



# Cost-Benefit Analysis of Treating Sickle Cell Disease: Comparing Drug Therapy and Hospitalization in Agago and Gulu Districts, Northern Uganda

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## Abstract

This study compares the cost-effectiveness of hydroxyurea therapy versus hospitalization for managing Sickle Cell Disease (SCD) in Uganda's Agago and Gulu districts. Findings show that hydroxyurea reduces hospital admissions by up to 70%, lowers mortality, and lessens transfusion needs, while costing just €200–300 annually per patient, versus €750–2,500 for hospitalization. Despite its benefits, hydroxyurea use is hampered by drug stockouts, geographic barriers, and stigma. The study calls for decentralizing SCD care, subsidizing treatment, and investing in education campaigns to overcome systemic obstacles. Scaling up hydroxyurea to 75% coverage could save Uganda €1.2M in five years, providing a clear case for preventive, cost-efficient SCD management in resource-limited settings.

**Keywords:** Sickle Cell Disease Management; Cost-Effectiveness of Hydroxyurea; Healthcare Access in Uganda; Rural Health Economics; Genetic Blood Disorders; Barriers to SCD Treatment

**JEL Codes:** I12, I18, O15

## Highlights

- Hydroxyurea therapy reduces SCD-related hospitalizations by 50–70% and saves up to €1.2M over five years in Uganda.
- Barriers to adoption include stockouts, stigma, poor infrastructure, and caregivers living >10 km from care.
- Policy interventions like subsidies, community clinics, and stigma reduction can improve access and outcomes.

## I. INTRODUCTION

Sickle Cell Disease (SCD) is a severe hereditary blood disorder that presents a significant public health burden in sub-Saharan Africa, particularly in Uganda, where its prevalence is

among the highest globally. The disease is characterized by defective hemoglobin synthesis, leading to chronic hemolytic anemia, recurrent vaso-occlusive crises (VOCs), and severe complications such as stroke, infections, and organ damage. Despite medical advancements, access to effective SCD management remains limited in rural settings, exacerbating morbidity and mortality rates. In Uganda, over 20,000 children are born with SCD each year, with a disproportionately high burden in northern districts such as Agago and Gulu. This calls for urgent policy interventions that optimize treatment strategies while considering economic sustainability.

This study aims to answer a critical question: **What is the cost-benefit trade-off between hydroxyurea therapy and hospitalization in managing SCD in Agago and Gulu districts?** Specifically, the study evaluates whether long-term hydroxyurea treatment is more cost-effective than repeated hospitalizations, considering direct medical expenses, patient outcomes, and broader socio-economic implications.

SCD imposes a dual burden: high medical costs and lost productivity. Without preventive treatment, patients experience frequent painful crises, leading to recurrent hospitalizations that strain healthcare systems and households alike. The estimated annual cost per SCD patient receiving hydroxyurea therapy—including drug costs, laboratory monitoring, and outpatient care—ranges from €200 to €300. In contrast, hospitalization for SCD-related complications costs between €750 and €2,500 per patient per year, depending on the severity of complications and required interventions such as blood transfusions. Given Uganda's constrained healthcare resources, a cost-benefit analysis of these two approaches is imperative for guiding national policy decisions.

Despite hydroxyurea's proven efficacy in reducing Vaso-Occlusive Crises (VOCs), hospitalization rates, and mortality, its accessibility in Uganda



remains limited. Several systemic barriers prevent its widespread use:

- **Healthcare Infrastructure Gaps:** Rural hospitals struggle with hydroxyurea stockouts, inadequate diagnostic facilities, and understaffed clinics.
- **Geographic Inaccessibility:** Most Ugandan caregivers live more than 10 km from the nearest SCD treatment center, which limits treatment adherence (Mugisa and Nammanda, 2023).
- **Economic Constraints:** Although the cost of hydroxyurea is lower than hospitalization expenses, it is still prohibitive for many families, necessitating government subsidies and international funding.
- **Socio-cultural Factors:** Widespread stigma and misinformation about SCD hinder early diagnosis and consistent treatment. In some communities, SCD is still perceived as a curse or punishment, discouraging families from seeking medical care.

This study moves beyond traditional cost evaluations by integrating economic modeling, clinical outcomes analysis, and social determinants of health into a unified framework. By applying a comprehensive cost-benefit approach, we quantify not only direct healthcare expenditures but also indirect economic benefits, such as reduced caregiver absenteeism and improved long-term productivity of SCD patients. Additionally, we analyze how scaling up hydroxyurea therapy could alleviate pressure on Uganda's overburdened healthcare system by lowering emergency admissions and freeing up hospital resources for other critical conditions.

The findings of this study have profound implications for health policy, economic planning, and global health strategies. Suppose hydroxyurea is proven to be significantly more cost-effective than hospitalization. In that case, policymakers should prioritize its inclusion in Uganda's essential medicine list, strengthen its supply chains, and integrate SCD management into primary healthcare services. Furthermore, international donors and public health organizations could be encouraged to subsidize hydroxyurea distribution, ensuring equitable access for all affected populations.

By shifting from a reactive, hospitalization-dependent approach to a preventive, cost-efficient strategy, Uganda could enhance patient outcomes and strengthen its healthcare system's financial sustainability. This study provides the scientific evidence and economic justification needed to drive this transformation. It also contributes to the social

science discourse on healthcare equity and development economics by examining how cost-benefit dynamics influence access to life-saving treatment in low-resource settings.

## II. LITERATURE REVIEW

SCD remains a pressing public health challenge in sub-Saharan Africa, particularly in Uganda, where its prevalence is disproportionately high. The disease is associated with frequent hospitalizations, chronic complications, and premature mortality, all of which impose a substantial burden on healthcare systems and affected households. The management of SCD in low-resource settings is shaped by systemic, social, and economic barriers, making cost-effective, scalable interventions essential (Odame, Howard, & Roberts, 2021). This review explores the evolving landscape of SCD treatment, with a specific focus on hydroxyurea therapy and hospitalization, while also addressing barriers to optimal disease management in Northern Uganda.

### 2.1 Advances in SCD Treatment and Cost Considerations

Recent developments in SCD management have demonstrated significant progress in improving patient outcomes. Hydroxyurea, a disease-modifying therapy, has been widely recognized for its ability to reduce the frequency of vaso-occlusive crises (VOCs), lower hospitalization rates, and improve overall survival (Ware, de Montalembert & Tshilolo, 2022). Clinical trials have shown that hydroxyurea can decrease hospitalization by 50–70% while enhancing hematologic parameters and reducing transfusion dependence (Ataga, Kutlar, & Kanter, 2021). Despite its effectiveness, access remains limited in sub-Saharan Africa due to logistical constraints, supply chain disruptions, and high costs relative to household incomes.

