR, Sarnaik SA, Rodeghier MJ, et al. Associated risk factors for silent cerebral infarcts in sickle cell anemia: low baseline hemoglobin, sex, and relative high systolic blood pressure. *Blood*. 2012;119:3684-3690. [PMID: 22096242] doi:10.1182/blood-2011-05-349621
- Jordan LC, King AA, Kanter J, et al. Incidence and risk factors for new and recurrent infarcts in adults with sickle cell disease. *J Am Heart Assoc*. 2024;13:e033278. [PMID: 38842282] doi:10.1161/JAHA.123.033278
- Jacob SA, Frei-Jones M, Saif-Ur-Rehman S, et al. National Alliance of Sickle Cell Centers consensus recommendations on sickle cell disease health maintenance: a consensus statement. *JAMA Netw Open*. 2025;8:e2543421. [PMID: 41231476] doi:10.1001/jamanetworkopen.2025.43421
- Liem RI, Lanzkron S, D Coates T, et al. American Society of Hematology 2019 guidelines for sickle cell disease: cardiopulmonary and kidney disease. *Blood Adv*. 2019;3:3867-3897. [PMID: 31794601] doi:10.1182/bloodadvances.2019000916

15. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018;71:1269-1324. [PMID: 29133354] doi:10.1161/HYP.0000000000000066
16. Zhou J, Han J, Nutescu EA, et al. Similar burden of type 2 diabetes among adult patients with sickle cell disease relative to African Americans in the U.S. population: a six-year population-based cohort analysis. *Br J Haematol*. 2019;185:116-127. [PMID: 30714090] doi:10.1111/bjh.15773
17. Jang T, Mo G, Stewart C, et al. Obesity and diabetes mellitus in patients with sickle cell disease. *Ann Hematol*. 2021;100:2203-2205. [PMID: 34148143] doi:10.1007/s00277-021-04578-w
18. Shah BN, Hassan TO, Zhang X, et al. Increased iron stores influence glucose metabolism in sickle cell anaemia. *Br J Haematol*. 2020;189:e184-7-e187. [PMID: 32232834] doi:10.1111/bjh.16596
19. Obeagu EI, Obeagu GU. Management of diabetes mellitus patients with sickle cell anemia: challenges and therapeutic approaches. *Medicine (Baltimore)*. 2024;103:e37941. [PMID: 38669382] doi:10.1097/MD.00000000000037941
20. Davidson KW, Barry MJ, Mangione CM, et al; US Preventive Services Task Force. Screening for prediabetes and type 2 diabetes: US Preventive Services Task Force recommendation statement. *JAMA*. 2021;326:736-743. [PMID: 34427594] doi:10.1001/jama.2021.12531
21. International Expert Committee. International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes. *Diabetes Care*. 2009;32:1327-1334. [PMID: 19502545] doi:10.2337/dc09-9033
22. Carrithers B, Klein R, Ovalle F, et al. Screening and diagnosis of type 2 diabetes in sickle cell disease. *J Am Board Fam Med*. 2024;37:919-922. [PMID: 39978849] doi:10.3122/jabfm.2024.240042R1
23. American Diabetes Association Professional Practice Committee. 2. Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes—2022. *Diabetes Care*. 2022;45:S17-S38. [PMID: 34964875] doi:10.2337/dc22-S002
24. American Diabetes Association Professional Practice Committee. 9. Pharmacologic approaches to glycemic treatment: Standards of Care in Diabetes—2025. *Diabetes Care*. 2025;48:S181-S206. [PMID: 39651989] doi:10.2337/dc25-S009
25. Badawy SM, Payne AB. Association between clinical outcomes and metformin use in adults with sickle cell disease and diabetes mellitus. *Blood Adv*. 2019;3:3297-3306. [PMID: 31698459] doi:10.1182/bloodadvances.2019000838
26. Halpern AB, Welch JGG, Hirway P, et al. Prevalence and complications of obesity in sickle cell disease. *Blood*. 2008;112:1434. doi:10.1182/blood.V112.11.1434.1434
27. Living with sickle cell disease. National Heart, Lung, and Blood Institute. Updated 22 August 2024. Accessed at www.nhlbi.nih.gov/health/sickle-cell-disease/living-with on 5 December 2025.
28. Sun R, Srivastava A, Derebail VK, et al. GLP-1 agonists and SGLT-2 inhibitors in adults with sickle cell disease. *Am J Hematol*. 2024;99:1610-1612. [PMID: 38655752] doi:10.1002/ajh.27348
29. Giordano P, Urbano F, Lassandro G, et al. Mechanisms of bone impairment in sickle bone disease. *Int J Environ Res Public Health*. 2021;18:1832. [PMID: 33668588] doi:10.3390/ijerph18041832
30. Blinder MA, Russel S, Barnes M. Prevalence of symptomatic avascular necrosis and the operative treatment in adult patients with sickle cell disease. *Blood*. 2014;124:1379. [10.1182/blood.V124.21.1379.1379]
