Genetic Diversity of Sickle Cell Disease in Nigeria: Implication for Emerging Gene Therapy and Health Equity

Godfrey Eshikhena Obaze [1*], Obinna Jacobs Chukwu [2], Obaro Princewill Idogho [3], Ademola Rasheed Olanrewaju [4], Yetunde Victoria Mene [5], Nyerovwo Charity Okei [6], Glory Abiola Ayemoba [7], Tobiloba Philip Olatokun [8], Fatima Tolulope Tijani [9], Auwal Shehu Ali [10]

[1-2] Department of Biochemistry, University of Nigeria, Nigeria
[3] Public Health Administration, First Moscow State University (Sechenov University), Russia
[4] Biomedical Engineering, Ulster University, United Kingdom
[5] Community Health, Obafemi Awolowo University, Nigeria
[6] Health Management, University of New Orleans, United States
[7] Nursing Science, Ladoke Akintola University of Technology, Nigeria
[8] Environment Health, University of Illinois Springfield, United States
[9] Department of Physiology, Bowen University, Nigeria
[10] Department of Pharmacy, Federal Teaching Hospital, Nigeria

* Corresponding Author: **Godfrey Eshikhena Obaze**

Article Info

ISSN (online): 2582-8940
Volume: 06
Issue: 04
October-December 2025
Received: 18-08-2025
Accepted: 19-09-2025
Published: 12-10-2025
Page No: 38-48

Abstract
Sickle cell disease (SCD) remains one of the most significant monogenic disorders globally, with Nigeria bearing the highest prevalence, accounting for nearly 50% of the world's annual births with SCD. The genetic landscape of SCD in Nigeria is remarkably heterogeneous, characterized by diverse β-globin haplotypes, varying allele frequencies, and multiple genetic modifiers influencing clinical outcomes. This review synthesizes current knowledge on the molecular and haplotypic diversity of SCD in Nigeria and highlights its implications for disease phenotype, prognosis, and therapeutic response. We critically evaluate the current management landscape, including hydroxyurea therapy, transfusion programs, and newborn screening efforts, while identifying barriers to equitable access. Furthermore, we examine emerging gene therapy approaches—lentiviral gene addition, CRISPR-Cas9 gene editing, and HbF reactivation—and assess their relevance to Nigeria's unique genotype distribution and healthcare infrastructure. Finally, we discuss health equity, policy priorities, and capacity-building strategies necessary to ensure broad, affordable access to curative therapies. Our review underscores the dual imperative of scientific innovation and health equity to transform SCD outcomes in Nigeria.

DOI: https://doi.org/10.54660/IJMBHR.2025.6.4.38-48

Keywords: β-Globin Haplotypes, Genomic Medicine, Genetic Diversity, Gene Therapy, Health Equity, Precision Medicine, Nigeria, Sickle Cell Disease

1. Introduction

Sickle cell disease is a genetic condition that was first identified more than a century ago, and since then it has been the subject of intensive research and clinical management. It is an inherited autosomal recessive disorder of the β-globin gene, characterized by recurring episodes of vascular occlusion and hemolytic anemia, among other clinical manifestations [1]. Although sickle cell disease is a global problem, its prevalence is highest in sub-Saharan Africa, with Nigeria bearing the greatest share of this burden. Nearly half of affected children die before the age of five, and survivors have a life expectancy of about 21 years, compared to

54 years in high-income countries [2–6].

Sickle cell disease (SCD) refers to a spectrum of inherited disorders affecting red blood cells, with sickle cell anemia being the most prevalent type. Its clinical course varies greatly: some individuals experience serious complications early in life, while others reach adulthood with fewer and milder symptoms. These differences in disease manifestation are believed to result not only from genetic factors and the extent of sickling but also from the influence of the vascular endothelium, platelets, leukocytes, plasma proteins, and environmental factors [7]. Owing to this variability, precision medicine—which involves customizing treatments based on clinical and genetic profiles—holds great potential. However, its use is still constrained by the limited number of available therapies and the difficulty of predicting disease trajectories.

Studies on genetic modifier loci in Nigerian patients, including BCL11A, HBS1L-MYB, and the β-globin cluster, have shown a clear correlation between certain variants and higher levels of fetal hemoglobin (HbF), which are linked to less severe disease outcomes [8].

The introduction of therapies such as hydroxyurea, newer agents like voxelotor and crizanlizumab, and preventive transfusion strategies for stroke provide opportunities to refine treatment strategies. In Nigeria, incorporating routine HbF measurement, genotyping, haplotype analysis, and systematic mapping of genetic modifiers could help establish clearer prognostic groups. These genetic insights provide a foundation for therapeutic interventions. Building on these therapeutic approaches, recent advances in molecular genetics and biotechnology, such as gene editing and gene addition strategies, have led to the development of gene-based therapies, thus providing new possibilities for curative treatment [10-12]. Equally important is ensuring fair access to healthcare. While gene therapies offer great promise, cost, infrastructural gaps, and availability risk leaving many patients behind [13, 14]. Addressing how genetic diversity, new treatments, and equity intersect in Nigeria is key to guiding research, clinical care, and policies that support inclusive healthcare [15].

This review aims to synthesize current evidence on the genetic diversity of SCD in Nigeria, examine its implications for advancing gene therapy, and discuss equity considerations in ensuring fair access to these emerging treatments.

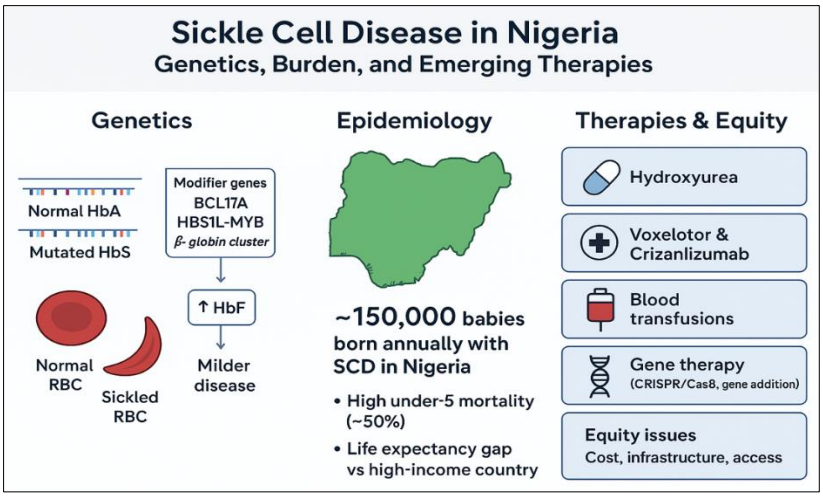

Fig 1: Genetics, burden, and emerging therapies of sickle cell disease in Nigeria, adapted from [4, 27, 52, 53]

2. Epidemiology of SCD in Nigeria

The genomic analysis carried on SCD has revealed that the mutant hemoglobin component β is African in origin, but the exact location of the mutation's origin and its accurate age currently remain unknown [17]. The single sickle hemoglobin allele (also referred to as the sickle cell trait) has proven that there is an evolutionary connection between haemoglobin subunit β variants and malaria since it provides protection against severe *P. falciparum* malaria, which forms the basis of the malaria hypothesis [18, 19].

