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REVIEW

Treating sickle cell disease in resource-limited sub-Saharan Africa: recent strategies and recommendations in addressing the gaps for the provision of evidence-based management

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ABSTRACT

Introduction: The management of Sickle cell disease (SCD) in sub-Saharan Africa (SSA) suffers from the lack of universal infant and population screening, inadequate access to standard treatment and poor public health prioritization amidst unstable political systems.

Areas covered: The state of evidencebased management of SCD in SSA was investigated including sustainability of international funding agencies.

Expert opinion: Current efforts are fragmentary along languages lines; sometimes driven by the funder's objectives and not the national agenda. The review highlighted the role of internal and external partnerships such as SPARCO, ARISE, CONSA, as well as technology-based support for the implementation of evidence-based care for SCD. We advocate for increased funding to implement SCD comprehensive care in line with the WHO SCD Framework for Primary, Secondary, Tertiary and Specialist Comprehensive Care at state and national level. To achieve this objective, it is important that SCD, as a leading non-communicable disease in Africa, be mandated as a standing agenda for the National Council of Ministers at the African Union, WHO and other regional bodies in Africa.

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1. Introduction

Sickle cell disease (SCD) is an inherited disorder of the HBB gene with amino acid substitution of glutamic acid for valine in the beta-globin protein, resulting in abnormal hemoglobin (HbS). HbS is autosomal recessive inheritance and affected individuals either have the homozygous (HbSS) or double heterozygous state when HbS co-inheritance occurs with another abnormal beta-globin chain such as HbSC, HbSβ thalassemia. The homozygous state (HbSS) is the most severe phenotype [1]. The central pathophysiology in SCD is the polymerization of hemoglobin on offloading oxygen, and therefore, in a low oxygen state, it forms rigid strands and sticky red blood cells (RBC), microvascular obstruction, tissue infarction and pain [1]. Pain is the cardinal feature of SCD, and together with other acute complications such as acute chest syndrome and acute splenic sequestration, is known as vaso-occlusive crises (VOCs) [2]. SCD is one of the leading life-threatening disorders in the world, and it is estimated that over 500,000 live births occur per year, with over 80% occurring in sub-Saharan Africa (SSA) [3,4] SCD has long been recognized as a global public health concern since it's associated with end-organ damage across the life span and premature death [5]. The outcome of SCD is variable, with high mortality in SSA, where 50% of infants with the disorder may not survive beyond the fifth birthday [4,5] compared to over 94% surviving into adulthood in high-income settings [6,7]. The management of SCD is complex, requiring early diagnosis, prevention of complications and end-organ damage.

Due to genetic, cultural, and anthropological factors, SSA patients are diverse [3]. SSA region is home to the most severe Sickle haplotype ranging from Bantu in Central and Southern Africa, Benin and Senegal variants in West and East Africa, which reflects severity of the disease phenotypes [8]. Additionally, the impact of conflicts in SSA countries has contributed to varied healthcare systems and capacities for managing SCD. The Lancet Haematology Commission 2023 has adequately described SCD in the continent by providing a spotlight on the interventions that are likely to yield the most significant benefits [3]. The commission's report stated, 'Simple, effective interventions to reduce the mortality and morbidity associated with sickle cell disease are available. Similarly, the Lancet Commission Non-Communicable Disease advocated 'that international development of assistance is to ensure that the poorest families affected by NCDIs are included in the progress toward universal health care [9]. The key challenges in SSA include the underdiagnosis of SCD, the absence of widespread NBS programs, the persistent

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Article highlights

- The Lancet Haematology Commission recommends that by 2025, policies, resources, and facilities should be in place to allow all babies worldwide to be screened for SC This emphasizes that Newborn and Early Infant Screening (NBS) must be a priority in Sub-Saharan Africa (SSA).
- NBS, as implemented across Africa, is limited in coverage, and faces significant challenges with patient follow-up after diagnosis.
- Laboratory diagnostic techniques currently implemented include high-performance liquid chromatography (HPLC), capillary electrophoresis (CE), isoelectric focusing (IEF), and point-of-care testing (POCT).
- Reducing high under-five mortality in SSA requires integrating early screening with timely prophylactic measures such as penicillin prophylaxis, pneumococcal and Hib vaccination, hydroxyurea use, and patient/caregiver education while addressing challenges inequitable access and implementation.
- There is need for further research to evaluate the effectiveness of currently available and novel antimalarial drug regimens as prophylactic agents for SCD patients, taking into consideration variations in malaria transmission intensity and parasite resistance rates across different regions in SSA,
- The Lancet paper (2024) calling for a global fund to support hydroxyurea and encouraging national and state governments to prioritize funding is both relevant and timely.
- New initiatives aimed at strengthening healthcare capacity, standardizing clinical practices, advancing research, and improving access to essential treatments in SSA are led by collaborative programmes like ARISE (African Research and Innovative Initiative for Sickle cell Education: improving Research Capacity for Service), CONSA (Consortium on Newborn in Africa), PEN-PLUS, and SPARCO (**Sickle** Pan-African Research Consortium), fostering sustainable improvements in SCD management.
- Limited availability of essential opioids in SSA, compounded by knowledge gaps among providers, restrictive regulations, and prescriber hesitancy, necessitates targeted education, regulatory reforms, improved supply chains, and public awareness campaigns to ensure effective and compassionate pain management for SCD patients.
- WHO global data highlights a stark contrast in blood supply between low- and middle-income countries (including Africa) and high-income countries, where the mean donation rate is over thirty-one donations per 1,000 people, compared to fewer than ten donations per 1,000 people in SSA countries.
- Transition planning in SSA may be improved by aligning with existing task-shifting and task-sharing policies, especially in situations where doctors are unavailable. These policies could allow the training and deployment of Community Health Extension Workers (CHEWs) – whom many patients are familiar with – or nurses to coordinate and assist adolescents and young adults (AYA) in navigating transition care interventions, making these services more accessible and acceptable. This would improve feasibility if transition activities were not completely hospital-based and could enhance accessibility of services.

neglect of SCD as a public health priority, limited access to health education, and the lack of robust health policy frameworks. These call for urgent attention by policymakers and increased public awareness of the issues. Moreover, there are gaps in long-term studies evaluating the impact of different SCD management strategies in SSA. In this paper, we aim to explore potential strategies that SSA countries can implement to enhance the diagnosis and management of SCD, to reduce the morbidity and mortality associated with the disease.

2. Newborn screenings (NBS) in SSA

The second recommendation of the Lancet Haematology Commission on Sickle cell disease to ensure that screening is available for all babies worldwide by by 2025 (Figure 1). This implies that policies, resources, and facilities must be in place to allow all babies to implement Universal NBS in SSA [3]. Newborn screening (NBS) is a public health system of testing babies for genetic, metabolic or developmental conditions that affect a child's long-term health or survival. Specifically, in SCD, a condition that, if not treated shortly after birth, will result in severe lifelong disability, chronic complications or even death, NBS is of crucial importance. When followed by minimal care, which includes penicillin and vaccination, NBS for SCD reduces the occurrence of life-threatening complications and reduces under-five mortality [10]. The implementation of Newborn screening for SCD in SSA would reduce the under-five mortality from 90% to 5%, according to some reports [11].

The concept of Newborn screening was introduced in the 1960s by Robert Guthrie. However, the first universal NBS for SCD was implemented in the 2000s in the U.S.A., UK and later Brazil and recently some European countries e.g. Netherlands, France and Germany have introduced universal NBS for SCD, while some only offer pilot.