31. Fountas A, Van Uum S, Karaviti N. Opioid-induced endocrinopathies. *Lancet Diabetes Endocrinol*. 2020;8:68-80. [PMID: 31624023] doi:10.1016/S2213-8587(19)30254-2
32. Söderberg KC, Laflamme L, Möller J. Newly initiated opioid treatment and the risk of fall-related injuries. A nationwide, register-based, case-crossover study in Sweden. *CNS Drugs*. 2013;27:155-161. [PMID: 23345030] doi:10.1007/s40263-013-0038-1
33. Prince E, Loeser P, Early M, et al. "Buprenorphine, it works so differently": adults with sickle cell disease describe transitioning to buprenorphine for treatment of chronic pain. *J Pain*. 2024;25:632-641. [PMID: 37742907] doi:10.1016/j.jpain.2023.09.014
34. David MS, Jones J, Lauriello A, et al. Converting adults with sickle cell disease from full agonist opioids to buprenorphine: a reliable method with safety and early evidence of reduced acute care utilization. *Am J Hematol*. 2022;97:1435-1442. [PMID: 36053825] doi:10.1002/ajh.26699
35. Walter O, Coughoul P, Maquet J, et al. Risk of vaso-occlusive episode after exposure to corticosteroids in patients with sickle cell disease. *Blood*. 2022;139:3771-3777. [PMID: 35471555] doi:10.1182/blood.2021014473
36. Evidence-Based Management of Sickle Cell Disease: Expert Panel Report, 2014. National Heart, Lung, and Blood Institute; 2014.
37. Lips P, van Schoor NM. The effect of vitamin D on bone and osteoporosis. *Best Pract Res Clin Endocrinol Metab*. 2011;25:585-591. [PMID: 21872800] doi:10.1016/j.beem.2011.05.002
38. Osunkwo I, Ziegler T, Alvarez J, et al. A randomized double blind, placebo controlled study of vitamin D to ameliorate sickle cell chronic pain [Abstract]. *J Pain*. 2012;13(Suppl):S73.
39. Dallas MH, Triplett B, Shook DR, et al. Long-term outcome and evaluation of organ function in pediatric patients undergoing haploidentical and matched related hematopoietic cell transplantation for sickle cell disease. *Biol Blood Marrow Transplant*. 2013;19:820-830. [PMID: 23416852] doi:10.1016/j.bbmt.2013.02.010
40. Adesina OO, Jenkins IC, Galvão F, et al. Alendronate preserves bone mineral density in adults with sickle cell disease and osteoporosis. *Osteoporos Int*. 2025;36:93-102. [PMID: 39433652] doi:10.1007/s00198-024-07268-1
41. Grimbly C, Escagado PD, Jaremko JL, et al. Sickle cell bone disease and response to intravenous bisphosphonates in children. *Osteoporos Int*. 2022;33:2397-2408. [PMID: 35904681] doi:10.1007/s00198-022-06455-2
42. O'Brien SH, Fan L, Kelleher KJ. Inpatient use of laxatives during opioid administration in children with sickle cell disease. *Pediatr Blood Cancer*. 2010;54:559-562. [PMID: 20049931] doi:10.1002/pbc.22395
43. Okpala I, Tawil A. Management of pain in sickle-cell disease. *J R Soc Med*. 2002;95:456-458. [PMID: 12205212] doi:10.1258/jrsm.95.9.456
44. Ebert EC, Nagar M, Hagspiel KD. Gastrointestinal and hepatic complications of sickle cell disease. *Clin Gastroenterol Hepatol*. 2010;8:483-489. [PMID: 20215064] doi:10.1016/j.cgh.2010.02.016
45. Michna E, Blonsky ER, Schulman S, et al. Subcutaneous methylnaltrexone for treatment of opioid-induced constipation in patients with chronic, nonmalignant pain: a randomized controlled study. *J Pain*. 2011;12:554-562. [PMID: 21429809] doi:10.1016/j.jpain.2010.11.008
46. Bader S, Jaroslawski K, Blum HE, et al. Opioid-induced constipation in advanced illness: safety and efficacy of methylnaltrexone bromide. *Clin Med Insights Oncol*. 2011;5:201-211. [PMID: 21836816] doi:10.4137/CMO.S4867
47. Segbefia C, Campbell J, Tartaglione I, et al. Pain frequency and health care utilization patterns in women with sickle cell disease experiencing menstruation-associated pain crises. *J Womens Health (Larchmt)*. 2023;32:1284-1291. [PMID: 38011013] doi:10.1089/jwh.2023.0023
48. De Sanctis V, Soliman AT, Daar S, et al. Current issues and options for hormonal contraception in adolescents and young adult women with sickle cell disease: an update for health care professionals. *Mediterr J Hematol Infect Dis*. 2020;12:e2020032. [PMID: 32395221] doi:10.4084/MJHID.2020.032
49. U.S. Centers for Disease Control and Prevention. U.S. Medical Eligibility Criteria for Contraceptive Use, 2024. Accessed at www.cdc.gov/medeligcritea.

