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ABSTRACT

ASCAT 2025 Abstract Book

ORAL PRESENTATIONS

OR01 | Real-world data demonstrating the correlation between increased fetal hemoglobin and reduced VOC rates in SCD

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Background: Sickle Cell Disease (SCD) is the most prevalent inherited blood disorder, caused by a mutation in the HBB gene, which results in dysfunctional hemoglobin (HbS). Under hypoxic conditions, HbS polymerizes, causing the characteristic erythrocyte deformation and is primarily responsible for clinical manifestations. Fetal hemoglobin inhibits HbS polymerization, and elevated HbF expression has been shown to improve both morbidity and mortality. Quantitative and correlative data linking HbF levels to clinical outcomes remain limited (Brunn-Rasmussen et al., 2024).
Aims: We present a real-world data analysis and modelling study using medical records obtained from Picnic Health to estimate the effect of HbF levels on the frequency of VOCs.
Methods: Included were 673 SCD patients (age 2–62 years, average follow-up of 6.31 years). HbF levels, transfusions, and VOCs were extracted and analysed. Data were collected between 1996 and 2021.The mean and median HbF levels were 8.6% and 5.8%, respectively. For each variable, data were summarized by observation year. HbF was analyzed as the annual mean per individual, while VOC and transfusions were counted as annual events. Missing HbF values were imputed using the individual's median HbF from other years. If HbF was recorded but VOCs were not, the VOC count was imputed as zero. Similarly, if HbF or VOCs were recorded but transfusions were missing, the number of transfusions was imputed as zero.
Data for modelling assumed that if a patient had an HbF measure in a year without a recorded VOC, the VOC/year was zero. These data were oversampled to account for potential bias from missing years with zero events through artificially increasing the number of data points in the minority category by replicating existing samples and to ensure that all HbF values had the same number of patient years. For the purposes of oversampling fractional HbF percentages were rounded down. Modeling was done using the nlmixr2 library in R.
Results: Higher HbF levels correlated with an increased proportion of patients experiencing zero VOCs/year. HbF levels were associated with improvements in the geometric mean VOC rate (Figure 1). Before oversampling, patients with 0%–10%, 10%–20%, and 20%–30% HbF had a mean of 3.3, 3.1, and 2.1 VOC/year respectively, based on 2381, 844, and 260 patient-years. With oversampling, the means decreased to 1.4, 0.5, and 0.1 VOC/year. A model was developed to estimate the effects of HbF on VOC; the model was a zero-inflated exponential distribution model to account for the skewness of the VOC rates and the increased probability of zero VOC as HbF increases. Based on the model, patients with HbF levels <1%, 10%, 20%, and 30% experienced an average of 2.3, 0.73, 0.2, and <0.1 VOC/year respectively. Using the model, we found that each 1% increase in HbF was associated with a 12% reduction in VOC rate (95% CI: 11%–13%).
Summary/Conclusion: Our data confirm the inverse correlation between HbF levels and VOC frequency, highlighting the clinical significance of HbF in reducing SCD morbidity and its potential as a therapeutic target. The probability of experiencing zero VOC/year approaches 100% once HbF levels reach 25%, a threshold also observed in milder SCD

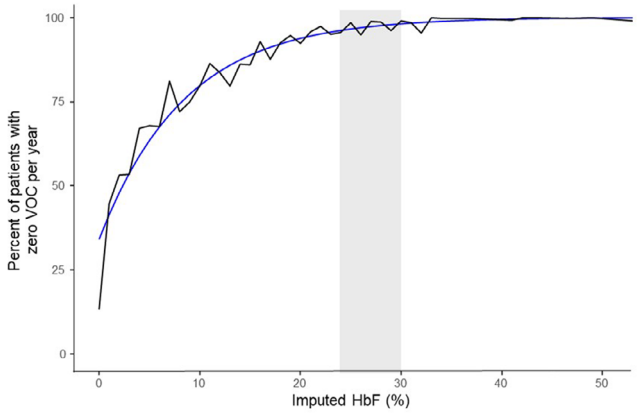

Figure 1. Probability of observing zero VOC per year by HbF %.
Blue line represents the model prediction; black line represents probability of observing zero VOC per year by HbF%.

phenotypes with heterozygous hereditary persistence of fetal hemoglobin (HbS/HPFH).

Importantly, even modest pharmacologic induction of HbF, could lead to a clinically meaningful reduction in annualized VOC rates. Our findings underscore HbF as an important biomarker correlating with clinical benefit in HbF-inducing treatment approaches.

OR02 | Voxelotor safety and effectiveness in patients with SCD in the RETRO and PROSPECT US Registries

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Introduction: Two US registry studies (RETRO and PROSPECT) evaluated real-world clinical and safety outcomes for patients with sickle cell disease (SCD) receiving voxelotor as part of their usual clinical care. The PROSPECT study was discontinued early in September 2024, after Pfizer withdrew voxelotor due to emerging preliminary data from 4 studies (including RETRO and PROSPECT) showing a potential imbalance in vaso-occlusive crises (VOCs) and an imbalance in fatal events in HOPE Kids 2 and RESOLVE studies (mostly in Sub-Saharan Africa). Preliminary data from an exploratory analysis of RETRO and PROSPECT suggested a potential increase in acute pain crisis (a surrogate for VOC) after initiation of voxelotor. The final assessment of RETRO and PROSPECT data following final database lock are presented.

Methods: After initial US approval of voxelotor in 2019, the RETRO registry (NCT04930328) collected retrospective data for participants with SCD treated with voxelotor for at least 2 weeks and aged ≥12 years at nine US sites from Q4 2019 to Q1 2022. The PROSPECT registry (NCT04930445) collected retrospective and prospective data for participants with SCD treated with voxelotor aged ≥4 years at 24 US sites starting in Q1 2022. Both registries collected data from healthcare records 1 year pre-voxelotor initiation. RETRO data were collected retrospectively for ~1 year post-voxelotor treatment and PROSPECT data were planned to be collected prospectively for up to 5 years post-voxelotor initiation. Safety analysis set included participants who met inclusion criteria and took at least one dose of voxelotor.

Results: RETRO enrolled 216 participants of mean (SD) age 33.1 (14.2) years. PROSPECT enrolled 265 participants (including 19 from RETRO), 260 of whom received a dose of voxelotor before the study was discontinued. The mean (SD) age of participants in PROSPECT was 32.0 (14.8) years: 33/265 (12.5%) were 12 to <18 years, and 23/265 (8.7%) were 4 to <12 years. The mean (SD) change in hemoglobin (Hb) from baseline ranged between 0.6 (1.6) and 0.8 (1.5) g/dL in RETRO and between 0.4 (1.5) and 0.7 (1.5) g/dL (through 48 months) in PROSPECT. The mean (SD) maximum change in Hb from baseline in RETRO was 1.3 (1.6) g/dL (range, 7.8 [1.5] to 9.2 [2.0] g/dL; $n = 179$) and in PROSPECT it was 2.0 (1.6) g/dL (range, 7.8 [1.4] to 9.8 [1.8] g/dL; $n = 251$). Voxelotor treatment also reduced markers of hemolysis in both studies. In both registries, acute pain crisis was the most common SCD-related adverse event, with annualized incidence rates (# of events/participant/year) of 1.33 pre-voxelotor and 1.54 post-voxelotor initiation in RETRO and 4.78 and 3.15 in PROSPECT. Overall, there were five fatal events in RETRO (ages 42–69 years at first dose of voxelotor) and six in PROSPECT (ages 20–56 years at first dose) none of which were considered related to voxelotor treatment per investigators (Table).

Conclusions: Despite differences in study designs and data collection methods for RETRO and PROSPECT, the limitations inherent in registry studies, as well as disruptions imposed on healthcare utilization by COVID-19 which may have impacted the reporting of acute pain crisis in RETRO and PROSPECT, the results of these two real-world studies were similar. Consistent with previous clinical and real-world studies, treatment with voxelotor in practice increased Hb and decreased markers of hemolysis with no evidence of voxelotor treatment leading to an increased frequency of acute pain crisis, new safety signals, or treatment-related deaths.

Table: Fatal events

Age at first dose, years/sex	Ethnicity	Adverse event	TEAE*	Treatment day†	Relationship to voxelotor	Cause of death
RETRO study participants						
68/F	Black/AA	Azotemia	Yes	N/A‡	Not related	Uremia
69/M	Black/AA	Death	Yes	92	Not related	Unknown
58/F	Black/AA	Renal failure	Yes	81	Not related	Acute on chronic renal failure
65/M	Black/AA	Chest pain (non-cardiac)	Yes	1	Not related	Chest pain, COVID-19
42/M	Black/AA	Shock hemorrhagic	No	195	Not related	Hemorrhagic and septic shock with acute liver failure
PROSPECT study participants						
21/F	Black/AA	Cardiac arrest	Yes	1154	Not related	Cardiac arrest
50/F	Black/AA	Sudden death	Yes	1303	Not related	Unknown
56/F	Black/AA	Hemolytic anemia	Yes	1562	Not related	Hemolytic anemia
20/F	Black/AA	Death	No	1003	Not related	Unknown
44/M	Black/AA	Pulmonary hypertension	No	921	Not related	Acute hypoxic respiratory failure
52/M	Black/AA	Death	No	934	Not related	Unknown

AA, African American; F, female; M, male; N/A, not available; TEAE, treatment-emergent adverse event.

*TEAE is defined as the adverse event that occurred at the time from the first dose of study drug through minimum of 28 days + last dose of study drug and the date of study completion/discontinuation.

†Treatment day was derived from date of first voxelotor treatment.

‡Date of AE onset not available; therefore, treatment day was unable to be calculated.

OR03 | Patient advocacy group involvement in the development of the MANAGE, MONITOR, REALIZE (MMR) framework

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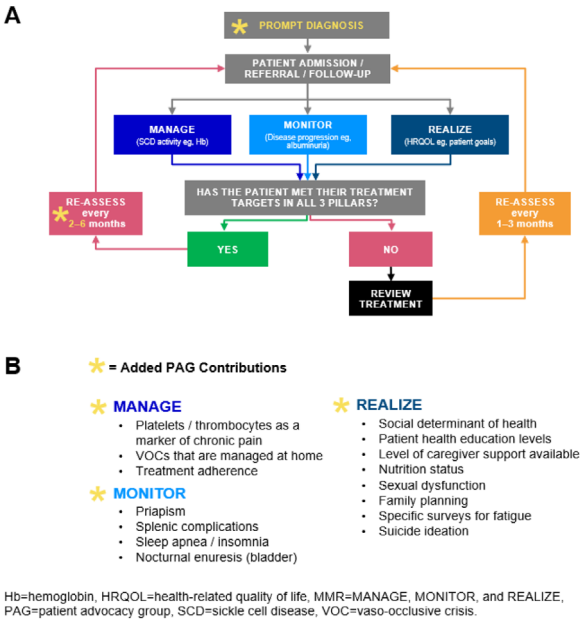
Introduction: The therapeutic landscape for sickle cell disease (SCD) continues to expand but guidance for goal-oriented treatment-decision-making is lacking. A treatment-decision-making tool for SCD management—the MANAGE, MONITOR, REALIZE (MMR) framework—was proposed by a team of global, SCD-expert healthcare providers (HCPs) who requested the inclusion of patient advocacy group (PAG) voices during framework development. The HCPs recognized the essential role of shared decision-making (SDM) in patient-centered care and wanted to address current gaps in SCD care that the PAG advisors identified in their regions. This collaborative approach aims to empower patients through informed choices and enables HCPs to tailor treatment goals to individual needs, enhancing patient satisfaction, adherence, and health outcomes.

Methods: In September 2024, 6 PAG advisors from Italy, Nigeria, the Kingdom of Saudi Arabia, the United Kingdom (UK), and the USA participated in virtual advisory boards chaired by HCPs who had participated in the MMR framework development. PAG advisors were selected from countries with high SCD prevalence, based on their advocacy work, and because of their lived experience with SCD. The advisors completed a 20-min online pre-meeting survey about the importance of 16 potential treatment outcomes (e.g. ability to make long-term plans, ability to do housework, avoiding chronic pain, etc). The relative importance of each treatment outcome was elicited using best-worst scaling (BWS). During these meetings, PAG advisors provided feedback on all 3 MMR pillars from the perspective and experiences of adults living with SCD and of caregivers of children with SCD. They commented on the accuracy and relevance of proposed assessment measures and identified potential discrepancies and/or missing framework components.

Results: Overall, the PAG advisors saw the MMR framework as a useful tool to help guide SDM in the treatment of SCD (Fig. A). Two advisors strongly advocated making prompt diagnosis the first step in the treatment-decision algorithm, highlighting that in many regions timely and accurate diagnosis is a critical unmet need. The advisors identified important gaps that were not addressed during initial framework development, highlighting areas requiring further attention and refinement, such as MANAGING treatment adherence, MONITORING insomnia, and REALIZING family planning goals, among others (Fig. B). Of the outcomes in the BWS, fertility had the most variation in relative importance—likely due to personal circumstances and life stage. There was consensus regarding the importance of other treatment outcomes, particularly those related to reducing or avoiding pain, and not worrying about hospitalization or sickness. Reducing the frequency of pain episodes and the impact of pain on usual activities were the most important outcomes of SCD care. Most advisors identified "managing pain" as the most critical aspect of SCD care as it impacts daily living. Reducing the frequency of pain was most important; it was ~2.4 and ~6.0 times more important than avoiding chronic pain or worry about sickness, respectively.

Conclusion: Patients, caregivers, and advocates were actively engaged, offering valuable and complimentary insights that helped shape the MMR framework to ensure this tool is relevant, comprehensive, and practical for both HCPs and patients.

Figure: The MMR treatment decision tool (A) and added PAG contributions (B).



Hb=hemoglobin, HRQOL=health-related quality of life, MMR=MANAGE, MONITOR, and REALIZE, PAG=patient advocacy group, SCD=sickle cell disease, VOC=vaso-occlusive crisis.

OR04 | Gene therapy in transfusion-dependant beta thalassaemia. Single centre experience: Manchester university hospitals

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Introduction: Gene therapy technology based on CRISPR-Cas9 is the first cellular therapy approved in the UK in September 2024 for the treatment of Transfusion Dependant

Thalassaemia (TDT). It corrects the underlying defect directly by reducing the BCL11A expression and increasing fetal haemoglobin production. Obtaining adequate CD34 positive haematopoietic stem cells (HSC) is a crucial step in order to proceed with this curative treatment. The CD34 cells collected takes 5–6 months to be edited. The edited CD34 stem cells are then reinfused back to the patient after 4 days of myeloablative busulphan conditioning chemotherapy.

Methods: All the eligible patients were discussed and approved at regional HCC and NHP. Seven patients underwent stem cell mobilisation with plerixafor and Granulocyte Colony stimulating factor (G-CSF). This was followed by leukapheresis over 3 days. Data was collected and analysed on patient characteristics, apheresis, and procedural complications retrospectively.

Results: The study cohort included seven patients, four males and three females. Age ranges were 13–37 years. One patient was splenectomised whilst all other patients had their spleen intact. All patients needed only one cycle of apheresis. GCSF was given over 5–7 days and plerixafor was given on the day of apheresis. The dose of G-CSF was 10 μg/kg daily and plerixafor 0.24 mg/kg. In splenectomised patient, the GCSF dose used was 5 μg/kg/daily.

Patient 1: WBC ranged from 65.6×10^9/L to 91.4×10^9/L. The total CD34 cell dose collected and sent for manufacturing was 70.24×10^6/kg. The CD34 cell dose of the gene edited stem cells were 18.5×10^6/kg.

Patient 2: WBC ranged from 73.2×10^9/L to 122.7×10^9/L. The total CD34 cell dose collected and sent for manufacturing was 38.8×10^6/kg. The CD34 cell dose of the gene-edited stem cells were 16.5×10^6/kg.

Patient 3: WBC count ranged from 132.2×10^9/L to 152.5×10^9/L. The total CD34 cell dose collected and sent for manufacturing was 22.54×10^6/kg.

Patient 4: WBC ranged from 56.8×10^9/L to 85.7×10^9/L. The total CD34 cell dose collected and sent for manufacturing was 29.22×10^6/kg.

Patient 5: WBC ranged from 68×10^9/L to 99.4×10^9/L. The total CD34 cell dose collected and sent for manufacturing was 21.96×10^6/kg.

Patient 6: WBC ranged from 71.7×10^9/L to 95.5×10^9/L. The total CD34 cell dose collected and sent for manufacturing was 77.39×10^6/kg. The CD34 cell dose of the gene-edited cells was 15.5×10^6/kg.

Patient 7: WBC ranged from 48.8×10^9/L to 60.8×10^9/L. The total CD34 cell dose collected and sent for manufacturing was 37.8×10^6/kg.

Conclusion: We successfully collected adequate CD34 stem cells in all patientswith one cycle of apheresis. In three out of the seven patients, the CD34 gene edited cell dose was 18.5×10^6/kg, 16.5×10^6/kg and 15.5×10^6/kg. The minimum requirement is 15×10^6/kg. For the remaining four patients, we are still awaiting the final CD34 cell dose.

We also report our first patient successfully undergoing gene therapy treatment for TDT in the UK since NICE Approval. He has engrafted and discharged home within 4 weeks. The adverse events seen were consistent with a myeloablative chemotherapy.

OR05 | Impact of SCD on daily lives and wellbeing of patients in Sub-Saharan Africa: SWAY findings

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Introduction: Sickle cell disease (SCD) is a group of inherited blood disorders associated with a range of clinical complications, primarily mediated by vaso-occlusion and hemolytic anemia. The objective of this SWAY data analysis was to compare the impact of SCD (examining symptoms—vaso-occlusive crises [VOCs], complications, and quality of life including emotional well-being, employment, and schooling) on patients in sub-Saharan Africa (SSA) compared to those in other low- and middle-income countries (LMICs) and high-income countries (HICs).

Methods: SWAY was a multicountry survey (Apr–Oct 2019) developed by international SCD experts, patient advocacy groups, and Novartis. Patients aged ≥6 years with SCD completed the survey (completion by proxy [parent/guardian/caregiver] was required for patients aged 6–11 years). The World Bank definition of high-income economy (gross national income/capita ≥US $12 536) was used to stratify countries into LMICs and HICs. VOCs (defined as "severe pain crises"), symptoms (experienced in the month preceding survey completion [excluding VOCs]), complications (ever

experienced), and genotype were all self-reported. Responses to questions on the impact of SCD were classified on a 1–7 Likert scale (1 = not severe/strongly disagree, 7 = worst imaginable/strongly agree).

Results: A total of 2145 patients were enrolled: SSA ($n = 519$), other LMICs ($n = 422$), and HICs ($n = 1204$). Patients in SSA were younger (median age: 15 years) than those in other LMICs (19 years) and HICs (29 years). The mean number of VOCs experienced in the year before survey completion was lower in SSA (4.5) and other LMICs (4.2) compared to HICs (6.0). Fatigue (34%–77%), headache (39%–58%), and bone aches (32%–58%) were the most frequently reported symptoms, while fever (60%–75%), infections (37%–66%), and joint issues (29%–65%) were the top 3 complications reported across countries. Patient-reported VOC burden was comparable across countries, with 30% of patients in SSA, 22% in other LMICs, and 27% in HICs experiencing ≥5 VOCs in the past year. The reported use of analgesics was lower in SSA compared to other LMICs/HICs, with 26% patients having ever been prescribed opioids (other LMICs 28%; HICs 73%) and only 30% patients received OTC analgesics (other LMICs 63%; HIC 64%). Hydroxyurea was most prescribed in other LMICs (67%) and HICs (51%) than in SSA (0%). The perceived burden of SCD on daily activities and emotional well-being was lower in SSA (32%, 52%) compared to other LMICs (31%, 56%) or HICs (43%, 64%). Patient-reported impact of SCD on career and schooling was also lower in SSA (vs. other LMICs and HICs), with 13% (vs. 47% and 43%) adults believing their income would be higher without SCD and 25% (vs. 56% and 56%) children reporting a negative impact on their school achievements, respectively.

Conclusion: The analysis of the SWAY survey data provides significant insights into SCD manifestations, management approaches, and the perceived burden of SCD, highlighting both commonalities and disparities across SSA, other LMICs, and HICs. Patients in SSA were younger and had a lower symptom burden but reported similar primary symptoms as in other LMICs and HICs, suggesting that the impact of SCD may progress with age. Despite a higher proportion of patients in SSA experiencing more than five VOCs annually—opiates use was still lower compared to other LMICs and HICs.

OR06 | Phase 3, randomized, HOPE Kids-2 trial of voxelotor in children with SCD and conditional TCD

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Introduction: Children with sickle cell disease (SCD) have an elevated risk of stroke, and the level of risk correlates with cerebral blood flow velocity (CBFV) as measured by transcranial Doppler (TCD) ultrasound. Treatment approaches for children with conditional TCD velocities (170 to <200 cm/s using STOP criteria) are not well defined.

Methods: HOPE Kids 2 (NCT04218084) was a phase 3, multicenter, double-blind, placebo-controlled trial designed to assess the effect of voxelotor on CBFV. Eligible participants were aged 2 to <15 years with SCD (HbSS/HbSβ^0 genotypes) and CBFV 170 to <200 cm/s. Participants were randomized 1:1 to voxelotor or placebo for 96 weeks. The primary endpoint was change from baseline to Week 24 in the time-averaged mean of the maximum velocity (TAMMV) of CBF, measured using TCD. Treatment-emergent adverse events (TEAEs) were classified as SCD-related (sickle cell anemia with crisis, acute chest syndrome, pneumonia, pneumonia viral, priapism, dactylitis, splenic sequestration, hepatic sequestration, and osteonecrosis) or non-SCD-related (any TEAE that was not an SCD-related event). Dosing was paused in May 2024, due to an imbalance of reported fatal TEAEs, and all active voxelotor trials were discontinued in September 2024. For efficacy analyses, all participants had reached 48 weeks (or had discontinued early) before the dosing pause. We report data from the final database lock (April 16, 2025).

Results: In total, 236 participants were randomized (voxelotor $n = 120$; placebo $n = 116$); 195 (83%) were enrolled in sub-Saharan Africa. For the primary endpoint, the decrease from baseline to Week 24 in CBFV was significantly greater with voxelotor (least-squares mean −12.06 cm/s [$n = 114$] vs. −4.29 cm/s with placebo [$n = 108$]; difference −7.77 cm/s; 95% CI, −13.18 to −2.37; $p = 0.0048$). Improvement was sustained through Week 48; −10.33 cm/s ($n = 111$) with voxelotor versus −3.86 cm/s with placebo ($n = 107$). At Week 24, a higher proportion of the voxelotor group had a CBFV response (≥15 cm/s reduction from baseline; 38.2% vs. 25.3% with placebo; $p = 0.0494$). Hemoglobin also increased at Weeks 24 and 48 with voxelotor. By end of study, adjusted annualized incidence rates of vaso-occlusive crisis (VOC) were 1.098 events/year in the voxelotor group and 0.580 events/year in the placebo group. During the trial (median [range] exposure: voxelotor 84 [3, 104] weeks, placebo 84 [3, 106] weeks), SCD-related TEAEs were reported for 59.2% (71/120) and 42.2% (49/116) of the voxelotor and placebo groups, respectively; the most common was sickle cell anemia with crisis, reported for 59.2% (71/120) and 37.9% (44/116) of the respective groups. TEAEs of stroke were reported for 0/120 participants in the voxelotor group and 3/116 in the placebo group, of which 1 was fatal. Fatal TEAEs were reported for 10 participants (voxelotor $n = 8$; placebo $n = 2$); all were in sub-Saharan Africa and four cases were associated with malaria. All fatal events were considered unrelated to study drug.

Conclusion: In children with SCD and conditional TCD velocities, HOPE Kids 2 demonstrated reduction in TCD flow velocity and improvement in hemoglobin with voxelotor. The fatal events in the study were consistent with known causes of death in patients with SCD. However, the

imbalance in VOCs suggests that enhanced monitoring for increases in VOC frequency may be needed for patients receiving voxelotor.

OR07 | RESOLVE: A phase 3, randomized trial evaluating voxelotor for leg ulcer healing in SCD

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Introduction: In sickle cell disease (SCD), leg ulcers are associated with a severe hemolytic phenotype and increased mortality rate, yet no treatments for leg ulcers in SCD have proven effective in clinical trials. After post hoc analysis of the HOPE trial suggested that voxelotor was associated with improved healing, the RESOLVE trial was designed to evaluate voxelotor for leg ulcer resolution.

Methods: RESOLVE was a phase 3, randomized, double-blind, placebo-controlled trial (NCT05561140). Participants aged ≥12 years with SCD (HbSS/HbSβ^0) and ≥1 active cutaneous leg/ankle/dorsal foot ulcer (size >2 cm^2; duration ≥2 weeks to <6 months) were randomized 1:1 to voxelotor 1500 mg or placebo for 12 weeks. The primary endpoint was complete resolution of target ulcer, requiring skin re-epithelialization at two consecutive study visits 2 weeks apart in the 12-week randomized period. After Week 12, both groups received open-label (OL) voxelotor for a further ≥12-week period (continuation after Week 24 was permitted if clinical benefit was derived and until alternative access to voxelotor was available). Treatment-emergent adverse events (TEAEs) were assessed throughout, including sickle cell anemia with crisis. The trial began in June 2022, study dosing was paused in May 2024, and the trial was discontinued in September 2024.

Results: RESOLVE randomized 88 participants (voxelotor $n=45$; placebo $n=43$) from Kenya ($n=62$), Nigeria ($n=17$), and Brazil ($n=9$). A higher proportion of the voxelotor group were receiving hydroxyurea (voxelotor 51%; placebo 33%) and had ≥2 VOCs during the past year (voxelotor 47%; placebo 35%). At baseline, mean (SD) target ulcer size was 20.8 (25.8) cm^2 for the voxelotor group and 25.8 (32.1) cm^2 for the placebo group. At Week 12, the primary endpoint was not met: 6.7% (3/45) of the voxelotor group versus 7.0% (3/43) of the placebo group achieved ulcer resolution (difference −0.3%, 95% CI −10.9%, 10.2%, two-sided $p=1.00$). The mean increase in hemoglobin with voxelotor was 1.9 g/dL versus no change with placebo. In the OL period, in which both groups received voxelotor, a further nine participants had ulcer resolution by Week 24 (total: continuing-voxelotor 16.3% [7/43]; delayed-voxelotor 18.6% [8/43]). Median (range) exposure was similar between groups (randomized period: voxelotor 12 [2–14], placebo 12 [12–14] weeks; OL period: continuing-voxelotor 21 [6–85], delayed-voxelotor 23 [11–83] weeks). For TEAEs, sickle cell anemia with crisis was the most common SCD-related TEAE (randomized period: voxelotor 44.4%; placebo 25.6%, OL period: continuing-voxelotor 60.5%; delayed-voxelotor 53.5%). By the trial end, fatal events were reported for 11 participants who received voxelotor (1 in the randomized period; 8 in the OL period, 1 at 118 days after the last voxelotor dose, and for 1 participant, it could not be confirmed when they had received their last voxelotor dose). The fatal events were consistent with known causes of death in populations with SCD living in malaria-endemic regions, and none were considered related to study treatment.

Conclusion: In RESOLVE, the primary endpoint was not met, as voxelotor treatment for 12 weeks did not result in complete resolution of more ulcers compared with placebo. In addition, participants receiving voxelotor had a higher rate of TEAEs of sickle cell anemia with crisis. The results reflect the challenges with management of leg ulcers in patients with SCD, underscoring the need for new treatments.

OR08 | Youth voices, lived experience and real world impact of a patient engagement day

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Introduction: The 2021 *No One's Listening* report highlighted a critical need to raise awareness of sickle cell (SC) among both healthcare professionals (HCP) and the public, despite being more prevalent than other genetic conditions. Engagement & trust between HCPs and SC patients remain poor.

This patient and public engagement event looked to progress and specifically engage younger members of the community

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to address empowerment. It offered a platform for innovative conversations between HCPs, other stakeholders and patients and community. Impact was evaluated both formally and informally.