Subsequent studies have revealed that more than 25% of the variation in severe malaria outcomes can be explained by human genetic factors, with sickle cell trait accounting for the largest proportion due to a single gene (up to 2%) [20]. Therefore, in areas where malaria has historically been endemic, the sickle hemoglobin allele is very common—up to 20% in some areas, but statistical estimations have set an upper limit at 18% [21].

Nigeria has the highest prevalence of SCD. It has statistically been established that between 150, 000 and 200, 000 children are born with sickle cell disease each year in Nigeria [22-23]. With regional variations, HbSS affects roughly 2–3% of live births, and the carrier rate is around 25%.

Again, due to migration considering the transatlantic slave trade in the past, the sickle hemoglobin allele is most common outside of Africa among people of African heritage, and has expanded to the Mediterranean, the Americas, the Indian subcontinent, and the Middle East [24, 25]. Hemoglobin C, the second most common contributor to sickle cell disease, occurs mainly in West Africa, with Burkina Faso as its center, though it is now spreading more widely [26]. In Africa, about 65–70% of cases arise from homozygous HBB mutations, around 30% from compound heterozygosity with hemoglobin C, and the rest from HbS/β⁰-thalassemia [21].

The sickle cell trait is the burden that is driving sickle cell disease in Nigeria. Projections suggest that by 2050, the number of affected newborns will rise by about 100, 000 globally, with Nigeria and the Democratic Republic of the Congo accounting for the largest share [27]. A 2019 survey further revealed that 10% of Nigerian children aged 6 months to 5 years with severe anemia also had sickle cell anemia [28]. The recessive sickle hemoglobin allele is highly lethal in malaria-endemic regions, with up to 80% of affected newborns dying before the age of five if untreated [29]. In

Nigeria, limited early diagnosis and inadequate care contribute to the death of about 100, 000 children with sickle cell disease each year before they turn five [4].

The likelihood of HbSS newborns is increased by high consanguineous marriage rates [31]. Outcomes are impacted by urban–rural differences; metropolitan areas have greater access to treatment facilities, whereas rural areas experience care gaps and low awareness [32]. Despite pilot programs showing lower mortality, nationwide newborn screening is still limited [33]. To lessen the burden, health education, premarital genetic counseling, and awareness campaigns are crucial [34].

3. Molecular and Genetic Diversity of SCD in Nigeria

3.1. Genotypic Variants

The frequencies of sickle cell alleles vary geographically in Nigeria. Sickle cell disease presents in several genetic forms depending on the hemoglobin genes inherited, HbSS, HbSC, HbS/β-thalassemia, and other compound heterozygous variants [35-36]. The HbS allele is common in the northern part of Nigeria and it is also the most prevalent nationwide, whereas HbC is more common in the western regions [28, 37]. In contrast, β-thalassemia is relatively rare in the Nigerian population [36, 38].

3.2. Haplotypic Diversity

Haemoglobin F (HbF) is the key modulator of the sickle cell disease (SCD). Haplotypic diversity in SCD is defined as the β-globin gene cluster, influences disease severity and clinical expression. Research studies have shown that there are five major haplotypes of the β-globin gene cluster associated with SCD which depends on geographical location: Senegal, Benin, Bantu/Central African Republic, Cameroon, and Arab-Indian [39–41]. The severity of the disease differs with HbF levels; for example, the Benin haplotype, which is associated with intermediate HbF levels and moderate disease severity, is the most common in West Africa, including Nigeria [42, 43]. The study of haplotypic diversity in SCD is advantageous as it provides insight into the genetics of the disease and aids in predicting prognosis, tailoring management strategies, and developing gene-targeted therapies [44].

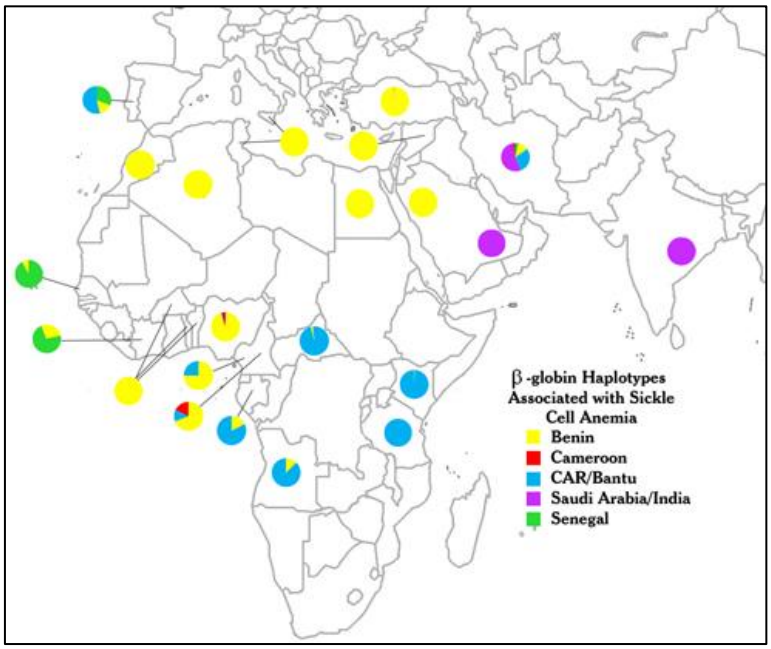

Fig 2: The distribution of sickle-cell anaemia haplotypes among nation with high prevalence of the disease [53]

3.3. Modifying Genetic Factors

The Mendelian condition, sickle cell anemia is characterized by remarkable clinical variability. Fetal hemoglobin (HbF) concentration and coincident α-thalassemia are two of the most significant genetic modifiers; they both have a direct impact on the sickled erythrocyte and influence the severity of the disease [45].

HbF is very important because it reduces the mean corpuscular HbS concentration and does not take part in HbS polymerization. Though its protective effect varies depending on the population and medical conditions, elevated HbF levels are linked to less painful episodes, fewer leg ulcers, and improved mortality [45, 46]. Three quantitative trait loci have been found to be important regulators of heritable HbF levels; The HBB cluster (chromosome 11p), where polymorphisms influence HbF production capacity, BCL11A (chromosome 2p16.1), where reduced expression variants increase HbF and ameliorate SCD severity, and the HBS1L-MYB region (chromosome 6q22–23), where variants lowering MYB expression elevate HbF and mitigate disease complications [47, 48].

Beyond HbF, α-thalassemia, found in more than 30% of individuals with SCD, modifies disease expression by lowering intracellular HbS concentration and reducing polymer-induced injury.

Additional genetic modifiers further shape disease heterogeneity: variants in ANXA2, TEK, TGFBR3, and ADCY9 are associated with stroke susceptibility [49]; the TGF-β/Smad/BMP signaling pathway is linked to multiple subphenotypes [50]; and genome-wide association studies have identified polymorphisms in UGT1A1 (bilirubin metabolism), NPRL3 (hemolysis), and CSMD1 (tricuspid regurgitant jet velocity) as contributors to disease outcomes [51].

