ARTICLE

Cost-effectiveness of gene therapy for sickle cell disease in Uganda: tailoring high-income evidence to Uganda's context

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Blood stem cell gene therapy to treat hemoglobinopathies is beginning to transform health for small numbers of patients in the U.S. and Europe, where these conditions qualify as rare diseases. Yet hemoglobinopathies are common globally, disproportionately affecting low- and middle-income countries (LMICs), creating an ethical imperative to ensure access where disease burden is greatest. Gene therapy could have blockbuster drug potential if distributable to these regions, but cost is a major barrier. Cost-effectiveness analysis (CEA) models are seldom adapted to low-income settings, where limited data and resources constrain efforts to contextualize high-income evidence. Here, we present a novel framework to evaluate high-income country authorized gene therapies in LMIC contexts. Uganda, where sickle cell disease (SCD) imposes a major burden and no curative therapies are available, is the test case. We evaluate cost-effectiveness of gene therapy for adolescents and adults with SCD in Uganda, adapting U.S. evidence to local economic conditions. Using a three-state Markov model to estimate lifetime costs of standard-of-care in Uganda, two U.S.-based CEA models were adapted using scaling factors and applied to two authorized gene therapies for SCD, Lyfgenia™ (lovo-cel) and Casgevy® (exa-cel), assuming biologically consistent efficacy across populations. Incremental cost-effectiveness ratios (ICERs) were calculated from healthcare and societal perspectives, with internationally accepted gross domestic product-based thresholds. This study demonstrates that Casgevy could be cost-effective in Uganda at a scaled cost when societal benefits are considered. This framework enables CEAs for emerging therapies where local clinical trial data are limited, supporting local decision-makers, global funders, and manufacturers in advancing equitable access to transformative therapies in LMICs.

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INTRODUCTION

Sickle cell disease (SCD) is a hereditary blood disorder and major public health concern in sub-Saharan Africa, where over 75% of the estimated 300,000 annual global births of children with SCD occur. Uganda is among the countries with the highest SCD burden, with 13.3% of the population carrying the sickle cell trait and 0.7% affected by SCD [1]. Prevalence rates are particularly high in regions such as East Central Uganda (1.6%) and Mid-Northern Uganda (1.5%), where sickle cell trait prevalence exceeds 20% in some districts. SCD is associated with significant morbidity, including chronic hemolytic anemia, recurrent vaso-occlusive crises (VOC), and organ damage, which result in reduced life expectancy and quality [2, 3].

The economic and social burden of SCD in Uganda extends beyond direct healthcare costs. Many individuals with SCD experience frequent hospitalizations and rely on treatments that can be expensive and often inaccessible, such as red blood cell transfusion exchange and hematopoietic stem cell transplantation (HCT). Hydroxyurea (HU) has been demonstrated to be safe and provide clinical benefits as a cost-effective disease modifying therapy, but its supply is limited [4]. Newer disease-modifying medications including voxelotor, L-glutamine, and crizanlizumab are not yet widely available and require additional clinical testing [5]. Additionally, caregivers face significant opportunity costs, particularly in rural and low-income areas. Despite efforts like the Uganda Sickle Surveillance Study (US3), which highlighted the need for targeted interventions, challenges remain in addressing the needs of adolescents and adults with SCD [2, 3, 6].

Uganda's health technology assessment (HTA) and regulatory functions are jointly coordinated by the Ministry of Health and the Uganda National Drug Authority (NDA), which oversees approval and post-market safety monitoring of medical products. The country does not yet have a formal HTA agency, though a national policy framework and proposed legal reforms seek to expand the NDA's authority to include structured HTA functions [7]. In the absence of a national health-insurance system, financing for advanced therapies generally relies on a mix of government funding, donor-supported programs, and out-of-pocket payments. Uganda also lacks an officially defined willingness-to-pay (WTP) threshold; therefore, cost-effectiveness studies typically reference WHO GDP-based benchmarks (1–3× GDP per capita) as contextual indicators of affordability.

Gene therapy offers transformative potential for individuals with SCD. Unlike traditional approaches, such as HU or

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symptomatic care, gene therapy addresses the underlying cause of the disease, offering the possibility of long-term remission or cure with a single intervention without the need to identify a healthy matched donor as is required for HCT. While Casgevy® (exagamglogene autotemcel (exa-cel)) and Lyfgenia™ (lovotibeglogene autotemcel (lovo-cel)) have been approved for SCD in high-income countries, the feasibility of making these curative therapies available in low-resource settings remains unexplored, in part due to the absence of localized cost-effectiveness data for these two drugs.

Gene therapies are primarily developed in high-income countries, with limited research and regulatory activity in low- and middle-income countries (LMICs). As of 2023, none of the 1100 active global clinical trials in gene therapy were open in low-income countries, and only 6% were recruiting patients in middle-income countries outside of China [8]. This disparity highlights significant translational gaps, particularly in regions like Africa, where diseases such as SCD impose substantial public health burdens [8]. A primary issue for expanding clinical trials into LMICs has been assessing cost effectiveness of gene therapies when there is a paucity of clinical data available for the region.