[3] with implementation limited to institutional or regional programs in countries like Benin, Nigeria, Uganda, DRC, Mali, Senegal, Ghana, Liberia, Tanzania, Kenya, Zambia, Burkina Faso, Cameron and Angola, Tanzania, Uganda and Liberia [3,12]. Key barriers to the sustainability of NBS in SSA and to the spread of national programs were reviewed by Archer et al. 2022 by identifying four themes related to the success of the programs, namely governance (the choice of staff to perform the program), technical (choice of process), cultural (knowledge and perceptions) and financial (capacity for self-financing) [10]. Also, they suggested that new programs in SSA should involve government funds from program's the start of the program. Multidisciplinary (nurses, physicians, biologists, biomedical laboratory technicians, psychologists, among others) teams are required for successful implementation. The involvement of primary /community health workers and hospitals (public and private) at various levels is needed for the programmes' success [13].

It is important to ensure reliable diagnosis through a commitment to sustained enforcement of robust quality control measures in diagnostic laboratories.

A successful newborn screening must be complemented by an effective follow-up, and patient well-being is paramount, starting with the introduction of penicillin V; this needs to be aligned with the health systems as advocated by the WHO [14] (Figure 2).

3. Laboratory diagnosis and capacity in SSA

Various laboratory techniques are available to diagnose SCD, but they vary in price, availability, and specificity. The first test described in the literature to identify the presence of sickle-shaped erythrocytes consisted of putting a drop of whole blood between a slide and coverslip, sealing it, and observing the preparation under a microscope after a few hours [15]. Although this is a simple and cheap test but no longer used due to the high rates of false-positive and false-negative results and the difficulty in distinguishing sickle cell anemia

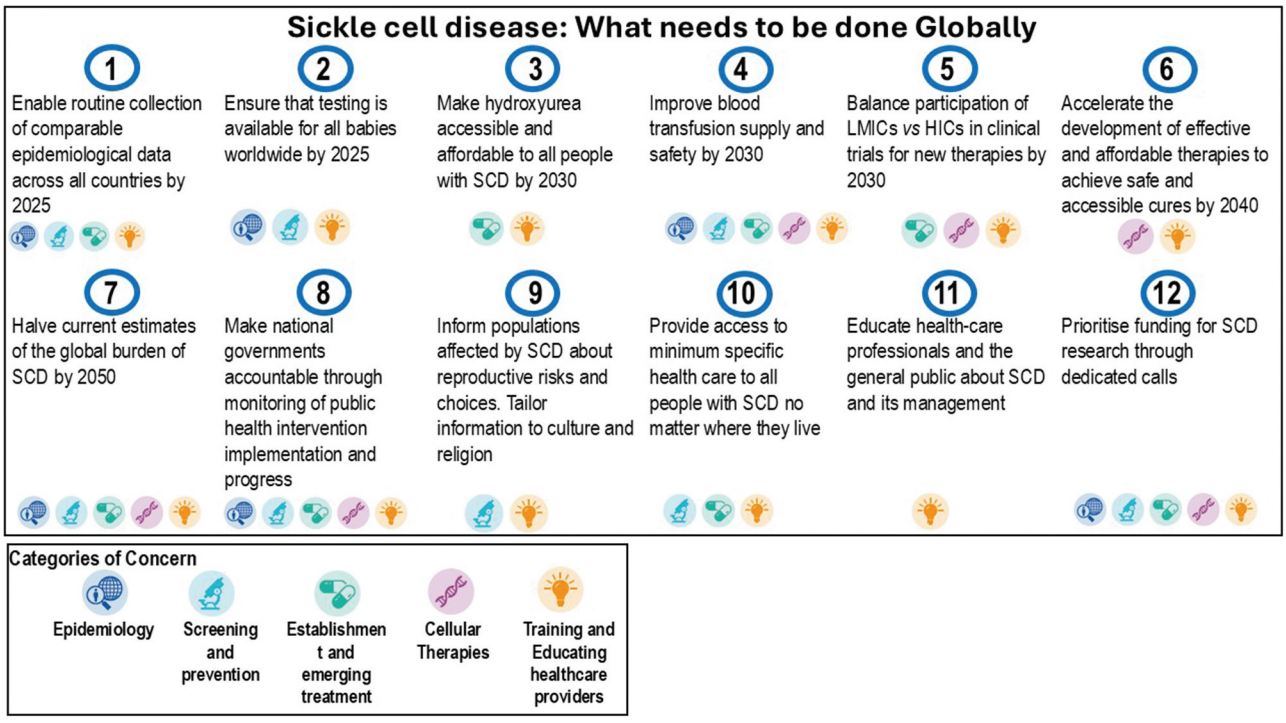

Figure 1. Summary of the twelve key recommendations from the lancet haematology commission 2023 for improving SCD care globally. (adapted from Piel FB, Rees DC, DeBaun MR, et al. Defining global strategies to improve outcomes in sickle cell disease: a lancet haematology commission. Lancet haematol [internet]. 2023 [cited 2024 Dec 20];10(8):e633–e686.).

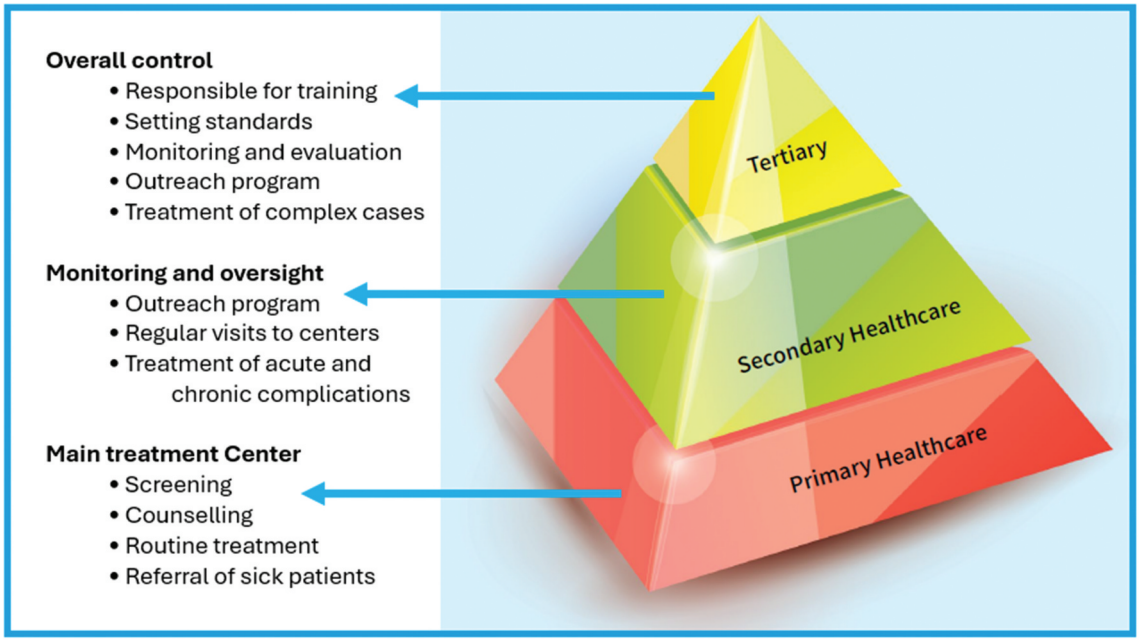

Figure 2. Summary of the WHO recommendations for the pyramidal management unit of SCD (adapted from WHO. WHO sickle package of interventions for sickle cell disease management. Brazzaville: WHO African region, 2024. Licence: CC BY-NC-SA 3.0 IGO. Office for Africa [internet]. 2024 [cited 2024 Dec 22]. Available from: https://www.afro.who.int/publications/who-sickle-package-interventions-sickle-cell-disease-management).

patients from sickle cell trait individuals. After this came solubility tests, which, despite high rates of false results, are still used nowadays because they are cheap and fast. They are based on the polymerization characteristics of S hemoglobin under deoxygenated conditions and its insolubility [16,17].