4. Current landscape of Sickle Cell Disease (SCD) management in Nigeria

Among countries with a high rate of people living with SCD, Nigeria has the highest burden of Sickle Cell Disease, and the treatment environment illustrates the conflict between significant programmatic advancements and high unmet demand. It's also critical to acknowledge the disparities in SCD clinical practice and treatment delivery that exist in Nigeria today. The majority of patients still face significant gaps in access to disease-altering medicine and care, while transfusion safety, curative therapeutic choices, and comprehensive genetic screening remains a serious challenge to grapple with despite the existence of several registries, pilot initiatives, and tertiary centers that offer good care. Each of the primary facets of modern SCD care in Nigeria is examined in the remaining portion of this section. Curative hematopoietic stem cell transplantation (HSCT), standard-of-care disease-modifying medications (hydroxyurea), transfusion services and iron management, basic medical care measures which often and are not limited include vaccination, administration of penicillin, malaria prevention health programs, and pain management). Other care systems include genetic screening (newborn screening, carrier screening, and genotyping) are all major components of this care process. This part also covers workforce and infrastructure constraints, the role of registries and data systems, and research and trial preparedness utilizing recent Nigerian and regional literature to uncover practical realities of the disease as well as evidence-based implementation lessons.

4.1. Standard-of-care medical therapies

Hydroxyurea: evidence, uptake and implementation barriers

The most often prescribed disease-modifying treatment for sickle cell disease (SCD) is hydroxyurea (HU), which has a proven track record of lowering hospitalization, transfusion reliance, and vaso-occlusive crises. Although implementation studies and analyses of Nigerian multicenter registries support clinically significant advantages for HU users, acceptance in Nigeria is still low in comparison to the number of eligible patients. Despite positive patient experiences and observable decreases in user problems, a multi-center survey related to SPARCO found that less than 15% of registered patients were using hydroxyurea at the time of reporting [54, 55].

It is also important to note that operational adoption of HU faces strict limitations by traditional monitoring paradigms that require clinical evaluation and periodic full blood counts; in many basic and secondary care settings, limited laboratory access increases clinician hesitancy to prescribe or escalate HU. According to recent research from Nigeria and cooperative African consortia in this area, task-sharing to community health workers and trained nurses, along with streamlined dosing and monitoring protocols, can improve adherence, reduce monitoring burden, and preserve safety [56]. Simplified pediatric HU regimen pilot trials suggest scale-ups that are safer in regions with very limited resources. However, to guarantee quality and safety, and achieve reliable results, these methods need standardized algorithms, systematic training, and result tracking systems to be enacted [56].

Support for adherence and financing models

According to previous studies, once patients are placed under HU, they often report better outcomes. These outcomes include fewer hospitalizations and pain crises; the most frequent reasons for stopping HU are availability and cost [55]. Nigerian data sources indicate that clinic-level adherence support which ranges from counselling and SMS reminders to integrated pharmacy supply increases treatment persistence. However, pooled procurement, local generic production, and the inclusion of HU in national insurance formularies or essential-medicines procurement frameworks may lower financial barriers [54-56].

4.2. Transfusion services and iron management

For people living with SCD, blood transfusions are still a traditional intervention and remain a vital component of long-term treatment plans including perioperative care and primary/secondary stroke prevention. In Nigeria, the transfusion ecosystem is plagued with low voluntary donation rate which is majorly due to non-renumeration practices among treatment centers. Other challenges are partly due to dependency on family/replacement donors in many centers, and ongoing shortages of safe blood are documented by national and facility surveys [57, 58]. In addition to complicating caregiving in emergencies during acute severe anemia and acute chest symptoms, the small pool of volunteer donors and sporadic blood service functionality make prolonged chronic transfusion programs less feasible [57, 58].

Transfusion safety and alloimmunization

The risk of alloimmunization and transfusion-transmitted infections is increased by pre-transfusion testing limitations, inconsistent donor screening quality, and the relative lack of systematic extended phenotyping. Significant alloimmunization rates among multiply transfused SCD patients are reported by systematic reviews and single-center studies conducted throughout sub-Saharan Africa, including Nigerian cohorts. Pooled analyses show a clinically significant alloimmunization prevalence, with some recent studies carried out in Nigeria, reporting rates that are clustered around a high teenage population range in heavily transfused groups [58, 59]. These findings highlight the necessity of better donor recruitment tactics, trustworthy transfusion-transmissible infection screening, and, whenever feasible, phenotype-matched care for patients who receive frequent transfusions [55].

Exchange transfusion and iron chelation

A small percentage of tertiary institutions offer exchange transfusions, which can be automated or manual and are useful for acute problems, reducing sickle hemoglobin burden prior to surgery, or in times of extreme emergency. However, the availability of routine exchange transfusion outside of metropolitan tertiary settings is limited by its technical and supply requirements, which include skilled personnel, the ability to perform manual exchange protocols or apheresis, and an appropriate supply of blood. This is due to the fact that chelation agents like deferoxamine, deferasirox, and deferiprone are expensive and not always readily available, iron overload from chronic transfusion is

acknowledged and often goes untreated; published experiences in Nigeria and other regions show varying but significant iron-overload prevalence and uneven chelation use [60, 61]. Safe long-term transfusion techniques are further hampered by limitations related to cost, supply, and monitoring.

4.3. Hematopoietic stem cell transplantation (HSCT)

Local experience and capacity

The only proven treatment for SCD is still allogeneic HSCT with sibling donors who match HLA. Over the past ten years, Nigeria has reported a few transplants and case series that show technical feasibility and acceptable results in certain individuals; nonetheless, local HSCT provision is not always available and at the time of this article, is yet a scalable alternative in Nigeria [56, 58]. The primary obstacles include the lack of donor registries and extensive HLA-typing services, the lack of skilled transplant teams, the capacity of intensive care units, the absence of regular apheresis and other facilities which include graft-processing tools, and the exorbitant out-of-pocket expenses for families [62].

Strategic opportunities and caveats

Experience from other low- and middle-income nations demonstrates that sustainable transplant programs may be established through international twinning and training alliances, staged infrastructure build-out, and carefully planned regionally targeted investments (centers of excellence). Though there still remains a persistent need for strong peri-transplant ecosystems and infrastructures and follow up programs initiated long-term for patients, novel transplant techniques including haploidentical transplants and reduced-intensity regimens may eventually increase donor pools and decrease toxicity (62). Therefore, investments in donor provision and registry facilities, laboratory assistance for HLA-typing and stem-cell processing, and finance approaches that shield families from unaffordable costs must go hand in hand with any HSCT scale-up in Nigeria.

5. Gene therapy for SCD: global advances and local opportunities

The development of gene-based treatments for SCD has advanced quickly from proof-of-concept studies to regulatory approvals and regulated clinical application. The two main clinical strategies are ex-vivo cell therapies that either (a) modify autologous hematopoietic stem and progenitor cells (HSPCs) to increase fetal hemoglobin (HbF) (CRISPR/Cas9-based editing of erythroid regulators such as BCL11A) or (b) introduce a corrective or anti-sickling globin transgene (lentiviral gene addition). Other approaches, such as non-viral vectors, small-molecule HbF inducers, and in-vivo editing, are still in the early phases of development and could eventually provide lower-infrastructure alternatives, but they are not yet licensed. The primary modalities, their clinical results to date, and known safety concerns are outlined in this section. It then looks at the prospects and particular difficulties of applying these developments to the Nigerian setting [59, 63-66].