Cost-effectiveness analyses for SCD have historically been scarce and largely limited to conventional treatments such as hydroxyurea, transfusions, or iron-chelation strategies, with few efforts addressing potentially curative approaches. More recently, comprehensive frameworks—such as the University of Washington Model for Economic Analysis of Sickle Cell Cure (UW-MEASURE) and the Fred Hutchinson Institute Sickle Cell Disease Outcomes Research and Economics Model (FH-HISCORE)—have advanced understanding of the long-term value of gene therapies by integrating both healthcare and societal perspectives to capture outcomes such as productivity gains and caregiver benefits. However, these models were developed in high-income contexts, underscoring the need to adapt such frameworks to low-resource settings like Uganda, where healthcare infrastructure and economic conditions differ substantially.

Evaluating the cost-effectiveness of gene therapy for SCD in Uganda is challenging due to significant data gaps, particularly regarding costs of delivering the therapy. While some data are available on costs of standard-of-care (SoC) in Uganda, information on gene therapy costs is virtually nonexistent. Importantly, because gene therapies target the underlying disease cause, there is a global expectation of biological consistency for gene therapy across populations [9]. Here, we leverage evidence from the U.S. for adapting costs and outcomes to the Ugandan context by calculating and applying scaling factors derived from the ratio of lifetime SoC costs between the two countries. By employing a dual-perspective approach that incorporates both healthcare system and societal impacts, this analysis aims to provide critical insights for policymakers considering advanced therapies for eligible populations in resource-constrained environments.

METHODS

We began by estimating the lifetime cost of standard care (SoC) for sickle cell disease (SCD) in Uganda using a three-state Markov model. We then compared this estimate to the lifetime SoC costs reported in two U.S. cost-effectiveness models (UW-MEASURE and FH-HISCORE) to derive proportional "scaling factors" that reflect the relative difference in healthcare costs between settings. These factors were then applied to all U.S. cost components—drug, administration, medical, productivity, patient time, caregiver time, and consumption—to approximate their equivalent value in Uganda's healthcare and economic context. Clinical effectiveness measures, including life-years, quality-adjusted life-years (QALYs), and health-years total (HYT), were assumed to remain constant across populations. Using these adjusted cost inputs, we conducted cost-effectiveness analyses from both healthcare and societal perspectives and examined affordability through willingness-to-pay threshold analyses.

Estimating the lifetime cost of SoC using a Markov model

To estimate the lifetime cost of SoC for SCD in Uganda, we employed a Markov model designed to simulate the progression of patients across three health states: (1) standalone SoC without HU, (2) SoC with HU, and (3) death, which serves as an absorbing state (schematic shown in Fig. 1). We considered transitions between these states to reflect real-world treatment dynamics, such as patients moving from HU-based SoC to standalone SoC due to treatment side effects and, in some cases, resuming HU after discontinuation. These transitions are modeled using probabilities informed by published literature (Table 1). The modeled population consisted of individuals 12 years and older with SCD who are eligible to receive gene therapy based on initial authorization trials for Casgvey and Lyfgenia (NCT03745287 and NCT02140554, respectively), to ensure that costs and outcomes accurately reflect the healthcare needs of this specific group.

We simulated the lifetime progression of patients in monthly cycles, starting with all individuals in the SoC with HU state, applying a yearly 3% discount factor [10]. Transition probabilities were age-dependent, with mortality rates increasing across three age groups: 13–18 years, 19–35 years, and 35+ years. The transitions between SoC types were modeled using probabilities that account for the real-world likelihood of switching due to treatment side effects and/or disease progression [11].

Costs for each health state were determined using Uganda's National Clinical Guidelines 2023 and categorized into management of acute or chronic complications [12]. These costs were tailored to reflect specifics of the two health states: standalone SoC and SoC with HU. The primary difference between these health states is inclusion of a fixed dose of HU (20 mg/kg) in the HU state. For patients on HU, we assumed the duration of complicated and uncomplicated episodes was 20% shorter with one fewer uncomplicated episode overall per year compared to those on standalone SoC. A complete list of all inputs to calculate total health state costs is shown in Table 2.