More recent techniques include high-performance liquid chromatography (HPLC), capillary electrophoresis (CE), cellulose acetate electrophoresis, agar gel electrophoresis and isoelectric focusing (IEF). These techniques are based on separating the different hemoglobin variants depending on

their retention time/peak of the curve, their migration on an electrical field or their isoelectric point [18]. Majority of the screening tests do not give immediate results, as samples must be processed in the laboratory. Some variants or some post-translational derivative forms of hemoglobin present the same retention time or migration pattern, result interpretation becomes more difficult, and a confirmatory test might be necessary [17].

Genetic testing is also a possibility in diagnosing hemoglobinopathies. The use of PCR, DNA microarrays or sequencing techniques allows the exact identification of the mutation associated with the disease [16]. These are highly precise techniques, but are also expensive, not available in most sub-Saharan countries' laboratories, and as the ones already mentioned, the diagnosis takes longer.

Point-of-care tests for hemoglobinopathies make screening faster, allowing the identification of S or C hemoglobin in a few minutes. Although they present several limitations, especially don't allow the identification of other variants, namely B-thalassemia, HbD or HbE or α-thalassemia, as the result is provided to the patients or caregivers right after the blood collection, the probability of enrollment in patient SCD care and programs can be substantially higher, as was described in Angola [19]. Through the years several POCT have been tested in different countries, namely Gazelle Hb Variant test, HemoTypeSC™ and Sickle SCAN®, and have proven their high sensitivity and specificity while requiring minimal training and producing results in less than ten minutes [20–22].

For the management and follow-up of SCD patients, complete cell blood count (CBC), including reticulocyte count, is essential. CBC allows us to determine anaemia severity by presenting red blood cell counts, total hemoglobin concentration, mean corpuscular volume, and mean corpuscular hemoglobin concentration. Reticulocyte count allows to evaluate the bone marrow compensatory response. Biochemical parameters such as lactate dehydrogenase, haptoglobin and unconjugated bilirubin are markers of intravascular hemolysis. A desirable follow-up also includes the determination of Fetal Hemoglobin, an important modulator of SCD, by HPLC or capillary electrophoresis [17].

4. Pneumococcal vaccination and penicillin V prophylaxis

Under-five mortality rates in children with SCD are exceptionally high in low or middle-income countries, like sub-Saharan countries [23]. To reduce these numbers, it is essential to associate early screening and diagnosis with prophylactic measures implemented soon after birth.

One of the leading causes of death in SCD children is infections, particularly *Streptococcus pneumoniae*, the more frequent etiological agent, among other encapsulated bacteria. The susceptibility to these polysaccharide-encapsulated bacteria is a functional asplenia, a common feature in SCD patients [24,25]. In the 1980s, a randomized, placebo-controlled clinical trial revealed an 84% reduction in pneumococcal infections in children with SCD taking penicillin prophylaxis [26]. Since then, penicillin prophylaxis has been prescribed to SCD patients to prevent these and other infections, and it is advised that this prophylactic measure starts around 3 months of age or soon after diagnosis until 5 years of age [3]. Accessibility to this prophylactic measure should be universal to all SCD patients, but it still varies from country to country.

Also, to prevent infections by *Streptococcus pneumoniae* and *Haemophilus influenza* that cause severe complications in these patients, such as pneumonia, meningitis, and septicemias, immunization is essential and advised. Two types of vaccines are available to prevent invasive pneumococcal infections and reduce the severity of the disease in case of exposure: PCV – a conjugate vaccine for children under 2 years of age, PPSV – a polysaccharide vaccine for children over two or adults and Hib vaccination to prevent *Haemophilus influenza* infections.

5. Pain management in SSA: opioid access and utilization

The cardinal feature of SCD presentation is pain, which may be the most common symptom that leads to diagnosis in the absence of newborn screening. Pain is a defining feature of SCD, and the leading cause of hospitalization and emergency room visits [27]. Acute pain results from vaso-occlusion, which causes tissue ischemia, reperfusion injury, and activation of nociceptors by inflammatory mediators [28].

Pain episodes are often unpredictable and triggered by known or unknown factors, including dehydration, infections, acidosis, extremes of temperature, stress, and strenuous exercise [1,28]. The frequency of pain episodes in SCD serves as a marker of clinical severity and is associated with an increased risk of early mortality [2].

Currently, there are no reliable biomarkers or imaging techniques to objectively confirm or quantify pain intensity in clinical settings. As a result, pain management depends on patients' self-reported pain severity [29]. Ongoing research is exploring the potential biomarkers and imaging tools that may help assess or predict pain levels more accurately [30].

Pain management in SCD is based on the World Health Organization analgesic ladder [31]. This framework recommends treatments based on the severity of pain. For mild pain, non-opioid medications such as non-steroidal anti-inflammatory drugs (NSAIDs), with the optional addition of adjuvant therapies as needed in the management of moderate-to-severe pain using opioids as appropriate [32].

While NSAIDs are available in the SSA, access to strong opioids remains poor [33–35]. For instance, in Nigeria, pentazocine, a weak synthetic opioid associated with significant psychological and physical dependence, is the most commonly available opioid for managing moderate-to-severe pain. In contrast, morphine and other parenteral opioids are either scarce or inaccessible [33]. This narrows the therapeutic options for effective pain management in Nigeria and other sub-Saharan African countries.

Barriers limiting opioid use in SSA include insufficient provider knowledge about opioid prescription and management,

restrictive prescription regulations, and prescriber hesitancy driven by concerns over adverse effects, dependency, and potential misuse [34,36]. These challenges are affected by systemic and socio-cultural issues. Studies have shown that opioid consumption across African countries has remained extremely low and stagnant over the past two decades, due to bureaucratic obstacles, regulatory restrictions, poor affordability, and widespread stigma associated with opioid use [37,38]. Additional barriers include limited training among healthcare providers, cultural expectations around pain endurance, and fears of addiction among both clinicians and patients [37]. To address these issues, there is a need for provider education on safe opioid prescribing, policy reform to streamline access, and improved opioid supply chains. Public education campaigns are also essential to dispel myths and promote compassionate care.

Finally, Hydroxyurea remains the standard of care and a key component of long-term SCD management globally [39].

6. Pharmacologic treatment

Hydroxyurea (HU), also known as hydroxycarbamide, is a ribonucleotide reductase inhibitor first used as an antineoplastic agent in myeloproliferative diseases. By inducing the production of Fetal Hemoglobin, the proportion of adult hemoglobin decreases, and reduces erythrocyte sickling [24,40]. HU is currently considered the standard of care in the prevention of vaso-occlusive and painful crises both in adults and children [23]. Despite its proven efficacy and safety, and the recommendations for including this medication in the minimum standard of care of SCD patients worldwide, its availability, accessibility and affordability in LMIC continues to be far from expected [23,41,42]. To fulfil this purpose of accessibility to medication for all, public–private partnerships between private companies, advocacy organizations, and governments might represent a key role, as happened in Ghana [43].