cdc.gov/contraception/hcp/usmec/index.html on 21 November 2025.

50. Roumen FJ. Review of the combined contraceptive vaginal ring, NuvaRing. *Ther Clin Risk Manag*. 2008;4:441-451. [PMID: 18728840] doi:10.2147/tcrm.s1964

51. Brito MB, Boas AQV, Silva AMN, et al. Impact of etonogestrel-releasing contraceptive implant use in cisgender women with sickle cell disease. *J Natl Med Assoc*. 2024;116:569-575. [PMID: 39428270] doi:10.1016/j.jnma.2024.09.003

52. Roe AH, Lang B, McAllister A, et al. Contraceptive use and preferences among females with sickle cell disease. *Contraception*. 2022;105:42-45. [PMID: 34418379] doi:10.1016/j.contraception.2021.08.009

53. Leroy-Melamed M, Jacob S, Shew ML, et al. Provider attitudes, preferences, and practices regarding sexual and reproductive health for adolescents and young adults with sickle cell disease. *J Adolesc Health*. 2021;69:970-975. [PMID: 34294508] doi:10.1016/j.jadohealth.2021.06.008

54. Oteng-Ntim E, Shangaris P. Evidence-based management of pregnant women with sickle cell disease in high-income countries. *Hematology Am Soc Hematol Educ Program*. 2022;2022:408-413. [PMID: 36485166] doi:10.1182/hematology.2022000378

55. Ghafari DL, Stimpson S-J, Day ME, et al. Fertility challenges for women with sickle cell disease. *Expert Rev Hematol*. 2017;10:891-901. [PMID: 28891355] doi:10.1080/17474086.2017.1367279

56. Pecker LH, Hussain S, Mahesh J, et al. Diminished ovarian reserve in young women with sickle cell anemia. *Blood*. 2022;139:1111-1115. [PMID: 34864892] doi:10.1182/blood.2021012756