Scaling factor derivation for gene therapy cost adjustment in Uganda

We derived scaling factors by comparing the lifetime discounted costs of SoC in Uganda and the U.S., expressed in 2021 USD. The scaling factor was derived using two standalone models (UW-MEASURE and FH-HISCORE) [13] as follows:

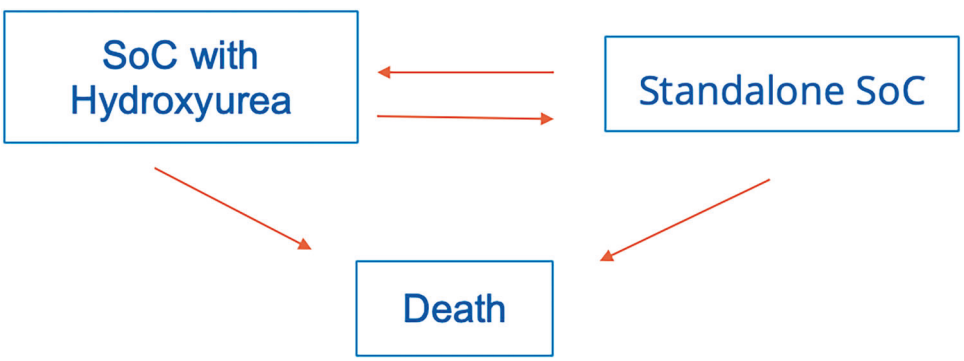

Fig. 1 Markov model structure for standard of care in sickle cell disease management in Uganda.

Table 1. Monthly transition probabilities between health states for standard of care in Uganda.

Description	Value	Source
Standalone SoC to SoC with HU	0.0602	(Shah, Bhor, Xie, Halloway, et al. 2019) [27]
SoC with HU to standalone SoC	0.0714	(Shah, Bhor, Xie, Halloway, et al. 2019) [27]
Probability of death for ages 13–18 (assumed identical for SoC and SoC with HU)	0.0010	(Desai, 2020; Nikitin et al. 2023) [11, 28]
Probability of death for ages 19–35 (assumed identical for SoC and SoC with HU)	0.0020	(Desai, 2020; Nikitin et al. 2023) [11, 28]
Probability of death for ages 35+ (assumed identical for SoC and SoC with HU)	0.0038	(Desai, 2020; Nikitin et al. 2023) [11, 28]

UW-MEASURE Model: This model integrates a broad range of comorbid conditions and healthcare dynamics, providing a comprehensive evaluation of SCD management.

$$Scaling\ Factor_{UW} = \frac{Lifetime\ Cost\ of\ SoC\ in\ Uganda\ (USD)}{UW-Measure\ Lifetime\ Cost\ of\ SoC\ in\ the\ U.S\ (USD)}$$

FH-HISCORE Model: This model focuses on a narrower set of health states with an emphasis on chronic conditions and long-term outcomes.

$$Scaling\ Factor_{FH} = \frac{Lifetime\ Cost\ of\ SoC\ in\ Uganda\ (USD)}{FH-HISCORE\ Lifetime\ Cost\ of\ SoC\ in\ the\ U.S\ (USD)}$$

The two scaling factors derived from these models capture the proportional differences in healthcare costs and utilization patterns between the two settings (U.S. and Uganda). Each scaling factor was applied to the U.S.-based cost estimates for gene therapy specific to its respective model, such that adjusted cost projections reflected economic realities and healthcare infrastructure of Uganda. The adjusted cost components included medical costs, gene therapy drug costs, administration costs, productivity costs, patient time use costs, caregiver time use costs, and consumption costs (see Supplemental Methods).

Evaluating the cost-effectiveness of gene therapy in Uganda

Lyfgenia for SCD is a lentiviral vector-based gene addition therapy developed by bluebird bio and Casgvey for SCD is the first CRISPR-based gene therapy developed and manufactured by CRISPR Therapeutics and Vertex Pharmaceuticals [14]. For analysis, we applied the current U.S. list price for Lyfgenia at $3.1 million and Casgevy at $2.2 million. U.S. pricing was applied here because both manufacturers are based in the U.S. and regulatory authorizations in the U.S. preceded all other countries. We performed CEA for each product separately to assess how pricing differences affect cost-effectiveness in the Ugandan context for both healthcare and societal stakeholders.

To adapt these models for Uganda, the derived scaling factors were applied to adjust U.S.-based cost components to the local context. Clinical effectiveness measures, including life-years gained, quality-adjusted life years (QALYs), and health years total (HYT), were assumed to be consistent across settings and based on robust evidence supporting gene therapy's biological efficacy [15].

Incremental cost-effectiveness ratios (ICERs) were calculated to quantify the value of gene therapy compared to SoC. Separate ICERs were estimated under the healthcare system and societal perspectives, capturing the differential burden across stakeholders. For the UW-MEASURE Model, both QALYs and HYT were used as effectiveness measures, whereas the FH-HISCORE Model focused exclusively on QALYs. This approach reflects the broader scope of the UW-MEASURE Model, which accommodates alternative metrics for equity-informed decision-making.

Sensitivity analysis to assess affordability in Uganda

Sensitivity analysis was conducted to assess the affordability of gene therapy under varying willingness-to-pay (WTP) thresholds based on Uganda's 2021 gross domestic product (GDP) per capita ($921) (World Bank). Thresholds at 1×, 2×, and 3× GDP per capita were considered, corresponding to $921, $1842, and $2763 USD, respectively. These thresholds are established by the World Health Organization (WHO) and widely accepted in health economic evaluations [16]. Calculated thresholds were used to determine the maximum gene therapy cost for maintaining cost-effectiveness under each model and stakeholder perspective as described above.