Pharmacological treatment for SCD has always been a challenge. The number of treatments is scarce, especially in SSA, where they are not available or affordable for the majority.

In fact, Hydroxyurea has been, for several years, the only approved therapy by the FDA (United States Food and Drug Administration) and EMA (European Medicines Agency). Recently, three medications were developed and subject to approval by these agencies. L-glutamine was approved by the FDA in 2017 but was never approved by EMA as they considered that it didn't show sufficiently proven efficacy [41]. The FDA and EMA approved Crizanlizumab, but the EMA revoked their approval in September 2023. Voxelotor was approved in 2019 but, in 2024, was suspended. Potentially curative hematopoietic stem cell transplantation and, more recently, gene therapy, are accessible only to a subgroup of children and young adults with SCD and are not available in SSA [41]. In sub-Saharan Africa, the majority, therefore, continue to experience the major causes of morbidity, including malaria, for which there is no uniform protocol for its prevention.

7. Antimalarial prophylaxis in SCD management

Malaria, a protozoan infection that targets red blood cells, remains a major cause of morbidity and mortality among children in SSA [44]. According to the World Health Organization, there were an estimated 249 million cases of malaria worldwide in 2022, resulting in approximately 608 thousand deaths. Most of these mortalities occurred among young children in SSA, a region that also has a high prevalence of SCD [45]. Individuals who carry the hemoglobin S gene are known to be less susceptible to malaria infection due to various mechanisms, including the 'sickling-phagocytosis phenomenon,' and other biochemical and immunological processes [46–48]. Collectively, these mechanisms are thought to confer a survival advantage and explain the retention of this gene in African populations. This relative protection is most evident among individuals with sickle cell trait (HbAS), who are less likely to experience severe malaria.

However, despite a similar or even lower risk of malaria infection among children with homozygous SCD (HbSS) compared to non-HbSS individuals, mortality from malaria infection is ten times higher in the HbSS group [47,49]. Malaria exacerbates hemolysis and worsens anemia in SCD, often to life-threatening levels. It also triggers acute complications such as vaso-occlusive crises and splenic sequestration, which significantly increase mortality risk. Impairment of splenic function also hinders the clearance of parasitized red blood cells [47]. Consequently, lifelong antimalarial prophylaxis is recommended for individuals with SCD in malaria-endemic regions like SSA [50].

However, the specific regimens for malaria chemoprophylaxis vary across countries in the region. For example, proguanil is the recommended prophylactic drug in Nigeria and Kenya, while sulfadoxine-pyrimethamine (SP) is used in Uganda and Malawi [51–53]. In Tanzania, recent updates to national guidelines have included proguanil-atovaquone and dihydroartemisinin-piperaquine as recommended prophylactic agents [54]. Despite widespread use, these regimens differ in efficacy and safety profiles, thereby complicating the selection of an optimal chemoprevention strategy for SCD patients [55–57].

The WHO notes that the success of malaria chemoprophylaxis programs depends on several factors, including the intensity of malaria transmission in a given area, the preventive efficacy of the chosen drugs, dosing frequency, duration of protection offered by each treatment course, the availability of the medications, and the level of adherence to the prescribed regimen among patients [58]. Several challenges hinder the effective implementation of malaria chemoprevention in SSA such as the emergence of parasite resistance, limited chemo preventive options, issues related to medication adherence and side effects, insufficient awareness of the need for prophylaxis among patients and their caregivers, low levels of education in affected populations, inadequate funding for prophylaxis programs, doubts about the efficacy of available medications, and the widespread use of high-dose folic acid (5 mg), which has been shown to interfere with the effectiveness of sulfadoxine-pyrimethamine [45,59–61]. Moreover,

standardized, evidence-based guidelines specifically tailored to SCD remain limited, as current recommendations often rely on general pediatric or adult guidance. Notably, in the recent WHO guidelines for malaria, SCD was omitted from the section listing special risk groups for malaria [58].

Despite these challenges, robust evidence supports the routine use of malaria chemoprophylaxis in individuals with SCD who live in malaria-endemic areas. For instance, a Cochrane review by Oniyangi and Omari and WHO recommendations emphasize the benefits of providing routine prophylaxis to this high-risk population [50,58]. Additionally, a systematic review and meta-analysis of six randomized controlled trials involving 912 children with SCD evaluated seven distinct chemoprophylactic regimens, including chloroquine, mefloquine, mefloquine-artesunate, proguanil, pyrimethamine, sulfadoxine-pyrimethamine, and sulfadoxine-pyrimethamine-amodiaquine demonstrated that antimalarial chemoprophylaxis significantly reduced parasitemia and clinical malaria episodes in this vulnerable population [46]. These findings highlight the critical role of chemoprophylaxis in protecting individuals with SCD from the severe consequences of malaria.

Nonetheless, there is an urgent need for large, well-designed, multicenter studies to evaluate the effectiveness of currently available and novel antimalarial drug regimens to establish definitive protocols for SCD patients. Such studies should consider the variations in malaria transmission intensity and parasite resistance rates across different regions in SSA, as these may influence the choice of prophylactic regimen. Furthermore, the increased use of antimalarial medications could accelerate the development of drug resistance, thereby undermining their long-term efficacy. To address this issue, it may be necessary to adopt strategies such as using distinct medications for prophylaxis and treatment or employing combination therapies that target resistance mechanisms to preserve the efficacy of existing drugs [45].

A comprehensive, integrated approach to malaria prevention that combines chemoprophylaxis with the use of the newly developed malaria vaccine, long-lasting insecticide-treated nets, and vector control measures offers the greatest potential for improving outcomes in this vulnerable population. However, recurrent malaria infections still contribute to both acute and chronic anemia in SCD, often necessitating blood transfusions – an essential yet challenging intervention in sub-Saharan Africa [48].

8. Blood transfusion for SCD in SSA

The administration of non-sickling HbAA red blood cell transfusions is an important disease modifier for managing SCD. The HbA introduced is used to treat acute life-threatening complications and prevent others such as strokes. Blood improves tissue oxygenation and replaces the HbS, thereby limiting vaso-occlusion, the basis of complications of SCD [62,63].

Indications for red blood cell transfusion in SCD include acute symptomatic exacerbations of hemolysis and anemia from acute splenic sequestration crisis in children, aplastic crises, acute chest syndrome, ischemic strokes, transient ischemic attacks, and pre-operative stabilization of patients. Blood transfusion in pregnancy to prevent and manage feto-maternal complications [64]. Therefore, safe blood availability is critical to the optimal care of patients with SCD.

The WHO recommends blood products from non-renumerated, unrelated blood donors. It also emphasizes screening for human immunodeficiency virus, hepatitis B and C, and Syphilis. Since the WHO established the framework for blood transfusion services in 2010, however, sub-Saharan Africa still lags in aligning with these recommended practices [65]. WHO global data shows a marked difference between blood supply in 60 low-middle-income countries, including 34 African countries, and high-income countries. The mean donation rate/per 1,000 people in HIC is triple the figures observed in African countries. The latter still use paid, replacement, and family donors. Blood-borne infection rates in SSA also exceed the incidence in high-income countries by far [65]. A large Nigerian study of blood transfusion services in 31 hospitals offering specialist services for the care of SCD across all zones of the country documented their capacity to provide blood transfusion needs of sickle cell patients. The greatest challenge was inadequate blood supply, as transfusion needs were often unmet. The most common blood component used, packed red blood cells were available in 45% of centers, only one center had the capacity to provide leukocyte-depleted blood. Screening for transfusion-transmitted infections (TTIs), is standard practice [66]. Immune-mediated complications of SCD may also make blood transfusion unsafe for recipients. No center had the capacity to prevent allo-immunization; the capacity to monitor and manage iron overload was quite limited as only serum ferritin could be monitored. They reported that iron chelators are expensive and often unavailable. Half the Nigerian hospitals were able to offer chronic transfusion therapy by top-up or manual exchange transfusion, as the majority had no access to automated apheresis machines [66].