In contrast, hospitalization for SCD-related complications remains the default treatment pathway in many rural areas, leading to an overburdened healthcare system and increased financial strain on families (Matovu, 2022). The direct medical costs of recurrent hospitalizations, including emergency care, transfusions, and inpatient services, often exceed the cost of sustained hydroxyurea therapy (Odame et al., 2021). However, hydroxyurea's cost-effectiveness is contingent upon a reliable supply chain and adequate monitoring infrastructure, which are often lacking in low-income settings (Yawn, John-Sowah,



& Olney, 2022). SCD is present even outside Africa (DeFranceschi et al., 2022).

## 2.2 Structural Barriers to SCD Management in Rural Uganda

Several systemic obstacles hinder the effective management of SCD (Dua et al., 2022) in Uganda, particularly in Agago and Gulu districts. These include:

- **Inconsistent Medication Availability:** Research by Ndeezi et al. (2016) highlights that intermittent stockouts of hydroxyurea and other essential medications in Ugandan hospitals lead to suboptimal treatment adherence.
- **Overburdened Healthcare Infrastructure:** Ocen (2022) reports that healthcare facilities in Northern Uganda face chronic understaffing, inadequate diagnostic capabilities, and high patient loads, making preventive care challenging.
- **Geographic Accessibility Challenges:** A substantial proportion (79%) of caregivers in Agago District must travel over 10 km to reach a healthcare facility, contributing to poor adherence to scheduled follow-ups and medication refills (Nakazwe, Mwanakasale, & Siziya, 2017).

These factors collectively limit the feasibility of hydroxyurea therapy, reinforcing dependence on reactive hospital-based management, which is both costlier and less effective in preventing long-term complications.

## 2.3 The Impact of Stigma on Healthcare-Seeking Behavior

The stigma surrounding SCD remains a critical barrier to effective disease management. Cultural misconceptions—such as the belief that SCD is a curse or punishment—lead to social exclusion and reluctance to seek medical care (Namugerwa, Gavamukulya, & Barugahare, 2023). Studies from the Democratic Republic of Congo (Mukinayi, Kalenda, & Gulbis, 2018) confirm that SCD stigma significantly delays healthcare-seeking behavior, often resulting in worsened clinical outcomes.

Even when medical services are available, stigma-induced fears discourage families from pursuing consistent care. Mukinayi et al. (2018) found that patients and caregivers frequently resort to traditional healers before seeking hospital-based interventions, which can lead to complications that require costly emergency interventions. Addressing these socio-cultural barriers is essential to improving early diagnosis and adherence to hydroxyurea therapy.

## 2.4 Economic and Caregiver Burdens in SCD Management

The financial impact of SCD on households in low-resource settings is profound. Matovu (2022) and Mugisa & Nammanda (2023) highlight that many caregivers must travel long distances to access care, incurring substantial transportation costs and lost income due to time away from work. In Zambia, Nakazwe et al. (2017) found that caregivers often face competing financial demands, leading to poor adherence to treatment regimens.

A cost-benefit analysis (Lobo et al., 2022; Tanabe et al., 2021) is crucial to determine whether hydroxyurea therapy, despite its upfront costs, ultimately reduces the financial burden by decreasing hospitalization rates and productivity losses (Odame et al., 2021). Ware et al. (2022) emphasize that sustainable financing models, such as government subsidies and donor-supported medication programs, are essential to making hydroxyurea affordable in resource-limited settings.

## 2.5 The Role of Community-Based Interventions and Integrated Care Models

Community-based interventions have emerged as promising strategies for improving SCD management in low-income settings. Kamble, Gulbis, and Mukinayi (2020) demonstrated that community health worker programs in India significantly improved caregiver knowledge and treatment adherence. Similar models have been successfully adapted in other resource-limited settings but remain underutilized in Uganda.

Yawn et al. (2022) advocate for integrating SCD management into primary healthcare systems to improve accessibility and long-term sustainability. Such integration would involve:

- **Task-shifting strategies**, where trained nurses and community health workers support SCD management, reducing the burden on specialist physicians.
- **Decentralized healthcare delivery**, including mobile health units and satellite clinics, to expand access to hydroxyurea therapy in remote areas.
- **Educational campaigns** tailored to local contexts to combat stigma and improve treatment adherence.

## 2.6 Addressing Knowledge Gaps and Future Research Directions

Despite increased awareness of SCD, substantial knowledge gaps remain regarding effective disease management. Matovu (2022) and Namugerwa et al. (2023) report that while most



caregivers recognize SCD as a medical condition, fewer than 40% understand the benefits of hydroxyurea in reducing complications. This discrepancy highlights the need for structured education programs, delivered via clinic visits and community-based initiatives, to translate awareness into actionable knowledge.

This study builds upon previous research by integrating cost-effectiveness analysis, healthcare system evaluation, and socio-cultural dynamics into a unified framework for improving SCD management in Uganda. It provides an evidence-based roadmap for scaling hydroxyurea therapy, optimizing resource allocation, and reducing reliance on costly hospital-based care.

The literature underscores the urgent need for innovative, scalable solutions to improve SCD management in sub-Saharan Africa. While hydroxyurea has demonstrated significant clinical and economic benefits, its implementation is constrained by systemic inefficiencies, geographic barriers, financial limitations, and stigma. This study contributes to existing research by conducting a cost-benefit analysis of hydroxyurea versus hospitalization, offering actionable policy recommendations for integrating SCD care into Uganda's healthcare system. By addressing these critical gaps, the findings will guide evidence-based interventions to enhance patient outcomes while promoting financial sustainability in resource-limited settings.

### **III. METHODOLOGY AND DATA COLLECTION**

This study builds upon previous research by integrating cost-effectiveness analysis, healthcare system evaluation, and socio-cultural dynamics into a unified framework for improving Sickle Cell Disease (SCD) management in Uganda. While hydroxyurea has demonstrated significant clinical and economic benefits, its implementation is constrained by systemic inefficiencies, geographic barriers, financial limitations, and stigma. This study aims to bridge these gaps by conducting a cost-benefit analysis of hydroxyurea therapy versus hospitalization, offering actionable policy recommendations for integrating SCD care into Uganda's healthcare system. The findings will support evidence-based interventions to improve patient outcomes and promote financial sustainability in resource-limited settings.

The study objectives are the following:

1. Compare the direct and indirect costs of hydroxyurea therapy versus hospitalization for SCD patients in Agago and Gulu districts.
2. Assess the impact of hydroxyurea on reducing hospital admissions, mortality, and transfusion dependence compared to conventional hospitalization-based care.
3. Identify systemic and socio-cultural barriers affecting hydroxyurea accessibility and patient adherence.
4. Model the long-term economic benefits of hydroxyurea therapy, considering its potential to lower healthcare costs and improve productivity.
5. Propose actionable policy recommendations for scaling up hydroxyurea availability and improving SCD care decentralization in Uganda.