RESULTS

Lifetime SoC costs in Uganda

We employed a novel approach to adapt robust baseline U.S.-based cost data to Uganda's economic context as well as social and healthcare landscape. Using a simplified Markov model with three health states (Fig. 1), we estimated the lifetime cost of SoC for SCD in Uganda using detailed cost analysis. All cost inputs are listed in Table 2.

Chronic SCD management costs accounted for life-long folic acid supplementation ($3.65/year), penicillin prophylaxis ($2.12/year), and malaria prophylaxis with monthly mefloquine ($53.16/year). Monitoring costs for SCD without HU were estimated at $91.91 annually, while monitoring costs for HU were higher due to more intensive follow-up requirements ($183.82 in the first year and $104 in subsequent years). Here, we applied a fixed-dose HU regimen costing $195.77 annually. Real-world data from a cross-sectional study conducted in Eastern Uganda informed the weighted average of eight outpatient visits per year (Olupot-Olupot et al. 2020). This study captured self-reported clinic attendance, reflecting variations in visit frequencies (monthly, bi-monthly, or quarterly) tailored to patient needs. These weighted averages provide a realistic representation of outpatient care utilization, with an average visit cost of $111.28 annually.

Acute complications, particularly VOC, were a significant driver of costs in the real-world data. Complicated episodes lasted an average of 7 days, while uncomplicated episodes lasted 5.1 days, with a cost per day of $30.20. Patients on HU experienced fewer uncomplicated episodes and their duration of all episodes was reduced by 20%. The number of VOC events was three per year for the SoC standalone, one complicated and two uncomplicated episodes, and two per year for the SoC with HU, one complicated and one uncomplicated episode. The average mass of red blood cell transfusions (58.2 kg) was also derived from the same study in Eastern Uganda. This informed the calculation of transfusion volumes and associated costs, ensuring that the estimates align with the real-world characteristics of the population being studied. The total cost of blood transfusions for patients with hemoglobin levels below 9 g/dL was calculated to be $453.31 annually, with a weighted average of 2.5 transfusions per year.

Based on this detailed costing estimate, the total discounted lifetime cost of the SoC for SCD in Uganda calculated by the model was estimated to be $21 877 USD (Table 3).

Scaling robust evidence from the U.S. to Uganda

To derive scaling factors for adjusting U.S.-based cost estimates to the Ugandan context, lifetime costs from two models were used (see "Methods"). In the UW-MEASURE model, the lifetime discounted cost of SoC in the United States was $1,197,111, resulting in a scaling factor of 0.018. In the FH-HISCORE model, the U.S. lifetime discounted cost of SoC was $668,136, yielding a scaling factor of 0.033. These scaling factors were applied to U.S.-based cost estimates for gene therapy (including gene therapy list prices) to enable the contextualization of U.S.-based cost data to reflect the economic realities of Uganda.

Table 2. Cost Inputs (in 2021 USD) for estimating the cost of standard of care in Uganda.

Category	Description	Yearly Cost	Source	Notes
Chronic Management				
General Measures				
	Life Folic Acid	3.65	("MSH (Management Sciences for Health) International Medical Products Price Guide," 2015) [29]	Administered as daily doses for lifelong supplementation
	Penicillin prophylaxis	2.12	("MSH (Management Sciences for Health) International Medical Products Price Guide," 2015) [29]	Two tablets per day
	Malaria prophylaxis with monthly mefloquine	53.16	("MSH (Management Sciences for Health) International Medical Products Price Guide," 2015) [29]	Three tablets monthly for malaria prevention
	Monitoring SCD, without HD	91.91	(Teigen et al. 2023) [4]	Includes routine laboratory tests and outpatient consultations
Treatment				
	HU starting dose, fixed dose, 19.2 mg/kg	195.77	(Teigen et al. 2023) [4]	Calculated for an average weight of 58.2 kg in Uganda.
	Monitoring, HU, first year	183.82	(Teigen et al. 2023) [4]	Reflects the additional monitoring required during the initiation phase.
	Monitoring, HU, subsequent years	104	(Teigen et al. 2023) [4]	Reduced monitoring frequency after stabilization.
	Yearly total cost of outpatient visits	111.28	(Olupot-Olupot et al. 2020; Teigen et al. 2023) [4, 30]	Includes eight outpatient visits annually, each costing $13.91 USD.
Acute Complications				
Painful Crisis - Hospital Management				
			(Teigen et al. 2023b) [4]	Hospitalization Daily Cost $30.20 USD.
	Complicated Episodes (Standalone SoC)	237.65	(Shah, Bhor, Xie, Paulose, et al. 2019; Teigen et al. 2023; Zaidi et al. 2021) [4, 31, 32]	One VOC crisis per year with a duration of 7 days
	Uncomplicated Episodes (Standalone SoC)	346.29	(Shah, Bhor, Xie, Paulose, et al. 2019; Teigen et al. 2023; Zaidi et al. 2021) [4, 31, 32]	Two VOC crises per year with an average duration of 5.1 each
	Complicated Episodes (SoC with HD)	190.12	(Shah, Bhor, Xie, Paulose, et al. 2019; Teigen et al. 2023; Zaidi et al. 2021) [4, 31, 32]	One VOC crisis per year with a duration of 5.6 days.
	Uncomplicated Episodes (SoC with HD)	138.52	(Shah, Bhor, Xie, Paulose, et al. 2019; Teigen et al. 2023; Zaidi et al. 2021) [4, 31, 32]	One VOC crises per year with a duration of 4.05 days.
Transfusion (Hb < 9 g/dL)				
	Total cost of transfusion (17 ml/kg)	453.31	(Olupot-Olupot et al. 2020; Teigen et al. 2023) [4, 30]	2.54 transfusions per year for an average weight of 58.2 kg, including transfusion sets and blood costs.