An extensive review of SSA transfusion safety showed a decline in capacity to provide safe blood to be associated with a reduction in external partnerships and funding from about 2009 [58], indicating heavy reliance on external funding and a need for the member countries to commit funds for this purpose.

To improve the supply of safe blood, there is a need for SSA nations to take responsibility for the improvement of donor recruitment, data management, epidemiological surveillance for TTIs, and hemovigilance [67]. Poor and expensive electric power supply also threatens the safe storage of blood.

Reliance on developed countries for reagents and equipment for processing, storing and delivering safe blood in the SSA is not sustainable [68].

9. Optimal management of pregnancy

Pregnancy in women with SCD is associated with an increase in feto-maternal adverse outcomes [69]. Pregnancy in SCD is associated with increased maternal morbidity and mortality include increased risk of acute chest syndrome, thromboembolism, infections, vaso-occlusive crises, pre-eclampsia, preterm labor, and cerebrovascular stroke. The leading fetal

complications include intrauterine growth restriction, premature birth and increased fetal loss. A study conducted in Tanzania showed that there was an excessive risk of maternal mortality in pregnant women with SCD compared to the others (11.4% vs 0.4%) [70]. During pregnancy, the classic adverse events of SCD, such as painful crises (Vaso-Occlusive Crises), acute chest syndrome, pulmonary embolism, stroke, hematological complications, and infections, should be managed [71].

Previous studies have shown that pregnancy exacerbates preexisting anemia, leading to an increase in the incidence of severe anemia and the need for transfusions [71]. Pregnant women with SCD and previous stroke history require close monitoring to avoid a new event, both ischemic and bleeding, throughout pregnancy and in the postpartum period [72]. All sickle-cell pregnant women should be evaluated for stroke risk, particularly pregnant women with hypertension [72]. Pregnant women with SCD, especially in low-resource settings, are therefore more likely to die in pregnancy or to miscarriage. In that sense, pregnancy-related studies should, thus, be a priority.

Preconception care with professional counseling and tests, regular consultations in prenatal care during pregnancy, and prompt diagnosis and treatment of the complications are key factors for SCD pregnancy management [73].

Frequent visits and obstetric scans during pregnancy (when feasible) increase the chance of detecting complications. During each visit, to ensure that vital signs (Pulse, respiratory rates, blood pressure and oxygen saturation) are routinely checked. The frequency of antenatal clinic visits need to reviewed to allow proper assessment and may be as often as every two weekly or more until delivery [73]. Each consultation is expected to evaluate Hb concentration, urinalysis and complete blood count. With regards to drug provision daily folic acid, Malaria chemoprophylaxis according to country guidelines, and low-dose aspirin can be considered [73].

Aspirin is a widely prescribed treatment in the prevention of cardiovascular complications, and at low doses, it is used to prevent pregnancy-related vascular disorders, such as pre-eclampsia, intrauterine growth restriction, and maternal disorders [74]. A number of studies have shown that the use of low-dose aspirin in pregnancy, specifically in women with SCD, is safe. The British Society for Haematology recommends prophylactic use of Aspirin, daily low dose, in women with SCD at high risk of pre-eclampsia [75]. A trial is being conducted in Nigeria comparing a daily dose of 100 mg aspirin to placebo, from 12 to 16 weeks' gestation until 36 weeks, in pregnant HbSS and HbSC women, with the primary outcome being the incidence of birth weight below 10th centile for gestational age or incidence of miscarriage or perinatal death [76]. Another trial is being conducted in Angola, LEARNER (ClinicalTrials.gov ID, NCT06417411), a prospective, open-label study to evaluate the effects of daily low-dose aspirin in pregnant women with SCD when initiated in the first trimester versus the second trimester of the gestational period. Recruiting started in April 2024 [77]. The role of Hydroxyurea in SCD pregnancy is debatable with studies suggesting that it may be safe up to conception [78], but is necessary that women must be advised about risks and benefits [73]. Asare et al in Ghana reported a reduction of mortality from over 60 per 1000 live births to 23 per 1000 live births in Ghana, this is in with the 9 evidence-based recommendations from Society for Maternal-Fetal Medicine Consult Series (US) and similar to Royal College of Obstetrics and Gynecology, British Society Haematology guideline.

The following are the 9 Society for Maternal-Fetal Medicine recommendations [78]:

1. We recommend that patients with sickle cell disease be managed by a multidisciplinary team that includes maternal–fetal medicine, hematology (ideally a hematologist specializing in sickle cell disease), genetics, pain management, and social work or behavioral health (as appropriate) starting in early pregnancy (best practice). 2. We recommend that pregnant patients with sickle cell disease receive all routinely recommended antenatal vaccinations in addition to meningococcal and pneumococcal vaccinations if due (GRADE 1A). 3. We recommend prenatal vitamins without iron unless iron deficiency is confirmed and initiation of 4 mg of folic acid for pregnant patients with sickle cell disease (GRADE 1B). 4. We recommend fetal growth surveillance every 4 weeks beginning in the 28th week of gestation (GRADE 1C). 5. For patients with uncomplicated sickle cell disease and a normally grown fetus, we suggest weekly or twice-weekly antenatal testing, beginning at 32–34 weeks of gestation. For patients with complicated sickle cell disease (i.e. maternal hypertension, vaso-occlusive crises, fetal growth restriction, or other coexisting complication), we suggest initiating individualized antenatal testing at diagnosis or at a gestational age when delivery would be considered if results are abnormal (GRADE 2B). 6. We recommend following evidence-based guidelines for the management of chronic and acute pain during pregnancy (best practice). 7. We suggest the use of prophylactic transfusions be individualized for high-risk patients with sickle cell disease in accordance with American Society of Hematology guidelines and directed by a hematologist and maternal–fetal medicine subspecialist in shared decision-making with the patient (GRADE 2B). 8. We recommend shared decision-making occur regarding the use of hydroxyurea in pregnancy, in conjunction with a sickle cell disease specialist and maternal–fetal medicine subspecialist, accounting for the timing of use and individual disease severity (GRADE 1C). 9. We recommend that reliable contraception be offered to patients with sickle cell disease to decrease the risk of an unintended pregnancy and associated maternal and perinatal risks (GRADE 1B).

10. Transition from pediatric to adult care services

The global standard of care for SCD is for affected adolescents and young adults (AYA) to access structured, adult-centered care directed by their pediatrician. This assumes early diagnosis, enrollment into comprehensive care for SCD with a pediatrician, survival into adolescence and life-long care thereafter, by an adult care team.

In high-burden SSA, newborn screening programs for SCD occur in pockets rather than nationwide, and specialist care is not always accessible. Late diagnosis in SSA and other low- and middle-income countries, sometimes occurs in

adolescence or adulthood [79–81]. This means that care by a pediatrician and a formal transition to adult-centered services would not be possible.