5.1. Overview of gene-therapy approaches

A. Ex-vivo lentiviral gene addition (β-globin transgene)

Lentiviral gene-addition works by using patient-derived autologous HSPCs, transducing them ex-vivo. This is usually carried out with the use of a lentiviral vector with a self-inactivating property that then encodes an anti-sickling β-globin gene, conditioning the patient (often with myeloablative chemotherapy), and then infusing the patient with the altered cells [67]. Consequently, the long-lasting manufacture of anti-sickling globin long term in erythroid cells derived from the modified HSPCs is what gives the treatment its efficacy. Lomotibeglogene autotemcel (Lyfgenia; LentiGlobin for SCD) is an example of a clinical product that was approved by the FDA in December 2023 after several years of clinical development and long-term follow-up that demonstrated a significant decrease or even complete elimination of events such as vaso-occlusion and also transfusion dependence that are popular occurrences in many treated patients [68, 69].

Clinical results and supporting data includes noticeable strong increases in anti-sickling hemoglobin species, combined with significant decreases that are observed also in vaso-occlusive crises (VOCs) [61, 70]. Other observations include transfusion independence in patients who were previously dependent on transfusions, and long-lasting engraftment in numerous participants were all shown in clinical trials with lentiviral β-globin addition. Although patient-level diversity has also been markedly observed in transgene expression and clinical response, the longest-running programs demonstrate lasting responses for many patients up to several years of follow-up [71, 72].

Although contemporary self-inactivating vectors have reduced the hazards of insertional mutagenesis and lentiviral vectors that have a lengthy history of clinical development, it is also important that strict long-term monitoring for occurrences like clonal growth and hematologic malignancy is still necessary to get the best results from patients [60]. Moreover, other clinical actions like GMP-grade vector manufacture, verified cell-processing facilities, apheresis, myeloablative conditioning, inpatient transplant care capacity, and long-term follow-up infrastructure are operational requirements for lentiviral gene addition [61, 72].

B. Ex-vivo CRISPR/Cas9-based editing to reactivate HbF (targeting BCL11A and related regulators)

Mechanism for this primarily relies on the erythroid-specific regulatory regions of BCL11A, a γ-globin repressor, are the focus of the most clinically sophisticated editing technique. Research from gene activation has shown that when erythroid BCL11A expression is disrupted, γ-globin is repressed, raising HbF levels and decreasing sickling. Also, autologous HSPCs that have been ex-vivo modified using CRISPR/Cas9 reagents and injected to make up the modified result of this. [68, 73]. The method has been shown to substantially decrease sickle hemoglobin polymerization by imitating hereditary persistence of fetal hemoglobin (HPFH) [69, 74].

Clinical results and supporting data include rapid also marked by significant increases in HbF and attendant decreases noticeable in VOC frequency. This is to say many patients became VOC-free throughout follow-up, and a decrease in the need for transfusions were all reported in pivotal trials for BCL11A-targeting medicines. Furthermore, the majority of adverse outcomes are linked to factors such as conditioning and the procedure adopted for transplantation, with little concerns relating to the editing itself. These observations are shown by the early and mid-term safety data. In order to keep an eye out for any delayed adverse outcomes, longer follow-up is being gathered [74, 75].

C. HbF reactivation by alternative molecular strategies and in-vivo editing (emerging)

The mechanism for this procedure involves procedures such as base editing, prime editing, shRNA/miRNA knockdown of BCL11A, and in-vivo delivery systems that modify HSPCs. This is done without ex-vivo manipulation. Additionally, gene-addition methods producing γ-globin and small-molecule HbF inducers are currently being investigated for their potency and if proven safe and successful, in-vivo editing which is a procedure that involves giving patients their editing reagents directly could significantly lower infrastructure requirements by avoiding the cell processing and conditioning that usually happens ex-vivo [68, 69, 71]. However, it is important to also note that in-vivo methods still face challenges ranging from delivery, specificity, to safety challenges and are still in the research stage [76, 77].

5.2. Applicability to the Nigerian context

It is necessary to assess biological applicability, programmatic preparation, infrastructure and personnel capacity, regulatory landscape, financial alternatives, and ethical issues in order to translate the promise of gene therapy into fair benefit for Nigeria. This area is discussed extensively in the sections below.

A. Biological applicability across genotypes and haplotypes

Mechanistic independence from the haplotype of β-globin: Regardless of the underlying β-globin haplotype (Benin, Senegal, Cameroon, Arab-Indian), or whether the patient has HbSS, HbSC, or HbS/β-thalassemia, the operationally accepted ex-vivo gene therapies which are primarily lentiviral β-globin addition and BCL11A-targeting CRISPR editing are activated by improving erythrocyte polymerization dynamics, a procedure that is made possible by increasing HbF levels or providing anti-sickling globin. Therefore, these treatments are mechanistically applicable to all frequent Nigerian genotypes [69, 71, 72, 74, 78].

Variability in clinical response and modifier alleles are other crucial factors to consider. It is observed that baseline genetic modifiers, which can affect baseline severity and HbF dynamics, vary among diverse groups and they include the co-inheritance of α-thalassaemia by patients, polymorphisms that occur at the BCL11A and HBS1L-MYB loci, and most occurring, haplotype-associated HbF levels. Hence, these variations may have considerable impact on not only the size of the clinical response, but also the absolute HbF levels attained following treatment of the patients. Local genetic data therefore are useful for interpreting trial results and for predicting various reactions or dangers in the Nigerian community, but it's important to note that none of the crucial approvals limited use to certain haplotypes. Thus, it is wise to include modifier genotyping and local genomic surveillance when designing and preparing trial materials and also following up with post-marketing monitoring [64, 75, 78].

B. Workforce, training and regulatory capacity

One of the impediments of SCD medical care in Nigeria is the current concentration of attention and caregiving in urban tertiary hospitals with varying transplant expertise; hence, ramping up care requires targeted training programs, international partnerships, and the creation of standard operating procedures and competency frameworks. Delivering effective cell therapies in underserved regions in Nigeria requires the experienced and well put together multidisciplinary teams which includes haematologists, transplant physicians, apheresis teams, cell-processing scientists. This of course wouldn't be in exclusion of specialized nursing and pharmacy support [62, 64].

Regulatory and ethical frameworks are other concerns in management of SCD in Nigeria. While many African national regulatory bodies are quickly expanding their ability to assess sophisticated biologics, post-marketing surveillance, an area that still needs critical attention is long-term follow-up, and standardized guidelines for somatic gene treatments. These two areas have shown an urgent need to be strengthened. Also, data processing for genomic and biobanking resources, thorough and balanced patient selection for trials and access, which also requires informed consent must all be covered under ethical frameworks. Hence, to guarantee that trials and access initiatives are morally and legally sound, Nigeria will require explicit cooperation between the regulator, industry, academia, and patient advocacy [67, 75].

C. Supply chain, manufacturing and cost barriers

Ex-vivo gene therapies globally, currently rely on highly specialized supply chains, including the creation of GMP vectors and cold-chain logistics for cell products. It also requires thoroughness in the verification of sterility as well as uncompromised quality-control testing, and frequently, cross-border shipping to specialist manufacturing facilities. It then follows that establishing reliable production at local level would drastically cut delivery time and costs but involves large production expenditure, technical skill and regulatory control. Moreover, shipping autologous cells across local processing units to foreign contract manufacturing companies and having the finished product returned are examples of interim models; these are costly and logistically challenging [71, 72].

D. Trial design, ethics and population prioritisation

Local epidemiology and trial inclusion criteria: Nigeria have a very high mortality rate of infants, a population rarely captured in the major early trials. This is often due to the fact that these trials were carried out in high-income urban statements. In order to curb this in the near future, Nigerian ethical trial design must balance the potential benefit of early therapeutic therapies against procedural hazards, particularly when conditioning regimens are necessary, as well as the local illness burden and mortality patterns (increased childhood mortality). As long as there is strong control and community involvement, protocols tailored to local realities such as capturing infants under well planned safety monitoring may be ethically acceptable [67, 75].