CEA analysis and ICERs

Tables 4 and 5 present the incremental effectiveness and costs of gene therapy compared to SoC in both the U.S. and Uganda using the UW-MEASURE and FH-HISCORE models. We report results separately for Casgevyand Lyfgenia, incorporating their respective pricing while assuming equivalent clinical effectiveness across settings and therapies.

For Casgevy, total incremental QALYs in Uganda were 11.9 in the UW-MEASURE model and 5.4 in the FH-HISCORE model. HYT were estimated at 19.7 in UW-MEASURE. Cost differences between Uganda and the U.S. reflect the application of scaling factors derived from the lifetime cost of SoC in each country. In Uganda, the total incremental medical cost of gene therapy was $45,664 for UW-MEASURE and $78,656 for FH-HISCORE. The totals (for UW-MEASURE and FH-HISCORE, respectively) are composed of baseline medical costs (−$3144 and −$8771), gene therapy drug costs ($40,205 and $72,035), and administration costs ($8604 and $15,392). The total societal costs, which include productivity losses, patient and caregiver time use, and consumption costs, were $31,053 for UW-MEASURE and $57,424 for FH-HISCORE. The resulting ICERs per QALY were $3837 (healthcare) and $2610 (societal) for UW-MEASURE, and $14,566 (healthcare) and $10,634 (societal) for FH-HISCORE—indicating that Casgevy may be considered cost-effective in Uganda under common WTP thresholds.

For Lyfgenia, results were directionally similar but less favorable due to higher drug pricing. ICERs per QALY in Uganda were $5219 (healthcare) and $3992 (societal) in UW-MEASURE and $20,023 (healthcare) and $16,091 (societal) in FH-HISCORE. While still yielding substantial health gains, Lyfgenia was less likely to meet cost-effectiveness thresholds under current pricing assumptions.

To illustrate the importance of applying context-adjusted cost inputs, we conducted an exploratory analysis assuming that the gene therapy drug prices remained at U.S. list levels (Casgevy at $2.2 million) while all other costs were locally scaled. Under this assumption, the incremental cost-effectiveness ratios (ICERs) increased to $185,332 per QALY (healthcare perspective) and $184,104 per QALY (societal perspective) in the UW-MEASURE model, and to $408,633 per QALY (healthcare perspective) and $404,701 per QALY (societal perspective) in the FH-HISCORE model. These substantially higher ICERs—well above any plausible affordability threshold for Uganda—underscore that applying unadjusted U.S. list prices would overstate both costs and ICERs, thereby supporting the use of context-adjusted pricing to reflect realistic market and policy conditions.

Table 3. Total Cost (in 2021 USD) for standalone SoC and SoC with HU and the life time cost for SoC.

	First Year	Subsequent Years	Total Cost
Health State			
Standalone SoC	$1 299	$1 299	
SoC with HU	$1 587	$1 257	
Life-Time Cost (Markov Model)			
Standard of Care			$21 877

Analysis of affordability

The scaled cost of delivering Casgevy in Uganda was estimated at $40,205–$72,035 across the two models (Table 4), while the scaled cost of delivering Lyfgenia in Uganda was estimated at $56,651.80–$101,504 (Table 5).

To assess affordability, we conducted a sensitivity analysis using varying WTP thresholds based on 1×, 2×, and 3× Uganda's GDP per capita ($921, $1842, and $2763 USD, respectively). These WTP thresholds were used to determine the maximum gene therapy cost in Uganda that would maintain cost-effectiveness from both

Table 4. Incremental effectiveness and costs of casgevy gene therapy compared to standard of care in the U.S. and Uganda.