Up to 50% now survive SCD into adolescence as improved care increasingly reaches SSA, however, SSA lags decades behind developed countries in the transformation of SCD from a disease of childhood, into a chronic lifelong disease [82]. Better survival has brought attention to heightened acute care needs, morbidity, and mortality among surviving AYA with SCD [83–85]. It has become necessary to adapt evidence-based strategies for transition care in AYA with SCD to sustain the gains of survival.

Transition is the concept of deliberately planning and changing the health care of AYA from child-centered to adult-oriented health-care systems [84] to improve disease outcomes. Transition care is a process rather than an event, as it involves a decision and actions required to prepare the adolescent for navigating their health care needs as an independent adult, training in self-management and self-efficacy, and finally, transfer to adult-centered care [86]. Transition care should pay attention to adolescents' and young adults' educational, psychosocial, and medical needs. Therefore, it is also best to engage their families [87]. The transition process culminates in a medical transfer of care to an identified adult provider who can accept responsibility for the care of the AYA. Medical records are best shared and logistic support offered where necessary and feasible [88].

The six SICKLE recommendations, which should be considered in any SCD care transition plan for young people are skills transfer, increasing self-efficacy, coordination of transition, knowledge transfer, linking to adult services, and evaluating readiness [89]. This begins with a transition policy showing a decision to inform and prepare adolescents for adult-centered care through tracking and monitoring progress to judge their readiness based on their acquisition of knowledge, self-management, self-efficacy, and confidence to access care independently without their parents. This should be followed by a joint team of pediatric and adult care providers seeing the adolescent together and subsequent transfer to adult care at about 16–18 years old. It is important to integrate adolescents into adult care after transfer to deem the transition successful when a first appointment and sustained utilization of adult-centered care in the long term have been observed [86,90–92].

Successful transition can be achieved through different programmes. Modalities employed vary from one program to another depending on the peculiarities of the health facility and locale. Modalities documented range from one-on-one training sessions, group counseling, methods incorporating information technology, in-person remote use, or any combination of modalities suited to a specific healthcare setting [93].

In SSA countries due to inadequate personnel, the capacity to offer specialist care for SICKLE recommendations for the transition from pediatric to adult-centered care are limited [66] comprehensive care mean that affected children are diagnosed late in childhood or adolescence [79,80] and may not receive care from a Paediatric team to offer purposeful transition care.

Transition to adult-centered care requires universal newborn and early infant diagnosis of SCD in public and private sector health institutions in SSA so that every child born with SCD and survives to adulthood gets an opportunity to access planned transition to adult-centered care. To increase the capacity for comprehensive multidisciplinary care, institutionalizing training and retraining of health care providers for children and adults, in both the public and private sectors is recommended. To further increase the reach of expert care, various other suitable cadres of health workers can be formally trained to offer SCD management in place of specialist doctors. There are existing task-shifting and task-sharing policies in the region for when there is no doctor. Transition care administered utilizing this healthcare delivery framework would allow for the deployment of community health workers (CHEW) with whom many patients are already familiar. This option of community-based transition care as opposed to hospital-based care would improve access and acceptability just as nurses coordinating and assisting AYA in navigating transition care activities can [89]. Appropriate training can make alternate care providers and navigators suitable for interacting with healthcare providers, family, and AYA as recommended for optimal transition care.

Appropriate training can make alternate care providers and navigators suitable for interacting with healthcare providers, family, and AYA as recommended for optimal transition care. Non-clinician community workers have successfully served in various capacities in the management of chronic diseases. They provide culturally acceptable support for positive behavioral change that can improve disease outcome and quality of life. They can also share the burden of training, build individual and community capacity, and bridge the gap between the patient and the medical facility by helping them navigate the hospital systems and adhere to multiple appointments. This would expand the reach of specialist care. Community health worker support to increase access to culturally acceptable transition to adult care in AYA living with SCD in SSA [94]. Community health worker-supported intervention programmes have been in use for a long time for enhancing the management of tuberculosis, malaria, HIV infections, diabetes, family planning, maternal and childhood mortality, and hypertension for a long time [95]. For an objective assessment of the efficacy of CHW-supported interventions to manage sickle cell transition care, transition care models for SCD need to establish standardized criteria for defining disease outcomes to evaluate the effectiveness of CHW-supported transition care for individuals with sickle cell disease [89,96]. [96]Evaluations of the effectiveness of CHW-supported transition programmes in AYA are, however, scarce [97].

In SSA, implementing standard transition care programmes tailored to fit high disease burdens, faces other barriers beyond human resources for health. These include limited healthcare provider awareness of the importance of transition care, insufficient understanding of the processes involved, and the absence of transition policies in facilities that offer specialist SCD care [98].

Digital media health interventions are a further consideration for enhancing transition care. Digital media offers

promising avenues for healthcare interventions, particularly for adolescents and young adults (AYA, whose significant online presence suggests that strategies leveraging this medium could be highly effective [99]. A comprehensive review of electronic health interventions, including mobile applications, internet-based cognitive behavioral therapy, games, and revealed that 94% of the participants experienced improvements in disease outcomes, such as self-management outcomes, with 63% expressing high satisfaction and acceptability of these interventions [100]. In sub-Saharan Africa (SSA), mobile digital media access varies widely, ranging from 3% in Tanzania to 40% in Burkina Faso and South Africa. However, a multi-country study on AYA in SSA did not include Nigeria [99]. In Nigeria, barriers to mobile phone ownership include erratic electricity supply and internet connectivity. Contrary to earlier findings that poverty was the primary obstacle, Forenbacher et al. identified low education, informal work, and unreliable electricity as the main barriers for adolescents aged 15 years or older. Interestingly, lower proficiency in English did not significantly hinder mobile phone ownership [101].

11. Prevention programs in SSA

SCD poses a significant burden in SSA, contributing to morbidity and mortality. It also creates substantial psychosocial and economic challenges for the affected individuals, their families, and society at large [3,102,103]. Preventing disease is a critical and worthwhile goal. Although curative therapies such as stem cell transplantation and advanced disease-modifying treatments like gene therapy hold promise, these interventions are likely to remain inaccessible to the majority of SCD patients in SSA for at least a decade or longer [3]. This reality calls for the need to prioritize prevention strategies to mitigate the burden of SCD in the region. A number of preventive strategies that may not be accessible or affordable for SSA setting include preimplantation genetic testing with prenatal diagnosis and pregnancy terminations present ethical dilemmas [104,105]. [105,106]. In addition, their uptake is faced with barriers such as prohibitive costs, religion, sociocultural, moral, and legal considerations. For example, in Nigeria, like in all African countries, abortion is illegal except when the woman's life is at risk [107,108].

As a result, even when prenatal diagnosis reveals a fetus affected by SCD, termination of pregnancy is not an option for most women.

Given these constraints, counseling and pre-conception testing is the most feasible and cost-effective strategy for reducing the burden of SCD in SSA [104]. Counseling offered through a structured communication process that provides individuals or couples with comprehensive information about genetic risks, inheritance patterns, and potential reproductive options. A key aspect of this process is addressing the emotional needs of the clients while ensuring they gain a clear understanding of the implications of transmitting SCD to their unborn children. A recent review emphasized the need for proper genetic counseling and scientific testing to enable informed decisions, indicating that the effectiveness of existing counseling models remains unclear [109].

Skilled genetic counselors to be dedicated to treatment centers [104]. Additionally, increasing public awareness about SCD and the importance of genetic counseling is vital for improving its uptake and effectiveness. While enforcing legal bans on marriages between sickle cell carriers may not be practical or productive, raising awareness and promoting voluntary participation in genetic counseling and testing are more effective strategies.