Methods: The event was produced by our Adult and Paediatric Haematology team, in collaboration with the ACTIVE Youth Health Board, the Red Cell Network, Sickle Cell Suffolk and the National Blood Service as part of the annual Cambridge Festival in a school close to the hospital, co-located and advertised with health related hands on activities on the same day and part funded by a NHS-X grant. The programme consisted of five screenings of "SICKLE", a 30 min coproduced film with a Q&A with patients and clinical cast.

A range of coproduced hands-on activities targeted different learning styles and age groups:

- Learning blood-taking on a model
- Crafting red blood cells from foam clay and playing a game with large soft wool cells and arty shape matching game
- A genotype activity with jelly bears
- Educational board games with a sickle cell theme
- Information on red cell apheresis and blood donation
- Focused topic poster: Parenting with sickle cell

Young person-designed t-shirts flattened the hierarchy between SC patients, HCPs, families and volunteers.

The event was designed as a drop-in session, with prebooking required for the film screening. Feedback was collected through structured forms after each screening, as well as creative methods such as a "Positivity Tree" poster where children left comments on red sickle-shaped notes. Volunteer reflections aided personal learning and observations.

Results: Of approximately 125 attendees, 36 completed the forms. All rated the event as 'helpful' and 97% would attend again. The most valued aspects were hearing directly from patients and engaging in hands-on learning. Attendees highlighted a public knowledge gap and expressed interest in future events exploring systemic NHS issues, mental health and holistic care around sickle cell. Suggestions for improvement included broader representation of heritage in patient stories, enhanced accessibility (e.g. subtitles), and more space for detailed post-screening dialogue. Future topics requested included treatment options, nutrition, mental health, and current clinical trials.

Conclusion: SC education is impactful when coproduced by those with lived experience of developmental stage and clinical diagnosis, and when delivered through active and hands-on learning. An inclusive coproduced design and careful consideration of the power dynamic between patients, carers, and community foster trust and cooperation between patients and HCPs. Such a non-hierarchical environment promoted open dialogue and empowered all attendees—regardless of prior knowledge, age or experience. Feedback highlighted a strong desire for more detailed, practical

information on treatment and holistic care, and representation of patient voices together. Experiential activities broke barriers and helped all ages gain mastery and knowledge that is pertinent to sickle cell impact improvements.

OR09 | Health literacy in thalassemia: Initial learnings from the thalassemia advocacy advisory council global patient survey

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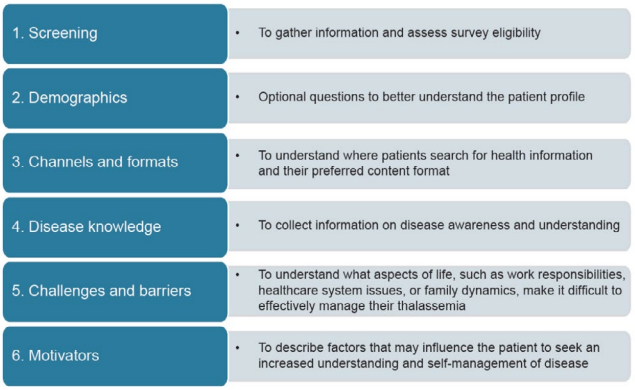
Introduction: Despite advances in the management of thalassemia, a rare and under-recognized hereditary anemia, unmet needs remain in this diverse patient population. The Thalassemia Advocacy Advisory Council (AAC), an international group of patients, caregivers, advocacy organizations, and healthcare professionals (HCPs), supported by Agios Pharmaceuticals, is a novel approach to better understand these needs and support initiatives to improve outcomes and care. An assessment and subsequent evidence audit of published literature and advocacy group/community-based research identified health literacy (i.e. understanding of thalassemia, its complications, and treatment approaches) as a critical gap for patients. Based on the findings, the Thalassemia AAC developed a patient survey to gain insights into the global community's perspectives and to identify strategies to potentially address health literacy needs and support informed patient advocacy. This study aimed to report the novel methodology and key operational learnings from deploying the Thalassemia AAC global patient survey.

Methods: A bespoke, 12–15-min survey was self-administered to adults (≥18 years) with a self-reported physician diagnosis of alpha (α)- or beta (β)-thalassemia, excluding those diagnosed with α- or β-thalassemia trait or those currently enrolled in mitapivat clinical trials (e.g. ENERGIZE [NCT04770753] or ENERGIZE-T [NCT04770779]). Participants from the United Arab Emirates, Saudi Arabia, Kuwait, Italy, USA, Greece, and Brazil were recruited via a specialist survey recruitment agency and/or a patient advocacy organization network. All participants provided informed consent. The primary objective was to describe health literacy in patients with thalassemia; secondary objectives included studying barriers and motivational aspects that affect disease understanding and self-management. The survey comprised six sections (Figure) and was completed online. Survey responses will be summarized as number and percentage for categorical variables, and as net percentages for continuous variables. Qualitative, free text responses will be reviewed and categorized.

Results: Initial key operational learnings include the importance of a collaborative approach across patients, caregivers, advocates, and HCPs, to help define meaningful survey questions and ensure an approach that incorporates emotional and experiential factors of importance to patients. Early integration of these representatives into the research process is vital to inform the most effective survey distribution methods and to allow tailored approaches based on regional and cultural factors. Survey data analysis is ongoing.

Conclusion: Health literacy plays a critical role in patient and caregiver understanding and management of rare diseases; empowering patients with the information they need to advocate for their own care is essential for improving outcomes. The novel Thalassemia AAC developed a collaborative framework to design and implement a global patient survey, with the aim of yielding insights that are meaningful and impactful to patients. Key learnings from this unique approach can serve as a valuable roadmap for addressing unmet needs in other rare disease communities.

Figure. The Thalassemia AAC global survey sections



AAC, Advocacy Advisory Council

OR10 | Supporting the psychological wellbeing of people with sickle cell when they are admitted to hospital

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Introduction: Sickle cell disorder (SCD) is a genetic condition which leads to the formation of sickle-shaped red blood cells which cause a range of complications including vaso-occlusive crises (VOC) and severe pain. VOC can require SCD patients to have hospital admissions to manage their pain. SCD mainly affects black people with African/Caribbean heritage and it is important to highlight the role of racism and stigma towards patients. Research has found that SCD patients often receive sub-standard care and lack of prioritisation which has impacted their trust of healthcare systems and increased their fear of being admitted into hospital. Care failings of SCD patients has in some cases led to early and avoidable deaths due to the lack of understanding of sickle cell and the systemic challenges that SCD patients face to access the treatment they need. Psychologists within the Haematology Psychology Service (HPS) at our acute hospital Trust offer psychological support to SCD patients through inpatient consultations to support with issues including coping with their inpatient experience, mental wellbeing (stress, anxiety, low mood), adjusting to being in hospital and managing treatment.

Methods: The aim of this audit was to explore the support the HPS team offers to inpatients with SCD, and identify areas for improvement. The HPS work closely with the wider Haematology team to offer psychological support to patients admitted to hospital. The duty psychologist role includes attending a weekly ward round, updating the wider team on patients currently admitted, offering face-to-face inpatient consultations, staff consultations and debriefs. Inpatient consultations are offered throughout Mondays, with capacity to see two further patients on Wednesdays and Fridays.

The data has been extracted from the HPS referral database covering consultations between April 2024 and March 2025.
Results: There were 162 inpatient referrals for patients with SCD; of these referrals 128 were seen for a consultation. The majority of these consultations were for support with coping with hospital admission (31.3%) followed by anxiety related to health (10.9%). 26% of the referrals seen were for patients whose primary problem might have been appropriately supported by a referral to a different service, for example bereavement, welfare or social support. Nearly 10% of patients seen disclosed thoughts about harm to themselves or others (usually suicidal ideation) and half of these merited onward referral to our liaison psychiatry team for support. 34 (21.0%) referrals did not result in a consultation; reasons for this included that psychological support was not indicated (50%) and patient declined to be seen (32.4%).
Conclusion: HPS plays a significant role in supporting the emotional wellbeing of SCD inpatients, particularly with hospital admissions and anxiety about their health. A significant number of patients were more appropriate for another service, or declined to see a psychologist. To develop the service and improve patient experience we will develop clearer referral pathways and offer more guidance to the wider team about alternative options for psychosocial support, as well as helping referrers to feel confident in how they explain the role of HPS, and to ensure that they have sought patient consent for the referral. We will also consider how we can work with the wider MDT and ward staff to improve awareness of the psychology service and what it can offer.

OR11 | Red blood cell movement under flow: A new marker of deformability for SCD patients

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Introduction: We propose a new marker of red blood cell (RBC) deformability, measured on individual cells, and sensitive to RBC membrane stiffness and internal viscosity. This marker is based on the individual mouvement of RBC under flow. In earlier study by our group, it was shown to be significantly reduced in sickle cell disease (SCD) patients compared to healthy subjects, and sensitive to RBC dehydration and density. The marker exhibited a high inter-patient variability at steady state and decreased significantly during vaso-occlusive crises (VOC). The study here aimed at comparing the marker with RBC deformability measured by gold-standard ektacytometry technique in SCD patients, and to identify its associations with clinical and biological parameters.
Methods: Under shear flow, a deformable RBC exhibits a droplet-like behavior when the stress exerted by the flow exceeds a threshold value: the membrane rotates around the cytoplasm in a so-called tank treading (TT) motion. The less deformable the RBC, the higher the threshold stress. Each stress value is associated with the minimum RBC deformability required for TT movement. The fraction of RBC displaying TT movement (f_{TT}) in a blood sample reflects the overall RBC deformability of the sample.
The f_{TT} marker and ektacytometry deformability parameters were measured in a group of 62 SCD patients (24 regularly transfused and 28 non-transfused). For f_{TT} measurement, 5 microliters of whole blood were diluted in a dextran solution (PBS, 9% dextran) and injected into a microfluidic flow chamber under a shear stress of 0.4 Pa. The movement of 2000 cells was recorded, analyzed and classified by artificial intelligence, to determine f_{TT} value. RBC deformability was also assessed at several shear-stresses by ektacytometry with blood diluted in PVP buffer supplied by the manufacturer and in the same dextran solution as the one used in the microfluidic measurements.
Results: For all patients, f_{TT} correlated with the elongation index EI at all shear stress values (0.3–30 Pa) in PVP buffer ($N=59$, Pearson correlation $r=0.37–0.51$, $p=3.7e^{-5}$ to $4.4e^{-3}$), at shear stress ≥1.69 Pa in dextran solution ($N=60$, $r=0.48–0.60$, $p=3.7e^{-7}$ to $2.3e^{-4}$), and with the maximum elongation index EI_{max} (PVP: $N=60$, $r=0.39$, $p=1.9e^{-3}$; dextran: $N=60$, $r=0.51$, $p=2.6e^{-5}$). Comparison of f_{TT} values by patient subgroups showed that it was lower in non-transfused patients (62% [$N=28$] vs. 72% [$N=24$], $p=0.033$) and in patients undergoing VOC (45% [$N=5$] vs. 67% [$N=22$], $p=0.026$). Based on this result, correlation analysis (Pearson [r] or Kendall [tau]) was performed for non-transfused patients between f_{TT} and quantitative laboratory parameters: it showed a positive correlation with fetal haemoglobin ($N=28$, $r=0.51$, $p=0.0056$), and negative correlations with haemoglobin S ($N=27$, $r=-0.67$, $p=0.0001$), total bilirubin ($N=25$, tau = −0.35, $p=0.01$), reticulocyte count ($N=24$, in g/l, $r=-0.52$, $p=0.009$; in %, $r=-0.59$, $p=0.002$), and C-reactive protein ($N=15$, CRP, tau = −0.53, $p=0.004$).
Conclusion: Our study shows that the f_{TT} marker correlates with ektacytometry measurements and with biological markers of hemolysis and inflammation (reticulocyte count, bilirubin and CRP). These findings indicate that this marker may act as a comprehensive indicator of RBC deformability for the development of new tests to be used in point-of-care or as companion test to monitore SCD patients.

OR12 | HELIOS action: Advancing research, education, and equity in haemoglobinopathies across Europe and beyond

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Introduction: Haemoglobinopathies, such as thalassaemia syndromes and sickle cell disease, are among the most prevalent inherited conditions worldwide. Despite their global impact, care remains inconsistent, with major disparities in diagnosis, treatment access, and research integration across regions. To address these challenges, the HELIOS COST Action (Haemoglobinopathies in European Liaison of Medicine and Science) was launched in 2023. This initiative aims to establish a sustainable, inclusive, and collaborative network to strengthen research capacity, harmonize clinical practices, and support equitable participation in haemoglobinopathy science and policy-making.

Methods: HELIOS is supported by the European Cooperation in Science and Technology (COST) and functions as an open, multidisciplinary network. Its activities are organized across five interconnected working groups: (1) molecular research and diagnosis; (2) clinical research and patient management; (3) data management and interoperability; (4) education and capacity building; and (5) dissemination and outreach. A comprehensive training program includes in-person schools, virtual webinars, and cross-border collaboration opportunities. The network also provides financial support through grants to facilitate member participation in international conferences and scientific missions.

Results: As of June 2025, HELIOS comprises over 235 members from 36 countries across Europe, Africa, Asia, North America, and Australia. The network demonstrates strong diversity, with 57% women, 47% early-career researchers (under 40), and 58% from COST Inclusiveness Target Countries. In its first 2 years, HELIOS training activities engaged more than 680 participants, 70% of whom were women, 46% early-career researchers, and 45% from target countries. Training initiatives have included molecular diagnostics schools, FAIR data workshops, transcranial Doppler training, virtual journal clubs, clinical webinar series, and expert lectures on recent advances in haemoglobinopathies. Through systematic mapping efforts and standardized assessment tools, HELIOS is actively identifying and addressing disparities in diagnosis, access to treatment, and professional development across participating regions. The network has established strategic collaborations with leading international initiatives such as ERN-EuroBloodNet, INHERENT, and HemaFAIR, enhancing coordination and avoiding duplication of effort. Additionally, HELIOS has financially supported 24 grant applications to date, enabling member participation in high-level international conferences and short-term scientific missions.

Conclusion: HELIOS is advancing the international response to haemoglobinopathies by promoting collaboration, standardization, and inclusive participation. Its coordinated approach supports the development of stronger research and care infrastructure to address shared challenges across diverse healthcare settings.

OR13 | High morbidity in adults with non-transfusion-dependent thalassemia referred to U.S. specialty centers

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Introduction: Non-transfusion-dependent thalassemia (NTDT) is associated with progressive morbidity that is often under-recognized. Many patients are referred to specialty centers only after complications have developed, reflecting gaps in recognition and management in community settings. We aimed to characterize the clinical features of adults with NTDT at the time of referral to U.S. thalassemia centers to identify opportunities for earlier intervention.

Methods: We conducted a cross-sectional study of adults with NTDT referred to three U.S. thalassemia centers between 2013 and 2023. NTDT was defined as α- or β-thalassemia not requiring regular transfusion support at referral. Demographics, genotype, lab values, organ-specific complications, and transfusion history were abstracted from

medical records. Descriptive statistics summarized clinical characteristics stratified by genotype.

Results: Eighty-two adults with NTDT were identified: 45% with α-thalassemia (deletional and non-deletional HbH disease) and 55% with β-thalassemia syndromes. The median age at referral was 36.5 years (range 18–74); 66% were female. Splenectomy was reported in 53% of β-thalassemia patients versus 11% of α-thalassemia patients. Pulmonary hypertension (14% vs. 3%) and paraspinal masses (29% vs. 5.5%) were more common in β-thalassemia. Arrhythmias occurred in 9% of β-thalassemia patients and none with α-thalassemia. Decreased bone mineral density was the most common endocrinopathy (38% overall). At referral, 52% had hemoglobin <9 g/dL; 38% had ferritin >800 ng/mL, exceeding the NTDT guideline threshold for tissue iron evaluation. Despite initial NTDT designation, 49% of patients ($n = 40$) were recommended to start on regular transfusion therapy. Most common indications were fatigue and symptomatic anemia (19 patients), pulmonary hypertension (4), and symptomatic extramedullary hematopoiesis (11).

Conclusion: This multi-center study highlights the substantial clinical burden among adults with NTDT at the time of referral, particularly among those with β-thalassemia syndromes. Many had already developed endocrine and cardiopulmonary complications. Nearly half ultimately required transfusions, challenging the notion that they are truly transfusion independent. These findings underscore the need for earlier recognition, risk stratification, and timely referral to thalassemia specialty centers. Interventions to facilitate earlier access to comprehensive care are urgently needed to prevent long-term morbidity in this population.

Table 1. Clinical and laboratory characteristics of adult patients with NTDT upon referral to U.S. thalassemia specialty centers.

	Alpha thalassemia	Beta thalassemia	p-value
N	37	45	
age, median (IQR)	35 (30, 46)	38 (32, 48)	0.41
sex			0.22
Male	10 (27%)	18 (40%)	
Female	27 (73%)	27 (60%)	
Started transfusions after referral			<0.001
No	32 (86%)	13 (29%)	
Yes	5 (14%)	32 (71%)	
History of splenectomy			<0.001
No	33 (89%)	21 (47%)	
Yes	4 (11%)	24 (53%)	
Hemoglobin (g/dL), median (IQR)	9.2 (8.2, 10)	8.6 (7.7, 9.5)	0.030
Ferritin (ng/mL), median (IQR)	419.7 (220, 657)	766.5 (385.55, 1558.345)	0.002
Over 5 lifetime units pRBC transfusion			0.081
No	23 (64%)	20 (44%)	
Yes	13 (36%)	25 (56%)	
Recommended transfusions after referral			<0.001
No	31 (84%)	11 (24%)	
Yes	6 (16%)	34 (76%)	

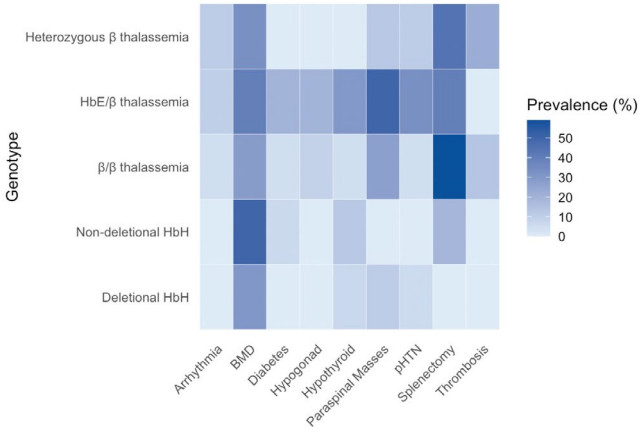

FIGURE 1 Heatmap of clinical complications by genotype. BMD, bone mineral density loss; pHTN, pulmonary hypertension.

OR14 | Reproductive health in women with sickle cell disease – A single center study

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Introduction: Sickle cell disease (SCD) is a genetic blood disorder affecting over 100 000 individuals in the United States (U.S.), with a high prevalence among non-Hispanic Black populations, including in Shelby County, TN. Advances in care have enabled more women with SCD reach key reproductive milestones, though they often experience complications such as delayed menarche, menstrual irregularities, pregnancy complications, and early menopause. Despite this, data on reproductive health outcomes in this population remain limited. This study was a retrospective cohort review conducted at the Diggs-Kraus Comprehensive Sickle Cell Center at Regional One Health, to evaluate the reproductive health of women with SCD.

Methods: The study protocol was approved by the Institutional Review Board (IRB) at the University of Tennessee Health Sciences Center (UTHSC). Female patients seen by sickle cell specialists were included if they had documentation of obstetric/gynecologic history. Clinical data were extracted from the electronic medical record, including age at menarche, menopausal status and onset, pregnancy outcomes, and reproductive health complications such as menstrual irregularities and fertility challenges. Odds ratios were computed comparing the frequency of events in the SCD group to those in the general U.S. population, using peer-reviewed population data as reference controls.

Results: A total of 251 females with SCD were included in the study, with a total of 494 pregnancies. Mean age of the cohort was 39.2 years (17–83), genotype 61% Hb SS, 32% Hb SC, 6% Hb Sβ+, 1% Hb Sβ0. The average age of menarche was calculated to be 13.5 years, and females with SCD were found to have an odds ratio (OR) of delayed menarche of 6.52 (95% CI: 4.69–9.07), compared to the general population. The average age of menopause was 46.4, with an OR of 7.33 (95% CI: 3.87–13.50) of early menopause compared to the general population. Females with SCD were more likely to have a preterm birth than the normal population (OR 2.61, 95% CI: 1.88–3.63). In addition, pregnant women with SCD were more likely to have preeclampsia than the general population (OR 1.48; 95% CI: 1.13–1.96).

Conclusion: This study highlights the significant reproductive health burden experienced by women with SCD. Delayed menarche, early menopause, and increased rates of pregnancy complications such as preeclampsia, stillbirth, and cesarean delivery were prevalent in our cohort. Quantitative analysis revealed that patients with SCD face disproportionately high odds of these outcomes compared to the general population. These findings underscore the need for structured reproductive counseling and interdisciplinary care models that integrate hematologic and obstetric/gynecologic management for women with SCD. Future research should build upon this work through prospective cohort studies that track reproductive milestones and complications in real time. Incorporating fertility biomarkers, such as Anti-Müllerian Hormone (AMH), would provide objective measures of ovarian reserve and help assess the reproductive impact of SCD and its treatments. Stratified analyses by genotype could offer personalized insights into reproductive risk. Interventional studies involving multidisciplinary care teams may improve reproductive planning, contraceptive counseling, and pregnancy outcomes for patients with SCD. Comparative studies with non-SCD controls are also needed to better isolate disease-attributable risks.

OR15 | Growth Differentiation factor-15 as a non-invasive biomarker of liver fibrosis in sickle cell disease

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Introduction: Sickle cell disease (SCD) can lead to progressive liver injury, including fibrosis, due to chronic hemolysis, inflammation, and iron overload. Growth Differentiation Factor-15 (GDF-15), a stress-induced cytokine, has been implicated in fibrogenesis and may serve as a biomarker of liver injury. This study aimed to investigate the association between GDF-15 levels and liver fibrosis in adult SCD patients.

Methods: Thirty adult patients with SCD, followed at a single Greek Thalassemia and Sickle Cell Unit, were prospectively enrolled. Clinical data, treatment history, laboratory results (including liver biochemistry, iron indices, hepcidin), and imaging (transient elastography, MRI T2*) were collected. Liver fibrosis was considered significant (≥F2) if FibroScan >7.2 kPa and either APRI >1.5 or FIB-4 >1.45. GDF-15 levels were measured by ELISA and evaluated in relation to fibrosis and other clinical parameters.

Results: Fourteen patients (46.7%) had significant liver fibrosis. GDF-15 levels were markedly elevated in these patients (5712.9 vs. 2991.7 pg/mL, $p < 0.002$) and positively correlated with liver stiffness ($r = 0.657$, $p < 0.001$), age, episodes of acute liver crises in the previous five years, creatinine, APRI, and FIB-4. In multivariate analysis adjusted for age, HbS%, albumin, and platelet count, GDF-15 remained independently associated with liver stiffness ($\beta = 0.619$, $p = 0.002$). No correlation was found with ferritin, hepcidin, or LIC. A GDF-15 cut-off of 4200 pg/mL yielded an AUC of 0.835 (95% CI: 0.686–0.983, $p = 0.002$), with 87.5% sensitivity and 64.3% specificity for detecting significant fibrosis.

Conclusion: GDF-15 levels are significantly increased in SCD patients with liver fibrosis and independently correlate with liver stiffness and liver crisis history. GDF-15 shows promise as a non-invasive marker for liver fibrosis in this population.

OR16 | Prevalence, characteristics and outcome of monoclonal gammopathies in adult β-thalassemic patients: A single center experience

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Introduction: As life expectancy of thalassemic patients (pts) has been extended over the past decades, several morbidities have emerged, including malignancies. Although the risk of solid tumors, especially hepatocellular carcinoma and its association to iron overload have been clearly reported, data on the incidence of hematologic malignancies and especially plasma cell dyscrasias remain scarce.

Aims: The aim of this study is to report the prevalence of monoclonal gammopathies (MGs), including monoclonal gammopathy of unknown significance (MGUS) and multiple myeloma (MM) and in adult β-thalassemic pts.

Methods: Capillary protein electrophoresis was performed as part of routine follow-up at least annually from 2015 until present. In cases with a monoclonal spike serum

immunofixation was performed. Clinical and laboratory patients' data were collected from medical files.

Results: In the total population of 239 patients with β-thalassemia, the median age was 53 years (range: 19–53), 47.7% were male and 31% were transfusion dependent (TDT). Overall, 17/239 (7.1%) pts had hypergammaglobulinemia in protein electrophoresis. A monoclonal spike was detectable and confirmed by immunofixation in eight cases (3.3%), of whom only two were TDT, five had undergone splenectomy, five had iron overload and 3 were on iron chelation treatment. The median age at the time of MG diagnosis was 56 years (range: 38–66). The paraprotein type according to immunofixation was IgGλ in three pts and IgGκ in two with median IgG levels of 1430 mg/dL (range 872–3050), IgAκ in two patients with IgA levels 831 and 1740 mg/dL and IgMλ in one pt with IgM levels of 199 mg/dL. A normal κ/λ ratio was found in all but one pt who had a κ/λ ration of 198.45 and was also the only one with proteinuria and positive urine immunofixation (κ light chain). None of the pts had elevated creatinine or calcium. Low dose CT was negative for lytic lesions in all pts. Bone marrow biopsy performed in four patients at diagnosis revealed plasmacytic infiltration ranging between 4% and 40%. In total out of the eight β-thalassemic pts with MG, diagnosis was MGUS in five pts, smoldering MM (SMM) in two and active MM in one. The prevalence of MG in our cohort by age group, is presented in Table 1.

All patients with MGs were under regular follow-up, as per IWGM guidelines. The single non-TDT patient with active MM, aged 38 at the time of diagnosis, was initially treated with lenalidomide–doxorubicine–dexamethasone, followed by autologous stem cell transplant (SCT) and consolidation with lenalidomide–dexamethasone. He relapsed 6 years later and received treatment with belantamab mafodotin–pomalidome–dexamethasone and remains in stringent complete remission until present.

Conclusion: In our adult patient population there seems to be an increased frequency of MGs, including MGUS and MM. The diagnosis of MG was made at an age younger than expected. Larger cohorts of patients and comparison to the general population data are required to confirm these observations. Standard treatment, including autologous SCT can be safely administered to young pts with β-thalassemia, leading to durable remissions.

Table 1: Prevalence of Monoclonal Gammopathies (MGs) in 239 adult β-thalassemic patients

AGE GROUP (yrs)	Pts (#)	MG # (%)	MGUS # (%)	MM # (%)
80-87	6	0	0	0
70-79	26	**1 (3.8%)**	0	**1 (3.8%)**
60-69	47	**2 (4.2%)**	**1 (2.1%)**	**1 (2.1%)**
50-59	69	**3 (4.3%)**	**3 (4.3%)**	0
40-49	55	**2 (3.6%)**	**1 (1.8%)**	**1 (1.8%)**
19-39	36	0	0	0
TOTAL	239	**8 (3.3%)**	**5 (2.1%)**	**3 (1.2%)**

OR17 | Knowledge and awareness of sickle cell disease among parents/caregivers in Khartoum, Sudan

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Introduction: Sickle Cell Disease (SCD) is a group of inherited haemoglobin disorders characterized by the abnormal shape of red blood cells and the presence of hemoglobin S (HbS). It is considered a major public health issue, particularly in sub-Saharan Africa. In Sudan, especially in western regions, SCD has a high prevalence and has significant morbidity and mortality risks, especially among children. Parental and caregiver involvement has an important role in the management of SCD. Understanding the level of knowledge and awareness among caregivers is crucial to improving early diagnosis, management practices, and outcomes for affected children.

Methods: This is a descriptive, cross-sectional, hospital-based study was conducted between April and December 2022 in the pediatric hematology clinic at Jafaar Ibn Ouf Hospital, Khartoum, Sudan. The study involved parents and caregivers of children with confirmed SCD who attended the clinic during the study period. Data were collected using a structured Google Forms questionnaire, which included a socio-demographic section and assessed caregiver knowledge of SCD. Informed consent was obtained. Data were analyzed using SPSS version 25. Statistical significance was set at $p < 0.05$.