57. Sewaralthahab S, Alsubki LA, Alhrabi MS, et al. Effects of hydroxyurea on fertility in male and female sickle cell disease patients. A systemic review and meta-analysis. *PLoS One*. 2024;19:e0304241. [PMID: 38848387] doi:10.1371/journal.pone.0304241

58. DeBaun MR, Kirkham FJ. Central nervous system complications and management in sickle cell disease. *Blood*. 2016;127:829-838. [PMID: 26758917] doi:10.1182/blood-2015-09-618579

59. Couette M, Roy J, Doglioni DO, et al. Screening for cognitive impairment in adults with sickle cell disease: a systematic review and meta-analysis. *Presse Med*. 2023;52:104207. [PMID: 37979834] doi:10.1016/j.lpm.2023.104207

60. Sahu T, Pande B, Sinha M, et al. Neurocognitive changes in sickle cell disease: a comprehensive review. *Ann Neurosci*. 2022;29:255-268. [PMID: 37064288] doi:10.1177/09727531221108871

61. Prussien KV, Jordan LC, DeBaun MR, et al. Cognitive function in sickle cell disease across domains, cerebral infarct status, and the

lifespan: a meta-analysis. *J Pediatr Psychol*. 2019;44:948-958. [PMID: 31050352] doi:10.1093/jpepsy/jsz031

62. Trzepacz AM, Vannatta K, Gerhardt CA, et al. Emotional, social, and behavioral functioning of children with sickle cell disease and comparison peers. *J Pediatr Hematol Oncol*. 2004;26:642-648. [PMID: 27811605] doi:10.1097/01.mph.0000139456.12036.8d

63. Taherifard E, Taherifard E, Hosseini-Bensenjan M, et al. The prevalence of obstructive sleep apnea and associated symptoms among patients with sickle cell disease: a systematic review and meta-analysis. *Hemoglobin*. 2023;47:215-226. [PMID: 38102839] doi:10.1080/03630269.2023.2290507

64. Acquazzino MA, Miller M, Myrvik M, et al. Attention deficit hyperactivity disorder in children with sickle cell disease referred for an evaluation. *J Pediatr Hematol Oncol*. 2017;39:350-354. [PMID: 28538513] doi:10.1097/MPH.0000000000000847

65. Thompson RJ, Gustafson KE, Bonner MJ, et al. Neurocognitive development of young children with sickle cell disease through three years of age. *J Pediatr Psychol*. 2002;27:235-244. [PMID: 11909931] doi:10.1093/jpepsy/27.3.235

66. Jonassaint CR, Jones VL, Leong S, et al. A systematic review of the association between depression and health care utilization in children and adults with sickle cell disease. *Br J Haematol*. 2016;174:136-147. [PMID: 26991317] doi:10.1111/bjh.14023

67. Treadwell MJ. Mental health and psychological resilience in sickle cell disease. *Lancet Haematol*. 2023;10:e569-e571. [PMID: 37451306] doi:10.1016/S2352-3026(23)00166-7

68. Adam SS, Flahiff CM, Kamble S, et al. Depression, quality of life, and medical resource utilization in sickle cell disease. *Blood Adv*. 2017;1:1983-1992. [PMID: 29296845] doi:10.1182/bloodadvances.2017006940

69. Njoku F, Pugh N, Brambilla D, et al. Mortality in adults with sickle cell disease: results from the Sickle Cell Disease Implementation Consortium (SCDIC) registry. *Am J Hematol*. 2024;99:900-909. [PMID: 38450756] doi:10.1002/ajh.27279

70. Lysandrou M, Quayle N, Landes K, et al. Evaluating self- vs interviewer-administered screening for depression in sickle cell disease. *Blood Adv*. 2024;8:699-702. [PMID: 38113469] doi:10.1182/bloodadvances.2023012083

71. Bangudi S, Stanek C, Shankar D, et al. Primary care use and depression screening among young adults with sickle cell disease during their final year of pediatric hematology care. *Pediatr Blood Cancer*. 2024;71:e30784. [PMID: 38037196] doi:10.1002/pbc.30784

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