To enhance the impact of genetic counseling in SSA, we recommend the integration of sickle cell education into the curricula of educational institutions from the primary to tertiary levels [3]. Genetic counseling and testing to be accessible to during routine health assessments and school entrance medical assessments. A task-shifting approach to train more genetic counselors, including community health workers, schoolteachers, and religious and opinion leaders [110]. Strengthening diagnostic laboratory capacities is equally important. False-negative results from substandard testing contribute to an increase in marriages between carriers, thereby undermining the efforts to reduce the prevalence of SCD in Africa [111].

12. South-south and north-south collaborations in SCD management

The progress made in managing SCD in SSA has been slow despite its high prevalence and significant contribution to morbidity and mortality. South–South and North–South collaborations are crucial to advance SCD management and improve clinical care for individuals living with the condition. These collaborations are vital to addressing resource gaps for SCD research, implementing proven interventions, and strengthening healthcare capacity in SSA [112]. On the other hand, high-income countries also require these collaborations to have insights into the complex pathophysiology and diversity of the disease and develop novel therapies [113]. The WHO has underscored the importance of local and global partnerships in the region to facilitate SCD diagnosis, treatment, and management [114].

Recent collaborative partnerships have emerged to address the SCD challenge in SSA. The NIH-funded SickleInAfrica Consortium, through its flagship initiative Sickle Pan African Research Consortium (SPARCO), builds research capacity by developing infrastructure, providing education, and training, and collecting longitudinal data to translate findings into practice [115,116]. The Consortium on Newborn Screening in Africa (CONSA), funded by the American Society of Hematology, operates in seven African countries to demonstrate the benefits of early SCD diagnosis and intervention, while fostering an international network to enhance newborn screening programs [117]. Similarly, the EU-funded African Research and Innovative Initiative for Sickle Cell Education (ARISE) facilitates multidisciplinary staff exchanges between researchers in Europe (Portugal, Italy, France, the United Kingdom, and Cyprus) and non-EU countries (Angola, Nigeria, Lebanon, Kenya, and the United States) to share best practices in newborn screening, diagnosis, and treatment of SCD (https://www.ariseinitiative.org/) In addition, several collaborative clinical trials such as REACH, NOHARM, and

SPRING have contributed to capacity-building efforts, focusing on hydroxyurea use, stroke prevention, and other aspects of SCD management [118,119].

These partnerships have fostered capacity development, standardized clinical procedures, established robust patient databases, improved diagnostics, expanded clinical care delivery, influenced health policies, advanced multi-site cohort studies, guided locally appropriate interventions, contributed to genomic research, and strengthened healthcare providers' skills to develop standardized care guidelines for SCD across the continent [115–117] (https://www.ariseinitiative.org/).

However, despite these successes, several challenges persist, the most notable of which is the sustainability of collaborative programs due to weak governmental commitment [119,120].

North-South and South–South collaborations offer mutual benefits, enhancing disease management in low-income countries, while providing high-income countries with insights into SCD pathophysiology and opportunities to develop novel therapies [113,119]. These partnerships should be guided by principles of mutual respect, benefit, and accountability [119]. Country ownership, including sustained funding and infrastructure investment, is critical for long-term success. Intersectoral collaboration between governments, academia, industry, and patients can further ensure the sustainability of these programs [114]. By prioritizing these efforts, SSA can reduce the burden of SCD, improve healthcare outcomes, and advance research that benefits global populations affected by the disease.

13. Challenges in SCD management in SSA

The management of SCD in SSA faces challenges, including insufficient public awareness, limited resources, inadequate healthcare infrastructure, and poor access to essential treatments. Addressing these challenges is crucial to reducing the disease burden.

Despite the high prevalence of SCD in SSA, studies have revealed a lack of basic knowledge about the disease, including its mode of inheritance, hemoglobin genotype testing, the importance of premarital genetic counseling, newborn screening, as well as its treatment with disease-modifying agents such as hydroxyurea among the various segments of the population [121–124]. These knowledge gaps perpetuate the high prevalence of SCD, as well as delayed diagnosis and treatment.

Also, the effective management of SCD requires a multidisciplinary team of healthcare professionals. SSA suffers from a critical shortage of skilled health workforce, which compromises the quality and outcomes of care [125–127]. Training and retention of skilled health workers, as well as task-shifting and task-sharing strategies, can help overcome this challenge [128].

Another major challenge is the inadequacy of healthcare infrastructure and funding to support SCD care. Many public health facilities lack essential diagnostic tools, such as equipment for genotype testing or transcranial Doppler ultrasonography, as well as the systems required for comprehensive care [35,129]. Without these services, early diagnosis and routine monitoring is often delayed or unavailable, resulting in missed opportunities for timely intervention. This directly contributes to preventable complications, higher rates of hospitalization, and early mortality. Moreover, low-income individuals frequently struggle to afford medications, regular testing, and access to specialized care, further compounding disease outcomes [129]. Improving access to quality health services, especially at the primary and secondary levels, is therefore critical. To address these challenges, efforts must be focused on increasing health funding, strengthening infrastructure, expanding access to health insurance, reducing treatment costs, and providing support to affected individuals.

Poor access to essential treatments such as safe blood transfusion, penicillin V, and hydroxyurea is a common occurrence in SSA. A study from Nigeria reported that 78% of hospitals in Nigeria could not provide consistent transfusion services, and only 45% have access to packed red blood cells [66] There is also a high risk of transfusion-transmitted infections (TTIs) due to their prevalence and insufficient infection-screening practices [66,130] Extended phenotypic matching for the detection of allo-immunization is rarely practised, and iron overload management is hindered by limited diagnostic tools and the high cost of treatment [66,130–132].

Hydroxyurea, the only affordable disease-modifying agent available in SSA, is reported to be both safe and effective for patients with SCD in SSA [122,133]. However, its use remains low due to various barriers. Healthcare system barriers include the drug's limited availability, high cost, and lack of coverage under healthcare insurance plans [134]. Healthcare providers face challenges such as inadequate knowledge and expertise in prescribing hydroxyurea, as well as negative attitudes toward its use [135]. Patients and caregivers face significant barriers, such as fear of side effects, the financial burden of out-of-pocket drug purchases, and doubt about hydroxyurea's effectiveness [136].

In conclusion, addressing the challenges of SCD management in SSA requires a multifaceted approach, including improving public awareness, building healthcare capacity, enhancing blood transfusion safety, promoting hydroxyurea access, and strengthening healthcare infrastructure. Collaborative efforts involving governments, international organizations, and local communities are essential to overcoming these barriers and improving outcomes for individuals living with SCD.

14. Capacity for comprehensive SCD care in SSA

The comprehensive care model of healthcare is a cost-effective model that delivers optimal care through the cooperation of the person living with SCD with a multidisciplinary team of medical and non-medical professionals offering holistic care to improve their quality of life, limit the need for inpatient care by screening, early detection of disease-related morbidity and treatment of acute and chronic complications of SCD [137]. This starts with newborn screening, early enrollment for multidisciplinary care, which offers relevant immunizations, penicillin prophylaxis to prevent infections, counseling, prevention of ischemic stroke prevention from the age of 2 years until 16 years of age, malaria prophylaxis necessary in SSA, prompt

recognition and expert management of acute and chronic complications of SCD, while covering psychosocial needs, consistent health screening for common complications, provision of evidence-based informed education to both patients and their families through counseling [138].