Results: A total of 206 caregivers participated, with a female predominance (57.8%). The majority (75.8%) were aged between 40 and 59 years, and 97% were aware of the hereditary nature of SCD. Half (49.5%) of the participants had good overall knowledge of the disease, including its clinical manifestations, risk factors, diagnostic criteria, preventive strategies, and complications. However, only 21% were found to be aware of the importance of premarital screening. Factors significantly associated with higher knowledge levels included being a mother (caregiver), having a higher educational level, and living in urban areas ($p < 0.05$). Additionally, families with more than one affected child, children diagnosed at an early age, and those with frequent hospital admissions demonstrated significantly higher knowledge and awareness scores ($p < 0.05$).

Conclusion: The study demonstrates an adequate level of knowledge and awareness regarding SCD among parents and caregivers attending a referral pediatric hematology clinic. Key factors that positively affect knowledge scores were maternal caregiving, higher education, urban residence, multiple affected children, early diagnosis, and frequent hospital visits. These findings highlight the need for educational interventions to improve caregiver awareness, especially preventive measures such as premarital screening.

OR18 | Influence of kinesiophobia and catastrophic thoughts on chronic pain in patients with sickle cell disease

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Introduction: In sickle cell disease (SCD), chronic pain is associated with increased morbidity, work absenteeism, difficulties in daily activities, and high healthcare costs. A large proportion of patients experience pain on more than 50% of days, predisposing them to other morbid conditions such as anxiety, depression and opioid dependence. This study aimed to explore the influence of biopsychosocial factors in the clinical presentation of pain syndromes in SCD patients and their association with clinical and functional parameters.

Methods: Participants were recruited from the Sickle Cell Disease Outpatient Clinic at the University of Campinas and categorized by gender, age and presence of chronic pain (defined as pain present on most days and lasting more than six months). Patients were evaluated using Pressure Pain Threshold (PPT) by digital pressure algometer, Western Ontario and McMaster Universities Arthritis Index (WOMAC), Tampa Scale for Kinesiophobia (TSK) questionnaire (the higher the score, the greater the degree of Kinesiophobia) and pain-related Catastrophizing Thoughts Scale (range = 0–5). Correlations were made between kinesiophobia and clinical and functional variables. We performed the Mann–Whitney test and Spearman's correlation for continuous variables, and the chi-squared test for categorical variables.

Results: The study included 62 patients, with a median age of 44 years (20–67), 43 female and 19 male, of which 46 are HbSS, 10 HbSC, 3 HbSβ^0 and 3 HbSβ^+. The median score in the kinesiophobia scale was 44.5 (28–65), catastrophic thoughts index was 1.66 (0.22–5.00), and functional capacity (Womac) was 16.5 (0.0–60.0); Comparing patients regarding genotype (HbSS and HbSβ0 vs. HbSC and HbSβ+), the level of kinesiophobia was 43 (28–65) and 48 (41–58) ($p = 0.039$), respectively, and the functional capacity (Womac) was 12 (0–60) and 27 (0–46) ($p = 0.105$), respectively. Left lumbar region pain threshold was 31.5 *N* (2.0–70.4) and 23.3 *N* (2.6–41.6) ($p = 0.053$), respectively; left hip pain threshold was 30.3 *N* (4.6–68.3) and 26.2 *N* (6.3–47.3) ($p = 0.395$), respectively, with no statistical difference between groups). Concerning the presence of chronic pain in the whole cohort, 53 (85.5%) participants were placed into the chronic pain group and 9 (14.5%) were placed into the no pain group: the level of kinesiophobia was 45.0 and 39.0 ($p = 0.043$), respectively; the median of catastrophic thoughts was 1.66 and 1.88 ($p = 0.779$), respectively (and interestingly, these measures were considerably low, in both groups); the functional capacity (Womac) was 21.0 and 3.0 ($p < 0.00$), respectively. There was a significant correlation between kinesiophobia and left hip pain threshold ($R = -0.335$; $p = 0.009$) and between left low back threshold ($R = -0.405$; $p = 0.001$) and WOMAC (FC) ($R = 0.459$; $p < 0.001$).

Conclusion: The levels of catastrophic thoughts in adults with SCD are generally low, reflecting the normalization of chronic pain and adaptive strategies. However, patients with higher kinesiophobia had worse physical performance, highlighting the influence of psychological pain processing on functionality. Additionally, the positive correlation between kinesiophobia and functional limitation reinforces that fear of movement may worsen motor dysfunction. Thus, this study highlights the need for a multidimensional approach to chronic pain management, considering physiological, psychological, and functional aspects for more effective care.

OR19 | Durable clinical benefits with exagamglogene autotemcel for transfusion-dependent thalassemia and severe sickle cell disease

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Introduction: Exagamglogene autotemcel (exa-cel) is a one-time, ex vivo CRISPR/Cas9 gene-edited, autologous cell therapy approved for patients (pts) ≥12 years old with transfusion-dependent β-thalassemia (TDT) or sickle cell disease (SCD) with recurrent vaso-occlusive crises (VOCs). We report long-term efficacy and safety from the CLIMB THAL-111, CLIMB SCD-121, and CLIMB-131 studies.

Aims: Evaluate long-term efficacy and safety of exa-cel in TDT and SCD pts, assess reversal of tissue iron accumulation in TDT pts, and factors associated with $CD34^+$ HSPC collection in SCD pts.

Methods: CLIMB-111 (TDT) and CLIMB-121 (SCD) are ongoing 2-year, Phase 3 studies of exa-cel in pts aged 12–35 years.

The CLIMB-111 primary endpoint is transfusion independence defined as proportion of pts maintaining a weighted average hemoglobin ≥9 g/dL without RBC transfusion for ≥12 consecutive months (TI12). The CLIMB-121 primary endpoint is proportion of pts free of severe VOCs for ≥12 consecutive months (VF12); key secondary endpoint is proportion of pts free from inpatient hospitalization for severe VOCs for ≥12 consecutive months (HF12).

In TDT, measures of tissue iron accumulation were assessed. In SCD, baseline (BL) factors potentially associated with $CD34^+$ HSPC collection were evaluated. Pts then enroll in CLIMB-131 for up to 13 y follow-up.

Results: As of 09 August 2024, 56 pts (mean age: 21.2 years) received exa-cel in CLIMB-111; median follow-up was 38.1 (7.9, 67.1) months. Of 54 pts evaluable for TI12, 98.1% (53/54) achieved TI12 in CLIMB-111 and CLIMB-131 combined. Median time to restart of chelation was 5.9 (range: 0, 30.1) months and phlebotomy was 9.4 (range: 2.9, 27.4) months after exa-cel infusion. Mean serum ferritin decreased to below BL by Month 12 and further over time to below 500 µg/L by Month 48. Mean liver iron content (LIC) decreased to below 5 mg/g by Month 48 and mean cardiac iron content remained stable at >30 ms. 25/56 (44.6%) pts discontinued iron removal therapy (IRT) for ≥6 months, with median follow-up after that of 10.7 (range: 2.5, 50.6) months. After IRT cessation, ferritin levels and LIC were generally stable without progressive increase over time.

As of 09 August 2024, 46 pts (mean age: 21.4 years) received exa-cel in CLIMB-121; median follow-up 33.2 (8.9, 62.2) months. Of 42 pts evaluable for VF12/HF12, 92.9% (39/42) achieved VF12 and 97.6% (41/42) achieved HF12 in CLIMB-121 and CLIMB-131 combined. Number of $CD34^+$ cells collected correlated positively with BL ($r = 0.65$, $p < 0.001$) and pre-apheresis blood $CD34^+$ cells/µL ($r = 0.67$, $p < 0.001$), BL platelet counts ($r = 0.30$, $p = 0.023$), BL alkaline phosphatase ($r = 0.43$, $p < 0.001$), and negatively with increasing age ($r = -0.48$, $p < 0.001$). There was no evidence of correlation with other factors analyzed: measures of hemolysis, other labs, or disease severity (BL annualized VOC and hospitalization rates, annualized RBC transfusion volume).

Exa-cel safety was consistent with myeloablative conditioning and autologous transplant in both TDT and SCD.

Conclusion: Exa-cel demonstrated durable clinical benefit in TDT and SCD pts and a safety profile consistent with busulfan myeloablative conditioning and autologous transplant. In TDT, there was no evidence of iron re-accumulation after IRT cessation. In SCD, younger age and

blood CD34$^+$ cells/μL at BL and pre-apheresis correlated most strongly with higher CD34$^+$ cell collection. These data continue to support exa-cel as a one-time functional cure for TDT and SCD.

OR20 | Pregnancy and SCD: Addressing the gaps in medical surveillance in low- and middle-income countries

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Introduction: Sickle Cell Disease (SCD) is a severe hereditary genetic condition, and pregnancy in these patients may lead to the exacerbation of symptoms and severe complications, such as eclampsia, pre-eclampsia, stroke, perinatal and maternal death. This study aimed to identify pregnancy complications and their association with genetic variability in women with SCD at Maternidade Lucrecia Paim, Luanda, Angola.

Methods: Pregnant SCD women followed at Maternidade Lucrecia Paim, Luanda, Angola, between June 2021 and March 2024, were invited to participate in the study. Sociodemographic data, information about previous manifestations of the disease and pregnancies were collected. Pregnancy monitoring included hematological, biochemical, and genetic analysis (SCD genotype, HBB haplotype, and 3.7 kb deletion of the α-globin gene).

Results: A total of 162 SCD patients were enrolled in this study, with ages ranging from 16 to 46. SS genotype was confirmed in 161 patients, and one patient presented with sickle beta-thalassemia. Moderate jaundice was identified in 15% and light jaundice in 59% of patients. Clinical history analysis shows that 91% of these patients have been hospitalized at least once, 81% of the times resulting from painful crisis episodes, and 79% received at least one transfusion. Overall, 18% of pregnancies resulted in stillbirth and 16% in spontaneous abortions.

Regarding HBB haplotypes, 87% of women had the CAR/CAR haplotype, which is considered the most severe. These CAR/CAR patients presented lower RBC ($p = 0.05$), hemoglobin ($p = 0.008$) and HCT ($p = 0.041$), and higher LDH ($p = 0.010$). The perinatal survival rate was also inferior in these patients (64% vs. 82%). Also, the presence of the T allele in the polymorphism rs968857, in the region of the δ-globin gene (HBD), seems to be associated with a lower rate of miscarriages ($p = 0.044$) and the number of livebirths ($p = 0.045$). The presence of 3.7 alpha thalassemia deletion has been associated with better prognosis in SCD patients. In this cohort, 12% of women were homozygous for the deletion and 36% were heterozygous. Homozygous patients presented lower WBC ($p = 0.004$), MCV ($p = 0.013$), MCH ($p < 0.001$), MCHC ($p = 0.003$), total and direct bilirubin ($p < 0.001$ and $p = 0.012$), and higher RBC ($p < 0.001$) and HCT ($p = 0.004$). Although not statistically significant ($p = 0.072$), homozygous presented a higher rate of livebirths (85% vs. 63%) than other genotypes.

Conclusion: The high rates of miscarriages and fetal death associated with SCD demonstrate the urgent need to invest in medical surveillance for these women, especially in countries where the prevalence of the disease is high and the resources are limited. The early identification of the most severe phenotypes will allow the implementation of preventive strategies to help reduce the risk of severe outcomes.

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OR21 | Co-developed pain plans improve engagement and care quality in pediatric sickle cell disease

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Introduction: Sickle cell disease (SCD) is a genetic blood disorder characterized by chronic hemolytic anemia, severe pain, and health disparities. The ASH Research Collaborative launched an SCD Learning Community (LC) to improve clinical practice and patient outcomes, prioritizing the reliable use of co-developed pain plans. These plans guide timely interventions, potentially reducing emergency department (ED) visits and hospitalizations. At our institution, no SCD patients initially had formal pain plans, and ED care pathways were non-individualized, primarily opioid-focused. Patients and families expressed interest in integrative health (IH) and nonpharmacologic pain management. We hypothesized that co-developing pain plans would enhance patient engagement and satisfaction.

Methods: A multidisciplinary team, including quality improvement (QI), hematology, ED, and IH staff, developed a key driver diagram, process map, and pain plan template with real-time provider and patient feedback. Materials from other LC pilot sites and institutional QI initiatives were reviewed. Using Epic EHR and Healthy Planet, eligible patients were identified based on age, genotype, and ≥1 narcotic

prescription in the past year. Initially, pain plans were completed on paper during routine visits, refined based on feedback, and integrated into an electronic smart form accessible via MyChart. A 3-item REDCap survey assessed caregiver engagement and satisfaction. The Child Opportunity Index (COI) and payor status were analyzed to evaluate equity and inclusion.

Results: At this academic medical center, ~950 children and young adults with SCD receive care. Among them, 74% have a Very Low to Low COI, ~70% have a governmental payor, and 88% self-identify as non-Hispanic Black. Of 46 patients eligible for the pilot phase, 35 (76.1%) completed pain plans by 10/30/2023. All 35 caregivers completed surveys, showing high engagement and satisfaction: 92% felt the plan was co-developed, and 89% were very likely to use it. Epic-based pain plans were incorporated into clinical workflows, with QR codes linking to IH videos for non-pharmacologic pain management. As of 06/01/2025, 509 patients (64% of the target population) have pain plans. Their preferences now automatically display for prescribing providers in the ED SCD pain orderset. No significant differences were observed in COI, payor status, or race/ethnicity between those with and without pain plans.

Conclusion: Co-developed pain management plans enhance SCD care and patient experience, offering a feasible, sustainable, and scalable approach. Efforts to expand pain plan implementation are ongoing. Priorities include adding an inpatient component and developing a QI-metric dashboard to track pain plan utilization and its impact on acute care use. Planned outcome measures include ED use, time to first opioid in the ED, and hospital admission rates.

OR22 | Introducing the "WHEEL": Psychosocial screening in haemoglobinopathy annual review clinics

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Introduction: Literature consistently reports increased psychological challenges from treatment and health complications for paediatric Haemoglobinopathy (HbO) patients and carers. Psychosocial issues can arise from the impact of pain, frequent hospital admissions and other symptoms on their daily lives. These difficulties often occur in the context of cultural barriers, socioeconomic challenges and stigma.

It is widely recognised that the specialist multidisciplinary team should include psychological professionals as a visible and accessible part of patient care, and that interventions should not be limited to direct therapeutic work. The role of the psychology team includes screening, assessment, formulation and intervention, as well as normalising and encouraging help-seeking for psychosocial issues. The Wellbeing and Health Experiences Evaluation Log (WHEEL) is a patient rated routine outcome measure comprising twelve domains as items on a self-report questionnaire. Each item is rated on a 5-point Likert scale indicating 'how things have been going' over the previous month.

Methods: An assistant psychologist contributed to patient annual review clinics at Birmingham Children's Hospital (a Haemoglobinopathy Coordinating Centre for the West Midlands) over a 12-month period. The WHEEL was completed with patients and/or carers and scores discussed during their appointment, in the presence of a clinical nurse specialist and medical consultant. The WHEEL scores were used to inform care planning decisions regarding follow-up support. A database of WHEEL scores has been kept for comparison of scores pre- and post-intervention and at different time points.

Results: Over the 12-month period: 240 WHEELs were administered; 16 patients consented to a psychology referral during clinic; 30 patients agreed to a follow-up psychology call after clinic—of these patients, five subsequently consented to a psychology referral. Psychology service leaflets were handed out to families who expressed an interest in learning more, and to provide our contact details—consistent data are not available for this. Patients and carers reported the highest scores (perceived as "going well") in domains of "family relationships" [mean = 4.5] and "accessing education/work" [mean = 4.4] and lowest scores (perceived as "problematic") in domains of "managing feelings" [mean = 3.7] and "how I feel about myself" [mean = 4.0]. It is worth noting that the most common domains for low scores were reported in "managing feelings" [19% low scores] and "doing the things I enjoy" [11% low scores].

Where no direct follow-up was indicated for psychology, WHEEL scores were still used to inform weekly multidisciplinary discussions. Next steps for further research include analysis of patient data over two time points, once more paired data is collected, as well as implementation in transition clinics and outpatient psychology appointments.

Conclusion: Routine use of the WHEEL in clinics has supported the multidisciplinary team to gain further insight into the lives of young people with HbO. It has facilitated conversations between families and healthcare staff about psychosocial wellbeing, helping staff to respond more flexibly and responsively to psychological need.

OR23 | Correlation of non-invasive hemoglobin measurement to vaso-occlusive crises in patients with sickle cell disease

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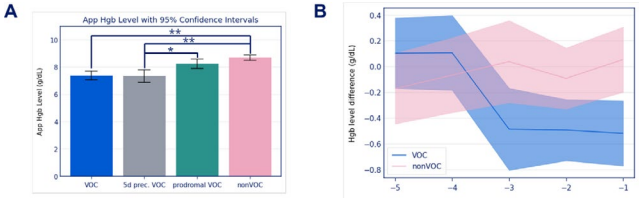
Introduction: The hallmark symptoms of sickle cell disease (SCD) are hemolytic anemia and vaso-occlusive crises (VOCs). These events can lead to severe pain, organ damage, and increased healthcare utilization. Early detection and intervention are crucial for improving patient outcomes and quality of life. This study investigates the potential to predict the occurrence of VOCs based on Hgb level trends determined via frequent non-invasive home-based monitoring.
Methods: Our smartphone app accurately measures Hgb levels non-invasively by analyzing fingernail bed pictures of SCD patients, comparable to complete blood count tests. Here we assessed the correlation of Hgb levels to VOC events in SCD. The study consisted of up to four site visits across a total of up to 8 weeks. For this study, 35 participants (26 female/9 male, 35 years old ± 7 years) with SCD (26 Hgb SS, 6 Hgb SC, 2 Hgb Sβ+ thalassemia, and 1 unknown) from three cities (Atlanta, Houston, and Washington D.C.) were enrolled. Participants took app tests every other day at home and recorded prodromal signs (e.g., numbness, paresthesia) or VOC-associated symptoms (e.g., severe pain, swelling), overall pain level, and medications in the app. Finally, participants took usability and acceptance surveys upon completion of the study.
Results: Mean Hgb level during VOCs was significantly lower (7.4 g/dL) compared to non-VOC periods (8.7 g/dL; $p < 0.001$). Additionally, results showed a decrease in Hgb levels when reporting prodromal l symptoms in the days prior to a VOC (8.3 g/dL), compared to non-VOC days ($p = 0.04$) (**Figure 1A**). The app detected significant variability in the lead up to a VOC compared to days where no VOC occurred. Hgb levels dropped significantly 3 days prior to a VOC event, with an average Hgb difference of 0.5 g/dL (**Figure 1B**). Participants reported that the app was easy to use, with all taking more than 11 app tests and 91% taking more than 21 app tests over the study duration. They expressed high satisfaction with the app's performance, with 13 participants indicating they acted on Hgb measurements, resulting in better health management. Additionally, 97% of participants expressed a desire to incorporate the app into their daily routine after the study. Finally, participants continued using the app with no instructions or financial incentive to do so, with more than 100 tests taken across the study population after completion of the study.
Conclusion: We demonstrated a correlation between Hgb levels and the occurrence of VOCs. Overall, the accuracy and correlations between Hgb levels and SCD symptoms suggest that this non-invasive app could be a useful tool for predicting VOCs in individuals with SCD. By providing early warnings of impending VOCs, the app can facilitate timely intervention, potentially reducing the severity and frequency of these events. Future research will validate these findings (e.g., by genotype stratification) and explore app integration into clinical trials and routine care to support SCD management and drug development.



OR24 | Factors influencing participation in sickle cell disease clinical trials: United Kingdom LISTEN survey findings

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Introduction: The success of clinical trials of new therapies for sickle cell disease (SCD) depends on recruiting and retaining a large and diverse group of people with SCD (PwSCD). The **L**earnings and **I**nsights into **S**ickle Cell **T**rial **E**xperie**n**ces (LISTEN) Survey was developed to understand the barriers and motivators to participation in clinical trials for PwSCD.[1] Here we present data from respondents in the United Kingdom (UK).
Methods: From October 2022 to August 2023, PwSCD (≥18 years) and healthcare professionals (HCPs) involved in the treatment of PwSCD in 17 countries completed quantitative surveys (online, telephone or face-to-face). PwSCD were asked about their awareness of, and prior participation in, clinical trials. They rated the importance of factors (grouped into five categories) that may affect their decision to participate in a clinical trial on a 7-point scale (not at all to extremely important) and ranked them from most to least important. HCPs provided their perspectives on the importance of these factors to PwSCD. HCPs and PwSCD also reported where they would typically go, or refer PwSCD, to find trial information.
Results: Of the 1145 PwSCD and 361 HCPs who completed the global LISTEN Survey, 112 PwSCD (66% female, median age 39 years) and 16 HCPs were from the UK. Almost all (96%, $n = 108$) PwSCD responded that they had heard of clinical trials, while 24% ($n = 27$) had previously participated in a clinical trial for SCD. Extremely or very important factors that motivated PwSCD to participate in a trial included the opportunity to try a treatment that might better manage their symptoms (58%) or might work better (54%; Figure). A key barrier to participation was that the treatment might have different side effects than those currently experienced (63%). Regarding trial information, PwSCD ranked (first or second of five) safety measures (79%) and how the treatment works (58%) as the most important factors. For further considerations, PwSCD ranked speaking to experts running the trial (62%) and other PwSCD involved in the trial (60%) as the most important. Compared with PwSCD, HCPs overstated the importance of trying a new treatment that might work better as a motivator to participation (81% vs. 54%), as well as barriers including the potential to experience different side effects (81% vs. 63%) and need for more medical tests (63% vs. 37%). HCPs understated the importance of PwSCD

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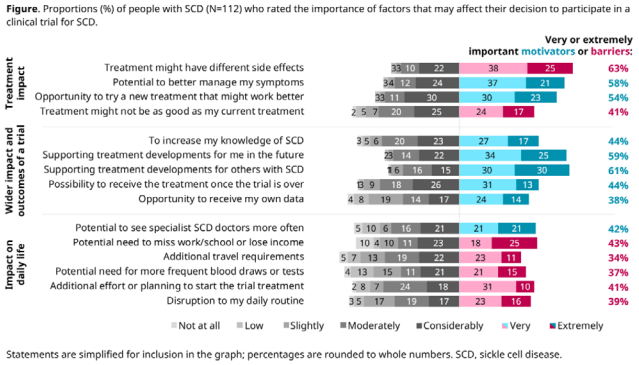

Figure. Proportions (%) of people with SCD (N=112) who rated the importance of factors that may affect their decision to participate in a clinical trial for SCD.

Statements are simplified for inclusion in the graph; percentages are rounded to whole numbers. SCD, sickle cell disease.

receiving their own data (13% vs. 38%) and supporting new treatment developments to benefit all PwSCD (38% vs. 61%). Common sources through which PwSCD had become aware of clinical trials were HCPs (20%), browsing the internet (13%), materials at medical centres (13%) and social media (12%) ($n = 108$). Whereas HCPs referred PwSCD to materials at medical centres (23%) and online/internet (23%), while social media (2.5%) was less common.

Conclusion: Compared with global LISTEN data, clinical trial awareness was higher in the UK, although the highest rated motivators and barriers to participation were similar to those reported globally. Improving recruitment into clinical trials in SCD in the UK will require clear communication of potential benefits and anticipated safety profiles, preferably by experts and PwSCD involved in the trial. Shared decision-making between PwSCD and HCPs, and optimisation of information materials in outpatient clinics in the UK, may also improve understanding and increase trial participation.

Reference

1. James et al, HemaSphere 2024;8:e70009.

OR25 | Paediatric haemoglobinopathies iron chelation audit: Liver iron concentration using R2 vs. R2*

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Introduction: Accurate measurement of iron overload is crucial for diagnosing and managing iron-related disorders.[1] MRI has gained widespread acceptance as a non-invasive method for assessing liver iron overload due to its strong correlation with biopsy results.[2] Several MRI-based techniques exist for estimating liver iron concentration (LIC) including R2 mapping and R2* mapping.[2] There was a clinical alert in 2017 to warn against the use of R2* in haemoglobinopathy patients, however, there have been many advances in R2* mapping since. Current haematology guidelines now endorse both techniques[1] while radiology guidelines suggest R2* is the preferred method.[4] In recent years scanner vendors have provided R2* mapping techniques and reporting, widening the access to R2* mapping.

In this audit, comparison was made between R2 and R2* mapping in a paediatric haemoglobinopathy population having iron overload surveillance, to establish comparability/superiority.

Methods: Seventy MRIs from 47 paediatric patients were acquired between August 2017 and March 2025, using 1.5T and 3T Siemens MRI scanners situated at Guy's and St Thomas' Hospitals. R2 mapping was performed using the Ferriscan technique that was analysed externally by Resonance Health to give LIC values. R2* mapping was performed using the Liverlab product provided by Siemens. Liver segmentation was performed using ITKSnap and LIC obtained using calibration equations[5] from a recent multicentre study. LIC was compared using Pearson's rho, scatter and Bland Altman plots. Motion on the images was scored by an MR Physicist, whilst a radiologist qualitatively reviewed all maps and segmentations.

Results: A significant and strong correlation in LIC was found between the two methods (e.g. at 1.5T, rho = 0.79, $p < 0.001$), a large bias was found (at 1.5T, mean positive difference of Ferriscan compared to Liverlab of 5.79 mg/g). For higher LIC values, the difference tended to be larger compared to lower LIC. No significant motion was seen on any of the R2* images, however, 45/70 of the R2 images showed moderate/high motion. Based on the segmentation and quality of the R2 maps, the radiologist deemed 8/70 R2 results were satisfactory, compared to positively reviewing all R2* cases. When the data was divided into low and high motion groups, the LIC values were more similar and the bias was smaller for the low motion data compared to the high motion data.

Cost comparison showed; for 50 patients under surveillance/year over 10 years, based on current prices, Ferriscan reporting would cost £95K, while Liverlab has a one-off cost of around £12.6K, that also covers Liver fat quantification software. There is no cost for Liverlab reporting.

Conclusion: It appears that LIC results correlate well between the two methods. However, there is a substantial positive bias for R2 LIC. The bias is lower when there is less motion in the R2 images, which may indicate that motion is one of the causes of the difference between the results. The difference tends to be larger for higher LIC values; to verify this a cohort of adults should be studied, where motion is likely to be less. We found that R2* offers motion robust, faster, lower cost images, which makes it preferable while giving comparable results to good quality R2 results. It may be particularly beneficial in paediatric patients, where motion is more likely. Further analysis in a larger population, including adults, is needed to verify these promising results.

OR26 | Development of a sickle cell disease specific transition tool: An MDT approach

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Background: There is evidence that Sickle Cell Disease, also known as Sickle Cell Disorder (SCD) paediatric patients' transition to adult services is linked with increased mortality (Kavanagh, Fasipe & Wun, 2022). It can be an extremely challenging time for young people (Fenchel et al., 2023), with high rates of non-attendance and non-adherence to medication. Preparation for this time is key, to ensure the patients and their care givers have a good understanding of their condition and how to navigate adult services. There is currently no widely used, user friendly SCD specific tool to assist with the transition preparation process. The aim of the study was to develop a user friendly, SCD specific transition passport with multidisciplinary team (MDT) input, to maximise the effectiveness of the transition preparation process.

Methods: A literature review was conducted to identify current assessment and education tools for SCD transition. Using peer review from the transition MDT and input from wider team members, the researchers combined previous literature, with knowledge of transition in practice. Components of the passport were designed with the young person at the centre, using a holistic approach. Some initial qualitative feedback of the tool, from service users and clinicians, was collected.

Results: The Evelina Transition Tool was developed, presented as a 10 section, scored transition readiness assessment. It is also an educational tool, as each section allows to assess and explore gaps in knowledge and it is filled by the clinician. Sections include knowledge about their condition and medications, sexual health, work and school, emotional wellbeing and knowledge of access to psychological services, lifestyle including diet, exercise, drugs and alcohol awareness. There are 10 points to be scored per section, totalling 100 points available. Initial feedback comments on the ease of use and clarity of scoring system.