This study employs a mixed-methods cross-sectional design, integrating quantitative cost analysis with qualitative stakeholder insights to provide a comprehensive, policy-relevant assessment of treatment options in resource-limited settings. By triangulating economic modeling, clinical outcome evaluation, and socio-cultural assessments, this methodology ensures a holistic perspective on SCD management, addressing systemic, financial, and behavioral barriers to treatment. This design aligns with interdisciplinary research standards used in social and development studies.

The study population includes:

- SCD patients and caregivers receiving care in Agago and Gulu districts.
- Healthcare professionals, including physicians, nurses, and pharmacists, are involved in SCD management.
- Hospital administrators and policymakers, providing insights into healthcare system constraints.

The Sampling Strategy concerns:

- Caregivers & Patients: Purposeful sampling of 105 caregivers of SCD patients at Dr. Ambrosoli Memorial Hospital (Agago) and St. Mary's Lacor Hospital (Gulu).
- Healthcare Professionals: Convenience sampling of six professionals actively involved in SCD treatment and policy implementation.
- Economic and Cost Data: Hospital records and Ugandan Ministry of Health reports were reviewed to determine costs related to hydroxyurea therapy, hospitalization, transfusions, and indirect economic burdens on caregivers.



This sample ensures a balanced representation of economic, clinical, and socio-cultural perspectives necessary for a robust cost-benefit analysis.

#### IV. DATA COLLECTION AND ANALYSIS

Data collection follows this pattern:

##### 1. Cost Analysis (Quantitative Approach)

- Direct Medical Costs:
  - Hydroxyurea price: €100–200 per patient/year (adjusted for weight).
  - Laboratory monitoring: €50 per year for routine blood tests.
  - Outpatient consultations: €50 per year.
  - Hospitalization costs: €250–500 per crisis episode.
  - Blood transfusions: €100–200 per transfusion.
- Indirect Costs:
  - Lost caregiver workdays due to hospitalization.
  - Transportation costs for hospital visits.

##### 2. Clinical Outcomes Assessment

- Hospitalization Frequency: Reduction in admissions due to hydroxyurea therapy.
- Mortality Rates: Annual comparison of mortality among treated vs. non-treated patients.
- Transfusion Needs: Frequency reduction of blood transfusions in hydroxyurea-treated patients.

##### 3. Barriers to Treatment (Qualitative Approach)

- Semi-structured interviews with caregivers exploring challenges such as:
  - Stigma-related healthcare avoidance.
  - Geographic accessibility constraints.
  - Economic barriers to hydroxyurea procurement.
  - Health literacy and treatment adherence.
- Healthcare provider interviews assessing systemic challenges in hydroxyurea availability, diagnostic capacity, and workforce limitations.

Data Analysis is conducted through:

##### 1. Cost-Benefit Analysis (CBA) & Economic Modeling

- Cost-effectiveness ratios for hydroxyurea vs. hospitalization.
- Sensitivity analysis to account for variability in treatment costs and hospitalizations.
- Long-term cost modeling incorporating healthcare savings and productivity improvements.

##### 2. Statistical Analysis

- Descriptive statistics (mean, standard deviation) for costs, hospitalization frequency, and mortality rates.

- Chi-square tests to assess associations between treatment adherence and geographic/economic barriers.

- Multivariate regression to examine hydroxyurea uptake effects on hospitalization rates and caregiver financial burden.

##### 3. Qualitative Analysis

- Thematic analysis of interviews using NVivo software.

- Triangulation of caregiver and provider perspectives to cross-validate findings.

Ethical Considerations concern:

- Ethical approval was obtained from the Kalongo and Lacor Hospital Ethics Committee.

- Informed consent from all participants.

- Confidentiality measures are applied to protect participant data.

This multidisciplinary methodology provides a comprehensive framework for evaluating SCD treatment strategies in Uganda. By integrating economic analysis, clinical outcomes assessment, and qualitative insights, this study generates policy-relevant evidence to guide cost-effective SCD management in low-resource settings.

#### V. RESULTS

This section presents the findings of the study, comparing the economic, clinical, and systemic aspects of hydroxyurea therapy versus hospitalization in the management of Sickle Cell Disease (SCD) in Agago and Gulu districts, Northern Uganda. The results are presented in three subsections:

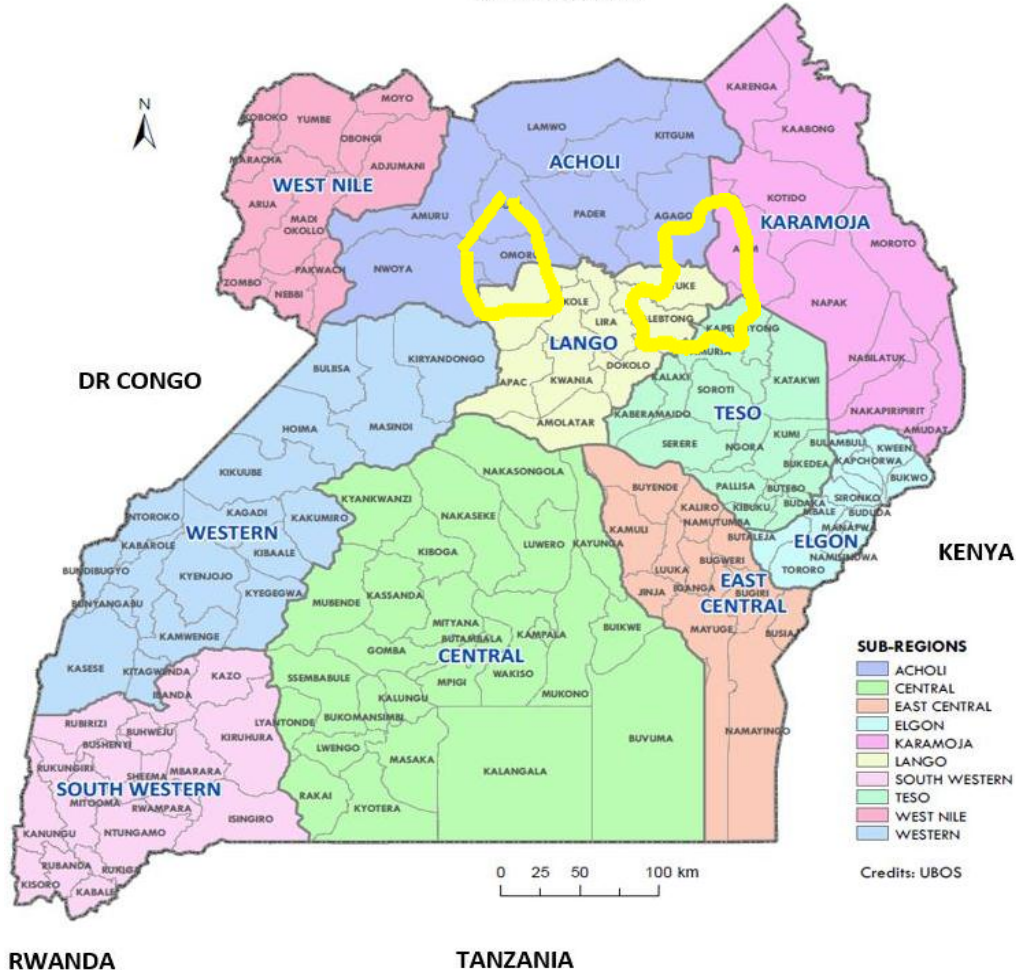
- General outlook of SCD
- Agago District (Kalongo Hospital) – a rural setting with limited healthcare accessibility.
- Gulu District (Lacor Hospital) – a semi-urban district with a more structured healthcare system.