	United States UW-Measure	Uganda UW-measure	United States FH-HISCORE	Uganda FH-HISCORE
Effectiveness				
Undiscounted Life-Years	17.4	17.4	17.0	17.0
Discounted Life-Years	7.9	7.9	6.4	6.4
QALYs (Patients)	9.8	9.8	5.1	5.1
QALYs (Family)	2.1	2.1	0.3	0.3
QALYs (Total)	11.9	11.9	5.4	5.4
HYT (Total)	19.7	19.7	NA	NA
Costs				
Medical Costs ($)	–172 065	–3 144	–267 872	–8 771
Gene Therapy Drug Costs ($)	2,200,000	40,205	2,200,000	72,035
Gene Therapy Administration Costs ($)	470,796	8604	470,089	15,392
Total Medical Costs ($)	2,498,731	45,664	2,402,217	78,656
Productivity Costs ($)	–1,247,805	–22,803	–1,015,378	–33,247
Patient Time Use Costs ($)	–28,620	–523	NA	NA
Caregiver Time Use Costs ($)	–19,035	–348	–25,402	–832
Consumption Costs ($)	495,968	9064	392,324	12,846
Total Societal Costs ($)	1,699,239	31,053	1,753,761	57,424
ICER (Health Care Sector) ($/QALY)	209,977	3837	444,855	14,566
ICER (Societal Perspective) ($/QALY)	142,793	2610	324,771	10,634
ICER (Health Care Sector) ($/HYT)	126,839	2318	NA	NA
ICER (Societal Perspective) ($/HYT)	86,256	1576	NA	NA

Table 5. Incremental effectiveness and costs of Lyfgenia gene therapy compared to standard of care in the U.S. and Uganda.

	United States UW-Measure	Uganda UW-Measure	United States FH-HISCORE	Uganda FH-HISCORE
Effectiveness				
Undiscounted Life-Years	17.4	17.4	17.0	17.0
Discounted Life-Years	7.9	7.9	6.4	6.4
QALYs (Patients)	9.8	9.8	5.1	5.1
QALYs (Family)	2.1	2.1	0.3	0.3
QALYs (Total)	11.9	11.9	5.4	5.4
HYT (Total)	19.7	19.7	NA	NA
Costs				
Medical Costs ($)	−172,065.0	−3144.5	−267,872.0	−8771.0
Gene Therapy Drug Costs ($)	3100000.0	56651.8	3,100,000.0	101,504.0
Gene Therapy Administration Costs ($)	470,796.0	8603.7	470,089.0	15,392.2
Total Medical Costs ($)	3,398,731.0	62,111.1	3,302,217.0	108,125.3
Productivity Costs ($)	−1,247,805.0	−22,803.4	−1,015,378.0	−33,246.8
Patient Time Use Costs ($)	−28,620.0	−523.0	NA	NA
Caregiver Time Use Costs ($)	−19,035.0	−347.9	−25,402.0	−831.7
Consumption Costs ($)	495,968.0	9063.7	392,324.0	12,846.0
Total Societal Costs ($)	2599,239.0	47,500.5	2,653,761.0	86,892.7
ICER (Health Care Sector) ($/QALY)	285,607.6	5219.4	611,521.7	2,0023.2
ICER (Societal Perspective) ($/QALY)	218,423.4	3991.6	49,1437.2	16091.2
ICER (Health Care Sector) ($/HYT)	172,524.4	3152.8	NA	NA
ICER (Societal Perspective) ($/HYT)	131,941.1	2411.2	NA	NA

Table 6. Maximum affordable costs of gene therapy for quality-adjusted life years (QALYs) under different willingness-to-pay (WTP) thresholds.

WTP	Healthcare sector perspective UW-measure	Societal perspective UW-measure	Healthcare sector perspective FH-HISCORE	Societal perspective FH-HISCORE
1× GDP	5501	20,111	−1648	19,585
2× GDP	16,461	31,071	3326	24,558
3× GDP	27,420	42,031	8299	29,532

Table 7. Maximum affordable costs of gene therapy for health years in total (HYT) under different WTP thresholds (UW-MEASURE model only).

WTP	Healthcare sector perspective UW-measure	Societal perspective UW-measure
1× GDP	12,684	27,295
2× GDP	30,828	45,439
3× GDP	48,972	63,582

healthcare and societal perspectives for the UW-MEASURE and FH-HISCORE models (Tables 6 and 7).

For QALYs, the maximum affordable costs under the UW-MEASURE model were $5501, $16,461, and $27,420 USD from a healthcare perspective and $20,111, $31,071, and $42,031 USD from a societal perspective at 1×, 2×, and 3× GDP thresholds, respectively. In contrast, the FH-HISCORE model yielded maximum affordable costs of −$1648 (negative value indicates non-affordability), $3326, and $8299 USD from a healthcare perspective and $19,585, $24,558, and $29,532 USD from a societal perspective at the same thresholds (Table 6).

For HYT, which were only available for the UW-MEASURE model, the maximum affordable costs were $12,684, $30,828, and $48,972 USD from a healthcare perspective and $27,295, $45,439, and $63,582 USD from a societal perspective for the respective 1×, 2×, and 3× GDP thresholds (Table 7).