Conclusions: The Evelina transition passport created is a sickle cell disease specific assessment readiness tool. Future research could assess the effectiveness of implementing this tool across hospitals in the UK, and further.

OR27 | Nanoparticle engineering for the prenatal therapy of sickle cell disease

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Sickle cell disease (SCD) is a severe, progressively debilitating, and life-threatening monogenic disease with an estimated 300 000 infants born with the disease every year. A single base mutation in the β-globin gene leads to protein misfolding and polymerisation of deoxygenated haemoglobin resulting in the characteristic sickle-shaped form of red blood cells. The abnormal structure results in haemolytic anemia, vasco-occlusive episodes, increased risk of infection and organ failure. Disease-elevating therapeutics exist but patients require life-long treatment. Few therapeutics offer curative treatment and those are only available to a limited number of patients.

With improvements in prenatal diagnostics, SCD can be diagnosed from ~10 weeks of gestation onwards. This, together with the development and improvement of lipid nanoparticles (LNPs) as carriers for nucleic acid therapies, showing an improved safety profile, has opened the possibility of in utero treatment. Hematopoietic stem cells proliferate in the fetal liver, before migrating to the bone marrow. We aim to deliver a base editor (BE) encapsulating LNPs targeting HSCs in the fetal liver to correct the missense mutation during this window.

We hypothesise that this can correct the SCD mutation in primary cells in vitro and successfully rescue the phenotype in vivo, following administration to the fetus in an SCD mouse model.

We successfully tested an ABE8e base editor which corrects the SCD mutation to a non-pathogenic variant (Makassar variant) in a HUDEP-2 cell line using mechanical and chemical transfection with 83% and 76% editing efficiency ($n = 1$).

Further, we have shown that mRNA can be successfully encapsulated using lipid nanoparticle formulations with known liver tropism, using DLIN-MC3, ALC0315, C12-200 and SM-102 ionisable lipid components for the formulations. Characterisation of those lipid nanoparticles showed favourable size and charge for delivery to the liver (size <200 nm; PDI <0.4 [$n = 3$]). We are currently encapsulating the BE mRNA into those lipid nanoparticle formulations for the delivery to primary HSCs. This lays the base for further testing of efficiency and toxicology in vitro and in vivo. Biodistribution and toxicology will be analysed following in utero injection into a mouse fetus at E13.5.

Institution Name: Kings College London.

OR28 | Cost-effectiveness of automated versus manual red blood cell exchange in sickle cell disease in France

Ghofran Kamoun[1], Camille Runelle-belliard[2], Pierre Cougoul[3], Stuart Mealing[4], Sarah Medland[4], Jamie Bainbridge[4], Matthew Cawson[1], Anna Yudina[1]
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Introduction: This study evaluated the lifetime clinical and economic impact of automated versus manual red blood cell exchange (aRBCX vs. mRBCX) in paediatric and adult patients with sickle cell disease (SCD) in France. The target

populations included high-risk individuals ineligible for, refractory to, or unwilling to undergo hydroxyurea therapy. Paediatric patients with elevated risk of stroke were modelled from age five to 18, while adults were modelled from a mean age of 38 over their remaining lifetime.

Methods: A global patient-level simulation model was adapted to the French healthcare system's perspective to estimate quality-adjusted life years (QALYs) and direct medical costs associated with aRBCX compared to mRBCX. Clinical inputs were drawn from peer-reviewed literature, while cost data were sourced from the national hospital discharge database (PMSI) and adjusted to 2022/23. Clinical experts were consulted to address data gaps.

Monte Carlo simulations were employed to capture variability in patient characteristics and estimate the likelihood of clinical events, including iron overload, VOCs, and survival rates. Baseline characteristics and event probabilities were modelled over the fixed time horizon. As events were not mutually exclusive, a patient's history influenced future risks. A discount rate of 2.5% was applied per French HAS guidelines. Second-order probabilistic sensitivity analysis was performed for 1000 individual lifetimes over 500 iterations. Outcomes included clinical event rates, healthcare resource utilization, and total costs.

Results: In both paediatric and adult cohorts, aRBCX was cost-saving and clinically beneficial compared to mRBCX.

Among the paediatric high-risk stroke subgroup, aRBCX led to a €34 302 reduction in cost per patient (15.5%) and a QALY gain of 0.15, confirming dominance. Disease-modifying transfusions (DMTs) were reduced by 45.2% (114 vs. 207), emergency transfusions by 38.4% (19 vs. 31), and chelation duration by 88.5% (1 vs. 7 months). The frequency of VOCs decreased by 40.3% (17 vs. 29), with corresponding cost reductions of 41.7% for VOC management and over 91% for chelation therapy.

In the adult population, aRBCX reduced total costs by €18 805 per patient (a 2.4% decrease) and yielded an additional 0.31 QALYs, driven by better clinical outcomes and reduced resource use. DMTs declined by 24.8% (240 vs. 319), emergency transfusions by 20.3% (61 vs. 76), and chelation duration by 88% (5 vs. 40 months). VOCs decreased by 21.5% (55 vs. 70), accompanied by a 10.2% reduction in acute chest syndrome events, as well as smaller but consistent declines in other acute complications. These gains translated into €29 486 in VOC-related savings and €28 669 in chelation cost reductions per patient. QALY gains (11.31 vs. 11.00) further reinforced the clinical value of aRBCX and an efficient reallocation of healthcare resources.

aRBCX is cost-effective in 70.4% of probabilistic sensitivity analysis iterations for both populations, illustrating the results are robust.

Conclusion: aRBCX was therefore both cost-saving and clinically superior, reinforcing its value in managing high-risk adult SCD patients in France. The therapy led to improved disease control, reduced acute complications, and decreased need for chelation, translating into better quality of life and significant cost savings. These findings support the case for broader access and funding of aRBCX within the French healthcare system.

OR29 | Re-defining high emergency department use for sickle cell disease

Mariam Kayle[1], Wei Pan[1], Audrey Blewer[1,2], Daniel Hatch[1], Camila Reyes[2], Lauren Siewny[2], John Strouse[2], Mathew Young[3], Paula Tanabe[1,2]

[1]Duke University School of Nursing, Durham, USA, [2]Duke University School of Medicine, Durham, USA, [3]Wake Emergency Physicians, Professional Association, Cary, USA

Introduction: Sickle cell disease (SCD) may result in high emergency department (ED) utilization primarily due to vaso-occlusive episodes (VOE). There is a lack of standardized definition for "high" ED utilization and cutoffs are often arbitrarily applied. This study describes ED utilization, proposes new categories for high ED utilization, and describes factors associated with high ED utilization among individuals with SCD.

Methods We conducted a retrospective cohort study which analyzed the North Carolina Hospital Discharge Data (2013–2019), a state-wide, all payer datasets. Participants were included if they had SCD, defined as at least three SCD visits (ED, inpatient, or outpatient surgery) in a rolling five-year period. All age groups, sexes, and payers, regardless of residence state, were included. The main outcome was the annual number of ED visits (ED treat and release and ED visits that resulted in hospitalizations). Exposure variables included sex, race, ethnicity, age, age at death, distance in miles to the closest SCD center, number of ED facilities visited, and the social vulnerability index (SVI).To determine ED utilization categories, we first examined the distribution of people based on the number of annual ED visits, then identified the categories across years to determine the data-informed cutoff for each category. Univariate analysis determined differences between participants based on ED utilization category, using chi square tests of independence or analysis of variance, as applicable. Descriptive statistics were conducted to describe characteristics of utilization, in the sample and by ED utilization group. A parsimonious multinomial regression was conducted using significant predictors from the univariate analysis.

Results: The cohort included 9964 patients, predominantly Black and <30 years old, with 100 188 total ED visits from 2013 to 2019. We categorized ED visits into four levels: low (0–1 visit in every year, $n = 3397$ [34.1%]), moderate (2–9 visits/year, $n = 5631$[56.5%]), high (10–32 visits/year, $n = 758$ [7.6%]), and super-high (33+ visits/year, $n = 178$ [1.79%]). Less than 10% of participants contributed 55% of ED visits. Almost one third of ED visits resulted in hospitalizations. Older age, younger age for in-facility deaths, and higher SVI significantly correlated with higher ED utilization. Patients with high utilization were more likely to die, die younger, use multiple EDs and reside in disadvantaged counties by

housing type and transportation. A total of 387 patients from 24 other states had ED visits in North Carolina, 43 (11%) of whom had ≥10 North Carolina ED visits in at least one of the study years.

Conclusions: In this cohort study of seven years of hospital discharge data, we defined four new categories of ED utilization in SCD. These categories are data-driven and reflect anecdotal clinical experience. Findings show that moderate ED utilization was common, but a small subset of patients exhibited high or super high ED utilization, contributing disproportionately to the total number of ED visits. These findings can help guide clinician-patient conversations. As ED visits begin to increase, there is an opportunity for interdisciplinary teams to collaborate to identify the cause of increasing ED visits. Linking patients to comprehensive sickle cell care, as well as social and behavioral health resources might help address health and psychosocial needs and reduce ED visits.

OR30 | A cost-conscious and highly succesful start-up strategy for hematopoietic cell transplantation in middle-income countries

Thomas Klingebiel[1-14]

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Introduction: An Indian NGO in collaboration with two international NGOs developed a cost-conscious pediatric BMT model for middle-income countries (MICs). The strategy is supported by the Access to Treatment and Transplant program (ATT) program of the international NGO and hinges on low-risk matched sibling donor (MSD) transplants for severe hemoglobinopathies delivered for an average cost of $12 000 including follow up.

Here we summarize the outcomes of 136 MSD BMTs for hemoglobinopathies done directly in MICs and compare experienced versus startup centres assisted by the ATT program.

Methods: On-site and online expert guidance relying on a comprehensive online IT platform including electronical medical records and continuing quality improvement tools (BMTPlus) was implemented. Major emphasis was given to nurses' training, and professional development. The protocol consisted of pre-transplant immunosuppression with fludarabine/dexamethasone followed one month later by fludarabine, busulfan and cyclophosphamide. G-CSF-primed bone marrow was used as stem cell source followed by cyclosporine/methotrexate prophylaxis. Moderate to severe graft-versus-host disease and event-free survival (GEFS) composite outcome was compared between established and startup centres.

Results: A total of 131 consecutive first bone marrow transplants (BMTs) were included in the analysis, consisting 118 patients (median age: 6.03 years; IQR: 4.1–9.1 years) from established centres and 13 patients (median age: 5.12 years; IQR: 4.1–7.1 years) from startup centres.

Of the 118 patients treated at established centres, 114 were diagnosed with thalassemia major and 5 with sickle cell disease (SCD). All 13 patients at the startup centres had thalassemia major with liver size ≤3 cm below the costal margin at transplantation. GEFS was 94% in the established centres and 100% in the startup centres. Overall survival was 97% in established centres and 100% in startup centres, with a median follow-up of 0.9 years at both centres. No statistically significant difference in GEFS was observed between the centres as determined by log-rank analysis.

Conclusions: The ATT platform focusing on low-risk MSD BMT for severe hemoglobinopathies seems to be a safe and effective BMT start up approach in MICs maximizing initial success rates while promoting sustainability.

OR31 | Regional perceptions of quality-of-life among people with sickle cell disease and their caregivers: LISTEN-survey findings

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Introduction: People with Sickle Cell Disease (PwSCD) experience recurrent pain episodes, fatigue and long-term complications, resulting in impaired wellbeing and quality of life (QoL). Learnings and Insights into Sickle cell Trial ExperieNces (LISTEN) survey assessed motivators and barriers for PwSCD to participate in SCD clinical research and also their lived experience with SCD.

Aim: This LISTEN survey analysis aimed to provide regional insights from PwSCD and caregivers (CGs) perspectives on well-being and QoL.

Methods: LISTEN survey was conducted between 06-Oct-2022 to 22-Aug-2023 in 17 countries. The eligible participants were diverse group of PwSCD aged ≥18-years and CGs must care for an SCD patient and involved in making decisions around SCD treatment for their PwSCD. Participants rated the importance of factors (grouped into five main

categories) affecting their decision to participate in a clinical trial on a Likert scale. Data for their well-being and QoL over the previous 4 weeks were collected and grouped into five regions: Sub-Saharan Africa (SSA), Europe (EUR), Latin America (LATAM), Middle East and North Africa (MENA) and South-Asia (SA).

Results: PwSCD ($n = 891$; 56% female, mean age 43 years) and CGs ($n = 163$; 75% female, mean age 37 years) completed the survey. Their responses to questions about the impact of living with SCD on their general, mental and overall health were collected. Across the regions, more than two-thirds of PwSCD from SA and MENA regions and one-thirds from other regions reported having difficulties in doing their usual activities. A greater proportion of PwSCD from LATAM and SA (both 55%) experienced anxiety (fairly to very often) compared to ~30%–40% in other regions. Notably, 30% of PwSCD from SSA region said that they never or rarely experienced anxiety. A larger proportion of PwSCD from MENA (54%) were satisfied with their overall health compared to other regions. Conversely, a majority (53%) from SA reported dissatisfaction. Majority of CGs in the SSA (66%), MENA (66%) and SA (67%) regions reported facing financial difficulties due to their caregiving responsibilities. Mood swings were reported by almost all CGs in LATAM (96%) followed by those from SA (75%), MENA (69%) and EUR (65%) regions due to their caregiving activities for PwSCD. Deterioration in their physical health was acknowledged by most CGs from LATAM (83%) and MENA (62%). Majority of CGs in the LATAM (70%), SSA (59%) and MENA (59%) and fewer than half in EUR (42%) and SA (33%) region somewhat to completely agreed in having difficulty in combining both caregiver responsibility and their (CGs) daily activities.

Conclusion: These findings underscore substantial challenges affecting the well-being, mental health, and quality of life of PwSCD and their CGs across all regions. This highlights that the treatment gaps still exist across the regions and emphasizes the necessity for a holistic treatment approach with heightened focus on these areas.

OR32 | The Cyprus haemoglobinopathy patient registry

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Introduction: Cyprus has one of the highest prevalences of thalassaemia globally and has been the first country to introduce a successful population-wide prevention programme, through premarital screening. As a result, the annual birth rate for β-thalassaemia has decreased to less than five cases from an expected 30–50. To further monitor disease epidemiology, treatment outcomes, and healthcare burden, the Cyprus Institute of Neurology and Genetics, in collaboration with the State Health Services Organization, has established the first national Registry of Patients with Haemoglobinopathies. The registry collects data on demographic characteristics, diagnosis, therapeutic approach, and clinical manifestations of patients with hemoglobinopathies in Cyprus.

Methods: Patients receiving follow-up care at two of the four Thalassaemia Clinics in Cyprus —Archbishop Makarios III Hospital and Larnaca General Hospital—are asked to voluntarily sign an informed consent form. Health-related data and other information obtained through medical records and questionnaires completed by collaborating physicians with the support of research investigators. Certain clinical parameters will be collected at different time points during the project. The registry developed using the best practices and guidelines of the European Platform on Rare Disease Registration and is aligned with the objectives of the European Reference Networks.

Results: To date, 409 patients have signed informed consent forms and been enrolled in the registry, with demographic, molecular and clinical data fully completed. Among them, 287 patients have been diagnosed with β-thalassemia, 105 patients with α-thalassemia, 11 patients with sickle cell disease, and 6 patients with other rare anaemias. The cohort is relatively balanced by gender, with ages ranging broadly from infancy to over 80 years old. Notably, there is a high concentration of patients between the ages 40 and 60, reflecting the typical profile of individuals receiving long-term follow-up care. Over 250 patients are transfusion-dependent, requiring regular blood transfusions for disease management. Approximately 40 patients receive occasional transfusions based on clinical need, while nearly 100 do not require transfusions as part of their routine care. Among patients with β-thalassaemia major, 96.9% receive transfusions every 1–3 weeks to maintain a pre-transfusion haemoglobin level close to 10 g/dL and 95.1% also undergoing iron chelation therapy. Common clinical manifestations include bone complications (78.7%), splenomegaly (30.6%), hepatic fibrosis (27.2%), type 2 diabetes (16.6%), hypothyroidism (11.5%) and cardiac arrhythmias (6.6%). As a result, patients undergo regular monitoring through abdominal ultrasound, liver and cardiac MRI, liver elastography, and bone mineral density scans to detect early organ damage and manage potential complications related to both the disease and its treatment.

Conclusion: The Cyprus Haemoglobinopathy Patient Registry strengthens Cyprus' participation in European and international initiatives and contributes to major collaborative efforts such as RADeep and INHERENT, by utilising the current registry case report forms for data sharing and harmonisation. As part of its future development, the integration of Patient-Reported Outcome Measures is planned, further enhancing the registry's value

in assessing patient well-being, advancing personalised medicine and supporting clinical decision-making.

OR33 | All-in-one --SEA, β-thalassaemia and haemoglobinopathy screening through the novel α-thalassaemia early eluting peak

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Introduction: Screening for α^0-thalassaemia, β-thalassaemia, and haemoglobin (Hb) E carriers is important in prevalent areas. The Southeast Asian type deletion (--^{SEA}) is the only prevalent reproductively significant double gene deletion locally. While high-performance liquid chromatography (HPLC) is effective in screening for β-thalassaemia and Hb E carriers (βT/HbE), phenotypic screening for α^0-thalassaemia is limited. The microscopy-based Hb H inclusion test (HbHi) is labour-intensive and has limited sensitivity. We pioneered the discovery of the α-thalassaemia early eluting peak (αEEP) in HPLC, which offers a potential screening method for --^{SEA}. This study aimed to determine the nature of the αEEP, assess its stability and robustness to interferences, and evaluate its diagnostic performance in a multi-centre setting.

Methods: First, liquid chromatography-tandem mass spectrometry (LC-MS/MS) was used to analyse 20 blood samples (10 αEEP-positive and 10 αEEP-negative) to determine the nature of the αEEP. Second, 92 blood samples were used to assess the stability and robustness of the αEEP to potential interferences, including lipaemia, icterus, and elevated glycated Hb and Hb F levels. Finally, a multi-centre evaluation of 694 haemoglobin pattern study samples from five tertiary referral hospitals in Hong Kong was conducted. The αEEP, HbHi, and an Hb Bart's-based immunochromatographic strip test (ICT) results were compared with --^{SEA} mutation status. The cost-effectiveness of the tests was also evaluated.

Results: LC-MS/MS analysis showed that the ζ-globin chain was present in all 10 αEEP-positive but absent in all 10 αEEP-negative samples ($p < 0.001$), demonstrating the association of αEEP with the embryonic ζ-globin chain.

The αEEP was stable for up to 14 days of storage at 4°C and was unaffected by lipaemia or icterus. The αEEP showed 100% sensitivity and 100% specificity in detecting --^{SEA} in samples with elevated glycated Hb ($N = 40$) and HbF ($N = 22$) levels.

For --^{SEA} detection, the αEEP showed superior diagnostic performance (sensitivity 99.6% [95% CI: 97.6%–100.0%], specificity 100% [95% CI: 99.2%–100.0%]) compared with HbHi (sensitivity 95.7% [95% CI: 92.2%–97.9%, $p = 0.012$], specificity 98.1% [95% CI: 96.3%–99.1%, $p = 0.004$]) and ICT (sensitivity 95.3% [95% CI: 91.7%–97.6%, $p = 0.006$], specificity 76.2% [95% CI: 72.0%–80.0%, $p < 0.001$]). Notably, the sensitivities of both HbHi and ICT dropped to 58.3% in individuals with βT/HbE, while αEEP sensitivity remained at 100%. ICT specificity was significantly lower when Hb F ≥1% compared with <1% (67.7% vs. 79.6%, $p = 0.006$), while αEEP specificity remained at 100%. The αEEP offered a 98.6% cost reduction compared with HbHi, while ICT offered a 47.6% reduction.

Conclusion: The αEEP represents embryonic ζ-globin chains, which are characteristically de-repressed in α^0-thalassaemia with --^{SEA}, underlying the scientific basis for --^{SEA} detection. The αEEP showed superior sensitivity and specificity for the detection of --^{SEA} compared with those of ICT and HbHi and was more robust in the presence of βT/HbE or elevated Hb F levels. The αEEP is a promising and highly cost-effective screening test for α^0-thalassaemia where --^{SEA} is predominant and enables all-in-one screening for --^{SEA}, β-thalassaemia and haemoglobinopathies by HPLC.

OR34 | Clinical landscape of parvovirus in SCD: A single-institution case series

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Introduction: Parvovirus B19 (PVB19) is the sole member of the Parvoviridae family known to be a human pathogen. The clinical manifestations of PVB19 varies based on the

host: immunocompetent children and adults with PVB19 present with self-limited febrile illness notable for rash (in children) and arthropathy (in adults). Due to tropism of PVB19 to erythroid progenitor cells, individuals with hemolytic disorders are at risk for more significant sequelae of PVB19. The most frequent clinical manifestation of PVB19 for children with sickle cell disease (SCD) is aplastic crisis which may require inpatient management and transfusion support. The 2024 PVB19 Outbreak garnered media attention and highlighted additional sequelae of parvovirus in the SCD population. Here, we describe our institutional experience with PVB19 over the past 10 years.

Methods: This single-center retrospective study included patients ≤21 years of age with SCD, aplastic crisis, and confirmed (IgM/IgG or PCR) PVB19 between January 1, 2015 and April 4, 2025. Data was collected from the electronic health record. This study obtained IRB approval.

Results: In the past 10 years, PVB19 testing was sent for 254 children with SCD and suspected aplastic crisis. PVB19 testing was positive in 51.5% of cases, yielding 130 cases in our study cohort. The majority of cases ($n = 69$, 53.1%) were between 2024 and 2025. The most frequent genotype observed in our study cohort is Hemoglobin (Hgb) SS ($n = 92$, 70.8%). Most received disease-modifying therapy such as hydroxyurea ($n = 86$, 66.7%), chronic transfusions ($n = 5$, 3.9%), or voxelotor ($n = 5$, 3.9%) at the time of PVB19 infection.

Most cases were identified with PVB19 titers ($n = 120$, 92.3%); PCR testing was sent for 36.9% of cases. Few had a concurrent infection at time of PVB19 ($n = 13$, 10.1%). All cases presented with aplastic crisis with median change of Hgb from baseline of 3.65 g/dL. In addition to aplastic crisis, cases presented with fever ($n = 91$, 70.5%), vaso-occlusive pain ($n = 72$, 55.8%), acute chest syndrome ($n = 23$, 17.8%), splenic sequestration ($n = 13$, 10.1%), hepatic sequestration ($n = 3$, 2.3%), and/or thrombosis ($n = 2$, 1.6%). The majority of cases required at least one red blood cell (RBC) transfusion for management ($n = 106$, 82.2%) with a median of 2 RBC transfusions in this cohort; interestingly, many cases ($n = 51$, 48.1%) never received an RBC transfusion prior to PVB19.

Almost all cases required inpatient admission ($n = 118$, 90.7%); a number of patients required management in the intensive care unit ($n = 25$, 19.4%). There were two fatalities secondary to PVB19 in this cohort.

Conclusion: We observed an increase in PVB19 cases between 2024 and 2025 as compared to 2015 and 2023. Most cases featured manifestations beyond aplastic crisis, highlighting the heterogenous clinical landscape of PVB19. This work calls to attention the range in severity in clinical manifestations of PVB19 in children with SCD. Early recognition of atypical presentations may decrease morbidity and mortality of PVB19 in this population.

OR35 | Impact of TGF-β pathway variants on luspatercept response in transfusion-dependent thalassemia

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Introduction: Despite being a monogenic disorder, beta-thalassemias exhibit significant clinical variability even among individuals with identical *HBB* genotypes. This heterogeneity is partly attributed to genetic modifiers, which influence disease expression, severity, and outcomes. Of particular interest are tertiary modifiers, genes that are unrelated to globin synthesis but may affect phenotype or treatment response, such as to luspatercept. Identifying such loci could enhance our understanding of pathophysiology and support personalized treatment strategies. The aim of our study was to identify genetic modifiers in the TGF-β signaling pathway and predictors of clinical response to luspatercept in patients with transfusion-dependent thalassemia (TDT).

Methods: We enrolled 51 TDT patients treated with luspatercept and followed at Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan. Patients were classified as Responders (R) or Non-Responders (NR), based on a ≥33% reduction in transfusion needs during any 12-week period, according to BELIEVE trial criteria.[2] Whole-exome sequencing (WES) was conducted in collaboration with CEINGE Advanced Biotechnology Institute, Naples. Sequencing reads were aligned to the reference human genome (GRCh37/hg19) using standard pipelines. Only variants with coverage ≥30× and a variant allele frequency (VAF) >0.3 were retained for further analysis.

Genotypes were coded as 0 (wild type), 1 (heterozygous), and 2 (homozygous) for each patient. Fisher's exact test and odds ratios (ORs) with Haldane's correction were used to assess variant-response associations ($p \leq 0.01$). Intragenic variants with $r^2 > 0.8$ were excluded to prevent variant load inflation due to linkage disequilibrium. Gene-based variant load was tested through logistic regression, using response status as the outcome and pooled variant load (β) as the predictor.

Results: Among the 51 tested patients, 19 were R and 32 NR. A total of 2282 variants in 343 different genes of the TGF-β pathway were detected. Twenty-three variants in 11 genes were associated with response to luspatercept, while 16 variants in 14 distinct genes were associated with a lack of response. After linkage disequilibrium filtering, nine

variants (three for NR and six for R) showed a statistically significant correlation with treatment response. Particularly, variants in the *PDGRFB* gene (involved in cellular migration and proliferation, and enhancement of TGF-β signaling through SMAD-independent mechanisms) were strongly associated with treatment failure ($p = 0.01$), although their functional impact on TGF-β modulation and luspatercept response remains to be clarified.

Conclusion: Although further data analyses are necessary, our findings suggest a potential role for TGF-β pathway variants in modulating the therapeutic response to luspatercept in TDT, contributing to the development of predictive algorithms for personalized therapy.

OR36 | Preliminary results of allogeneic hematopoietic stem cell transplantation for sickle cell disease in Tanzania

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Introduction: Around 11 000–14 000 children are born with SCD in Tanzania annually. While life expectancy of SCD patients in high-income settings has improved, the mortality rate is 50%–90% in low-income countries. Curative options (allogeneic hematopoietic stem cell transplantation HSCT, gene therapy) have been virtually unavailable in sub-Saharan Africa. Here we present preliminary results of the first patients with severe SCD receiving HLA-matched allogeneic HSCT at a newly established HSCT Unit in Tanzania.

Methods: Tanzania launched a development program in 2018 to establish HSCT in a tertiary Hospital in Dodoma. Supported by Italian organisation from 2019 international experts trained Tanzanian professionals via videoconference lectures and observational internships in Italy. In January 2023 HSCT program started with initial Italian on-site support transitioning to ongoing weekly online clinical-logistical round. All patients with symptomatic SCD, received bone marrow (BM) stem cells from HLA-identical siblings. Conditioning consisted of Busulfan, Rabbit ATG, Rituximab and Cyclophosphamide; GvHD prophylaxis included methotrexate and cyclosporine. HbS level was maintained <30% by automatic red cell exchange before transplant. Median follow-up is 13 months (IQR 3–28).

Results: From January 2023 to March 2025, 19 patients underwent allogeneic HSCT. Donors median age was 8 years (IQR, 2–22); 13 of them had sickle cell trait. BM was unmanipulated, except for one patient with major ABO-incompatible graft. Median TNC infused was 4.6×10^8 cells/kg of recipient (IQR; $2.6–8.9 \times 10^8$ cells/kg). Patients median age was 8 years (IQR, 4–14), 10 patients were male, 9 female. Conditioning was well tolerated without grade III-IV events. Engraftment was achieved in all patients at a median of 26 days (IQR, 13–41) for neutrophil and 19 days for platelets (IQR 14–35). All patients experienced febrile neutropenia responding to antibiotics. Microbiological findings on blood cultures included *P. aeruginosa*, Gram negative rods and Coagulase-negative Staphylococci, all resolved. One patient was positive for *P.falciparum*, two patients developed CMV reactivation, treated and recovered. One case of extrapulmonary tuberculosis was treated successfully. Three patients experienced acute GVHD (grade I–II), with complete response to treatment. At median follow-up of 13 months (IQR, 3–28) no transplant-related mortality occurred. One patient developed moderate skin chronic GHVD, currently on treatment. One patient was diagnosed with oral HPV, resolved with cryotherapy; another was diagnosed with probable Invasive Fungal Disease, treated with Voriconazole. No other long-term complications were diagnosed. All patients remain transfusion-free with blood counts and HbS levels compatible with complete engraftment and chimerism. 7/19 patients stopped immune-suppressants at median of 300 days after HSCT (range 265–365), and 6 of them went back to school after revaccination.