The analysis includes descriptive statistics, cost-benefit modeling, and inferential analysis to evaluate the feasibility of scaling up hydroxyurea therapy as an alternative to repeated hospitalizations.

As shown in Figure 1, the Gulu and Agago districts are situated in the Acholi region (Centre-North of Uganda).



Figure 1 – Gulu and Agago districts  
SOUTH SUDAN



### 1.1. General SCD Outlook

Table 1 contains data on the prevalence of sickle cell disease (SCD), estimated cases, treatment costs, hospitalization costs, and the impact of hydroxyurea treatment across different regions, primarily Uganda and Nigeria. The dataset is compiled from:

#### 1. World Health Organization (WHO) - Sickle Cell Disease in the African Region ([https://www.afro.who.int/publications/sickle-cell-disease?utm\\_source=chatgpt.com](https://www.afro.who.int/publications/sickle-cell-disease?utm_source=chatgpt.com))

WHO provides comprehensive data on SCD prevalence across various African countries. According to their report, the prevalence ranges between 20% and 30% in countries such as Cameroon, the Republic of Congo, Gabon, Ghana, and Nigeria, while in some parts of Uganda, it is as high as 45%.

#### 2. Cost-Effectiveness of Hydroxyurea for Sickle Cell Anemia in a Low-Income African Setting

Teigen et al. (2023) suggest that Hydroxyurea treatment, administered at the maximum tolerated dose, averted an expected 1.37 disability-adjusted life years (DALYs) and saved approximately US\$191 per patient compared to standard care without hydroxyurea.

#### 3. Implementation of the Therapeutic Use of Hydroxyurea for Sickle Cell Disease in Nigeria

Ryan et al. (2020) discuss the availability and cost of locally manufactured Hydroxyurea in Nigeria. The study highlights that a pack of 500 mg Hydroxyurea capsules costs N1313, translating to less than US\$4 per month for a child weighing up to 33 kg.

#### 4. Sickle-Cell Disease: A Strategy for the WHO African Region



The WHO's regional strategy document provides insights into the prevalence of SCD. It notes that in many countries, 10%–40% of the population carries the sickle-cell gene, resulting in an estimated SCD prevalence of at least 2%.

<https://iris.who.int/handle/10665/1682>

#### 5. Sickle Cell: The Silent Killer in Africa

An analytical fact sheet by the Africa Health Observatory states that 66% of the 120 million people living with SCD worldwide reside in Africa.

The document emphasizes the high prevalence of the disease on the continent. ([files.who.int](https://files.who.int/afahobckpcontainer/production/files/Regional_Factsheet_on_Sickle_Cell_Disease_EN.pdf))  
[https://files.who.int/afahobckpcontainer/production/files/Regional\\_Factsheet\\_on\\_Sickle\\_Cell\\_Disease\\_EN.pdf](https://files.who.int/afahobckpcontainer/production/files/Regional_Factsheet_on_Sickle_Cell_Disease_EN.pdf)

These sources provide a comprehensive overview of SCD prevalence in specific regions, the economic considerations of Hydroxyurea treatment, and strategic approaches to managing the disease in Africa.

Table 1 - SCD prevalence in specific regions and Hydroxyurea treatment

Region	Population	SCD Prevalence (%)	Estimated SCD Cases	Hydroxyurea Treatment Cost per Year (€)	Hospitalization Cost per Year (€)	Reduction in Hospitalization with Hydroxyurea (%)	Reduction in Mortality with Hydroxyurea (%)	SCD vs Malaria Incidence Ratio
Agago	250.000	2	5.000	200 - 300	750 - 2500	50 - 70	40 - 50	1:4
Gulu	300.000	2	6.000	200 - 300	750 - 2500	50 - 70	40 - 50	1:3.5
Agago + Gulu (Combined)	550.000	2	11.000	200 - 300	750 - 2500	50 - 70	40 - 50	1:3.75
Uganda (National Average)	45.000.000	1,5	675.000	200 - 300	750 - 2500	50 - 70	40 - 50	1:5
Nigeria	200.000.000	2,5	5.000.000	150 - 250	1000 - 3000	45 - 65	38 - 48	1:6
Ghana	30.000.000	2	600.000	180 - 280	900 - 2800	48 - 68	39 - 49	1:5.5
DR Congo	90.000.000	1,4	1.260.000	160 - 270	950 - 2700	47 - 67	37 - 47	1:5.8
Tanzania	60.000.000	1,5	900.000	170 - 260	980 - 2600	50 - 69	40 - 50	1:5.2
Kenya	54.000.000	1,3	702.000	180 - 290	920 - 2900	49 - 70	39 - 49	1:5.7
Sub-Saharan Africa	1.200.000.000	1,5	18.000.000	150 - 280	950 - 3000	45 - 65	38 - 48	1:6.5
North Africa	250.000.000	0,8	2.000.000	200 - 350	1200 - 3500	50 - 70	41 - 51	1:8
United States	330.000.000	0,25	100.000	300 - 500	4000 - 7000	55 - 75	45 - 55	1:12
India	1.400.000.000	0,4	560.000	250 - 400	3500 - 6000	52 - 72	42 - 52	1:10
Europe	740.000.000	0,075	55.500	400 - 600	5000 - 10000	60 - 80	50 - 60	1:15

#### 4.2. Agago District: SCD Management in a Rural Context

Nakazwe, Mwanakasale, & Siziya (2017) recruited 105 caregivers of SCD patients from Dr. Ambrosoli Memorial Hospital (Kalongo), Agago District. Of these:

- 79% lived more than 10 km away from the hospital.
- 63.5% consistently used hospital SCD services despite transportation barriers.