The results indicate that Casgevy gene therapy offers substantial health gains, but at a high cost. From a healthcare system perspective, the ICER for Casgevy was estimated at $3837 per QALY and $2318 per HYT in the UW-MEASURE model and $14,566 per QALY in the FH-HISCORE model. When broader societal costs and benefits were considered, ICERs declined to $2610 per QALY, $1576 per HYT (UW-MEASURE), and $9421 per QALY (FH-HISCORE). Based on WHO cost-effectiveness thresholds where interventions with ICERs between 1× and 3× Uganda's GDP per capita ($921–$2763) are considered cost-effective the societal ICERs in UW-MEASURE fall within the cost-effective range, with the HYT-based ICER approaching the highly cost-effective threshold.

Altogether, this analysis suggests that Casgevy gene therapy is cost-effective in Uganda at a cost of $40,205 per drug product when societal benefits are considered and that this drug product cost is within internationally accepted WTP thresholds.

DISCUSSION

This study performed CEA of gene therapy for SCD in Uganda, addressing limited cost data and economic disparities. We applied

a novel approach that scaled U.S. cost estimates using the ratio of lifetime SoC costs in both countries. This method reflects Uganda's economic context and aligns with global cost-effectiveness practices. Our results support pricing strategies to make gene therapies feasible for SCD patients in resource-limited settings.

SCD is a common global monogenic blood disorder, with the highest prevalence in countries of sub-Saharan Africa and southeast Asia [17]. Uganda has the 5th highest prevalence of SCD in Africa [18] and is a co-founding member of the Global Gene Therapy Initiative, which aims to facilitate capacity building for gene therapy in LMICs [19]. The WHO named Uganda a test case country for guidance on regulatory reform to support gene therapy development and implementation and the Ugandan government has agreed to support gene therapy infrastructural development in phases over the next few years [8].

Gene therapy for SCD is a recent innovation, with therapies such as Lyfgenia and Casgevy receiving U.S. authorization in late 2023 following promising clinical trials [13]. However, no clinical trials have been performed in any high-incidence region to date. To perform CEA here, we assumed that the clinical benefits from gene therapies in Uganda would match those observed in the U.S., including gains in life-years, QALYs, and HYT. This assumption, which is necessary because of the absence of Uganda-specific clinical trial data, aligns with the global expectation of biological consistency for gene therapy across populations [9]. By integrating scaled cost estimates with assumed effectiveness, we calculated ICERs for gene therapy compared to SoC in Uganda.

Importantly, the scaled cost of delivering Casgevy in Uganda was estimated at $40,205. This figure is notably higher than the reported local manufacturing cost of chimeric antigen receptor (CAR) T-cell therapies in India, which was reported to be $35,107 per product [20]. This pricing differential suggests that even with the high cost, a positive profit margin could exist for gene therapy products in Uganda under appropriate pricing and delivery models. In comparison, the cost of haploidentical or unrelated matched donor HCT in India, where Ugandan patients with available donors are referred for this procedure, is up to $70,000 per procedure (https://www.drrahulbhargavahematologist.com/treatments/sickle-cell-anemia) [21].

The price threshold sensitivity analysis demonstrated that the maximum affordable cost of gene therapy depends significantly on the WTP level and perspective considered. For example, under a WTP threshold of 1× GDP per capita, the maximum affordable cost of gene therapy from the healthcare perspective was $5501 (UW-MEASURE), but it was non-affordable (–$1648) under the FH-HISCORE model. However, these values increased to $20,111 and $19,585, respectively, from a societal perspective. This emphasizes how societal perspectives provide greater flexibility in pricing due to the inclusion of downstream benefits such as productivity gains and reduced caregiver burdens. In particular, the UW-MEASURE societal ICER of $2610 per QALY suggests that gene therapy could be a feasible investment under current economic conditions if societal benefits are prioritized [22].

Historically, there has been a scarcity of CEAs focused on SCD, even prior to the emergence of curative gene therapies. A review of published CEAs identified only 13 studies, most of which assessed conventional treatments such as HU, blood transfusions, or interventions for complications like iron overload [23]. Few studies explored genetic therapies and none were conducted in low-resource settings like Africa. This highlights a significant gap in our understanding of the economic feasibility of advanced SCD interventions in these contexts.

With the approval of gene therapy for SCD, three major cost-effectiveness models have been developed to evaluate its economic value. Herring et al. (2024) used a patient-level simulation model to assess Lyfgenia, emphasizing long-term health outcomes and societal benefits, such as reductions in caregiver burden and productivity losses [24]. Goshua et al. (2023) introduced a distributional CEA framework, applying equity weights to evaluate how gene therapy could reduce health disparities—a novel approach in SCD economic evaluations [25]. Basu et al. (2024) employed two distinct simulation models (UW-MEASURE and FH-HISCORE) to evaluate cost-effectiveness from both healthcare and societal perspectives, highlighting the importance of dual-model frameworks in addressing variability and uncertainty across patient populations. Building on these frameworks, particularly Basu et al.'s dual-model approach, our study leverages UW-MEASURE and FH-HISCORE for their inclusion of comprehensive health states, such as chronic and subacute complications, and their alignment with both healthcare system and societal perspectives [13]. Major differences in this study include fixed WHO thresholds for pricing and scaling factors to adapt to a local economic context, which may partially explain why we observed cost effectiveness for one drug product and not the other.