Conclusion: Our experience highlights the feasibility and safety of HSCT in Tanzania through local capacity building and serves as a model for expanding curative SCD therapies in LMICs. Tanzanian staff, despite not having previous experience in HSCT, performed over half the transplants independently after training. Ensuring long-term sustainability is crucial, requiring affordable costs, reliable supply chains, and continuous training to potentially expand HSCT to other disorders and donor types.

OR37 | In utero gene editing tools for sickle cell disease

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Introduction: Sickle Cell Disease (SCD) is a severe monogenic disorder caused by a single point mutation in the HBB gene, resulting in the production of sickle hemoglobin (HbS). Curative therapies such as HLA-matched hematopoietic stem cell (HSC) transplantation are limited by donor availability, while ex vivo gene therapies remain constrained by complexity, risks, and limited accessibility. Prenatal base editing offers a unique opportunity to correct the underlying mutation before disease onset, leveraging immune tolerance and the accessibility of fetal hematopoietic stem and progenitor cells (HSPCs). This study investigates the potential of ABE8e-NRCH-mediated in utero base

editing to introduce the non-pathogenic Makassar β-globin variant as a therapeutic strategy for SCD.

Methods: We evaluated adenine base editing efficiency in vitro using human SS HUDEP-2 erythroid cells and primary fetal and adult SS CD34⁺ HSPCs isolated from peripheral blood. Cells were electroporated with ABE8e-NRCH mRNA, sgRNA targeting the SCD mutation, and GFP mRNA. Editing at the HBB locus was quantified via Sanger sequencing. Transfection efficiency and apoptosis were assessed by flow cytometry, and cell proliferation was tracked over time. Clonogenic potential was measured using colony-forming unit (CFU) assays. Lineage-negative HSPCs were isolated from fetal livers (E13.5) of humanized Townes SCD mice carrying the SCD mutation, edited ex vivo, and assessed for editing efficiency, erythroid differentiation, and viability. Mice were phenotypically characterized through hematological parameters, histology, organ weight, and hematopoiesis profiling.

Results: ABE8e-NRCH achieved high A-to-G editing efficiencies in SS HUDEP-2 cells (78.3 ± 15.7%, $n = 4$), adult SS CD34⁺ HSPCs (85.0 ± 1.0%, $n = 3$), and fetal SS CD34⁺ HSPCs (86.7 ± 2.5%, $n = 3$). Fetal HSPCs showed greater viability and proliferation post-transfection than adult cells, with sustained transfection observed at day 1 in fetal (87.5 ± 5.7%, $n = 3$) and adult (85.6 ± 1.5%, $n = 3$) HSPCs. Editing in colony-derived BFU-E and CFU-GM progenitors was similarly efficient between fetal (92.7 ± 2.5%, 91.7 ± 2.1%) and adult (91.7 ± 2.1%, 85.7 ± 2.1%) HSPCs. In the Townes SCD mouse model, fetal liver Lin⁻ HSPCs edited ex vivo with ABE8e-NRCH showed efficient A-to-G conversion (64.3 ± 13.8%, $n = 6$). SS mice recapitulated human SCD features, including anemia, leukocytosis, splenomegaly, and disrupted splenic architecture ($n = 6$ per group).

Conclusion: Fetal CD34⁺ and Lin⁻ liver-derived HSPCs are highly amenable to adenine base editing, with robust editing efficiency and minimal impact on viability or differentiation. Compared to adult cells, fetal HSPCs demonstrate enhanced proliferation, sustained transfection, and preserved clonogenic capacity, reinforcing their suitability for in utero therapeutic intervention. These findings support prenatal base editing as a promising strategy to correct SCD before birth. Ongoing work will focus on optimizing in vivo delivery systems and evaluating long-term correction and safety in preclinical models.

OR38 | Sickle cell disease ECHO: Kenya leading with care in Sub-Saharan Africa

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Introduction: Sickle cell disease (SCD) is an inherited blood disorder which affects millions of people worldwide marked with significant morbidity and mortality from severe complication. Over 300 000 children are born annually with SCD; over 70% of these births occur in Sub-Saharan Africa. In Kenya, approximately 14 000 children are born with SCD each year with a greater incidence in malaria endemic areas. The disease related mortality in the resource-limited countries of Sub-Saharan Africa is greater than 50% compared to <3% of high-resourced settings. Since 2011, hematologists from North American institutions partnered with Kenyan specialists to deliver educational seminars in Kenya focusing on Western Kenya, a region with the highest prevalence of SCD.

Methods: A multidisciplinary, collaborative team of Kenyan and North American health providers aimed to launch a Project ECHO (Extension for Community Health Outcomes) program focused on SCD; the first SCD ECHO in sub-Saharan Africa. The "hub" team included pediatric and adult hematologists from Kenya and the United States, nurses, clinical officers, patient advocates, social workers, and local physician leaders. "Spoke" participant recruitment for the SCD ECHO program began months prior to the launch through interpersonal networking and contact logs of participants from prior educational workshops and other ECHO programs in the region. Paring with existing technology in the region, the WhatsApp smartphone messaging platform acted as a notification network for coordinating ECHO logistics. The adapted curriculum focused on key areas: Screening and diagnosis, infection prevention, utilization of Hydroxyurea and management of acute and chronic complications. The "hub" team members participated in programmatic planning activities for the SCD ECHO launch for a 6-month duration.

Results: The SCD ECHO program successfully launched in June 2022 with once monthly sessions. Participation at early sessions averaged 120 attendees with participants attending from 24 of the 47 total counties in Kenya; all target counties in Western Kenya with a high prevalence participated. ECHO leadership maintained fidelity to the model with an emphasis on dialogue, collaboration, and mentorship. Program monitoring utilized iECHO platform in combination with survey instruments for educational assessments and participant feedback. The ECHO community continues to flourish outside of the virtual sessions with increased dialogue between "spoke" participants and "hub" members via electronic messaging. An unintended beneficial outcome from the SCD ECHO was an increase in SCD referral patterns from "spoke" sites to the referral centers.

Conclusion: The mortality rate from SCD disease in low-resourced countries with high prevalence rates in sub-Saharan Africa remains disproportionately high, and education at the community level is a key component to end these disparities. Increased utilization of Project ECHO represents a strong mechanism to continue building local, regional, and international partnerships to collaborative improve SCD care and outcomes together. The program after

3 years of running looks at the horizon to be a superhub for other African countries to join the ECHO movement.

OR39 | Long term outcomes of haemoglobinopathy patients infected with hepatitis C: A single centre experience

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Introduction: Routine hepatitis C screening began in the UK in 1991, with the last transfusion-transmitted case reported in 1997. While screening has reduced new infections and treatment—particularly direct-acting antivirals (DAAs)—has proven highly effective, long-term outcomes in haemoglobinopathy patients with hepatitis C remain poorly defined. The UK's 2019 Infected Blood Inquiry highlighted concerns around a "lack of ongoing monitoring" in those who cleared the virus. Chronic hepatitis C can lead to cirrhosis and hepatocellular carcinoma (HCC), and patients with haemoglobinopathies face added risk from iron overload and other liver-related complications.
Methods: We conducted a retrospective review of clinical notes, radiology, and biopsy results for all haemoglobinopathy patients at our centre with prior hepatitis C infection. Mean liver iron concentration as measured by R2-MRI was calculated for each patient over a 15-year period (the period is due to availability of historic results).
Results: Twenty-eight patients were identified: 27 with transfusion-dependent thalassaemia and 1 with sickle cell disorder; 18 were male. There were six cases of HCC. Eleven patients had biopsy-proven cirrhosis. six have died—four from HCC, one from complications of chronic liver disease, and one from heart failure related to iron overload, who also had HCC. One other patient with HCC required liver transplantation. The median age of surviving patients is 57 years.
HCV clearance data was available for 25 patients: 23 achieved sustained viral response (SVR); the 2 who did not have both died from liver-related complications. Treatment data was available for 22: 2 cleared the virus spontaneously, 20 were treated with interferon (±ribavirin), and 7 required additional treatment with DAAs. Three achieved SVR with interferon alone; the latest SVRs were achieved in 2016.
Biopsy data at diagnosis was available for 17 patients: 10 had grade 3 or 4 fibrosis. Of these, four have died. Among the six who are alive, one was transplanted due to HCC, two had a kPa of <10 on recent vibration-controlled transient elastography (VCTE), with a mean 15-year LIC of 1.9 mg/g/dw. Three had kPa >10 with mean LIC of 4.03 mg/g/dw.
Of the seven patients without advanced fibrosis on initial biopsy, four subsequently developed cirrhosis. All had chronic hepatitis C for over 10 years and achieved SVR with DAA therapy in 2015–2016. Three now have kPa <10 on VCTE. Their mean LIC was 6.6 mg/g/dw. The three who did not develop cirrhosis all achieved SVR in the 1990s; two had chronic HCV for under a year. Their mean LIC was 4.7 mg/g/dw.
Among the 11 patients with biopsy-confirmed cirrhosis, four have died. Of the remaining seven: 6/7 have normal serum transaminases, 7/7 maintain normal albumin, none have had ascites and 1 has grade 1 oesophageal varices.
Conclusion: This is, to our knowledge, the first UK-based retrospective dataset describing 30-year outcomes in haemoglobinopathy patients with HCV. Limitations include incomplete data due to multi-centre care and gaps in historic records. Outcomes appear to be consistent with the literature in that prolonged infection and liver iron content are risk factors in developing HCV liver-related complications. Whether current monitoring guidelines—such as annual AFP, 6-monthly ultrasound, and the frequency of VCTE—are appropriate for all patients remains uncertain. Further longitudinal studies are needed to inform future care pathways.

OR40 | Survival and morbidity among adults with thalassemia in England: Retrospective analysis using routine healthcare data

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Introduction: Thalassemia is associated with ineffective erythropoiesis and hemolysis, leading to chronic anemia and complications that can impact life expectancy. Limited studies have compared mortality between patients with non-transfusion-dependent thalassemia (NTDT) or transfusion-dependent thalassemia (TDT) and non-thalassemia populations. This study aimed to assess overall survival (OS) among adults with TDT and NTDT compared to a non-thalassemia population and the association of hemoglobin (Hb) with complications in NTDT in England.
Methods: Clinical Practice Research Datalink (CPRD) Aurum linked to Hospital Episode Statistics and death registrations were used to identify adults with α- or β-thalassemia from 2008 to 2019, indexed on the latest of 18th birthday, start of CPRD registration, or 1 Jan 2008. TDT was defined as ≥8 red blood cell transfusions (RBCT) each ≤42 days apart in the 12 months pre-index. Among patients with non-TDT, to limit the possible inclusion of trait/carriers, four definitions (Def) were used: (1) diagnosis codes; (2) hematology or inpatient visits with a primary

diagnosis of thalassemia; (3) Def 1 and 2; and (4) Def 1 or 2 (Figure). Patients with another hemoglobinopathy or prior hematopoietic stem cell transplantation were excluded. Adults with TDT or NTDT were matched to non-thalassemia controls (1:5 ratio) on age, sex, geography and ethnicity. OS from birth to study period end (31 Dec 2020) was assessed among adults with TDT or NTDT and controls using the Kaplan–Meier method and compared using log-rank test and Cox proportional hazards regression. A sensitivity analysis assessed OS from index. Multivariable Poisson and logistic regressions were used to assess the association of mean Hb, excluding readings within 8 weeks of RBCTs, with number of complications (43 considered) and presence of seven selected composite thalassemia-related complications, respectively, during follow-up. For these analyses, patients with NTDT and ≥1 Hb reading were included and re-indexed at their earliest Hb reading. Incidence rate ratios (IRR) and odds ratios (OR) were adjusted for age, sex, and follow-up (offset in Poisson model).

Results: Ninety-six patients with TDT and 480 controls and 288, 296, 68, and 516 patients with NTDT and 1440, 1480, 340, and 2580 controls for Def 1–4, respectively, were included. The mean index ages were 32–38 years, and median follow-ups were 5.2–7.3 years across groups. OS was statistically significantly worse for adults with TDT and NTDT compared to controls in the main (all NTDT Def, Figure) and sensitivity analyses (except NTDT Def 3, data not shown). Hazard ratios in the main analyses ranged from 2.85 (NTDT Def 1) to 11.68 (TDT) compared to controls (Figure). Among patients with NTDT who had ≥1 Hb reading (Def 1–4, $n = 222$, 227, 45, and 404), there was a statistically significant decrease in the number of complications for each 1 g/dL increment in Hb for Def 2 (IRR = 0.93, 95% confidence interval [CI] 0.89–0.97) and 4 (0.94, 0.91–0.98), but not for Def 1 (0.96, 0.92–1.01) or 3 (0.90, 0.79–1.02). For each 1 g/dL increment in Hb, odds of osteopathy statistically significantly reduced for NTDT Def 2 (OR = 0.54, 95%CI 0.39–0.74) and 4 (0.70, 0.56–0.88), but not for Def 1 or 3.

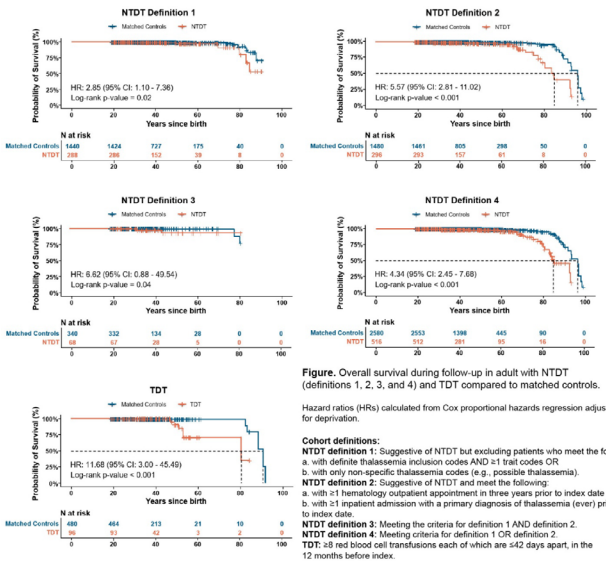

Figure. Overall survival during follow-up in adult with NTDT (definitions 1, 2, 3, and 4) and TDT compared to matched controls.

Hazard ratios (HRs) calculated from Cox proportional hazards regression adjusted for deprivation.

Cohort definitions:
NTDT definition 1: Suggestive of NTDT but excluding patients who meet the following:
a. with definite thalassemia inclusion codes AND ≥1 trait codes OR
b. with only non-specific thalassemia codes (e.g., possible thalassemia).
NTDT definition 2: Suggestive of NTDT and meet the following:
a. with ≥1 hematology outpatient appointment in three years prior to index date OR
b. with ≥1 inpatient admission with a primary diagnosis of thalassemia (ever) prior to index date.
NTDT definition 3: Meeting the criteria for definition 1 AND definition 2.
NTDT definition 4: Meeting criteria for definition 1 OR definition 2.
TDT: ≥8 red blood cell transfusions each of which are ≤42 days apart, in the 12 months before index.

Conclusion: Adults with NTDT and TDT are more likely to die at younger ages than those without this condition. In adults with NTDT, higher Hb was generally associated with lower likelihood of thalassemia-related complications.

OR41 | Impact of non-transfusion-dependent thalassemia on health-related quality of life and work productivity: A real-world survey

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Introduction: Thalassemia is associated with ineffective erythropoiesis and hemolysis, leading to chronic anemia and complications that can impact life expectancy, health-related quality of life (HRQoL) and work productivity. Research on the patient-reported impacts of non-transfusion-dependent thalassemia (NTDT), including α- and β-thalassemia is limited. This multi-region study aimed to investigate HRQoL and work productivity of adult patients with NTDT.

Methods: Data were drawn from the Adelphi Real World Thalassemia Disease Specific Programme™, a cross-sectional retrospective survey of physicians (hematologists/hematologist-oncologists) and their adult patients with a physician-confirmed diagnosis of NTDT (α and β) conducted from February to November 2024.

Physicians reported patient demographics and clinical characteristics in a patient record form (PRF) for up to 15 consecutive consultations. Each patient with a physician-completed PRF was invited to fill out a voluntary patient self-completion form (PSC). The PSC captured demographics, clinical characteristics, symptoms and outcomes, through individual questions and established patient-reported outcome measures, including the Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue, the Patient-Reported Outcomes Measurement Information System (PROMIS) Physical Function (PF), and the Work Productivity and Activity Impairment (WPAI) questionnaire for thalassemia.

Descriptive analysis was conducted only on data specific to the patient group who completed a PSC; patients who

Figure

	Genotype			Region				Age		Gender		Hb Level	
	Overall NTDT	α-NTD	β-NTD	Asia	EU and N. America	MENA	South America	<35 years	≥35 years	Male	Female	≤10g/dL	>10g/dL
*FACIT-Fatigue total scores**													
N	163	81	82	46	60	56	1	86	77	81	82	119	26
Mean (SD)	36.8 (10.5)	38.8 (10.3)	34.9 (9.8)	33.9 (11.7)	41.3 (8.6)	33.6 (9.5)	22.0 (0.0)	36.7 (11.5)	36.9 (9.3)	37.3 (9.8)	36.2 (11.2)	36.1 (10.9)	34.6 (9.7)
Median (IQR)	39.0 (29.0-46.0)	42.2 (30.2-47.0)	35.0 (27.0-44.0)	34.5 (24.0-45.2)	44.0 (36.0-47.0)	33.0 (25.5-42.1)	22.0 (N/A)	39.5 (29.0-47.0)	37.0 (30.0-45.0)	39.0 (29.0-45.8)	38.5 (27.8-46.0)	37.0 (29.0-46.0)	39.0 (25.5-44.5)
PROMIS Physical Function T-scores‡													
N	158	79	79	45	52	59	1	82	76	81	77	109	33
Mean (SD)	48.3 (8.2)	49.9 (8.3)	46.6 (7.8)	48.1 (8.5)	51.2 (8.0)	44.9 (6.5)	43.1 (0.0)	48.7 (8.8)	47.8 (7.5)	48.9 (8.0)	47.6 (8.4)	47.7 (8.3)	47.3 (7.1)
Median (IQR)	48.7 (41.5-60.1)	50.8 (43.1-60.1)	48.7 (40.6-49.2)	44.7 (41.5-60.1)	49.2 (48.4-60.1)	45.2 (39.5-49.2)	43.1 (N/A)	47.8 (41.4-60.1)	48.7 (41.8-52.4)	47.8 (42.0-60.1)	48.7 (41.6-53.0)	48.7 (41.6-53.0)	48.7 (42.0-51.8)
WPAI - Thalassemia§													
N	88	40	48	26	29	34	0	42	46	54	34	55	22
Mean (SD) % absenteeism	10.0 (16.6)	9.8 (17.7)	10.1 (15.8)	12.9 (5.8)	4.5 (18.9)	17.3 (18.2)	-	9.6 (16.2)	10.3 (17.1)	11.8 (16.8)	7.1 (9.3)	10.7 (16.9)	13.1 (23.4)
Median score (IQR)	6.7 (0.0-13.5)	3.1 (0.0-12.9)	8.8 (0.0-14.3)	12.8 (6.3-15.4)	0.0 (0.0-0.0)	9.5 (0.0-16.7)	-	6.3 (0.0-13.0)	5.3 (0.0-14.5)	7.6 (0.0-14.3)	4.6 (0.0-12.5)	7.1 (0.0-14.3)	8.3 (0.0-13.8)
N	95	45	50	32	29	34	0	46	49	55	40	64	20
Mean (SD) % presenteeism	30.6 (25.5)	29.6 (26.6)	31.6 (25.5)	32.3 (27.6)	35.7 (22.3)	27.6 (25.1)	-	31.1 (26.4)	30.2 (25.7)	33.1 (26.5)	27.5 (25.1)	30.0 (26.1)	42.3 (19.4)
Median score (IQR)	20.0 (10.0-50.0)	20.0 (0.0-50.0)	20.0 (10.0-50.0)	30.0 (2.5-60.0)	20.0 (0.0-40.0)	40.0 (17.5-50.0)	-	20.0 (0.0-50.0)	20.0 (10.0-50.0)	20.0 (10.0-60.0)	20.0 (0.0-55.0)	25.0 (0.0-50.0)	50.0 (10.0-67.5)
N	83	39	44	26	26	33	0	41	44	51	34	54	20
Mean (SD) % overall work impairment	35.2 (27.6)	35.2 (26.0)	35.1 (27.6)	41.6 (26.2)	26.1 (21.4)	42.0 (27.5)	-	35.2 (28.0)	35.2 (27.5)	36.0 (26.6)	30.9 (28.6)	35.2 (27.5)	45.8 (30.1)
Median score (IQR)	26.7 (10.0-55.0)	38.8 (10.0-55.3)	25.4 (12.3-56.2)	45.8 (13.0-65.8)	18.5 (0.0-26.8)	50.0 (15.0-56.2)	-	25.1 (10.0-56.2)	28.3 (10.0-55.3)	30.0 (13.0-69.8)	24.3 (4.4-50.8)	30.7 (10.0-55.7)	54.7 (12.5-70.6)
N	156	77	79	44	65	45	1	80	75	79	76	106	32
Mean (SD) % activity impairment	30.0 (25.0)	29.4 (26.6)	30.6 (22.9)	32.7 (28.6)	20.8 (20.7)	40.9 (24.7)	20.0 (0.0)	29.5 (25.6)	30.5 (24.5)	32.4 (26.1)	27.5 (23.7)	30.3 (24.8)	33.8 (27.0)
Median score (IQR)	30.0 (10.0-50.0)	20.0 (0.0-50.0)	40.0 (10.0-50.0)	35.0 (5.0-57.5)	10.0 (0.0-40.0)	50.0 (15.0-60.0)	20.0 (N/A)	20.0 (2.5-50.0)	30.0 (10.0-50.0)	30.0 (10.0-50.0)	30.0 (0.0-50.0)		45.0 (10.0-57.5)

*The higher the score, the lower the fatigue. US general population FACIT-Fatigue mean (SD): 43.6 (9.4) (Cella, 2002). †The higher the score, the better the physical function. US general population PROMIS Physical Function mean T-score (SD): 59.7 (8.0) (Fransvoi, 2015). ‡The higher the score, the more impairment to work or activities. US general population WPAI mean (SD): absenteeism 3.49% (13.88%), presenteeism 12.91% (21.58%), overall work impairment 19.51% (25.56%), and activity impairment 22.08% (28.33%) (Witt, 2015). Countries included in Asia region: Malaysia, Thailand; countries included in Europe (EU) and North America region: France, Germany, Greece, Italy, Spain and United States; countries included in Middle East and North Africa (MENA) region: Saudi Arabia, Turkey, United Arab Emirates, Egypt; countries included in South America region: Brazil. Abbreviation: NTDT, non-transfusion-dependent thalassemia; Hb, hemoglobin; SD, standard deviation; IQR, interquartile range; WPAI, Work Productivity and Activity Impairment; %, percent

received a hematopoietic stem cell transplantation or gene therapy were excluded from the analysis. Data were reported from the following countries: Brazil, Egypt, France, Germany, Greece, Italy, Malaysia, Saudi Arabia, Spain, Thailand, Turkey, the United Arab Emirates, and the United States. Data were analyzed by thalassemia genotype, region, and patient age, gender, and average hemoglobin (Hb) level (in the past 12 months prior to survey).

Results: Overall, 164 patients with NTDT (81 α-thalassemia; 83 β-thalassemia) completed a PSC and had corresponding PRF data completed by 51 physicians. At the time of data collection, patient-reported mean (standard deviation [SD]) age was 36.0 (12.4) years, 50.0% were female, and 64.5% were working full/part time. Physician-reported average Hb value over the past 12 months was (mean [SD]) 9.4 (1.3) g/dL.

When asked about symptoms ever experienced, 51.9% and 38.0% of patients reported fatigue and weakness, respectively. At survey completion, 33.5% and 26.1% of patients reported that fatigue and shortness of breath, respectively, interfered with their ability to carry out daily activities, and 61.4% reported they are worried about the risk of long-term complications.

Mean (SD) FACIT-Fatigue score was 36.8 (10.5; Figure). Mean (SD) PROMIS PF T-score was 48.3 (8.2; Figure). From the WPAI-Thalassemia, mean (SD) absenteeism was 10.0% (16.6%), presenteeism was 30.6% (25.9%), overall work impairment was 35.2% (27.6%), and activity impairment was 30.0% (25.0%).

These scores were all worse for patients with NTDT (both α and β) than published US population norms (Figure).

Conclusions: Overall, adult patients with NTDT (both α and β) experience worse fatigue, impaired physical function, and greater impairment in work productivity and daily activities relative to the general population, highlighting an unmet need to reduce the humanistic burden of thalassemia.

OR42 | Trends in hospitalisations for sickle cell disease, cystic fibrosis and haemophilia in England

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Introduction: Recent evidence suggests inequalities exist in secondary healthcare for people living with sickle cell disease (SCD). However, evidence quantifying these inequalities is lacking, nor have they been compared with other similar genetic conditions using routine hospital data in the UK. We aimed to describe recent trends in hospital admissions for SCD, cystic fibrosis (CF) and haemophilia in England.

Methods: We conducted a retrospective observational study using NHS England Hospital Episode Statistics (HES) Admitted Patient Care (APC) data of all individuals with a primary diagnosis of SCD, CF or haemophilia between 1st January 2013 and 31st December 2022. We compared the number and proportion of hospital admissions, 30-day emergency readmissions, length of stay (LoS) and costs of hospitalisations by age groups over time for the three conditions considered.

Results: Using HES APC, we identified 19 506 individuals with SCD, 9569 with CF and 7289 with haemophilia. People with SCD had a higher proportion of five or more elective hospital admissions ranging from 43.4% to 52.1%, compared with 14.3% to 22.3% for CF and 10.4% to 14.5% for haemophilia over the study period. The proportion of 30-day emergency readmissions was higher for individuals with SCD (9.0%) and CF (7.5%) compared to those with haemophilia (3.2%), particularly in the 10–19 and 20–29 age groups. The overall mean LoS (days) was longer among people with CF admitted for sepsis (24.3 vs. 16.7 in SCD and 20.8 in haemophilia) and acute appendicitis (6.1 vs. 5.9 for SCD and 5.4 for haemophilia). Overall estimated hospitalisation costs were much higher for SCD (£109.9M) compared with CF (£44.2M) and haemophilia (£14.4M) in the 2021/22 financial year.

Conclusion: We found substantial inequalities in all the indicators considered for SCD, CF and haemophilia. This comparative analysis can help guiding public health policies to reduce potentially preventable emergency readmissions, optimise LoS, and generate healthcare cost savings.

OR43 | Qualitative study on socio-cultural impacts on sickle cell disease newborn screening and public health solutions

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Introduction: Evidence indicates the importance and effectiveness of Newborn Screening for Sickle Cell Disease

(NBS-SCD) for timely detection and management. Despite this, NBS-SCD has not gained significant momentum, particularly in India, where Sickle Cell Disease (SCD) is a pressing public health issue. The incidence of SCD at birth in India was 16% in 2021, predominantly affecting socio-economically marginalised tribal and rural populations with limited access to quality health care. Effective NBS programs are crucial for preventing SCD and for early diagnosis to reduce morbidity and mortality. The recently launched National Sickle Cell Anaemia Mission in India proposes universal newborn screening as a key strategy. However, socio-cultural practices, local beliefs, and stigma surrounding SCD pose significant challenges to effective screening. This paper explores how these factors impact NBS-SCD implementation in resource-constrained, high SCD-prevalent regions of India, and suggests recommendations through an integrated social work in public health approach. The objective is to advocate for the right to health of marginalised communities.