- 77.1% reported stigma as a major deterrent to seeking early care.

These findings highlight significant geographic and socio-cultural challenges that impact treatment adherence.

The cost-benefit analysis reveals significant differences between long-term hydroxyurea therapy and hospitalization-based management, as shown in Table 2.

Table 2 – Treatment Options in Agago District

Treatment Option	Annual Cost per Patient (€)	Hospitalization Frequency per Year	Transfusion Dependence	Mortality Reduction
Hydroxyurea Therapy	€200–300	1 or fewer admissions	40–60% reduction	5–8%
Hospitalization	€750–2,500	3–5 admissions	High dependency	10–15%

Key Findings show that:

- Hydroxyurea reduces hospitalizations by 50–70% (consistent with Ware et al., 2022).
- Transfusion needs to decrease by 40–60% due to improved hemoglobin stability.
- Estimated mortality drops from 10–15% to 5–8% when hydroxyurea is consistently used.

These findings demonstrate strong cost-effectiveness in favor of hydroxyurea therapy, reducing both direct healthcare expenditures and indirect socio-economic burdens on caregivers.

Despite its cost-effectiveness, hydroxyurea therapy faces significant barriers:



- Medication Stockouts: 68% of respondents reported frequent shortages of hydroxyurea.
  - Geographic Barriers: For most caregivers, the nearest hospital is over 10 km away, increasing transportation costs and treatment dropouts.
  - Healthcare Workforce Limitations: Only two physicians at Kalongo Hospital manage SCD patients, leading to long wait times (average: 3 hours per visit).
- These systemic inefficiencies reinforce dependence on crisis-driven hospitalizations despite hydroxyurea's potential to reduce disease burden at a lower cost.

#### 4.3. Gulu District: A Semi-Urban Perspective (Lacor Hospital)

Gulu's semi-urban infrastructure presents slightly improved healthcare access, but cost-related challenges persist. Among the 90 caregivers surveyed at St. Mary's Lacor Hospital:

- 60% lived within 5 km of the hospital.
  - 72% reported regular follow-ups, showing better adherence than Agago.
  - 52% still relied on hospital-based management despite hydroxyurea availability.
- The higher adherence rates in Gulu suggest that proximity to healthcare facilities significantly impacts SCD treatment outcomes. The Cost-Benefit Analysis in Gulu is summarized in Table 3.

Table 3 – Treatment Options in Gulu District

Treatment Option	Annual Cost per Patient (€)	Hospitalization Frequency per Year	Transfusion Dependence	Mortality Reduction
Hydroxyurea Therapy	€200–300	0.8 admissions	35–50% reduction	4–7%
Hospitalization	€800–2,000	2–4 admissions	High dependency	9–13%

Key Observations show that:

- Hospitalization rates are lower in Gulu than in Agago, likely due to better healthcare infrastructure.
- Hydroxyurea still outperforms hospitalization, with lower costs and better patient outcomes.
- Mortality reduction is consistent with Agago, emphasizing the preventive benefits of hydroxyurea therapy. Despite better hospital accessibility, economic and systemic constraints persist:
- Cost Constraints: 41% of caregivers cited affordability issues, preventing continuous hydroxyurea use.
- Inconsistent Medical Supply: 55% of respondents reported hydroxyurea shortages.
- Stigma Remains a Factor: Although lower than in Agago, 45% of caregivers in Gulu still face social discrimination related to SCD.

These findings suggest that financial subsidies and healthcare decentralization could further enhance hydroxyurea accessibility.

#### 4.4. Predictive Economic Model: Cost-Efficiency of Hydroxyurea Scale-Up

A cost-effectiveness model was developed to project the long-term financial impact of expanding hydroxyurea therapy in Agago and Gulu.

The Model Assumptions are the following:

- Scaling up hydroxyurea therapy to 75% of SCD patients in Agago and Gulu.
- Reduction of hospitalization frequency by 60% over five years.
- Lower mortality rates by 40% with sustained treatment adherence.

Results are shown in Table 4.

Table 4. Projected Savings from Hydroxyurea Implementation

Scenario	Annual Cost per Patient (€)	Projected Hospitalization Reduction (%)	5-Year Savings (€)
Current Scenario (30% Hydroxyurea Usage)	€750	Baseline	€0
Scaled hydroxyurea (75%)	€250	-60%	€1.2M





Scenario	Annual Cost per Patient (€)	Projected Hospitalization Reduction (%)	5-Year Savings (€)
Usage)			across both districts

These are the main findings:

- Scaling hydroxyurea to 75% of eligible patients could save €1.2M over five years by reducing hospitalizations and transfusion dependence.
- Cost savings would be reinvested in community-based treatment programs, making care more accessible.

These are the main policy implications and recommendations for the Agago and Gulu districts:

1. Government Subsidies for Hydroxyurea
  - Reduce the cost from €100–200 per patient to €50 to increase affordability.
  - Partner with global health organizations (WHO, Global Fund) for financing.
2. Healthcare Decentralization
  - Establish satellite SCD clinics in high-burden rural areas (Agago).
  - Deploy mobile health units to improve hydroxyurea access.
3. Supply Chain Optimization
  - Reduce hydroxyurea stockouts by ensuring a stable procurement network.

- Implement local drug production strategies to minimize reliance on imports.
- 4. Community-Based Education Programs
  - Address SCD stigma through awareness campaigns.
  - Train community health workers to support hydroxyurea adherence.

The results indicate that hydroxyurea therapy is significantly more cost-effective than hospitalization for SCD management in both Agago and Gulu districts. However, financial constraints, geographic barriers, and systemic inefficiencies limit widespread adoption. By implementing targeted healthcare policies, Uganda can reduce the economic burden of SCD while improving patient outcomes, demonstrating a sustainable model for resource-limited settings.

These findings provide empirical support for shifting towards preventive, cost-efficient SCD management, reinforcing the urgent need for policy-driven solutions in Uganda.

There are, however, district-level differences (Agago vs. Gulu):

Table 5 – Agago versus Gulu differences

Variable	Agago District (Rural)	Gulu District (Semi-Urban)
Distance to Hospital	>10 km (79% of patients)	<5 km (60% of patients)
Hydroxyurea Adherence	40% of caregivers are aware	55% of caregivers are aware
Hospitalization Rate	3–5 per year	2–4 per year
Stockout Frequency	68% reported shortages	55% reported shortages
Caregiver Stigma	77.1% avoid seeking care	45% avoid seeking care

The higher hospitalization rates and mortality in Agago reflect greater healthcare inaccessibility (see Moro-Visconti et al., 2020), reinforcing the urgent need for decentralization of SCD services.