Furthermore, explicit equity safety protocols must be included in roll-out plans to prevent gaps from expanding. These protocols include clear selection criteria, subsidized access for low-income patients, a clear-cut commitment to capacity-building, and, where practical, attention to local manufacture and training. In order to guarantee culturally appropriate consent procedures and post-treatment care (long-term follow-up, fertility counseling), patient groups should be at the center of the planning process [67, 75].

Table 5.1: Comparison matrix of gene-therapy modalities matched against Nigerian health ecosystem & constraints

Modality	Clinical Evidence	Core Infrastructure Required	Compatibility status to Nigerian Genotypes/Haplotypes	Cost and Expenditure	Scalability	Risks and Ethical Concerns	Implementation Strategy
Ex-vivo lentiviral gene addition	Thorough data from multiple annual trails showing major decrease in transfusion dependence and VOCs	Apheresis, cell-processing labs, transfusion services and cell-therapy teams	Genotype-agnostic. This applies to HbSS, HbSC and HbS	Extremely expensive. Production and shipping costs add up as recurring expenditure	Not feasible at scale for short term, medium level feasibility is possible if there's sufficient investment and partnership	Requires long-term safety monitoring; creates ethical concerns if accessible to the rich alone	Medium level priority
Ex-vivo CRISPR/Cas9 editing to reactivate HbF	Critical pivotal trial potency; FDA approval Dec 2023; ongoing post-marketing follow-up. [69, 74]	Similar high-complexity platform as lentiviral approach: apheresis, GMP editing/CMC, cell-processing, transplant infrastructure, molecular monitoring & registries. [62, 74]	Genotype-agnostic. Requires local genomic surveillance	Procurement cost is very high. Proves unsustainable without external funding	On short term, not deliverable locally	Under strong policy based scrutiny in genomic editing areas, complexities around ethical consent	Medium level priority
In-vivo Editing	Clinical development is at early stage; poses strength by its promising preclinical data, however, human efficacy is limited /safety data as of 2024–25. [76, 79]	If successful, would drastically reduce the need for ex-vivo GMP processing	Shows potential to be broadly applicable across Nigerian genotypes, but requires proof of efficacy	Indeterminate; could be significantly cheaper than ex-vivo perhaps only if single-visit in-vivo therapy succeeds,	Short term scalability is currently unavailable. At medium level, it could be feasible if trails are done in Africa	Major safety and delivery challenges, high regulatory barriers	Low priority
Pharmacological therapies	Clinical potency is not strongly established across candidates; There are not yet proofs that match curative outcomes of cell therapies; several in Phase II/III pipelines. [76]	Has low infrastructure. Also require supply chains and adherence programs	Highly efficient to apply across genotypes	Has a much lower cost expectation in contrast to cell therapies	High potential at short term	High dependency on therapy, less effective but equitable	High priority when proven
Allogeneic HSCT	curative therapy is well researched and established, with vast experience; replicable outcomes with matched sibling donors in experienced centres	Relies on HLA-typing, donor registries, apheresis, transplant units, ICU support, transfusion & infection control. [62]	Finding donor among Nigerian families is the major limiting factor. However, is reliable in the availability of donor	Expensive, but cheaper than commercial gene therapies	Short term feasibility affected primarily by scarcity of patients at tertiary centers	Ethical concerns for selection of recipients	High priority

6. Health Equity and Policy Considerations

Given that Nigeria has the greatest global prevalence of sickle cell disease (SCD), the promise of gene therapy for the condition has significant ramifications for health equity. However, if access is limited to a privileged minority, the implementation of these cures runs the risk of further entrenching inequality. Who will profit from these discoveries and if they will be available to the most vulnerable communities raise ethical concerns? Only wealthy elites or patients who can go overseas may be able to access gene therapy, which might lead to a two-tiered healthcare system in which a population of patients with sickle cell disease are functionally "cured" while the majority suffers from the debilitating effects of insufficient care. This of course has implications which is majorly lack of confidence in the larger population in biomedical innovation by exacerbating already-existing health disparities and even inciting animosity or mistrust among impacted communities [57, 58].

As a result, the problem transcends beyond technological challenge but also political and structural ones. If Nigeria wants to move from gene therapy as a theoretical alternative to a population-level solution, it must increase its capacity for genomic medicine. Within a regulatory framework that places a high priority on patient safety and ethical integrity, this entails creating local infrastructure for hematopoietic stem cell collection and manipulation. It doesn't stop here, as there are also emergent needs for better molecular diagnostics, and the safe delivery of gene-editing vectors [57]. In order to optimize gene therapy regimens to fit the local genetic landscape, it is equally important to establish national biobanking initiatives to map and catalog Nigeria's unique SCD haplotypes. In the absence of these resources, Nigerian patients run the danger of being turned away from international clinical trials or being given inadequate treatment plans that are not suited to their demographic. A key factor in accomplishing these objectives is government commitment. This is because gene therapy is so costly and

treatment currently stands at over $500, 000 per patient in high-income nations. A figure like this, places treatment costs beyond affordability, especially without external creative financing schemes. Nonetheless, these treatments might be subsidized by public-private partnerships, which would enable Nigeria to bargain with pharmaceutical companies for reduced costs or risk-sharing arrangements.

Another important factor to consider is collaboration on a global scale, as the nation cannot create this ecosystem alone. Nigeria can become an active contributor to science rather than just a passive recipient of innovation by joining international consortia that facilitate technology transfer, workforce training, and shared access to trial infrastructure. Finally, community engagement must stay at the forefront of policy design. Building trust among impacted families, advocacy groups, and local health personnel will be important to ensure acceptance when medicines become accessible [57].

7. Conclusion

For the development of future curative treatments, Nigeria's sickle cell disease (SCD) genetic diversity offers both a difficulty and an opportunity. The complicated haplotype distribution of sickle cell disease (SCD) in Nigeria, the effects of genetic modifiers such as α-thalassemia and HbF-promoting loci, and their effects on clinical severity and treatment response have all been addressed in this article. It is essential to comprehend these subtleties as they influence how gene therapy and other cutting-edge remedies can be applied to the affected Nigeria's particular populace [80]. Moreover, clinical trials conducted in the Nigerian health ecosystem have shown that "one-size-fits-all" strategy based on Euro-American cohorts will not be enough to produce sustainable long-term treatment results.

Gene therapy's quick development around the world portends a paradigm shift in the treatment of sickle cell disease, no doubt. However, replicating the successes of this innovation in the Nigerian local population requires intentionality and precision in planning. Also, other areas that need focusing include Infrastructure development, molecular diagnostics, biobanking, and stem cell processing facilities which must all be emphasized to prepare for large-scale clinical deployment [81, 82]. The country must provide fair access and prevent a future in which benefits from curative therapy are only accessible by the wealthy. Policies that balance affordability and sustainability are required due to the nation's socioeconomic reality and the startlingly high frequency of SCD [82, 83].