Methods: We conducted qualitative exploratory research at seven high SCD prevalence sites across six Indian states. In-depth interviews with 127 participants, including healthcare providers and parents of newborns with SCD, were conducted. Data was coded and analysed thematically using NVivo14. An interface analysis examined the impact of various factors at different levels on newborn screening. Findings are presented through mind maps, word clouds, and participant narratives. The study followed the Consolidated criteria for Reporting Qualitative research (COREQ) checklist.

Results: The study revealed that socio-cultural practices, local beliefs, and stigma significantly hinder the implementation of NBS-SCD. Negative stereotyping and stigmatisation of children with SCD led parents to delay screening and diagnosis, adversely affecting treatment and care. Community beliefs related to ancestral curses and witchcraft promoted secrecy surrounding the disease, leading to a preference for traditional remedies over medical interventions. The paper analyses the nuanced expressions of stigma and local beliefs and their impact on NBS-SCD. An intersectional analysis highlights variations based on gender and ethnic identity, underscoring the need to address these aspects for effective control and management of SCD.

Conclusion: Although global advancements have been made in technology, treatment, and drug development for SCD, socio-cultural and behavioural factors remain underacknowledged. It is crucial to address the social determinants and perceptions related to SCD to manage it effectively. There is a pressing need for collaboration among various stakeholders to reach marginalised communities that are often overlooked due to social and structural barriers.

OR44 | PTSD symptoms and pain interference in children with sickle cell disease: Prevalence and associated factors

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Introduction: Children with sickle cell disease (SCD) are regularly exposed to vaso-occlusive crises (VOCs), hospitalizations, and medical complications. These experiences may lead to psychological distress and post-traumatic stress disorder (PTSD) symptoms, potentially resulting in elevated levels of pain interference (PI) in daily functioning. Although pain is a known aspect of SCD, the psychological dimensions—particularly PTSD and PI—remain underexplored, with their prevalence and associated factors not well understood. This study aims to report the prevalence of PTSD symptoms and clinically relevant PI in children with SCD and to investigate associated factors. Hereby we seek to improve awareness and identify the urgent need for the development of multidisciplinary care approaches.

Methods: This is a single-center, cross-sectional substudy of baseline measurements embedded in a larger randomized controlled trial investigating the effect of EMDR on PI reduction in children with SCD (the RELAX study), conducted at Amsterdam UMC. All children aged 6–18 years with SCD were eligible. Exclusion criteria were major interfering acute medical or psychiatric conditions and estimated IQ <80. After informed consent, participants completed the Child and Adolescent Trauma Screen (CATS), the PROMIS Pain Interference questionnaire, and a sociodemographic survey. For children ≥8 years, self-report questionnaires were analyzed; for younger children, parent proxy-reports were used. Additional clinical data were extracted from records. Primary outcomes include the prevalence of PTSD symptoms and PI. Secondary outcomes involve exploring associations between these outcomes and demographic (age, sex, and parental education, psychological (comorbid mental health conditions), and clinical variables (SCD genotype, prescribed medications, prior complications or organ

damage, and the frequency and duration of hospitalizations). Descriptive statistics will be used to characterize the cohort, and regression analyses will assess associations.

Results: Data collection will continue until December 2025. Preliminary analyses of 69 children with SCD (mean age = 12 years, SD = 3.53; 46% female) show that 26 (38%) reported clinically relevant PI (PROMIS *T*-score >49). PTSD symptoms were analyzed in the subgroup ($n = 54$) who reported one or more traumatic events (mean age 13 years (SD = 3.07), with 46% female). Among them, nine (16.7%) scored ≥21 on the CATS, indicating subclinical or clinical PTSD symptoms. Analyses of associated factors are ongoing and will be presented at the ASCAT conference.

Conclusion: Preliminary findings indicate a psychological and functional burden in children with SCD. Over one-third of children experienced clinically relevant PI, suggesting a high level of daily functioning disruption. Additionally, 16.7% of children with trauma exposure show PTSD symptoms, suggesting this comorbidity may be underrecognized in clinical practice. These results illustrate the importance of psychosocial screening in pediatric SCD care and support the inclusion of mental health services into routine treatment. They also provide a baseline for evaluating interventions such as EMDR in the ongoing RELAX study.

OR45 | Consortium on newborn screening in Africa—Progress update

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Introduction: Sickle cell disease (SCD) is a serious inherited red blood cell disorder with stark regional differences in childhood survival. For the 300 000 babies born with SCD annually in sub-Saharan Africa, under-5 mortality (U5M) has been estimated to be ≥50%. Deaths before SCD diagnosis lead to underestimates of disease-associated mortality.

Multinational population-based research on the impact of early screening is crucial for demonstrating the potential of low-income countries with high SCD burdens to improve outcomes. As part of the American Society of Hematology's SCD Initiative, the society developed the Consortium on Newborn Screening in Africa (CONSA) to address these challenges.

CONSA's hypothesis is that early infant SCD screening and entry into standardized continuous care will reduce U5M compared with historical estimates. The primary objectives of this implementation trial are to determine (1) the population-based birth incidence of SCD and (2) the effectiveness of early standardized care in preventing early mortality in children with SCD consortium-wide at each country's site(s). The secondary objectives are to (1) measure the overall 5-year survival rate of affected children enrolled in the newborn screening cohorts; (2) assess the program uptake, reach, fidelity; (3) evaluate sustainability; and (4) assess the costs of newborn screening and early interventions for each site.

Methods: CONSA is a registry trial based on standard screening and diagnostic procedures and early intervention therapies, specifically penicillin prophylaxis and childhood immunizations. Clinical SCD standards for the consortium were established based on existing national and global guidelines.

The consortium's main implementation focus include (1) register patient data and medical history of babies diagnosed with SCD within the first 3 months of life in a shared database, (2) initiate antibacterial and antimalarial prophylaxis within the first 3 months of life and ensure immunization of each baby (3) monitor each patient at required intervals and update the patient's record in the registry after each visit, and (4) estimate the incidence of specific SCD genotypes and identify other hemoglobin variants among populations in CONSA countries.

Results: As of March 2025, the following data have been received:

- 130 477 children have received results
- 23 222 diagnosed with SCT (17.8%)
- 1721 diagnosed with SCD (1.32%)

Efforts to monitor clinical care are ongoing, with interventions being implemented to strengthen retention in care (currently 44% retention). Of the children coming back to clinical care:

- Over 90% are receiving clinical interventions including penicillin, folic acid, and bed nets.
- We are implementing several activities now to strengthen retention efforts.

Conclusion: The 2020, CONSA has demonstrated that newborn screening and early clinical interventions can be implemented in diverse resource settings. Ongoing efforts are focused on strengthening retention and building health system capacity, showcasing to governments and partners the feasibility of such approaches.

As CONSA continues to implement its programs, focus will be on expanding hydroxyurea access, working with governments and partners to scale up screening and clinical interventions across countries, and prioritize research in the clinical care of the children diagnosed with SCD.

OR46 | Blood group antigen diversity among blood donors and individuals with sickle cell disease in Kenya

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Introduction: Sickle cell disease (SCD) patients rely on blood transfusion to manage the complications of the condition and have been shown to be significant consumers of this limited resource. The risk of erythrocyte alloimmunization increases if the donor erythrocyte antigens are not well matched to the recipient. However, neither pre-transfusion alloantibody screening nor extended matching beyond ABO and Rhesus D is routinely undertaken in Africa. Even with extended blood group antigen matching, a mismatch can happen due to genetic diversity and variable expression of the blood group antigens. An alloimmunization prevalence of 14.3% among individuals with SCD was recently reported. Most of the alloantibodies were specific to the Rhesus and MNS blood groups. However, the phenotypic expression of blood group antigens in these individuals and blood donors has not been described. This study aimed to describe the phenotypic diversity of clinically significant blood group antigens.

Methods: This was a cross-sectional study of 280 blood donors and 254 individuals with SCD and history of transfusion conducted on the coast of Kenya. Phenotyping of the red cell antigens Rh (C, c, D, E, e), Kell (K, k, Kpa, Kpb), Duffy (Fya, Fyb), Kidd (Jka, Jkb), Lewis (Lea, Leb), Lutheran (Lua, Lub), P1 and MNS (M, N, S, s) using Bio-Rad phenotyping gel-cards was undertaken.

Results: Phenotype diversity was highest in the MNS ($N = 14$) and Rhesus ($N = 9$) blood groups, with majority of the participants expressing ccDee (58.43%) and M+N+S–s+ (33.57%). The rare phenotypes observed included Rh (CCDEE), MNS (M–N–S–s+), Duffy (Fya+Fyb+, Fya–Fyb+), Kidd (Kpa+Kpb+, Kpa–Kpb–), Lutheran (Lua+Lub+, Lua–Lub–), Lewis (Lea+Leb+), Kell (K+k+) and Kidd (Jka–Jkb+, Jka–Jkb–). Some phenotypes were exclusively expressed in blood donors (M–N–S+s+ and M+N–S+s–) or individuals with SCD (CCDEE, M+N+S–s–, M-N+S+s– and M–N–S–s+). 14 (5.5%) of the individuals with SCD were alloimmunized and expressed at least one rare phenotype across the different blood group systems.

Conclusion: Red cell antigen and phenotype diversity is present among blood donors and individuals with SCD in Kenya. The presence of phenotypic diversity and rare phenotypes puts unmatched transfusion recipients at risk for the development of alloimmunization. A better understanding of the molecular diversity of red blood cell antigens in the local population of donors and transfusion recipients in Africa is needed.

OR47 | Triple effect of caregiver education in enhancing health outcomes of sickle cell patients in Nigeria

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Background: Sickle cell disease (SCD) is a serious genetic and inherited disorder. It has physical, psychological, and socio-economic impacts on affected individuals including children and families. Nigeria bears the highest burden with about 150000 newborns affected yearly. In the rural communities, there are many issues arising from ignorance about the disease, lack of access to health services, underutilization of available healthcare services due to ignorance from religious and cultural beliefs, financial constraints, and delayed diagnosis. These factors result in high morbidity and mortality of children living with sickle cell disease. Despite extensive patient education efforts, sickle cell disease (SCD) outcomes remain poor in Nigeria because a critical gap exists. While patients receive education, caregivers who make actual care decisions and control resources remain undereducated about sickle cell disease. This disconnection keeps creating preventable crises, false beliefs, family stigma, psychological and emotional stress, and healthcare system failures where parents reject proper treatment.

Objective: To demonstrate that comprehensive caregiver education creates a triple effect improving clinical outcomes, family dynamics, and healthcare system engagement simultaneously.

Methods: A five-year caregiver-centered intervention program (2019–2024) was implemented, which targeted 300 families under the umbrella of Ignite Sickle Cell Initiative in Ondo State, Nigeria. The program integrated monthly free clinics and sickle cell parents' education curriculum. Modules included hydration strategies, pain management at home, infection prevention, emergency recognition, psychological support, effective communication with healthcare personnel, medication adherence and navigating local health systems. Caregivers (majorly 95% parents) received this intensive education every month at the clinic. We measured clinical indicators (crisis frequency, adherence), family functioning (disease understanding, stigma levels, emotional stress), and system engagement (referral, insurance enrollment, advocacy capacity).

Results: The caregiver education intervention produced remarkable improvements across all three domains. (Clinical outcomes, family system and healthcare system engagement). Clinical outcomes showed crisis episodes decreased by 67%, treatment adherence improved by 42%, and hospital visits reduced by 58%. Family resilience strengthened with disease misunderstandings decreased by 61% and family stigma reduced by 49%. Healthcare system engagement transformed dramatically with hospital usage from trained families increased by 65%, 486 families enrolled in state health insurance through advocacy efforts, and 8% of trained caregivers became community advocates.

Conclusion: Caregiver education produced threefold better outcomes when compared to traditional patient-focused approaches by targeting the actual decision-makers. This triple effect model addresses the fundamental mismatch between who receives education and who makes the care decisions. The intervention creates sustainable, community-driven improvements that extend beyond individual families to strengthen entire healthcare systems. This scalable approach offers a paradigm shift for SCD management in resource limit settings.

OR48 | Genotype

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Introduction: *Genotype* is a short film that addresses the urgent need for greater awareness of Sickle Cell Disease, particularly in African communities. With a rise in cases among newborns, the film explores the emotional and medical consequences of genetic incompatibility between couples.
Through the story of a Ghanaian-Kenyan couple who unknowingly pass on the disease to their child, *Genotype* emphasizes the importance of genotype testing before marriage. This film is both a personal narrative and a public health message, urging viewers to make informed choices to protect future generations.
Methods: The film *Genotype* was developed using a narrative storytelling approach to engage audiences emotionally while delivering a critical public health message. The production followed these key steps:

a. *Research and Development*: In-depth research was conducted on Sickle Cell Disease, including its genetic causes, prevalence in African populations, and the psychological impact on families. Interviews with medical professionals and affected families informed the script to ensure accuracy and authenticity.
b. *Scriptwriting*: The script was crafted to reflect a relatable story that bridges cultural boundaries—following a Ghanaian man and a Kenyan woman to emphasize that Sickle Cell Disease is not confined by borders.
c. *Casting and production*: The film employed actors from diverse East and West African backgrounds to represent the cross-cultural nature of the narrative. Filming focused on intimate settings such as the home and hospital to highlight the emotional weight of the diagnosis.
d. *Post-production and messaging*: The editing process emphasized emotional pacing, sound design, and visual cues that reinforce the film's core message: the importance of genotype testing before marriage.
e. *Awareness and Distribution strategy*: The final film is intended for use in health education campaigns, community screenings, schools, and online platforms. Subtitles and translations are considered to widen accessibility across regions.

Results: The short film *Genotype* successfully delivered its core message on the importance of genotype testing through a compelling narrative format. Key outcomes include:

(i) *Audience engagement*: Early screenings of the film generated strong emotional responses from viewers, particularly among young adults and couples. Many audience members reported a heightened awareness of Sickle Cell Disease and the role of genetic testing.
(ii) *Behavioral impact*: Post-screening surveys indicated that a significant number of viewers who had never considered genotype testing expressed intent to get tested and to encourage their partners to do the same. Health professionals at community screenings also reported increased inquiries about Sickle Cell screening.
(iii) *Community reach*: The film was screened in schools, churches, health centers, and community events across Kenya and Ghana, reaching a wide demographic. Social media shares and online distribution through You Tube further extended its reach beyond physical screenings.
(iv) *Collaborations and support*: The film sparked interest from health organizations and advocacy groups, leading to partnerships for future awareness campaigns. NGOs have expressed intent to use the film as an educational tool in genotype counseling sessions.

Conclusion: *Genotype* demonstrates the power of storytelling in driving health awareness. By portraying the emotional journey of a couple blindsided by their child's Sickle Cell diagnosis, the film delivers a simple but urgent message: know your genotype before marriage.
The film not only educates but also encourages critical conversations among couples, families, and communities. As cases of Sickle Cell Disease continue to rise, *Genotype* stands as a creative intervention that can help prevent future suffering through informed choices and early testing.

OR49 | Daily living experiences of people living with sickle cell in Ireland

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Introduction: Sickle cell disease (SCD) is a complex inherited hemoglobinopathy disproportionately affecting people of African descent. While widely researched in global contexts, there remains a significant gap in understanding how individuals experience SCD in Ireland, where its prevalence is increasing due to migration. This study explores the daily lived experiences of people with SCD in Ireland, with a particular focus on the psychosocial impacts of the disease and its implications for education and employment.
Methods: A qualitative methodology was employed to gather in-depth data from individuals living with SCD in Ireland. Six participants, aged 18–35, were selected through purposive sampling and interviewed using semi-structured questions. Data was analysed using Braun and Clarke's reflexive thematic analysis framework, ensuring that emerging themes were grounded in participant narratives. Research assistants with clinical backgrounds were trained and supervised to conduct interviews, ensuring cultural sensitivity and consistency in data collection.

Results: Five major themes emerged: (1) inconsistent and inadequate healthcare access; (2) stigma and psychological strain, including anxiety, depression, and societal disbelief of SCD-related pain; (3) the central role of family in disease management and emotional resilience; (4) barriers in education, such as high absenteeism, neurocognitive impacts from stroke, and a lack of institutional understanding; and (5) employment challenges, including workplace discrimination, fear of disclosure, and limited legal protections or accommodations. Participants frequently reported being misunderstood by healthcare professionals and educators, compounding both physical suffering and emotional distress. Caregiver burden, especially on mothers, was also a recurring sub-theme. These findings highlight the intersectionality of race, disability, and chronic illness, particularly within under-represented health systems.
Conclusion: This study offers a critical insight into the under-researched experience of living with SCD in Ireland. It demonstrates how physical, psychological, and structural barriers reinforce cycles of exclusion in healthcare, education, and employment. The findings underscore the urgent need for policy reform, increased awareness, and integrated support systems that recognise SCD as a complex condition requiring multi-sectoral responses. A patient-centred, rights-based approach is essential to address stigma, improve care pathways, and ensure equity in educational and professional opportunities for individuals living with SCD in Ireland.

OR50 | Positioning Africa towards equitable access to cell and gene therapies for sickle cell disease

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Introduction: The sub-Saharan African (SSA) region remains disproportionately burdened with sickle cell disease (SCD), bearing about 80% of the global burden, with over 1600 new births annually in Ghana alone. Yet, innovative cell and gene therapies (ICGTs) for SCD with potential to prevent end-organ damage or offer cure is inaccessible to this very population most burdened by the disease. The cost of ICGTs is extremely high ($2.2 to $3.1 million per person) and clinical studies on their efficacy and safety are conducted largely in Western populations with less genetic diversity compared to the African population. In addition, there are issues of regulation and intellectual property regarding the commercialization of affordable ICGTs. However, with strategic preparation, SSA can be well positioned by the year 2035 to address the gap in equitable access to ICGTs for people living with SCD (PLWSCD) in the region. While several recommendations for bridging this gap have been proposed, their implementation have been hindered largely by lack of funds. An evidence-based funding model that supports co-production of sustainable resource mobilisation, contextual research, and quality clinical care is needed.
Objectives: Using Ghana as an example, a set of recommendations for positioning the country towards the provision of ICGTs for SCD management is outlined. This could serve as a framework for other areas in SSA and for promoting access to advanced management of other diseases of global health significance in similar settings.
Methods: Drawing on the funding models of the Global Fund, International Monetary Fund, and Ghana National Association of Teachers Cancer Foundation, recommendations for sustainably funding the range of strategies necessary to ensure access to ICGTs for PLWSCD in Ghana and beyond by 2035 are outlined.
Results: It is recommended that a well-established private ICGT company sets-up a branch in Ghana in partnership with an internationally certified pharmaceutical company in Ghana. This co-operation should operate three main arms – research, clinical services, and a foundation. The research arm will investigate ICGTs among Ghanaians over the next 5–7years; the clinical arm will ensure infrastructural and resource readiness from year 8 to 10; the foundation arm, acting on the principles of insurance, will mobilize funds to support activities of arms 1 and 2 over the next decade and thereafter, to cover/subsidize the cost of treatment with ICGT for eligible PLWSCD. The government should establish an alliance of sickle cell organizations in Ghana (ASCOG) to coordinate all efforts of sickle cell organizations in Ghana; lead the development of ICGT treatment eligibility and regulatory guidelines in collaboration with PLWSCD and stakeholders; set-up a fund and actively meet fund-raising targets; together with health economists, determine reasonable contributions to the fund by PLWCD/their families; and coordinate contributions from the fund into the ICGT foundation arm, so that there is continuous funding for ongoing research and ICGT treatment.
Conclusion: With an estimated population of 400 000 PLWSCD in Ghana and over 16 000 new births annually, reasonable continuous contributions from the SCD community and donations from across the globe could ensure that by 2035, Ghana can increase reach of PLWSCD to ICGTs, helping to address the current gap in access to global advancements in SCD management.

OR51 | Generation of sickle cell disease model systems using CRISPR-Cas9 technology

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Background: Sickle cell disease (SCD) is a group of inherited blood disorders characterized by the presence of the Glu6Val (Hemoglobin S) sickle mutation either in homozygous form

(sickle cell anemia; SCA) or in a compound heterozygous form with other mutations in the beta globin gene, such as the Haemoglobin C (Glu6Lys). Polymerization of these globins leads to sickling of red blood cells (RBC), which causes painful episodes, anaemia, and, in worse cases, organ damage. SCA (HbSS) is the most extensively studied since it is the most clinically severe form. HbSC is the second most clinically significant form of SCD; nonetheless, it is understudied and under-represented in trials and drug discovery processes because it is considered a "mild" form of SCD. However, data has shown that individuals with HbSC present with same complications as HbSS, although generally to a lesser extent, and that some complications such as retinopathy and splenomegaly are more prevalent in HbSC.

With the recent recall of Voxelotor and Crizanlizumab, there is a urgent to develop new drugs for the management of SCD. Recent drug discovery approaches for SCD have focused on phenotype-modifying abilities, therefore it has become increasingly important to understand the process and kinetics involved in the sickling and unsickling of RBCs in all forms of SCD. This project aims to develop an array of immortalised cell lines with different SCD genotypes to provide a sustainable supply of cells for analysis and drug discovery.

Methods: The erythroid cell line BEL-A, created in our lab, recapitulates normal human erythropoiesis. It was used as founder line for ribonucleoprotein (RNP)-mediated CRISPR-Cas9 genome editing to introduce mutations, creating a catalogue of sickle cell lines (HbSS, HbSC, HbAS, HbCC and HbAC). The lines were extensively characterised by assessing cell viability, expansion, globin expression profile (RP-HPLC and western blotting), cell morphology, and sickling characteristics, using a range of cell biology, molecular biology, and biochemical approaches. Alongside, HbSS and HbSC patient RBCs sickling characteristics were analysed for comparison.

Results: Expansion and differentiation characteristics of the SCD cell lines was not significantly different to to wildtype BEL-A, with the lines thus providing a sustainable and consistent supply of SCD cells. RP-HPLC and western blot analyses confirmed production of the expected globin variants at the protein level. Hypoxia live imaging of patient RBCs revealed differences in sickling dynamics and morphology between HbSS and HbSC genotypes. Importantly, sickling analysis of late-stage erythroblasts and reticulocytes provides functional validation of the cell lines as physiologically relevant model systems and enables analysis of differences in sickling characteristics in the different SCD genotypes.

Conclusion: The SCD lines provide a reproducible and sustainable supply of SCD cells for analysis of different SCD genotypes, importantly with an identical genetic background. These lines can be used to study the effect of genetic variants on sickling and serve as a platform for drug discovery.

OR52 | Patient-driven insights in sickle cell disease: Results from a global survey informing public health strategies

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Introduction: An effective public health strategy aimed at improving outcomes in sickle cell disease (SCD) must be grounded in the lived experiences and needs of those directly affected. To ensure that these perspectives are recognised and integrated into community health plans, ERN-EuroBloodNet, the SCD *Lancet Haematology* Commission, and ASCAT jointly launched a global initiative to collect patient-driven insights of people living with SCD. This initiative has the objectives of making the voices, priorities and needs of those living with the condition more visible in the definition of health policy objectives, public health and research agendas, thus guiding future actions to promote education, and consequentially achieving patient driven evidence to support advocacy efforts.

Methods: A two-round global survey was designed to assess through patient-driven insights the public health objectives preidentified. The survey targeted patients, as well as their parents, caregivers, partners, children, siblings and advocates. The first round (September 2023–January 2024) was conducted in English. Based on feedback, the second round (June 2024–February 2025) included a redesign of the structure and simplification of language, and it was as well translated into eight languages to ensure accessibility and reduce possible identified bias. This survey included a scoring-based prioritization of strategic actions for three topics: Research, Education and Policy. Respondents selected the priority of each element within each area from the most urgent to the less urgent. There were also open-ended questions to capture unmet needs potentially missing in the structured scoring part. The participation to the survey was anonymous. Responses were analysed quantitatively and qualitatively, indeed open-text entries were thematically coded by macro areas.

Results: The first and second rounds of the survey collected 196 and 199 responses, respectively. The final round

gathered answers from 30 countries, with the highest participation from the UK, France, USA, Portugal, Belgium, The Netherlands, Italy, and Nigeria.
The top-ranked priorities were:

- Research: Development of new drugs and innovative therapies (confirmed in both rounds).
- Education: Training for health professionals (confirmed in both rounds).
- Policy: Implementation of neonatal and prenatal screening. (In round one, this followed closely behind the recognition of SCD in national disease classifications).

From 210 free-text responses, five key themes emerged: Equitable access to treatments and curative therapies globally; Recognition of SCD as a disability; Combatting racial bias in healthcare; Need for psychosocial and financial support; Creation of expert centres and support for low-resource settings.
Conclusion: The survey confirms the critical need for patient-driven, equity-oriented approaches in shaping healthcare responses to SCD. A strong global consensus emerged around investment in innovative therapies, training of health professionals, and early screening. Free-text insights reveal persistent structural inequities, stigma, and the psychosocial burden experienced by individuals living with SCD. These findings should inform international, EU-wide and national strategies for supporting the inclusion of SCD communities as active stakeholders in policy-making, research, and service care planning.

OR53 | Sickle cell meets lupus: A rare case of cardiac tamponade in a young adult

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Introduction: The coexistence of Sickle Cell Disease (SCD) and systemic lupus erythematosus (SLE) presents a rare and complex clinical scenario. This case highlights the diagnostic and therapeutic challenges involved in managing both conditions, emphasizing the interplay between vaso-occlusive crisis, inflammatory responses and autoimmune manifestations.
Case Presentation: A 23-year-old male with a history SCD, recurrent vaso-occlusive crisis, cholelithiasis, and atopy presented with acute pericarditis complicated by cardiac tamponade and bilateral pneumonia. Laboratory evaluation revealed markedly elevated liver enzymes (AST 567 U/L, ALT 770 U/L), elevated C-reactive protein (peak 21.65 mg/dL), anaemia (hemoglobin 6.4 g/dL) and reticulocytosis (5.9%). Autoantibody testing showed a positive ANA (1:640) with a nuclear multiple dot and reticular cytoplasmic pattern, along with anti-Sm, anti-SSA, anti-RNP, anti-Sp100, and weakly positive anti-PL-7 and anti-PL-12 antibodies. Anti-SSB, anti-dsDNA, and anti-Scl-70 were negative. Complement levels were reduced (C4 <2.0 mg/dL; C3 24 mg/dL). Inflammatory markers were elevated, including ferritin (13 919 ng/mL) and circulating immune complexes (5.5 μg Eq/mL). Cardiac biomarkers indicated myocardial strain with elevated troponin T (5.02 ng/L) and NT-proBNP (352 pg/mL). The overall clinical and laboratory picture was consistent with active autoimmune and inflammatory processes. The patient developed obstructive shock requiring pericardiocentesis, followed by pulses of methylprednisolone and hydroxychloroquine therapy, leading to rapid clinical and biochemical improvement.
Discussion: This case illustrates the challenge of distinguishing between SCD complications and SLE-related autoimmune phenomena. The serological profile—including positive ANA, specific autoantibodies, hypocomplementemia, and markedly elevated ferritin—supported the diagnosis of active autoimmune disease. The combination of nuclear and cytoplasmic antibodies, together with heightened inflammatory markers, reflects complex immune activation. The coexistence of SCD and SLE demands a multidisciplinary approach for accurate diagnosis and individualized treatment.
Conclusion: Clinicians should be aware of overlapping features between SCD and SLE. A comprehensive laboratorial screening—including autoantibody screening, complement levels, immunoglobulin profiles and inflammatory markers—is essential for accurate diagnosis. Early recognition and tailored immunomodulatory therapy are crucial for achieving optimal outcomes in such complex clinical scenarios.