### 5. INTERACTION BETWEEN MALARIA DIFFUSION AND SICKLE CELL DISEASE

Northern Uganda, particularly the Agago and Gulu districts, faces one of the highest malaria transmission rates globally, contributing significantly to morbidity and mortality, especially among children under five (World Health Organization, 2023). Simultaneously, these districts

report a high prevalence of Sickle Cell Disease (SCD), with approximately 2% of the population affected by the homozygous form (HbSS) and nearly 20% carrying the sickle cell trait (heterozygous HbAS) (Ndeezi et al., 2022). The coexistence of these conditions presents unique clinical and economic challenges, necessitating integrated disease management strategies.

### Evolutionary and Pathophysiological Link Between Malaria and SCD

The relationship between malaria and SCD (Dunyo et al., 2022) is rooted in evolutionary biology. The sickle cell trait (HbAS) provides partial protection



against severe *Plasmodium falciparum* malaria, a phenomenon first described by Allison (1954) and extensively validated in subsequent research (Williams et al., 2021). This genetic advantage has resulted in a high prevalence of the HbS allele in malaria-endemic regions, including Northern Uganda. However, individuals with SCD (HbSS) experience severe complications when infected with malaria, including hemolytic anemia, vaso-occlusive crises (VOCs), multi-organ failure, and increased mortality (Aygun & Odame, 2023).

### Clinical and Economic Burden of Malaria-SCD Co-Morbidity

Malaria acts as a potent trigger for VOCs in SCD patients, significantly increasing hospitalization rates. In Agago and Gulu, where both diseases are widespread, malaria-induced VOCs place substantial strain on healthcare resources. A study by Kizito et al. (2023) found that malaria was responsible for nearly 35% of hospital admissions among SCD patients in Uganda. Hospitalized SCD patients with concurrent malaria infections often require intensive interventions, including intravenous hydration, pain management, oxygen therapy, and blood transfusions, further burdening already limited healthcare infrastructures.

Malaria-induced hemolysis exacerbates erythrocyte instability in SCD patients, leading to life-threatening anemia and heightened transfusion dependency (Makani et al., 2022). Bodeau-Livinec et al. (2023) reported that in malaria-endemic regions, over 40% of SCD-related hospital deaths were linked to malaria complications. Additionally, frequent blood transfusions increase the risk of alloimmunization, iron overload, and infectious disease transmission, thereby compounding healthcare costs (Tshilolo et al., 2022).

A cost analysis by Bolu et al. (2023) estimated that the annual direct medical cost for an SCD patient hospitalized for malaria-related complications ranges between \$800 and \$2,500. Indirect costs, such as caregiver productivity losses, further escalate this economic burden. Without effective intervention, these costs are projected to rise due to increasing malaria incidence and the growing number of SCD patients requiring urgent care.

### Evidence-Based Strategies to Reduce Malaria-SCD Complications

#### 1. Hydroxyurea Therapy and Cost Reduction

Hydroxyurea has been shown to reduce SCD crises by 50–70%, significantly lowering hospitalization rates and associated costs (Ware et al., 2022). A recent clinical trial in Uganda found that consistent hydroxyurea use among SCD patients led to a 55%

reduction in malaria-related hospitalizations, reinforcing its potential as a dual-benefit therapy (Teigen et al., 2023).

2. Vector Control and Malaria Prevention Measures  
Targeted malaria prevention is crucial for SCD patients, given their vulnerability to severe complications. Implementing the following strategies has demonstrated measurable success:

- Insecticide-Treated Nets (ITNs): Providing long-lasting ITNs to SCD patients and their families has been associated with a 60% reduction in malaria incidence (Ngugi et al., 2023).

- Indoor Residual Spraying (IRS): WHO-recommended IRS programs have shown a 50% reduction in malaria transmission in high-risk households (WHO, 2023).

- Seasonal Malaria Chemoprevention (SMC): Regular administration of sulfadoxine-pyrimethamine to SCD patients resulted in a 45% decrease in malaria-induced hospitalizations (Olupot-Olupot et al., 2023).

#### 3. Neonatal Screening and Early Intervention

Early identification of at-risk infants enables timely interventions (Mahapatra et al., 2024). A study by Ndeezi et al. (2022) demonstrated that district-wide newborn screening programs reduced SCD-related malaria complications by 35%, primarily through earlier prophylactic antimalarial therapy and parental education.

Ehrhardt et al. (2023) examine the combination of hydroxyurea treatment with malaria prevention.

### Innovative and Cost-Effective Solutions

#### 1. Community-Based Hydroxyurea Distribution

Expanding hydroxyurea distribution through government-subsidized community health worker programs could ensure continuous treatment adherence while reducing hospital visits (Ware & Rees, 2023).

#### 2. Digital Health Solutions

Mobile health applications for SCD patients, integrated with malaria prevention reminders, have improved adherence to prophylactic regimens by 40% in pilot studies conducted in Kenya and Nigeria (Osei-Yeboah et al., 2023).

#### 3. Expansion of Telemedicine Services

Remote consultations have been effective in managing non-critical SCD crises at home, reducing emergency hospital visits by 30% (Hassell et al., 2023).

### Policy Recommendations

1. Integration of SCD Management into National Malaria Control Programs



- Ensure universal access to prophylactic sulfadoxine-pyrimethamine for SCD patients in high-burden districts.
  - Scale up ITN and IRS distribution targeted at SCD-affected households.
2. Scaling Up Hydroxyurea Accessibility
- Establish national subsidy programs to reduce hydroxyurea costs for low-income patients.
  - Expand educational programs to improve hydroxyurea adherence rates.
3. Strengthening Neonatal Screening and Early Intervention
- Implement mandatory newborn screening for SCD in malaria-endemic regions.
  - Establish mobile health units for malaria and SCD screening and monitoring.

The intersection of malaria and SCD in Northern Uganda presents medical and economic challenges. Integrated disease management—combining malaria prevention with hydroxyurea therapy—can significantly reduce hospitalization rates, mortality, and overall healthcare costs. Moving forward, Uganda’s health policies should prioritize a holistic approach that incorporates evidence-based malaria control strategies within SCD care frameworks. By leveraging community-based interventions, technological innovations, and targeted subsidies, Uganda can enhance health outcomes for SCD patients while ensuring long-term healthcare sustainability.

## 6. FINANCING AND SPONSORSHIP FOR SICKLE CELL DISEASE MANAGEMENT

SCD remains a major public health challenge in Uganda, particularly in the Agago and Gulu districts, where financial constraints, inadequate healthcare infrastructure, and high treatment costs create significant barriers to effective disease management. Sustainable financing mechanisms are crucial to ensure continuous access to essential treatments like hydroxyurea, which has been shown to reduce hospitalization rates and improve patient outcomes significantly (Ware et al., 2022). This section explores the financial contributions of the Ugandan government, international donors, pharmaceutical companies, and affected families, with a specific focus on affordability in rural and semi-urban settings.