Hydroxyurea from 9 months of age has become an integral part of comprehensive care and SSA struggles with unreliable supply, poor health worker knowledge and hence prescription apathy and high cost of toxicity monitoring where infrastructure for monitoring is available. Hydroxyurea is, however, locally produced in Nigeria.

Low awareness of the benefit of Penicillin prophylaxis and its utilization among healthcare providers in SSA countries is poor and would limit prescriptions [139]. Penicillin V access is poor in Nigeria due to unavailability and relatively high cost as the medicine is not produced locally but imported.

Currently, universal newborn screening for SCD is not yet implemented in any available in SSA country [10] despite policies mandating it [52]. [140] Models of care employing task shifting could benefit access to health interventions by offering comprehensive care services at primary and secondary healthcare facilities to address logistical barriers to follow-up and enrollment caused by insufficient funding for transportation [141]. Even when the facilities are available, the cost of providing comprehensive care is too high and inaccessible for most patients due to out-of-pocket expenditure [142].

External research funding has held up a modicum of comprehensive care, but governments need to own the programs and commit funds and implement policies for comprehensive care. A map of thirty-one secondary and tertiary-level hospitals able to offer specialist SCD care across Nigeria, where the SCD burden is high, showed inequitably distributed resources [66].

While substantial progress has led to improvement in SCD care, significant gaps remain due to the fragile nature of healthcare infrastructure, human resources, diagnostic and laboratory capacity. Addressing these challenges is crucial to providing comprehensive care for SCD patients in the region [143].

Comprehensive care can potentially prolong life and enhance the quality of life for individuals living with SCD [138]. Of note is the reduction in morbidity and mortality achieved through newborn screening, immunization, penicillin prophylaxis and hydroxyurea, a disease modifier which reduces morbidity and mortality [144] and hence reduces years of life lost (YLL) from premature death and disability-adjusted lived years (DALYs). Episodic treatment of sickle cell disease complications has been shown to cost significantly more than managing in a comprehensive care setting in high-income [144] as well as in SSA settings [145]. A cost–benefit analysis would support interventions that align with evidence-based standards of care, as no form of compensation can compare to a life lost. Comprehensive care is therefore desirable for low-resource, high-burden SSA. Its adaption to local realities is, however, crucial to make care cost-effective in the region.

15. Conclusion

We advocate for increased funding to implement SCD comprehensive care in line with the WHO SCD Framework for Primary Secondary, Tertiary and Specialist Comprehensive Care at state and national level. To achieve this objective, it is important that for SCD as a leading non-communicable disease in Africa and mandate it as a standing agenda for the National Council of Ministers at the African Union, the WHO and regional bodies.

16. Expert opinion

Following this targeted literature review, including unpublished data, we have come to the following conclusions and make recommendations for the management and control of Sickle cell disease (SCD) in SSA (SSA).

That a successful Newborn and Early infant diagnosis of SCD implementation is pivotal to achieving a sustainable program for SSA. Screening followed by effective follow-up, starting with the introduction of penicillin V, as advocated by the WHO [14]. We propose consideration for diagnostic techniques include high-performance liquid chromatography (HPLC), capillary electrophoresis (CE), isoelectric focusing (IEF), and point-of-care testing. See WHO Table 1.

Barriers limiting opioid use in SSA include insufficient provider knowledge about opioid prescription and management, restrictive prescription regulations, the absence of morphine in rural healthcare facilities, challenges in securing foreign currency for morphine importation, and prescriber hesitancy driven by concerns over adverse effects, dependency, and potential misuse. We recommend the incorporation of analgesia training for undergraduate and postgraduate medical education on SCD.

Evidence supports the routine use of malaria chemoprophylaxis in individuals with SCD who live in malaria-endemic areas [50] and the WHO recommendations emphasize the benefits of providing routine prophylaxis to this high-risk population [50,58].

WHO global data shows that of 60 low-middle-income countries with less than 10 blood donations per 1,000 people, 34 are in Africa compared to high-income countries where the mean donation rate is over thirty-one donations/1,000 people. To improve the supply of safe blood, we recommend that SSA nations strengthen donor recruitment, data management, TTI surveillance, and hemovigilance while addressing power supply challenges and reducing dependence on imported reagents and equipment for sustainability.

The six SICKLE recommendations, which should be considered in any SCD care transition plan for young people are skills transfer, increasing self-efficacy, coordination of transition, knowledge transfer, linking to adult services, and evaluating readiness. We recommend that transition planning in SSA can be optimized through alignment with existing task-shifting and task-sharing policies for when there is no doctor. This policy could also allow for the training and deployment of Community Health extension workers (CHEW) with whom many patients are familiar or nurses to coordinate and assist adolescents and young adults (AYA) in navigating transition care interventions, making it more accessible and acceptable.

Poor access to essential treatments such as safe blood transfusion, penicillin V, and hydroxyurea is a common occurrence in SSA.

Table 1. Approaches to the initial diagnosis of SCD in SSA (adapted from WHO [14]).

	Neonatal screening	Screening campaigns	Intrafamily screening	Diagnosis of clinical manifestations and/or complications
Specific objectives	▲ Early diagnosis of SCD ▲ Early management of children with SCD	▲ Screening subjects with undiagnosed major SC syndromes ▲ Screen subjects with heterozygous hemoglobinopathies (AS, AC, αthal)	▲ Screening for undiagnosed SCD in the family ▲ Screen family members with heterozygous hemoglobinopathy (AS, AC, αthal)	▲ Diagnosing SCD in a patient with signs or complications suggestive of major SC syndrome
Terms and conditions	▲ Availability of a laboratory and methods for neonatal diagnosis of hemoglobinopathies ▲ Setting up care conditions for children with SCD	▲ Availability of screening methods or rapid diagnostic tests ▲ Possibility of referral to SCD care structure ▲ Access to information and genetic counseling	▲ Availability of diagnostic methods for various major SC syndromes ▲ Possible management of SCD ▲ Access to information and genetic counseling	

We recommend that the provision of affordable hydroxyurea is key to improving adherence to patient follow-up and improving the lives of people living with SCD, especially in Africa.

To address the question of malaria prophylaxis in high endemic areas we advocate for well-designed Randomized Clinical trials to identify appropriate chemoprevention in malaria endemic settings [50,58].

Policies promoting early diagnosis and enrollment into comprehensive care are necessary tools to improve transition from pediatric to adult care.

It is our opinion that successful implementation of sickle cell programmes in Sub-Saharan Africa is possible as evidenced by new initiatives across the continent from Anglophone, Francophone, and Portuguese speaking countries, this is now the time to strengthen clinical follow-up, hydroxyurea provision and comprehensive care programmes. These new initiatives must align within the respective countries' health systems to maximize benefits for patients and their families. A coordinated approach to ensure that all external and international funding partners commit to work together and in consonant with the health priorities in the countries. This could reduce the tendency for programme 'silos' which even though lead to high impact publications makes very little impact in the health systems and the efforts quickly fizzle out.

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Author contributions

M Brito co-designed the manuscript structure, allocated specific writing tasks to A Ofakunrin, I Akinwumi, and C Ginete, organized the referencing, arranged sections in order, and completed the referencing. C Ginete contributed to the manuscript writing, provided substantial intellectual revisions, and refined the content for clarity and accuracy. A Ofakunrin contributed to manuscript writing, provided substantial intellectual revisions, and refined the content for clarity and accuracy. I Diaku-Akinwumi contributed to manuscript writing, provided substantial intellectual revisions, and refined the content for clarity and accuracy. BPD Insua initiated the manuscript design, edited the draft, recommended structural changes to the format, and finalized the manuscript.

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