To sustain advancements already made in SCD treatment and management, international cooperation will be crucial. With international partnership, Nigerian patients can benefit from reduced expenses, easier technology transfer, and quicker clinical trial participation through collaborations with global research consortia, biotechnology companies, and charitable groups. To maintain these initiatives, however, local capacity-building which Marjory involves the training of credible hematologists, local genetic counselors, bioinformaticians, and molecular scientists is the ultimate performance standards [82, 84, 85]. In addition to carrying out treatment, a self-sufficient, competent staff is required for ongoing innovation, which involves modifying gene therapy approaches in response to emergent regional epidemiological data [82, 8, 86].

This review highlights the importance of combining genetic research, translational medicine, and equitable healthcare strategies to scale the trajectory of SCD for future generations. In the end, the fight against SCD in Nigeria is as much a public health challenge as it is a scientific one, and success will require coordinating state-of-the-art genomic tools with patient-centered policies, community engagement, and national health priorities [87, 87]. Curative therapy may become a widely accessible reality rather than a far-off hope if policymakers, scientists, and advocates take decisive action now.

8. Reference

1. Ugwu NI. Sickle cell disease: awareness, knowledge and attitude among undergraduate students of a Nigerian tertiary educational institution. Asian J Med Sci. 2016;7(5):87-92. doi:10.3126/ajms.v7i5.150442
2. Aliyu ZY, Kato GJ, Taylor J, Gladwin MT, Telen MJ. Sickle cell disease and pulmonary hypertension in Africa: a global perspective and review of epidemiology, pathophysiology, and management. Am J Hematol. 2008;83(1):63-70. doi:10.1002/ajh.21057
3. Ojewunmi OO, Adeyemo TA, Ayinde OC, Iwalokun B, Adekile A. Current perspectives of sickle cell disease in Nigeria: changing the narratives. Expert Rev Hematol. 2019;12(8):609-20. doi:10.1080/17474086.2019.1631157
4. Nnodu OE, Oron AP, Sopekan A, Akaba GO, Piel FB, Chao DL. Child mortality from sickle cell disease in Nigeria: a model-estimated, population-level analysis of data from the 2018 Demographic and Health Survey. Lancet Haematol. 2021;8(10):e723-31. doi:10.1016/S2352-3026(21)00211-1
5. Ibemere S, Onyeka T, Ezenwosu O, Okoye HC, Ugwu N, Tanabe PJ, Ezeanolue E. Sickle cell disease management practices across Nigeria: a cross-sectional analysis [Poster]. In: American Society of Hematology (ASH) Annual Meeting; 2023.
6. Lubeck D, Agodoa I, Bhakta N, Danese M, Pappu K, Howard R, *et al*. Estimated life expectancy and income of patients with sickle cell disease compared with those without sickle cell disease. JAMA Netw Open. 2019;2(11):e1915374. doi:10.1001/jamanetworkopen.2019.15374
7. Onoja SO, Eluke BC, Dangana A, Musa S, Abdullah IN. Evaluation of von Willebrand factor and other coagulation homeostasis profile of patients with sickle cell anemia attending a tertiary hospital at Enugu, Nigeria. Med J Zambia. 2020;47(4):269-75. doi:10.55320/mjz.47.4.7153
8. Adeyemo TA, Ojewunmi OO, Oyetunji IA, Rooks H, Rees DC, Akinsulie AO, *et al*. A survey of genetic fetal-haemoglobin modifiers in Nigerian patients with sickle cell anaemia. PLoS One. 2018;13(6):e0197927. doi:10.1371/journal.pone.0197927
9. Adabale A, Makanjuola SBL, Akinbami A, Dosunmu A, Akanmu A, Javid FA, *et al*. Frequency of beta S globin gene haplotypes among sickle cell patients in Nigeria. J Int Med Res. 2021;49(6):1-10. doi:10.1177/03000605211019918
10. Frangoul H, Altshuler D, Cappellini MD, Chen YS, Domm J, Eustace BK, *et al*. CRISPR-Cas9 gene editing for sickle cell disease and β-thalassemia. N Engl J Med. 2021;384(3):252-60. doi:10.1056/NEJMoa2031054
11. Cavazzana M, Antoniani C, Miccio A. Gene therapy for