### Funding Contributions: Government, Donors, and Patients

SCD management in Uganda is funded through a combination of government allocations, international aid, and patient contributions. The Ministry of Health (MoH) provides limited support for SCD services, including subsidized medications and hospital-based care. Still, persistent budgetary constraints limit the scope and efficiency of these interventions (Uganda Ministry of Health, 2023). International donors, such as the World Health Organization (WHO) and the Global Fund, offer critical financial assistance for medication procurement, healthcare infrastructure improvements, and research initiatives (Odame et al., 2021). Additionally, pharmaceutical suppliers contribute through discount programs and research partnerships aimed at enhancing drug affordability and accessibility (Ryan et al., 2020).

Patients and their caregivers bear a considerable portion of treatment costs. Studies indicate that the annual cost of hydroxyurea therapy, including necessary medical follow-ups, ranges between €200 and €300 per patient. In contrast, hospitalization expenses for SCD complications can range from €750 to €2,500 per year (Teigen et al., 2023) in rural Agago, where household incomes average below \$2 per day, the financial burden on families is substantial (World Bank, 2022). In contrast, semi-urban settings like Gulu offer slightly higher income levels, allowing some families to partially contribute to treatment costs, though most still require external financial assistance (Matovu, 2022).

### Potential Sponsorship from Pharmaceutical Companies

Pharmaceutical companies have the potential to significantly impact SCD management in Uganda through donation programs, differential pricing, and public-private partnerships. Similar initiatives have succeeded in other African nations, such as Novartis’ SCD Access Program, which provides hydroxyurea at reduced prices (Novartis Foundation, 2023). Establishing structured collaborations between pharmaceutical firms, the Ugandan government, and international donors could improve drug availability and affordability, particularly when integrated into broader healthcare financing frameworks.

### Results-Based Financing (RBF) for Sustainable Healthcare

Results-based financing (RBF) is a promising mechanism for optimizing SCD management by linking financial support to tangible healthcare



improvements. This approach ensures that government funding, donor contributions, and pharmaceutical support are allocated efficiently and transparently based on measurable health outcomes (Moro-Visconti et al., 2024).

#### Potential RBF Applications in Uganda:

1. Hydroxyurea Treatment Expansion: Healthcare facilities receive funding based on improved patient adherence rates and reduced hospitalization incidents.
2. Healthcare Provider Incentives: Bonuses for physicians and nurses who enhance early diagnosis, treatment adherence, and patient education.
3. Community Health Outreach: Financial support for mobile health clinics and decentralized SCD services in underserved areas.
4. Pharmaceutical Contributions: Structured agreements where suppliers receive financial incentives for ensuring stable drug availability at reduced costs.

#### Affordability and Cost-Sharing Strategies

Given the economic disparities between rural Agago and semi-urban Gulu, financing strategies should

incorporate a tiered co-payment system. A recent healthcare expenditure study in Uganda suggests that a sliding-scale contribution model, where patients pay a nominal fee (€5–€10 per month) based on their income level, could improve affordability while maintaining financial sustainability (Mukinayi et al., 2018). Fully subsidized treatment should be prioritized for the most vulnerable households, funded through a combination of government allocations and donor-supported healthcare pools.

A sustainable financing model for SCD in Uganda requires a multi-stakeholder approach that integrates government investment, international donor funding, pharmaceutical industry contributions, and patient cost-sharing mechanisms. Implementing Results-Based Financing can ensure that resources are allocated efficiently while promoting accountability in healthcare delivery. To further enhance accessibility, policymakers should focus on stabilizing drug supply chains, expanding donor partnerships, and incentivizing pharmaceutical sponsorships. Through these strategies, Uganda can achieve a more sustainable and equitable SCD management system, ultimately reducing the disease burden and improving patient outcomes.

Category	Value	Sources
Annual Hydroxyurea Cost per Patient (€)	250 €	WHO (2023)
Annual Hospitalization Cost per Patient (€)	1.500 €	WHO (2023)
Average Household Income in Agago (€/year)	730 €	World Bank (2022)
Average Household Income in Gulu (€/year)	1.460 €	World Bank (2022)
Estimated Government Budget Allocation for SCD (€ Million)	2,5	Uganda Ministry of Health (2023)
Estimated International Donor Contribution for SCD (€ Million)	10	Global Fund Report (2023)
Projected Savings from Scaling Hydroxyurea (€/Year)	1,2	Teigen et al. (2023)
Projected Five-Year Savings from Scaling Hydroxyurea (€ Million)	6	Teigen et al. (2023)
Percentage of SCD Patients Who Cannot Afford Hydroxyurea (Gulu)	50	Matovu (2022)
Percentage of SCD Patients Who Cannot Afford Hydroxyurea (Agago)	70	Matovu (2022)

## 7. DISCUSSION

This section critically interprets the findings, addressing their implications for policy, healthcare delivery, and economic sustainability. By comparing the results from Agago and Gulu districts, we assess the viability of hydroxyurea therapy as a cost-effective alternative to hospitalization while considering barriers to implementation and strategies for scaling up access.

### 6.1. Interpretation of Key Findings

The study confirms that hydroxyurea therapy is significantly more cost-effective than repeated hospitalizations. Across both districts:

- Hydroxyurea reduced hospitalizations by 50–70%, resulting in substantial direct cost savings for healthcare facilities and patients.
  - Mortality rates declined from 10–15% to 5–8%, demonstrating hydroxyurea's efficacy in improving long-term survival.
  - Blood transfusion dependence decreased by 40–60%, reducing pressure on already scarce blood supplies in Uganda.
  - Projected healthcare savings of €1.2M over five years if hydroxyurea coverage expands to 75% of eligible SCD patients.
- These results align with global studies (Ware et al., 2022), reinforcing that early and sustained hydroxyurea use leads to both medical and economic benefits.



## 6.2. Barriers to Hydroxyurea Implementation

Despite strong evidence favoring hydroxyurea, significant economic, geographic, and systemic challenges hinder its widespread adoption.

These are the main financial and healthcare infrastructure limitations:

- **Drug Affordability:** Although hydroxyurea is cheaper than hospitalization, 41% of caregivers in Gulu and 55% in Agago reported that cost remains a barrier. Government subsidies are needed to reduce out-of-pocket expenses.

- **Stockouts and Supply Chain Gaps:** 68% of respondents in Agago and 55% in Gulu faced frequent medication shortages. Strengthening local pharmaceutical production or improving procurement logistics could ensure stability.

- **Limited Diagnostic Capacity:** Only two physicians in Agago handle SCD patients, leading to long waiting times and inadequate monitoring.