OR54 | Impaired pyruvate kinase correlates with hemolysis, ineffective erythropoiesis, and endothelial dysfunction in sickle cell disease

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Introduction: Sickle cell disease (SCD) is characterized by chronic hemolytic anemia and painful vaso-occlusive episodes. Abnormal hemoglobin S polymerizes upon deoxygenation, resulting in sickled red blood cells (RBC). Intravascular lysis of sickled RBCs results in oxidative stress, endothelial dysfunction, and inflammation. Until recently, treatment has been limited to hydroxyurea (HU) and blood transfusion. However, new strategies are emerging including

pyruvate kinase (PK) activators that enhance PK activity, a key enzyme of glycolysis. Activation of PK has been reported to increase ATP, improve membrane health, and decrease RBC sickling. In this study, we investigate whether impaired PK associates with hemolysis, ineffective erythropoiesis, proinflammatory cytokines, and endothelial dysfunction in patients with SCD.

Methods: Patients with HbSS or HbSβ^0-thalassemia patients at steady state, who did not receive a blood transfusion <2 months were enrolled. PK and hexokinase (HK) activity were measured, and PK thermostability (i.e., % residual PK activity) was measured after 1 h of incubation (53°C). RBC adhesion to laminin (Biolamina) was carried out on IBIDI μ-Slide I 0.4. Oxygen gradient ektacytometry was used to assess point of sickling (PoS, Lorrca, RR Mechatronics). Soluble transferrin receptor (sTFR), hemopexin, heme oxygenase-1 (HO-1), CD40 Ligand (CD40L), myeloperoxidase (MPO), and VEGF were assessed with MSD ELISA in plasma. Plasma proinflammatory cytokines were measured with OLINK technology. The association was assessed using the Spearman's correlation with level of significance 0.05 (GraphPad Prism v10).

Results: Ninety-one patients were enrolled, median age was 27 years (range 6 – 58 years), 56% female, and 67% were on HU therapy (Table 1). PK thermostability correlated with hemoglobin ($r = 0.225$, $p = 0.032$), absolute reticulocyte count ($r = -0.415$ $p \leq 0.001$), erythroblast count ($r = -.378$, $p < 0.001$), and sTFR ($r = -0.365$, $p < 0.001$, Figure 1). These findings indicate that reduced PK thermostability is associated with increased hemolysis and ineffective erythropoiesis. Furthermore, PK thermostability correlated with neutrophil count ($r = -0.292$, $p = 0.014$), and CD40L ($r = -0.265$, $p = 0.027$). The association with CD40L, a platelet-associated pro-inflammatory molecule linked to endothelial cell activation, indicates increased endothelial dysfunction in individuals with reduced PK thermostability. In addition, PK thermostability correlated with PoS ($r = -0.415$, $p < 0.001$) and HbF levels ($r = 0.385$, $p \leq 0.001$). PK/HK ratio associated with hemoglobin ($r = 0.299$, $p = 0.004$), bilirubin levels ($r = -0.239$, $p = 0.026$), and hemopexin ($r = 0.228$, $p = 0.031$). PK thermostability or PK/HK ratio did not correlate with other thromboinflammatory parameters (IL-1b, IL-7, IL-8, IL-10, IL-18, HO-1, interferon-α, TNF-α). Despite a significant correlation between PK thermostability and RBC adhesion ($r = -0.309$, $p = 0.037$), we did not find a significant correlation of PK thermostability with adhesion markers (sVCAM, sICAM, P-selectin, E-selectin), or other markers of endothelial dysfunction (vWF, VEGF, MPO).

Conclusion: This study demonstrates that impaired PK function, reflected by decreased PK/HK ratio and reduced PK thermostability, is associated with increased hemolysis, ineffective erythropoiesis and endothelial dysfunction. Future research is needed to determine whether in vivo activation of PK can reduce inflammation, improve erythropoiesis and endothelial dysfunction.

TABLE 1 Baseline characteristics.

Table 1. Baseline characteristics	SCD (n = 91)	Reference values
Age, years	26 (6 - 58)	
Sex, female, n (%)	51 (56%)	
SCD genotype, n (%)		
HbS/β0	7 (7.7%)	
HbSS	84 (92.3%)	
Hydroxyurea, n (%)	61 (67.0%)	
Laboratory parameters (median, range)		
PK Activity (U/gHb)	13.1 (3.5 - 24.3)	5.0 - 8.8
HK Activity (U/gHb)	2.3 (0.7 - 6.4)	0.5 - 1.0
PK/HK Ratio	5.6 (3.2 - 12.4)	8.0 - 18.7
PK thermostability, residual activity at T=60 (%)	74.8 (39.4 - 98.7)	76.0 - 100.7
Hb (g/dL)	9.1 (6.4-13.5)	12.1-17.2
Reticulocyte count (10.9/L)	232 (76 - 563)	40 - 110
Erythroblast count (10.9/L)	0.0 (0.0 - 9.6)	0.0
Leucocyte count (10.9/L)	8.1 (3.5 - 15.7)	4.0 - 10.0
Neutrophil count (10.9/L)	4.1 (1.3 - 10.8	1.5 - 4.0
LDH (U/L)	393 (164 - 827)	<240
Total bilirubin (umol/L)	40 (6 - 135)	<17
HbF (%)	8.0 (0.1 - 35.3)	0.8 - 2.0
Thrombo inflammatory markers	**SCD (n = 91)**	**controls (n = 20)**
Soluble transferrin receptor (sTFR, ug/mL)	5.55 (1.91 - 12.02)	1.05 (0.68 - 2.32)
Hemopexin (ug/mL)	97.42 (5.19 - 307.78)	288,97 (0.50 - 319.10)
CD40 Ligand (CD40L, pg/mL)	385.65 (40.18 - 2668.59)	1.22 (33.57 - 882.94)
HO-1 (ng/mL)	1.06 (1.43 - 28.60)	0.92 (0.09 - 1.93)
Myeloperoxidase (MPO, ng/mL)	23.44 (4.13 - 265.43)	30.70 (1.16 - 279.01)
VEGF (pg/mL)	502.66 (229.46 - 3261.34)	366.98 (220.02 - 919.55)
IL-6 (pg/mL)	3.39 (1.16 - 47.49)	1.54 (0.78 - 8.19)
Functional assays		
Point of sickling (mmHg)	40.9 (17.1 - 80.5)	n/a
RBC Adhesion	11.40 (3.10 - 39.10)	4.95 (3.20 - 14.30)

Numbers represent median (range)

SCD, sickle cell disease; PK, pyruvate kinase; HK, hexokinase; RBC, red blood cell

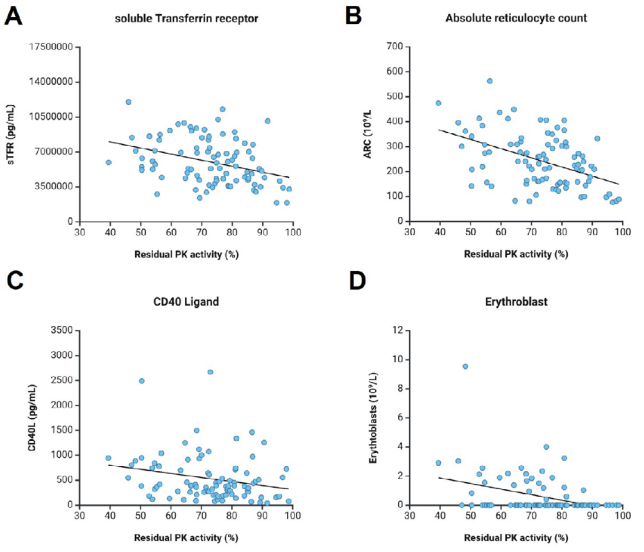

FIGURE 1 Correlation of PK thermostability with sTFR, absolute reticulocyte count, erythroblasts and CD40 ligand.

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OR55 | Venous thromboembolism in HbSC and sickle cell anemia and associations with hematological and thromboinflammatory parameters

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Introduction: Sickle cell disease (SCD) is a monogenetic disorder that is characterized by vaso-occlusion and chronic hemolytic anemia. Hemoglobin SC disease (HbSC, heterozygosity for hemoglobin S [HbS] and HbC), is the second most common form of SCD. Compared to the most prevalent form sickle cell anemia (SCA), HbSC has a clearly distinct phenotype and is considered to have a milder phenotype. Growing evidence suggests a high burden of venous thromboembolism (VTE) in SCD patients. Recently it has been postulated that thromboinflammation is a key factor in development of VTE in SCD. This study aimed to investigate the differences in VTE occurrence between HbSC and SCA and identify potential associations with occurrence of VTE.
Methods: This was a single-center cross sectional study using electronic chart review of adults with SCD was carried out. General demographic information, genotype, location of VTE, and lifetime admissions for most common SCD-related complications were collected. Laboratory values, both at steady state during outpatient clinic visit and during the VTE, were analyzed. From a subset of patients plasma was obtained at steady state to measure thromboinflammatory parameters and adhesion parameters. CD40 Ligand (CD40L), VEGF, cytokines, and adhesion molecules were measured with OLINK technology or MSD ELISA. Blood viscosity was measured in whole blood with a viscometer (Brookfield). Statistical analysis was performed with Graphpad Prism, and differences between groups were calculated using a Mann–Whitney *U*-test.
Results: Among 260 individuals with SCD, 22% (58/260) had experienced a VTE in the past, 77% was considered as provoked. There was no significant difference in VTE incidence between genotypes (HbSC 16/62 20%, SCA 37/111, 25%), age or gender. Pulmonary embolism (PE) was the most common type of VTE in patients with HbSC (13/16, 81%) and SCA (30/37, 76%). Patients with HbSC experienced VTE at a relatively older age compared to SCA patients with VTE ($p < 0.001$) or patients with HbSC without VTE ($p = 0.044$). In 7/16 HbSC patients VTE occurred when admitted for VOE or ACS compared to 22/37 in SCA. In individuals with VTE, significantly lower hemoglobin and higher leucocyte counts were found in SCA and HbSC patients during VTE compared with steady state (all $p < 0.05$). In SCA, a significant higher lactate dehydrogenase (LD) was found during VTE compared with steady state levels ($p = 0.025$). We found increased platelet counts, IL-6, IL-7, IL-8, CXCL8, VEGF, CDL40, P-selectin and E-selectin in 8 HbSC patients with VTE at steady state compared to 32 without VTE (Figure 1). Hemoglobin, hematocrit and viscosity levels were not significantly different between these two groups. In contrast, the hematocrit to viscosity ratio (HVR) was lower in HbSC with VTE compared to individuals without VTE. No differences were found in laboratory parameters in adults with SCA (10 with VTE, 49 without VTE; Figure 2).
Conclusion: A high burden of venous thromboembolism, particularly PE, was observed in patients with SCD. Although the prevalence of VTE is similar between SCA and HbSC, it is associated with elevated inflammatory and adhesion markers in the HbSC group only. Notably, HbSC or SCA patients who developed VTE did not exhibit elevated blood viscosity, hemoglobin, or hematocrit levels, suggesting that other factors, such as inflammation might play a role. Future studies are warranted to further explore associations with VTE in SCD.

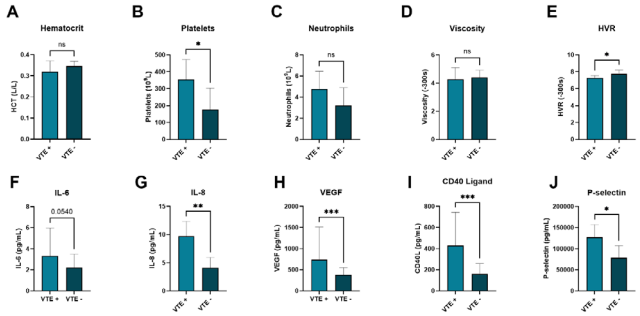

FIGURE 1 Thromboinflammatory parameters in adults with HbSC with and without venous thromboembolism.

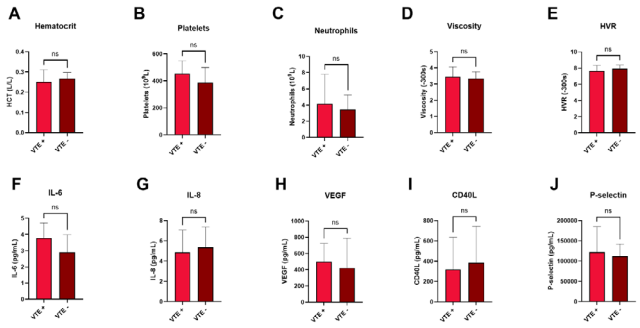

FIGURE 2 Thromboinflammatory parameters in adults with SCA with and without venous thromboembolism.

OR56 | Patient-reported quality of life and biometric signals: A real-time window into vaso-occlusive crisis risk

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Introduction: Accounting for approximately 95% of SCD-related hospitalisations and with severe impacts on quality of life, vaso-occlusive crises (VOCs) remain a significant challenge for individuals with Sickle Cell Disease (SCD). This work therefore explored the potential for predicting VOCs through biometric signals collected by wearables and electronic patient-reported outcomes (ePROs), aiming to enable earlier intervention and improve outcomes.

Methods: Data was analysed from 62 UK patients (Jul 24–Feb 25) who had provided informed consent, including continuously captured wearable biometric data at minute-level resolution, and daily ePROs collected through a dedicated app. Using linear models adjusted for sex, gender, and genotype, variation in ePRO and activity data was analysed across the 7 days pre- and peri-VOC, with significance defined at $p < 0.05$. Health states were assessed using EQ-5D-5L at baseline, pre-VOC (7 days), and during VOCs, deriving health utility index scores from the UK/England EuroQoL value set.

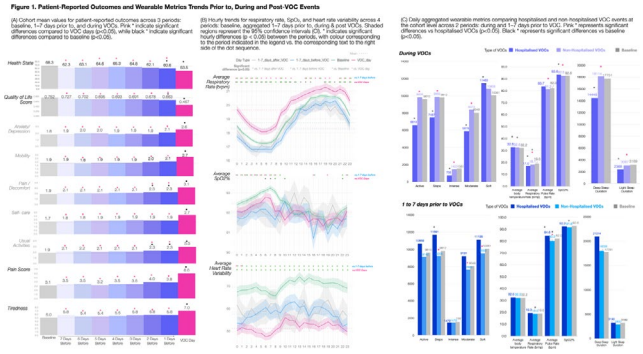
VOCs and linked hospitalisations were self-reported as Yes or No, and days with recorded "Maybe" VOC responses were excluded to reduce misclassification. VOC events <5 days apart were treated as a single episode. Baseline was defined as excluding the 7 days pre- and post-Yes VOCs.

Results: Median age was 36 (range 17–68), and 76% were female. Genotype distribution included HbSS (73%), HbSC (23%), and others (5%).

Compared to both pre-VOC and baseline values, VOC days exhibited the lowest Health State and EQ-5D-5L scores and declined significantly (Figure 1A), with scores 1 day pre-VOC already significantly lower than baseline. All five EQ-5D-5L domain severity scores were in turn significantly elevated on VOC days, with significant elevation from baseline of pain/discomfort and usual activity scores 1–2 days prior to VOC.

Significant reductions were revealed through hour-by-hour analysis (Figure 1B) in night-time respiratory rate (21:00–04:00) and SpO_2 levels (22:00–09:00) pre- and during VOCs, compared to baseline, in parallel with lower heart rate variability (HRV) at each timepoint.

Across 180 VOCs, 32 (18%) were associated with a patient-reported hospitalisation. In the 1–7 days pre-hospitalised VOC, participants recorded increased activity than non-hospitalised VOCs: longer moderate and soft



activity duration, higher step counts, and elevated pulse rates (Figure 1C). Activity levels exhibited significant drops during hospitalised VOCs compared to non-hospitalised VOCs, including step counts, active time, moderate and intense activity, alongside sleep duration. Hospitalised VOCs were furthermore associated with higher mean pulse rates and SpO_2 than non-hospitalised VOCs, in addition to lower respiratory rates.

Conclusion: This work observed significant pre-VOC changes in ePROs, particularly regarding increased pain/discomfort and decreased QoL scores. Real-time biometric monitoring revealed hourly-level deviations in respiratory rate, SpO_2, and HRV pre-VOC in comparison to baseline, highlighting their potential utility as early indicators in VOC prediction.

With hospitalised VOCs exhibiting distinct wearable patterns both pre- and during VOCs, indicating particular potential in stratifying hospitalisation risk, these findings ultimately support the feasibility of future remote VOC prediction strategies in disease management, and highlight key physiological signals pre-VOC that could inform critical proactive decision-making.

OR57 | Organ damage since childhood in sickle cell disease: Evolution and influence of disease-modifying therapies

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Introduction: Individuals with sickle cell disease (SCD) progressively develop chronic organ injuries that limit their life expectancy. Age-related evolution of organ damage and effect of disease-modifying therapies on its progression have not been fully elucidated. Biomarkers of organ damage and treatment response are still not included in routine prediction models; oxygenscan parameters could serve this function. The aims of the project were: to describe the prevalence

of chronic damage in the mainly affected organs in a cohort of children, adolescents and young adults with SCD followed according to a standardized protocol; to analyse the effect of disease-modifying therapies on the development of organ damage; to explore the role of oxygenscan parameters as biomarkers of organ damage in SCD.

Methods: This is a retrospective analysis of prospectively collected real-world data on organ damage in SCD patients monitored from 2007 in the Paediatric Haematology Unit of a University Hospital. Individuals with SCD, any genotype, were included in a Natural History study at diagnosis, treated and monitored for chronic organ complications according to a standardized protocol based on national guidelines. Since 2023 steady state peripheral blood samples of untreated and treated patients were prospectively collected to measure oxygenscan parameters according to a standardized European protocol.

Results: The study included 242 SCD patients (186 HbSS, 15 HbSβ0, 36 HbSC, 5 HbSβ+). Median age was 2.1 years (range 0–18.8) at diagnosis and 11.3 years (range 0.7–28.7) at last follow-up. Median time of follow-up was 8 years, with 2139.9 patient-years of observation. Patients received disease-modifying treatments as follows: 20.7% no therapy, 59.9% hydroxyurea (HU) only, 5.0% chronic red blood cell (RBC) transfusions only, 14.4% HU and chronic RBC transfusions. The prevalence of SCD-related organ injuries among patients with at least one evaluation was: 56.7% for brain large vessels vasculopathy at magnetic resonance (MR) angiography and 34.0% for silent cerebral infarcts at MR imaging; 33.6% for retinopathy; 36.8% for lung restrictive dysfunction; 28.4% for albuminuria; 37.8% for renal ultrasound abnormalities. The earliest organ damage to appear overall was brain injury, followed by lung dysfunction, renal involvement and retinopathy (Figure 1). The cumulative incidence of organ injuries affecting brain, lung and kidney at different timepoints from SCD diagnosis was significantly higher in untreated patients than in those who had received at least one disease-modifying treatment before the onset of damage ($p < 0.0001$). Reduced RBCs' deformability at oxygenscan correlated with the presence of abnormalities at ophthalmological examination and at renal ultrasound.

Conclusion: Long-term follow-up documents the evolution of injuries in children with SCD, with progressive involvement of different organs across ages. Wider and earlier use of disease-modifying treatments might allow the prevention or delay of organ damage, with further improvement of life expectancy and quality. Some oxygenscan parameters appear promising as biomarkers of SCD chronic complications and treatment response, but further investigations would be necessary to confirm these results.

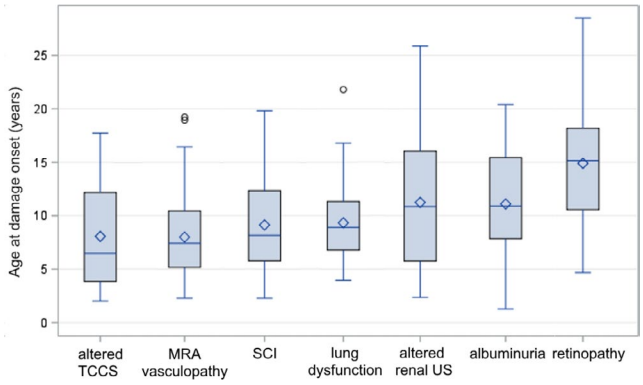

FIGURE 1 Variance of median age at the onset of chronic damage in different organs (p 0.0001).

OR58 | Research that reflects us: Insights from young people living with sickle cell and chronic pain

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Introduction: Pain is often dismissed or ignored in CYP and remains undermanaged in acute and chronic care contexts. Children and young people (CYP) from racialised (e.g., Black Caribbean/African, South-East Asian) communities are often excluded from chronic pain research. Including CYP living with sickle cell disease (SCD), where CYP from racialised groups represent the *majority* in the Global North, and from CYP living with other pain conditions (e.g., rheumatic conditions), where CYP from racialised groups represent the *minority* in the Global North, will provide critical insights as to the similarities and differences in why they may choose to be involved in research, how research delivery can be improved, potential language changes, and how to make relevant research more approachable. Critically, as caregivers play a crucial role in CYP participation, we will also include their valuable insights.

Methods: Purposive sampling was employed to recruit participants from across the UK through charities like Juvenile Arthritis Research and Crescent Kids, along with study advertisements disseminated through social media posts on Instagram, Facebook (closed groups), and LinkedIn using specific hashtags related to chronic pain and SCD. Twelve CYP aged 16–24 years from racialised groups (SCD = 8) living with chronic pain and 4 caregivers aged 33–47 years (SCD = 2) participated in separate online focus groups lasting 90 min. The groups were facilitated using semi-structured and online poll questions. Two patient and public involvement advisors (1 SCD caregiver; 1 CYP living with chronic pain) contributed to the study design and analysis to ensure inclusivity.

Results: Reflexive thematic analysis using an inductive approach with semantic coding identified five overarching themes. Participants expressed mistrust due to past injustices and ongoing negative experiences, emphasised

shared decision-making with families and trusted sources, and found research materials overly complex. They recommended simpler, culturally relevant materials, shorter consent forms, and clearer explanations. They also stressed involving CYP and child-friendly formats with reinforcements to encourage participation. Significantly, CYP living with SCD expressed the most concerns with anonymity and privacy regarding their data. All participants indicated that co-creating research materials with input from the community can help build trust and relevance.

Conclusion: To improve the inclusion of racialised CYP in chronic pain research, trust must be actively built through the co-creation of culturally sensitive, accessible materials and engagement with community voices. CYP living with SCD expressed heightened sensitivity to anonymity and called for greater transparency and cultural relevance in study design. Co-creating materials with CYP and caregivers from the SCD community emerged as key to building trust and improving engagement. Involving families and trusted networks in decision-making processes further supports participation. These outcomes highlight the urgent need for inclusive, community-driven approaches to research that reflect the lived realities of racialised CYP with SCD and chronic pain. These insights are critical to reshaping research approaches and ultimately improving health equity and outcomes for CYP living with chronic pain across racialised backgrounds.

OR59 | Small activating RNA-mediated induction of HBG with liposome delivery for in vivo treatment of SCD

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Introduction: Haemoglobin is an oxygen carrying tetramer composed of two alpha and two beta globin chains. The beta globin gene locus includes embryonic (epsilon, ε, *HBE*), fetal (gamma, g, *HBG*), and adult (beta b, *HBB*) forms of beta globin chains, which form the tetramers Gower II, HbF, and HbA, respectively. Sickle cell disease (SCD) is caused by a mutation in the *HBB* gene. The resulting tetramer, haemoglobin S (HbS), distorts red blood cells under hypoxic conditions leading to painful vaso-occlusive episodes, anaemia, and other complications. Expression of fetal g-globin and concurrent HbF tetramer can compensate for dysfunctional HbS in patients if %HbF reaches 25%, a level considered transformational. Recent drug development work focused on reactivating *HBG* using small molecules or CRISPR technology. CRISPR is highly effective but poses a high treatment burden and challenging accessibility for patients. Small molecules can achieve strong activation, but specificity and the consequent risk of adverse events is an obstacle.

Small activating RNAs (saRNAs) are short, double-stranded RNA molecules that leverage an evolutionarily conserved mechanism to selectively induce transcription of target genes. saRNA-mediated RNA activation by in vivo delivery has been demonstrated in clinical studies using the liposome NOV340 (PMID 34407972). Previously, we demonstrated that NOV340 liposomal formulation can target erythroid progenitor cells (ErPs) in the bone marrow of non-human primates (NHP) with high efficiency, supporting the development of an in vivo delivered HbF inducer. In December 2024, we presented data describing the identification of the saRNA development candidate, MT011391, which demonstrated induction of pan-cellular, dose-dependent g-globin RNA and protein in a primary erythroid-derived progenitor cell model using bone marrow-derived CD34 cells isolated from healthy human donors. Pharmacodynamic activity of liposome-formulated MT011391 was observed in an NHP model previously induced to an anaemic state and treated with hydroxyurea (HU), as used elsewhere (PMID 39642886).

Methods: Two-phase erythroid differentiation model, CD34+ cells isolated from sickle cell patients. HbF tetramer was measured by HPLC.

Results: Here we show that, as in healthy donors, MT011391 induces pan-cellular HbF in primary erythroid cells from SCD donors, with 84% ErP cells expressing HbF (compared to 37% oligo control; mean across four donors). Furthermore, we show that MT011391 induces an average of 30% HbF in healthy donors and increases the % HbF by 45% in cells from SCD donors compared with oligo control. In the clinic, HU, which is the standard of care, induces HbF in most patients, however higher levels required to prevent SCD symptoms are seldom reached and some patients do not respond at all. Our data shows that MT011391 is active in both HU responsive and non-responsive donors. Finally, we present data supporting a synergistic effect of HU and MT011391 on HbF induction on in vitro differentiated ErPs from healthy donors.

Conclusion: Collectively, these studies establish that in vivo-delivered saRNA oligonucleotides hold promise for best-in-class in vivo HbF induction, with the potential to achieve protective levels of HbF with a high degree of specificity. This approach offers significant improvements in safety, tolerability, and accessibility over current gene editing and small molecules therapies under development.

OR60 | Vincamine as a potential therapeutic agent for sickle cell disease: An in silico study

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Introduction: Sickle cell disease (SCD) refers to a point mutation in β-globin gene that leads to production of sickle shaped red blood cells and formation of haemoglobin S (HbS). Under low oxygen condition, HbS form hydrophobic bonds between the valine on one polypeptide and various amino acids on adjacent chains like phenylalanine, alanine and leucine. These interactions trigger polymerization. Hydroxyurea (HU) serves as the primary pharmacological agent for clinical management of SCD by promoting the synthesis of HbF. HU causes programmed cell death in late-stage erythroid progenitor cells that leads to many cascading effects. Secondary metabolites of plants are reported to be potential novel anti-sickling agents.

Molecular docking and molecular dynamics (MD) simulations have emerged as in silico method for examining the interactions and stability between small molecules and biological macromolecules at the atomic scale. This work is designed to utilize in-silico methods to examine the anti-sickling efficacy of selected plant secondary metabolites to identify potential lead compounds for formulation of effective treatment agents for SCD.

Methods: Sixty-four natural compounds reported to have anti-sickling properties was collected from available literature and databases. The crystallographic structure of carbon monoxy HbS in complex with GBT440 (PDB ID: 5E83) was retrieved from the Protein Data Bank (PDB). Refinement of the structure was done by utilizing BIOVIA Discovery Studio software and Auto Dock Tools. The ligand files were subsequently translated into PDB file format, Gasteiger charges were integrated into the ligands, non-polar hydrogen atoms were amalgamated. The files were preserved in PDBQT file format for docking purposes. Active site and grid generation was also performed. The Auto Dock Vina software was employed to predict energetically favourable binding orientations between the selected ligands and the HbS protein. The configuration and alignment of the binding sites were analysed. The Swiss ADME analytical tool was utilized for evaluation of the pharmaco-dynamics of the compounds under investigation, displaying maximum affinity of binding, accompanied by a binding conformation that closely resembles to that of the bound ligand GBT440. The Gromacs-2019.4 software was utilized to conduct molecular dynamics simulations on the protein-ligand complex.

Result: The ligands that showed highest affinity of binding were Apigenin, B Sitosterol, Barbaloin, Biflavanone, Cajanin, Carotenoid, CassaneFuranoditerpene, Catechin, Cepharantine, Chamuvaritin, Coleon U, Emodin, Epicatechin, Epigallocatechin gallate, Isovitexin, Kolaviron, Lupeol, Pfaffic acid, Piperine, Rutin, Stigmasterol, Uvarinol, Vincamine, Vitexin. Vincamine exhibited a comparable interaction with the co-crystallized ligand GBT440. Swiss ADME server was used to analyse the ADME properties of vincamine. Vincamine passes the ADME filters with bioavailability score of 0.55. The vincamine-HbS complex relative stability during simulation.