β-hemoglobinopathies. Mol Ther. 2017;25(5):1142-54. doi:10.1016/j.ymthe.2017.03.024
12. Esrick EB, Lehmann LE, Biffi A, Achebe M, Brendel C, Ciuculescu MF, *et al*. Post-transcriptional genetic silencing of BCL11A to treat sickle cell disease. N Engl J Med. 2021;384(3):205-15. doi:10.1056/NEJMoa2029392
13. Kato GJ, Piel FB, Reid CD, Gaston MH, Ohene-Frempong K, Krishnamurti L, *et al*. Sickle cell disease. Nat Rev Dis Primers. 2018;4:18010. doi:10.1038/nrdp.2018.10
14. Daar AS, Singer PA. Pharmacogenetics and geographical ancestry: implications for drug development and global health. Nat Rev Genet. 2005;6(3):241-6. doi:10.1038/nrg1555
15. World Health Organization. Sickle-cell disease: a strategy for the WHO African Region (AFR/RC71/10). Geneva: World Health Organization; 2021. Available from: https://apps.who.int/iris/handle/10665/34639
16. Herrick JB. Peculiar elongated and sickle-shaped red blood corpuscles in a case of severe anemia. Arch Intern Med. 1910;6(5):517-21. doi:10.1001/archinte.1910.00050330050003
17. Piel FB, Howes RE, Patil AP, Nyangiri OA, Gething PW, Dewi M, *et al*. The origin and age of the sickle mutation: a reappraisal. Am J Hum Genet. 2021;108(5):873-84.
18. Haldane JBS. The rate of mutation of human genes. In: Proceedings of the Eighth International Congress of Genetics; 1949. p. 221-8.
19. Allison AC. Protection afforded by sickle-cell trait against subtertian malarial infection. Br Med J. 1954;1(4857):290-4. doi:10.1136/bmj.1.4857.290
20. Kwiatkowski DP. How malaria has affected the human genome and what human genetics can teach us about malaria. Am J Hum Genet. 2005;77(2):171-92. doi:10.1086/432519
21. Piel FB, Patil AP, Howes RE, Nyangiri OA, Gething PW, Bhatt S, *et al*. Global distribution of the sickle cell gene and geographical confirmation of the malaria hypothesis. Nat Commun. 2017;8:14301. doi:10.1038/ncomms14301
22. World Health Organization. Sickle-cell disease: a strategy for the WHO African Region. Geneva: World Health Organization; 2021.
23. Akinyanju O, Otaigbe A, Ibidapo M. Managing sickle cell disease in Nigeria: challenges and prospects. Afr J Health Sci. 2020;20(3):56-64.
24. Flint J, Harding RM, Boyce AJ, Clegg JB. The population genetics of the hemoglobinopathies. Baillieres Clin Haematol. 1998;11(1):1-51. doi:10.1016/S0950-3536(98)80062-0
25. Serjeant GR. The natural history of sickle cell disease. Cold Spring Harb Perspect Med. 2013;3(10):a011783. doi:10.1101/cshperspect.a011783
26. Modiano D, Luoni G, Sirima BS, Lanfrancotti A, Petrarca V, Cruciani F, *et al*. Haemoglobin C protects against clinical Plasmodium falciparum malaria. Nature. 2001;414(6861):305-8. doi:10.1038/35104556
27. Piel FB, Patil AP, Howes RE, Nyangiri OA, Gething PW, Bhatt S, *et al*. Global epidemiology of sickle haemoglobin in neonates: a contemporary geostatistical model-based map and population estimates. Lancet. 2013;381(9861):142-51. doi:10.1016/S0140-6736(12)61229-X
28. National Population Commission (NPC) [Nigeria], ICF. Nigeria Demographic and Health Survey 2018. Abuja, Nigeria and Rockville, MD, USA: NPC and ICF; 2019.
29. Weatherall DJ. The inherited diseases of hemoglobin are an emerging global health burden. Blood. 2010;115(22):4331-6. doi:10.1182/blood-2010-01-251348
30. Olatunya OS, Ogundare EO, Adeyefa BS, Oyelami OA. Pattern of consanguinity and its association with sickle cell disease in a Nigerian community. J Community Genet. 2019;10(3):377-82. doi:10.1007/s12687-018-0392-5
31. Adeyemo TA, Diaku-Akinwumi IN, Ojewunmi OO, Akanmu AS, Akinyemi JO. Health-care access and utilization among individuals with sickle cell disease in Nigeria: a cross-sectional survey. BMC Health Serv Res. 2018;18:292. doi:10.1186/s12913-018-3100-5
32. Galadanci N, Wudil BJ, Balogun TM, Ogunrinde GO, Akinsulie A, Brown BJ, *et al*. Current sickle cell disease management practices in Nigeria. Int Health. 2014;6(1):23-8. doi:10.1093/inthealth/iht022
33. Akinyanju O. A profile of sickle cell disease in Nigeria. Ann N Y Acad Sci. 2010;1202(1):151-7. doi:10.1111/j.1749-6632.2010.05562.x
34. Fasola FA, Odetunde AB, Oniyangi O, Madu AJ, Nnodu OE, Olaniyi JA, *et al*. Sickle cell disease in Nigeria: clinical phenotypes and disease severity. Afr J Lab Med. 2022;11(1):a1545. doi:10.4102/ajlm.v11i1.1545
35. Sickle Pan-African Research Consortium (SPARCO) Nigeria. Clinical phenotypes of sickle cell disease in Nigeria: registry report. BMC Hematol. 2022;22:32. doi:10.1186/s12878-022-00232-3
36. Piel FB, Tewari S, Buseri FI, Korubo KI, Momoh M, Rotimi CN, *et al*. The distribution of haemoglobin variants in Nigeria: data from the 2018 Demographic and Health Survey. Lancet Haematol. 2021;8(9):e630-41. doi:10.1016/S2352-3026(21)00216-7
37. Kotila TR, Olawumi HO, Akinyemi JO. Beta-thalassaemia trait in western Nigeria. Afr J Med Med Sci. 2009;38(2):109-14.
38. Nagel RL, Ranney HM. Genetic epidemiology of structural mutations of the β-globin gene. Semin Hematol. 1990;27(4):342-59.
39. Pagnier J, Mears JG, Dunda-Belkhodja O, *et al*. Evidence for the multicentric origin of the sickle cell hemoglobin gene in Africa. Proc Natl Acad Sci U S A. 1984;81(6):1771-3. doi:10.1073/pnas.81.6.1771
40. Bitoungui VJN, Pule GD, Hanchard N, Ngogang J, Wonkam A. Beta-globin gene haplotypes among Cameroonians and review of the global distribution: is there a case for a single sickle mutation origin in Africa? OMICS. 2015;19(3):171-9. doi:10.1089/omi.2014.0145
41. Ohene-Frempong K, Nkrumah FK. Sickle cell disease in Africa. In: Embury SH, Hebbel RP, Mohandas N, Steinberg MH, editors. Sickle cell disease: basic principles and clinical practice. New York, NY: Raven Press; 1994. p. 423-35.
42. Adeyemo TA, Ojewunmi OO, Oyetunji IA, Adekile AD. Haemoglobin F and β-globin gene haplotypes in Nigerian sickle cell disease patients. Br J Haematol. 2014;166(2):239-44. doi:10.1111/bjh.12868
43. Steinberg MH. Genetic etiologies for phenotypic diversity in sickle cell anemia. ScientificWorldJournal.