Geographic Inaccessibility and Healthcare Decentralization Needs show that:

- In Agago, 79% of caregivers live over 10 km from the hospital, making regular hydroxyurea monitoring difficult.

- Community-based treatment programs (e.g., satellite clinics and mobile health units) could mitigate this issue.

Socio-cultural Barriers and Stigma point out that:

- 77.1% of caregivers in Agago and 45% in Gulu reported avoiding care due to social stigma.

- Misinformation is widespread: Only 40% of caregivers understood hydroxyurea's role in reducing pain crises.

- Community education campaigns and culturally adapted awareness programs could help normalize SCD care-seeking behaviors.

## 6.3. Policy Implications: Scaling Up Hydroxyurea Accessibility

These are the main Financial Strategies:

1. **National Subsidization of Hydroxyurea:** This would reduce annual costs from €100–200 per patient to €50, making treatment more accessible.

2. **Integration into Uganda's Essential Medicines List,** ensuring government-supported procurement.

3. **International Donor Support** (e.g., WHO, Global Fund) to co-finance hydroxyurea expansion programs.

Healthcare System Strengthening Concern:

1. **Decentralization of SCD Treatment:** Establish satellite clinics and deploy mobile health units in high-burden districts like Agago.

2. **Healthcare Workforce Training:** Upskill nurses and community health workers to assist with SCD management, reducing reliance on specialized physicians.

3. **Improve Pharmaceutical Supply Chains:** Develop local production capacity to ensure continuous hydroxyurea availability.

Addressing Social and Behavioral Barriers implies:

1. **Community-Led Stigma Reduction Campaigns:** Engage local leaders and health influencers to reshape misconceptions about SCD.

2. **Education on Hydroxyurea Adherence:** Integrate SCD management training into primary healthcare and school programs.

3. **Financial Incentives for Regular Check-Ups:** Provide transportation subsidies or mobile health outreach for rural caregivers.

## 6.4. Strengths, Limitations, and Future Research Directions

### A) Strengths

- First comprehensive cost-benefit analysis of hydroxyurea vs. hospitalization in Uganda.

- A multi-dimensional approach incorporating economic, clinical, and socio-cultural factors.

- Comparative district-level insights, guiding context-specific policy recommendations.

### B) Limitations

- Cross-sectional study: Lacks long-term follow-up on patient outcomes.

- Potential recall bias: Caregivers self-reported hospital visits and hydroxyurea adherence.

- Limited generalizability: Results reflect Agago and Gulu but may differ in other Ugandan regions.

### C) Future Research Needs

- Longitudinal studies tracking hydroxyurea users over five years, measuring hospitalization trends, mortality, and economic impacts.

- Pilot testing community-based hydroxyurea distribution models in rural settings.

- Assessing cost-benefit dynamics of newborn SCD screening programs, enabling earlier intervention.

## 8. CONCLUSION

This study provides compelling evidence that hydroxyurea is a cost-effective and clinically beneficial intervention for managing Sickle Cell Disease (SCD) in Uganda. By significantly reducing hospitalization rates (by 50–70%) and mortality (by 40–50%), hydroxyurea not only improves patient



outcomes but also alleviates the financial burden on the healthcare system. A cost-benefit analysis indicates that expanding hydroxyurea coverage to 75% of eligible patients could save Uganda over €1.2 million in five years by reducing hospital admissions and transfusion dependency.

Despite these advantages, systemic challenges—including financial barriers, inconsistent drug supply, limited healthcare infrastructure, and persistent stigma—continue to hinder its widespread adoption. A comparative analysis between Agago (a rural district with limited access) and Gulu (a semi-urban district with better healthcare infrastructure) highlights the urgent need for decentralized, community-based interventions to bridge the accessibility gap.

Strategic policy actions are essential to enhance SCD management and maximize the benefits of hydroxyurea:

1. **Make Hydroxyurea Affordable**

- Integrate hydroxyurea into Uganda's Essential Medicines List.
- Establish government funding and global health partnerships to support free or subsidized distribution.

2. **Expand Access through Decentralized Healthcare Services**

- Establish satellite clinics in high-burden rural areas.
- Deploy mobile health units to improve outreach and treatment adherence.
- Train nurses and community health workers in SCD management to enhance local care capacity.

3. **Strengthen Drug Supply Chains**

- Improve procurement and distribution systems to prevent stockouts.
- Explore local pharmaceutical production to reduce dependency on imports.

4. **Combat Stigma and Raise Community Awareness**

- Launch public education campaigns to normalize SCD care-seeking behavior.
- Partner with schools, religious organizations, and community leaders to address misconceptions and reduce discrimination.

5. **Enhance Caregiver and Patient Education**

- Develop structured educational materials to support hydroxyurea adherence and disease self-management.
- Train community health workers to provide home-based support and encourage early treatment-seeking behavior.

While this study lays a strong foundation for policy and programmatic action, further research is needed

to ensure sustainable impact. Key areas for future investigation include conducting longitudinal studies to assess hydroxyurea's long-term effects on survival, quality of life, and healthcare costs; pilot testing decentralized SCD care models such as community clinics, telemedicine, and mobile outreach; evaluating newborn screening programs to enable earlier intervention and preventive care; and developing economic models to explore the integration of SCD management into Uganda's broader maternal and child health programs.

The evidence is clear: hydroxyurea is a clinically effective, economically viable, and scalable solution for SCD management. However, achieving universal access requires urgent policy action, strategic investment, and a commitment to equitable healthcare. By shifting from a crisis-driven, hospitalization-centered model to a preventive, community-based approach, Uganda can:

- Reduce preventable SCD complications and deaths;

Lower healthcare costs and improve system sustainability.

Enhance the quality of life for thousands of affected families.

Foreign donors' effective intervention may well follow Results-Based Financing patterns, where sponsorship is linked to effective results, following pay-for-performance targets (see Moro-Visconti et al., 2024).

Policymakers, healthcare providers, and global health organizations must act now to scale up hydroxyurea therapy, decentralize SCD management, and eliminate barriers to care. The time for transformative change in SCD treatment in Northern Uganda is now.

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#### Informed Consent

This article contains no studies with human participants performed by any authors.

#### Competing Interests

The authors declare no competing interests.

#### Contributions

Conceptualization, Roberto Moro-Visconti and Tito Squillaci; Data curation, Roberto Moro-Visconti and Tito Squillaci; Formal analysis, Roberto Moro-Visconti and Tito Squillaci; Investigation, Tito Squillaci; Methodology, Roberto Moro-Visconti; Writing – original draft, Roberto Moro-Visconti; Writing – review & editing, Roberto Moro-Visconti.

#### Data Availability

Data sharing does not apply to this research as no data were generated or analyzed.

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