Despite the advances of gene therapy products into clinical trials, CEAs for gene therapies in low-resource settings remain scarce. To date, only the study by Morgan et al. (2024) has addressed this, which estimated the value-based price (VBP) of gene therapy for SCD across seven LMICs, including Uganda [26]. Using a Markov model, Morgan et al. identified Uganda's VBP for gene therapy as $700–$4100, depending on therapeutic outcomes and WTP thresholds. However, this study did not assess cost-effectiveness. Our analysis addresses this gap by adapting high-income country evidence to evaluate the cost-effectiveness of gene therapy within Uganda's healthcare context. This approach is especially valuable given the limited availability of country-specific data, providing policymakers with critical insights for implementing advanced therapies in resource-constrained environments.

We note several limitations in this study. First, our analysis only considers adolescents and adults for whom drug products are authorized in the U.S.; however, the majority of all individuals with SCD in Uganda are children, as high early-life mortality prevents many from surviving into adolescent or adulthood. Ongoing efforts of others are attempting to identify the severity predictors in children with SCD, but global alignment is critical. Future re-analyses of cost effectiveness will be needed once pediatric indications or trial data become available to fully capture the population-level impact of gene therapy in Uganda. Second, although HU is the standard of care in high-income countries, it remains broadly unavailable to most SCD patients in Uganda as a fixed-dose regimen. In this analysis, we modeled HU as a fixed dose rather than a maximum tolerated dose, which may underestimate its potential effectiveness and cost-efficiency. Third, the standard of care for SCD is heterogeneous—not only between countries, but also within Uganda—varying by disease severity, region, and facility type. HU is often only available at specialized centers, limiting its accessibility for patients. Additionally, the absence of a national health insurance system means that out-of-pocket costs—which are often substantial—are not fully captured. Finally, due to limited local data in Uganda on gene therapy delivery, we relied on scaled U.S.-based cost estimates, which may not fully reflect the operational and contextual realities in Uganda, and may therefore overestimate the value of gene therapy under current health system conditions. Because our analysis adapts existing cost-effectiveness models using a scaling approach to translate parameters across settings, formal probabilistic sensitivity analysis was not applicable; this represents a conceptual limitation of our framework. The U.K. also recently authorized Casgevy at a negotiated price that is lower than the current list price of £1.6 M, but the agreed upon price has not been disclosed. However, analysis of our model with this information was not possible for two pragmatic reasons: (1) the actual cost per drug product is unknown and (2) SoC costs in the U.K. are different than

in the U.S., thus the cost assumptions in the model do not align with the U.K. market and healthcare systems

Our model results suggest that gene therapy for SCD could be cost-effective in Uganda when societal benefits are considered. These findings can support local decision-makers, global funders, and manufacturers in advancing equitable access to transformative therapies in LMICs. This study bridges a critical gap in the literature by providing a novel framework for health technology assessments of adopting gene therapies in LMICs by estimating the cost-effectiveness of gene therapy for SCD in Uganda. Our model represents an important initial step in estimating the value of gene therapy for SCD in Uganda by adapting evidence from high-income countries to appropriate local economies, offering a framework for guiding future feasibility studies and policy decisions.

DATA AVAILABILITY

All data used to draw conclusions from this study are included in this manuscript.

CODE AVAILABILITY

The analytical model and simulation code used to generate the results presented in this study are available from the corresponding author upon request.

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AUTHOR CONTRIBUTIONS

FM-C, RH, AB, and JEA conceived ideas. FM-C, RH, and JEA wrote the paper. JEA and RH supervised this research, secured funding, and edited the paper. FM-C performed research. LB, RKB, and CK-M provided Ugandan context for this study and feedback on the study design. All authors read and approved the manuscript.

COMPETING INTERESTS

JA and CK-M are co-founders of the Global Gene Therapy Initiative (GGTI). JA is a Fellow of the Ugandan National Academy of Sciences (FUNAS). Work conducted for this study was performed while JA was employed at the Fred Hutchinson Cancer Center. JA is now Professor and Vice Chair of the Department of Genetic and Cellular Medicine at the University of Massachusetts Chan Medical School. FM-C and RH have assigned an innovation related to this study (Scalable Methodology for Adapting High-Income Cost-Effectiveness Evidence to Low-Resource Healthcare Settings) to the University of Washington. At the time of manuscript submission, this innovation is not protected by a patent. None of the remaining authors declare any conflicts of interest.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study did not involve human participants, animals, or the collection of identifiable personal data. All analyses were conducted using publicly available, previously published data sources and simulation models. All methods were performed in accordance with the relevant guidelines and regulations. Because no primary data collection involving human participants or live vertebrates was performed, approval from an ethics committee was not required, and informed consent was not applicable. No identifiable images of human research participants are included in this article; therefore, written informed consent for publication of images was not required.

ADDITIONAL INFORMATION

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