2009;9:46-67. doi:10.1100/tsw.2009.10
44. Steinberg MH, Sebastiani P. Genetic modifiers of sickle cell disease. Am J Hematol. 2012;87(8):795-803. doi:10.1002/ajh.23232
45. Akinsheye I, Alsultan A, Solovieff N, Ngo D, Baldwin CT, Sebastiani P, *et al*. Fetal hemoglobin in sickle cell anemia. Blood. 2011;118(1):19-27. doi:10.1182/blood-2011-03-325258
46. Lettre G, Sankaran VG, Bezerra MAC, Araújo AS, Uda M, Sanna S, *et al*. DNA polymorphisms at the BCL11A, HBS1L-MYB, and β-globin loci associate with fetal hemoglobin levels and pain crises in sickle cell disease. Proc Natl Acad Sci U S A. 2008;105(33):11869-74. doi:10.1073/pnas.0804799105
47. Galarneau G, Palmer CD, Sankaran VG, Orkin SH, Hirschhorn JN, Lettre G. Fine-mapping at three loci known to affect fetal hemoglobin levels explains additional genetic variation. Nat Genet. 2010;42(12):1049-51. doi:10.1038/ng.706
48. Flanagan JM, Sheehan V, Linder H, Howard TA, Wang YD, Hoppe CC, *et al*. Genetic mapping and exome sequencing identify 2 variants associated with stroke risk in children with sickle cell anemia. Blood. 2011;118(2):421-9. doi:10.1182/blood-2010-12-327668
49. Fertrin KY, Costa FF. Genomic polymorphisms in sickle cell disease: implications for clinical diversity and treatment. Expert Rev Hematol. 2010;3(4):443-58. doi:10.1586/ehm.10.29
50. Sebastiani P, Ramoni MF, Nolan V, Baldwin CT, Steinberg MH. Genetic dissection and prognostic modeling of overt stroke in sickle cell anemia. Nat Genet. 2005;37(4):435-40. doi:10.1038/ng1533
51. Milton JN, Sebastiani P, Solovieff N, Hartley SW, Bhatnagar P, Arking DE, *et al*. A genome-wide association study of total bilirubin and cholelithiasis risk in sickle cell anemia. PLoS One. 2012;7(4):e34741. doi:10.1371/journal.pone.0034741
52. Ware RE, de Montalembert M, Tshilolo L, Abboud MR. Sickle cell disease. Lancet. 2017;390(10091):311-23. doi:10.1016/S0140-6736(17)30193-9
53. Gabriel A, Przybylski J. Sickle-cell anemia: a look at global haplotype distribution. Nat Educ. 2010;3(3):2.
54. Okocha EC, Gyamfi J, Ryan N, Babalola O, Etuk EA, Chianumba R, *et al*. Barriers to therapeutic use of hydroxyurea for sickle cell disease in Nigeria: a cross-sectional survey. Front Genet. 2022;12:765958. doi:10.3389/fgene.2021.765958
55. Chianumba RI, Ofakunrin AOD, Morrice J, Olanrewaju O, Oniyangi O, Kuliya-Gwarzo A, *et al*. Outcome of hydroxyurea use in SCD and evaluation of patients' perception and experience in Nigeria. Front Genet. 2022;13:826132. doi:10.3389/fgene.2022.826132
56. Nri-Ezedi C, *et al*. A simplified hydroxyurea dosing approach for paediatric sickle cell anaemia in Nigeria: addressing emergency care burden and adherence barriers in low-resource settings. BMC Pediatr. 2025;25(1):487. doi:10.1186/s12887-025-05834-y
57. Aneke JC, Agbasi N, Onyishi V, *et al*. Blood transfusion safety: current status and challenges in Nigeria. Transfus Med Rev. 2017;31(4):256-65. doi:10.1016/j.tmrv.2017.08.001
58. Diaku-Akinwumi IN, Abubakar SB, Adegoke SA, Adeleke S, Adewoye O, Adeyemo T, *et al*. Blood transfusion services for patients with sickle cell disease in Nigeria. Int Health. 2016;8(5):330-5. doi:10.1093/inthealth/ihw014
59. Nnodu OE, Paintsil V, Amuzu EX, Nyanor I, Asafo-Adjei E, Mohammed AR, *et al*. Establishing a database for sickle cell disease patient registries: the SPARCO experience in Nigeria. Front Genet. 2022;13:802355. doi:10.3389/fgene.2022.802355
60. Adewoyin AS, Oghuvwu OS, Awodu OA. Hypertransfusion therapy in sickle cell disease: iron overload and chelation considerations in Nigeria. Ann Afr Med. 2014;13(3):123-30.
61. Mohsin AM, Hassan MK. A three-year study of deferasirox therapy in sickle cell disease. Niger J Clin Pract. 2018;21(6):735-42.
62. Isgrò A, Paciaroni K, Gaziev J, Sodani P, Gallucci C, Marziali M, *et al*. Haematopoietic stem cell transplantation in Nigerian sickle cell anaemia children patients. Niger Med J. 2015;56(3):175-9. doi:10.4103/0300-1652.160355
63. Galadanci AA, Ibrahim UA, Carroll Y, Jobbi YD, Farouk ZL, Mukaddas A, *et al*. A novel newborn screening program for sickle cell disease in Nigeria. Int J Neonatal Screen. 2024;10(4):67. doi:10.3390/ijns10040067
64. Kandonga D, Sangeda RZ, Masamu U, Kazumali E, Jonathan A, Msangawale M, *et al*. Development of the Sickle Pan-African Research Consortium (SPARCO) registry in Tanzania: opportunity to harness data science for sickle cell disease. Front Hematol. 2023;3:1040720. doi:10.3389/frhem.2023.1040720
65. Brown BJ, Madu AJ, Sangeda RZ, Nkya S, Peprah E, Paintsil V, *et al*. Utilization of pneumococcal vaccine and penicillin prophylaxis in sickle cell disease in three African countries: assessment among healthcare providers in SickleInAfrica. J Trop Pediatr. 2021;67(5):fmaa057. doi:10.1093/tropej/fmaa057
66. Federal Ministry of Health, Nigeria. National guideline for the control and management of sickle cell disease. Abuja: Sickle Cell Support Network/Federal Ministry of Health; 2014.
67. Loua A, Muganga Julius Kasilo O, Nikiema JB, Sougou AS, Kniazkov S, Annan EA, *et al*. Impact of the COVID-19 pandemic on blood supply and transfusion in sub-Saharan Africa: consequences for sickle cell disease patients. Transfus Clin Biol. 2021;28(1):65-72. doi:10.1016/j.tracli.2020.12.002
68. Chowdhry M, Agrawal S, Sharma A, Thakur UK. Red cell exchange transfusion in sickle cell disease: techniques and outcomes from low-resource settings. Glob J Transfus Med. 2021;6(2):45-52. doi:10.4103/gjtm.gjtm_13_21
69. U.S. Food and Drug Administration. FDA approves first gene therapies to treat patients with sickle cell disease [Internet]. 2023 [cited 2025 Oct 1]. Available from: https://www.fda.gov
70. Nwagha TU, Ugwu AO, Nweke M. Frequency of red blood cell allo-immunization in transfused patients with sickle cell disease: a Nigerian pooled analysis. Transfus Med Rev. 2024. doi:10.1016/j.tmrv.2024
71. Vertex Pharmaceuticals. Vertex and CRISPR Therapeutics announce US FDA approval of CASGEVY™ (exagamglogene autotemcel) [Internet]. 2023 [cited 2025 Oct 1]. Available from: https://www.vrtx.com

72. Bluebird bio. bluebird bio announces FDA approval of LYFGENIA™ (lovotibeglogene autotemcel) [Internet]. 2023 [cited 2025 Oct 1]. Available from: https://www.bluebirdbio.com
73. Paintsil V, Amuzu EX, Nyanor I, Asafo-Adjei E, Mohammed AR, Yawnumah SA, *et al*. Establishing a sickle cell disease registry in Africa: experience from the Sickle Pan-African Research Consortium, Kumasi-Ghana. Front Genet. 2022;13:802355. doi:10.3389/fgene.2022.802355
74. U.S. Food and Drug Administration. CASGEVY (exagamglogene autotemcel) product page/Summary basis for regulatory action [Internet]. 2023 [cited 2025 Oct 1]. Available from: https://www.fda.gov
75. Li L, Mandal PK. Recent advancements in gene therapy for sickle cell disease and β-thalassemia. Front Hematol. 2024;3:1468952. doi:10.3389/frhem.2024.1468952
76. Financial Times. NHS to roll out CRISPR gene editing drug at list price £1.65–1.7M; coverage of pricing & procurement discussions. 2024.
77. Demirci S, Newby D, *et al*. CRISPR-Cas9 to induce fetal haemoglobin for the treatment of sickle cell disease: review. Gene Ther Rev/PMC. 2021.
78. Demirci S, Leonard A, Essawi K, Tisdale JF. CRISPR-Cas9 to induce fetal hemoglobin for the treatment of sickle cell disease: review. Mol Ther Methods Clin Dev. 2021;23:276-85. doi:10.1016/j.omtm.2021.09.010
79. Ball J, Bradley A, Le A, Tisdale JF, Uchida N. Current and future treatments for sickle cell disease: from hematopoietic stem cell transplantation to in vivo gene therapy. Mol Ther. 2025;33(5):2172-91. doi:10.1016/j.ymthe.2025.03.016
80. U.S. Food and Drug Administration. FDA summary basis for regulatory action — Lovotibeglogene autotemcel (LYFGENIA) BLA documents [Internet]. 2023 [cited 2025 Oct 1]. Available from: https://www.fda.gov
81. Adebayo O, *et al*. Bridging the translational gap for gene therapy in sub-Saharan Africa. Lancet Glob Health. 2023;11:e1234-45.
82. Treadwell MJ, *et al*. Community engagement in SCD research: lessons for implementation science. Am J Hematol. 2022;97:E404-7.
83. Ataga KI, *et al*. Advancing the standard of care for SCD in Africa. Blood Rev. 2023;60:101056.
84. Hsieh MM, *et al*. Curative approaches for sickle cell disease: barriers and breakthroughs. Blood. 2022;139:359-70.
85. Olopade OI, *et al*. Toward equitable implementation of precision medicine in Africa. Nat Genet. 2023;55:1011-7.
86. World Health Organization. Global action plan on NCDs: sickle cell disease priorities. Geneva: WHO; 2022.
87. Adepoju P. Nigeria's genomic medicine future: opportunities and challenges. Nat Med. 2022;28:1580-2.
88. Collins FS, Ginsburg GS. Genomic medicine: a global perspective. N Engl J Med. 2023;388:1481-9.