Conclusion: Vincamine was identified to possess favourable binding affinity with HbS, in addition to possessing suitable drug likeness and pharmacokinetic profile. Molecular dynamics simulation of vincamine-HbS complex has demonstrated a stable interaction, indicating its potential as a promising candidate for further exploration as anti-sickling agent.

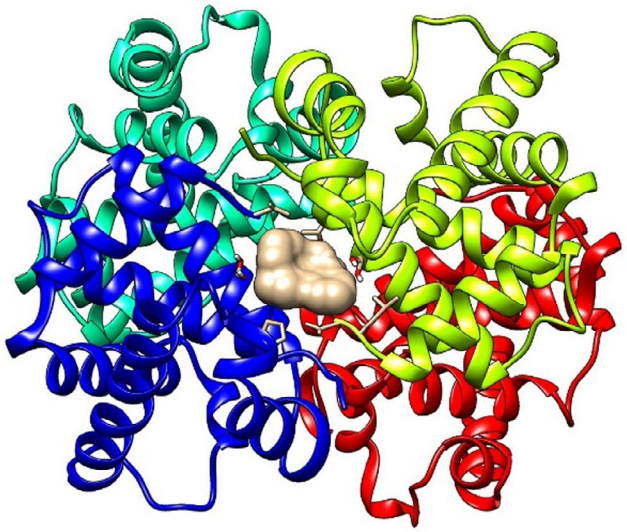

FIGURE Docked pose and orientation of Vincamine with HbS (PDB ID: 5E83).

OR61 | Atherosclerosis and atherosclerotic cardiovascular disease in an ageing cohort of beta thalassemia patients

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Introduction: In recent decades, the improvement in thalassemia management has led to a significant increase in life expectancy, with non-transfusion-dependent (NTDT) and transfusion-dependent (TDT) beta-thalassemia patients now reaching their sixth decade of life. Consequently, age-related complications are emerging. In the general population, the most prevalent age-related disease is atherosclerosis. Data on

the prevalence of atherosclerosis in thalassemia patients is limited, typically involving small cohorts or pediatric and young adult subjects. No data have been published from cohorts that reflect the current ageing thalassemia population. This cross-sectional study aims to evaluate the prevalence of atherosclerotic plaques and atherosclerotic cardiovascular disease (ASCVD) as defined by the European Society of Cardiology (ESC) in a cohort of adult TDT and NTDT patients, as well as to explore potential risk factors for atherosclerosis in this population.

Methods: We collected clinical and laboratory parameters and performed Doppler ultrasound of the carotid artery to detect atherosclerotic plaques and measure the intima-media thickness (IMT).

Results: A total of 196 patients were enrolled, including 131 TDT with 65 NTDT, of whom 58% were female. The prevalence of ASCVD was 6.9% (9/13, IC 6.1%–7.7%) in TDT and 32% (21/65; IC 15.3%–48.7%) in NTDT. The median IMT, an indirect assessment of the degree of ASCVD, was 0.55 mm in both cohorts (range 0.4–1 mm), significantly lower than that of the age- and sex-matched general population. IMT increases with age, with IMT in males slightly higher than in females. No difference in IMT was observed between TDT and NTDT. Regarding known risk factors for atherosclerosis, our data suggest that our patients do not exhibit an atherogenic lipid profile, indicated by low total cholesterol and LDL, preventing us from using the 10-year cardiovascular disease risk score proposed by ESC. Notably, there is a difference in oxidized LDL between patients with and without ASCVD in both the TDT and NTDT cohorts, suggesting that it may not be the quantity of LDL but rather the quality of LDL that predisposes individuals to ASCVD. As in the general population, a history of smoking, alcohol use, and diabetes increases the risk for plaques in these patients. Physical activity was measured using the IPAQ score, revealing that our cohort was largely sedentary, with most patients categorized as minimally active.

Regarding disease-specific risk factors that are hypothesized to contribute to the development of atherosclerosis, when comparing patients with and without ASCVD, no differences in iron, inflammation, and hemolysis parameters were observed. Notably, as indicated by ferritin levels and NTBI, our cohort is overall well-chelated.

Conclusion: To our knowledge, this is the largest and oldest cohort of thalassemia patients in which atherosclerosis and its risk factors have been investigated. Our data showed a higher prevalence of atherosclerotic plaques in the NTDT cohort compared to the general population and highlighted the risks associated with aging, smoking history, and alcohol consumption. Current guidelines for thalassemia do not include carotid Doppler ultrasound in the follow-up; however, our data suggest the importance of conducting the exam in the at-risk population.

Further studies are needed to investigate the unique lipid profile in these patients and develop a specific cardiovascular risk score that considers the peculiarities of the disease.

OR62 | An interpretative phenomenological analysis study on mothers living with sickle cell disease in the UK

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Introduction: Medical advancements in Sickle Cell Disease (SCD) have improved the life expectancy of women enabling the opportunity to experience motherhood. However, qualitative inquiries documenting women's lived experiences in their transition to motherhood remain limited and particularly unexplored in the UK. This phenomenological study responds to the existing knowledge gap by presenting a detailed understanding of these women's lifeworld. The main aim is to capture shared and individual experiences of the impact of SCD on women's transition to motherhood. This comprises: the effect of SCD on women's feelings, thoughts, behaviours and interactions with others, exploring women's self-identity in their maternal journey as well as their personal thoughts of societal perception in becoming and being a mother and identifying what health and well-being strategies were utilised during their transition to motherhood.

Methods: The study conducted 22 purposive, semi-structured interviews with women living with SCD and utilised Interpretative Phenomenological Analysis (IPA) to analyse women's existential narratives on the experience of becoming and being mothers.

Results: The findings of this study demonstrate that participants were uncertain about their reproductive capacity and valued health compatibility when selecting a partner. These experiences were not without aspects of stigmatization relating to narratives of how women viewed themselves over societal judgement and systemic inequality within their reproductive decision-making processes. The lack of information on SCD pregnancy brought on feelings of abnormality and the need to preserve pregnancy through being hyper-vigilant about their episodic triggers, avoiding stress and changing nutritional habits. Women also describe feelings of fear and loneliness that derived from the lack of information on SCD pregnancies and detrimental views of SCD. Women highlighted relying on their spiritual faith and being in the company of others to feel less alone. Women's journey into motherhood holds intrinsic insights into the individual worlds of women's physical, mental, social, reproductive and occupational selves. Fatigue marks the everyday experience of mothering with SCD, with maternal identity and role challenged by the capability of bodily function, driving adjustments in maternal expectations.

Conclusion: This study provides valuable insights into the impact of living with SCD on women's transition to motherhood. The findings may inspire healthcare service providers to deliver a holistic and comprehensive care that meets the needs of mothers with SCD, improve psychological support and build initiatives to enhance maternal health and well-being.

OR63 | Real-world safety profile of twice-daily deferiprone for iron overload in patients with sickle cell disease

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Introduction: Achieving long-term adherence to iron chelation therapy is key to optimizing outcomes for patients with transfusion-dependent sickle cell disease (SCD). Deferiprone (DFP) is an oral iron chelator with >28 years of safety and efficacy data. Whilst DFP was originally formulated for administration three times-a-day (TID), a twice-a-day (BID) formulation was developed to improve patient adherence. Both DFP TID and BID formulations were approved by the United States (US) Food and Drug Administration (FDA) for transfusional iron overload in patients with SCD in 2021. The long-term safety profile of DFP BID has not previously been assessed in patients with SCD as an independent subgroup. Here, we utilize data from the Ferriprox® Total Care Registry (FTCR) to assess the safety of DFP BID in patients with SCD in real-world US clinical practice.
Methods: Collective safety data were obtained from the FTCR including all patients who received DFP BID between July 1st 2020 to August 31st 2023. Primary diagnosis (PD) was extracted from case narratives, defined as the diagnosis for which DFP BID was prescribed. Cases with a PD classified as SCD were analyzed. DFP exposure was defined as time active in the registry. The frequency of adverse events (AEs) and serious AEs (SAEs) was assessed, categorized by Medical Dictionary for Regulatory Activities Preferred Term, including all events reported through the centralized pharmacy.
Results: A total of 197 patients with a PD of SCD were referred to the FTCR for DFP BID, of which 179 (90.9%) were ≥18 years of age. In 189 patients who received ≥1 BID shipment, the mean (standard deviation) DFP BID exposure was 319.1 (256.5) days; total estimated exposure was 165 patient-years. In total, 531 AEs and 238 SAEs were reported. The most frequently reported AEs and SAEs are shown in Table 1. One neutropenia event and none of agranulocytosis were reported, defined as per the treating physician's clinical practice. The case of neutropenia recovered and was not associated with a fatal outcome (case not ongoing with no further follow up reported/required). Fatal outcomes were reported in 16 patients at a median (range) age of 43 (14–69) years. No fatal outcomes were assessed as possibly or probably related to DFP treatment.

TABLE 1 Most frequently reported AEs and SAEs in patients with SCD on DFP BID.

Preferred term (PT)	Total reports, *n* (%)
Total AEs	531 (100)
Most frequently reported AEs	
Sickle cell anemia with crisis	54 (10.2)
Abdominal discomfort	16 (3.0)
Nausea	14 (2.6)
Vomiting	13 (2.4)
Ill-defined disorder	12 (2.3)
Total SAEs	238 (100)
Most frequently reported SAEs	
Sickle cell anemia with crisis	54 (22.7)
Ill-defined disorder	11 (4.6)
Death	10 (4.2)
COVID-19	6 (2.5)
Infection	6 (2.5)
Pneumonia	6 (2.5)
Sepsis	6 (2.5)

Note: PT of no. of adverse event is not included. Off label use (81 events) and Product dose omission issue (12 events) are amongst the top 10 AE PTs, and Product dose omission issue is amongst the top 10 SAE PTs (6 events), but are not considered as AEs on their own. Ill-defined disorder is a medical problem of unclear type. Data was extracted from a spontaneous reporting system; Death refers to fatal outcomes with unknown causes of death or lack of full medical history.

Conclusion: Data from the FTCR indicates that DFP BID is well-tolerated in patients with SCD in real-world clinical practice with no new safety concerns identified. Limitations associated with real-world data collection must be acknowledged.

OR64 | Real-world safety profile of twice-daily deferiprone for iron overload in patients with thalassemia syndromes

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Introduction: Transfusional iron overload leads to significant morbidity and mortality, meaning long-term adherence to iron chelation therapy is key to reducing organ damage and optimizing survival outcomes. Deferiprone (DFP) is an

established oral iron chelator with >28 years of safety and efficacy data. DFP was first approved for administration three times-a-day (TID) for transfusional iron overload in patients with thalassemia by the European Medicines Agency in 1999, and by the United States (US) Food and Drug Administration (FDA) in 2011. A twice-a-day (BID) formulation, developed to improve patient adherence, was approved by the FDA for patients with thalassemia in 2020. The Ferriprox® Total Care Registry (FTCR) is a drug-surveillance program established in the US to evaluate the safety profile of DFP under conditions of routine clinical care. Here, we assess the safety of DFP BID in patients with thalassemia in real-world US clinical practice.

Methods: Collective safety data were obtained from the FTCR including all US patients receiving DFP BID between July 1st 2020 to August 31st 2023. Primary diagnosis (PD), defined as the diagnosis for which DFP BID was prescribed, was extracted from case narratives. All cases with a PD classified as 'Thalassemia syndromes' were included in this analysis. DFP exposure was defined as time active in the registry. The frequency of adverse events (AEs) and serious AEs (SAEs) by Medical Dictionary for Regulatory Activities Preferred Term was assessed, including all events reported through the centralized pharmacy.

Results: Out of 425 patients referred to the FTCR between July 2020 and August 2023 for DFP BID, 133 patients (31.3%) reported a PD of thalassemia syndromes. Of these, 96 patients (72.2%) were ≥18 years of age. In 129 patients who received ≥1 BID shipment, the mean (standard deviation) DFP BID exposure was 407.4 (311.1) days; total estimated exposure was 144 patient-years. In total, 396 AEs and 92 SAEs were reported. The top five most frequently reported AEs and SAEs are shown in Table 1. There were two episodes of agranulocytosis and five of neutropenia reported, defined as per the treating physician's clinical practice, none of which were associated with a fatal outcome and all of which recovered. Fatal outcomes were reported in six patients at a median (range) age of 47 (12–78) years. No fatal outcomes were assessed as possibly or probably related to DFP treatment.

Conclusion: Data from the FTCR indicate that since launch, DFP BID is well-tolerated in routine clinical practice in patients with a PD of thalassemia syndromes. No new safety concerns were identified compared to the safety profile of DFP TID. Limitations associated with real-world data collection must be acknowledged.

TABLE 1 Most frequently reported AEs and SAEs in patients with Thalassemia syndromes on DFP BID.

Preferred term (PT)	Total reports, *n* (%)
Total AEs	396 (100)
Most frequently reported AEs	
Nausea	19 (4.8)
COVID-19	14 (3.5)
Fatigue	10 (2.5)
Vomiting	9 (2.3)
Nasopharyngitis	8 (2.0)
Total SAEs	92 (100)
Most frequently reported SAEs	
Ill-defined disorder	5 (5.4)
Neutropenia	5 (5.4)
Death	4 (4.3)
Thrombosis	3 (3.3)
Upper limb fracture	3 (3.3)

Note: PT of No adverse event is not included. Ill-defined disorder is a medical problem of unclear type. Neutropenia includes PTs of Neutropenia and Febrile neutropenia. Data was extracted from a spontaneous reporting system; Death refers to fatal outcomes with unknown causes of death or lack of full medical history.

OR65 | A single-centre experience of bone mineral density assessment in adults with sickle cell disease

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Introduction: Bone health in sickle cell disease (SCD) is poorly documented. Avascular necrosis (AVN) is a hallmark complication in SCD. Other factors like haematopoietic stress, vitamin D deficiency and iron overload may also contribute to poor bone health. Bone mineral density (BMD) assessment is not routinely performed in SCD and the validity of BMD assessment in SCD and the predictive value of dual-energy X-ray absorptiometry (DXA) scores for fractures is unclear.

We evaluated DXA scan practice in a single-centre cohort of 966 adults with SCD.

Methods: The departmental Governance Committee approved the audit. We reviewed records of all patients attending for annual review at King's College Hospital to identify DXA scan results. From these records, additional data were extracted, including demographics, non-elective hospital attendances, comorbidities, full blood count, haemolytic and inflammatory markers, presence of chronic pain, regular opioid use, iron overload, steroid exposure, smoking, and history of AVN or fractures. Osteopenia and osteoporosis were grouped together as 'abnormal' for comparison with normal DXA scans.

Results: In total, 39 patients (4%) had DXA scans. 21/201 (10%) of people ≥50 years old underwent a DXA scan (9 normal, 12 abnormal). 18/765 (2%) of people younger than 50 had a DXA scan (10 normal, 8 abnormal). The cohort comprised 30 patients with HbSS, 8 patients with HbSC, and 1 patient with HbS/β^0 genotype.

For most patients, follow-up was compliant with NOGG standards. 7/9 osteoporosis patients received bisphosphonates, 8/9 were assessed for secondary causes, and 19/20 patients with an abnormal DXA scan received appropriate follow-up.

Multivariate analysis demonstrated a statistically significant association between DXA scan outcome (normal vs. abnormal) and both haemoglobin (80.9 vs. 101.9 g/L) and bilirubin

levels (33.0 vs. 18.1 μmol/L), as indicated by Wilks' Lambda ($p = 0.048$). Logistic regression analysis identified regular use of strong opiates (OR 3.9, $p = 0.036$) and a history of AVN (OR 0.025, $p = 0.025$) as independent factors associated with an increased likelihood of an abnormal DXA scan outcome (OR 3.9, $p = 0.036$). Oddly, exposure to steroids (OR −5.7, $p = 0.037$) and chronic pain (OR −3.8, $p = 0.04$) were associated with a lower likelihood of an abnormal scan. Other, non-SCD-related conditions (auto-immune disease, rheumatoid arthritis, smoking, previous fracture, DM2, CKD and history of transplantation) did not contribute to the model.

Vertebral spine involvement was also associated with a reduced likelihood of an abnormal DX scan (OR −3.5, $p = 0.027$). Also, there was discordance between BMD scores of the spine versus the hip, spine *T* and *Z* scores being significantly lower than hip *T* and *Z* scores.

Conclusion: BMD assessment was performed in 10% of our over 50s cohort, which is somewhat lower than would be expected. Compliance with national standards was otherwise adequate. Lower BMD was independently linked to higher haemolysis, presence of AVN and frequent strong opiate use, including people below the age of 50. However, artefacts from sclerosis secondary to infarction in sickle cell bone disease may overestimate BMD on conventional DXA, limiting its accuracy at affected sites and supporting the rationale for incorporating trabecular bone score (TBS) as a complimentary assessment tool. There is a need for prospective studies to address gaps in knowledge about bone health in sickle cell disease.

OR66 | Atrial fibrillation prevalence and its management in the aging transfusion-dependent beta-thalassemia

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Raffaella Origa, Prof Matteo Bertini, and Prof Irene Motta equally contributed to this work.

Introduction: Atrial fibrillation (AF) represents an emerging issue in transfusion-dependent beta-thalassemia (β-TDT) adults given their increasing life expectancy. However, data on AF in these patients (pts) are limited, and the current management is based on the guidelines for the general population, although distinctive features could require specific management.

Methods: In collaboration with Società Italiana Talassemie ed Emoglobinopatie, we conducted a multicentric retrospective study that aims to study the prevalence of AF and its management in β-TDT adults in Italy. Pts followed between January 1, 2003 and December 31st, 2023 with a diagnosis of β-TDT and AF were included in the study. Clinical data have been collected with digital CRF.

Results: As of December 31st, 2023, nine Italian thalassemia centers participated in the study, following a total of 1389 β-TDT. Data of 188 β-TDT pts with a history of AF were included.

At enrolment, 165 pts were alive (males 101, 61.2%), the mean age was 51.9 ± 8.5 years, and 73% were splenectomized. The majority was β-thalassemia major, and one out of four was thalassemia intermedia who became transfusion-dependent during life. The mean age at the first AF episode was 40.3 ± 11.5 years. AF prevalence was 11.9%, with a prevalence that reaches 31% above the age of 66, differently from the general population in which the prevalence is 2%–4% and pts are older. As in the general population, prevalence was higher in males (16.1% vs. 8.4%). Among the known risk factors for AF, the most frequent were diabetes (25/182, 13.7%), heart failure (43/183, 23.5%), and smoking (24/140, 17.1%). Moreover, a history of supraventricular arrhythmias was reported in 15.6% (28/179) of pts. Regarding disease-specific factors contributing to the pathophysiology of AF, cardiac iron overload was present in 68/108 pts (63%) at any time before AF and in 55/120 pts (45.8%) at the time of the first event. Interestingly, at least 35/188 pts (18.6%) did not show cardiac iron overload either prior to or at the time of the first AF episode. Most subjects had left atrial dilatation (73/112, 65.2%), which can result from anemia that leads to increased cardiac output. Rhythm control attempt was implemented at any time in 161/185 pts (87.0%). Amiodarone was the most widely used drug. Transcatheter ablation was performed in 50/188 pts (26.6%) without any procedure-related complication, and 32/43 pts (74.4%) reported improvement in symptoms, which is the primary scope of the procedure. The prevalence of stroke was 5.5% (9/165), rising to 7.9% (13/165) if also considering transient ischaemic attacks, which is higher than the general population, despite the risk of thromboembolism at the first AF episode evaluated with CHA2DS2-VASc score was low in 55.6% pts (100/180). Interestingly, 9 events happened during anticoagulant therapy. Of note, splenectomy, a well-known risk factor for thrombosis, was present in 88% (15/17) of those pts.

Conclusion: This is the first study evaluating AF prevalence and its management in TDT. AF is a clinically relevant

issue in thalassemia pts with a prevalence higher than the general population. Also, stroke prevalence in this cohort is higher than in the thalassemia population in general, and the CHA2DS2-VASc score presents some limitations. Surprisingly some strokes happened during anticoagulant treatment. Altogether these data suggest that specific guidelines are necessary to provide the best care to thalassemia pts.

OR67 | Mind the gap: A 10-year audit of emergency pain management in transition-age sickle cell patients

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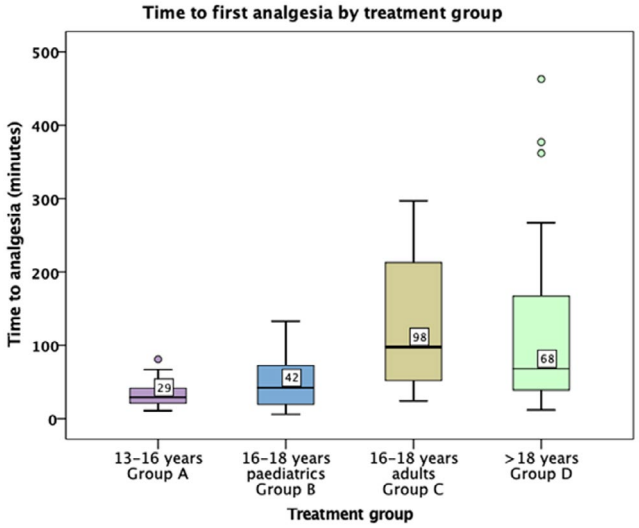
Introduction: The transition from paediatric to adult services represents a vulnerable period for patients with sickle cell disease (SCD), during which differences in the management of vaso-occlusive crises (VOCs), particularly in analgesia delivery, can negatively impact outcomes. This single-centre audit evaluated the timeliness of analgesia administration in patients aged 13–22 years presenting with VOC in our institution, with the aim of assessing adherence to national guidelines and identifying areas for improvement during this transitional phase.
Methods: This retrospective 10-year audit included patients aged 13–22 years presenting with VOC at a single centre, categorized into four age groups: 13–16 years (A), 16–18 years seen by paediatrics (B), 16–18 years seen by adults (C), and >18 years (D). Clinical and demographic data were obtained from electronic health records. The primary metric was time from arrival to first analgesia. Patients who did not receive analgesia in the emergency department (ED) were excluded. A mixed linear regression model accounted for repeated presentations by the same patients.
Results: We analysed 93 VOC presentations from 53 patients. The mean age at transition was 17.5 ± 0.7 years (range: 16–18.8 years). Patient level pre-post transition analysis showed that mean time to analgesia increased threefold post transition (from 37 to 117 min, $p = 0.003$). In the 16–18 age group, 53% of cases were managed by the paediatric team (group B) in the paediatric assessment unit (PAU) and 47% were managed in adult ED (group C). Group C experienced significantly longer time to analgesia than Group B (121 vs. 52 min, $p = 0.01$), and also compared to Group A (mean difference: 86 min, $p = 0.002$). Timely analgesia within 30 min was delivered in only 11% of group C, versus 47% in group B (relative risk 1.7, $p = 0.02$). Pain scores were documented in 100% of 16–18 year-olds seen in PAU, but in only 47% seen in adult ED. Mean time to inpatient admission was longer in adult ED compared to PAU, although the difference was not statistically significant (9.7 h vs. 6.9 h, $p = 0.08$). Route of analgesia was intranasal and oral in PAU, whereas for patients managed in adult ED it varied significantly, with intravenous used in the majority (60%).



Conclusion: This audit reveals significant disparities in VOC management between paediatric and adult services, particularly in the 16–18 age group. Delays in analgesia, lower rates of pain score documentation, and delays for inpatient admissions were more common in adult ED settings. In addition to ongoing quality improvement efforts (including the use of universal care plans, and the implementation of the ACT NOW acronym), we recommend deferring the completion of transition to adult services until age 18 for adolescents with SCD in our institution, to ensure continued access to PAU and better alignment with national care standards.

OR68 | Reflections from patients with SCD in Ontario on hospital care experiences

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Background: Sickle cell disease (SCD) is an inherited blood disorder associated with a range of complex biopsychosocial challenges, including chronic pain, frequent hospitalizations, stigma, and mental health burdens. In 2020, in response to numerous testimonials and personal feedback from patients and families, the Sickle Cell Awareness Group of Ontario (SCAGO) conducted a study to evaluate the standard of care in Ontario by analyzing firsthand accounts of healthcare experiences from individuals living with SCD.
Methods: An online self-reporting survey was deployed to collect detailed accounts of healthcare encounters between July 2019 and February 2020. Each survey response focused on a single hospital visit such as emergency department presentations or admissions related to vaso-occlusive episodes. Thematic analysis was performed to identify patterns and concerns across responses.
Results: A total of 66 responses were collected. The majority of participants were between 18 and 64 years of age, with 12 surveys completed by caregivers on behalf of patients under 18. Findings from the study highlighted two major issues

consistently reported by participants: prolonged wait times when seeking care and a perceived lack of responsiveness by healthcare professionals to patient needs. Regarding wait times exceeding 1 h, 31% (5/16) reported delays before initial nurse contact, 56% (10/18) experienced delays before seeing a physician, and 50% (8/16) reported waiting over 1 h for pain medication administration. When asked about their first point of contact at triage, 60% (9/15) described the staff member as respectful, empathetic, and caring. However, 22% (4/18) of respondents reported feeling stigmatized or fearful for their life during the hospital visit. Feelings of loneliness or helplessness were reported by 44% (7/16) of respondents.

Conclusion: In response, SCAGO engaged in follow-up consultations with three Ontario hospitals. These meetings fostered productive dialogue, during which hospitals proposed targeted strategies to enhance SCD care delivery and identified educational opportunities to improve provider awareness and competence.

Building on these insights, SCAGO collaborated with Ontario Health to publish a Quality Standard for SCD in January 2023. This standard outlined eight key Quality Statements aimed at ensuring equitable, timely, and person-centered care. Topics included addressing discrimination in clinical settings, improving responses to vaso-occlusive crises, and managing chronic complications.

To assess the implementation of this Quality Standard, SCAGO will repeat the survey using the same methodology. Findings will inform whether the Quality Statements are being met and identify areas requiring further improvement. Ultimately, this research aims to promote accountability within the healthcare system, drive policy and practice changes, and uphold a high standard of care for individuals living with SCD in Ontario.

OR69 | Erythrocyte alloimmunisation in children with sickle cell anemia in Kilifi, Kenya

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Introduction: Sickle cell disease (SCD) is a severe genetic disorder, with over 75% of cases occurring in sub-Saharan Africa. Transfusion therapy is crucial for managing SCD; however, in African countries, transfusion safety is often compromised by a lack of extended blood group matching beyond ABO and Rhesus D antigens, along with the absence of routine alloantibody screening. This study aimed to determine the incidence of erythrocyte alloimmunization in multiply transfused children with SCD in Kilifi, Kenya.

Methods: This is a retrospective study of 98 children with SCD aged 0–13 years who were admitted to Kilifi County Hospital between 2003 and 2023. SCD was diagnosed using high-performance liquid chromatography and confirmed by PCR. Plasma samples collected during the follow-up period through routine surveillance the SCD clinic and paediatric wards were retrieved, and screening for alloantibodies was performed on these stored samples using the standard 3-Diacell and the 11-ID-Diapanel cells (DiaMed GmbH, Bio-Rad, Switzerland).

Results: Alloantibodies were detected in 14/98 (14.3%) participants, and 1/98 (1.0%) had an autoantibody. Among the identified alloantibodies, anti-e was found in two children, anti-E, anti-M, anti-S, anti-s, anti-Lua and anti-Leb in a single individual each. Five children had pan-reactive alloantibodies, and three had antibodies of unidentified specificity. Older age was significantly associated with the development of alloantibodies ($p = 0.027$).

Conclusion: The alloimmunization rate of 14.3% seen in this study is higher than that reported in previous studies from East Africa (2.9%–8%). Since most alloantibodies were specific to Rhesus and MNS blood groups, and older age was significantly associated with alloimmunization, this underscores the importance of routine alloantibody screening in multiply transfused children and suggests the need for extended antigen matching in SCA patients to improve transfusion safety.

OR70 | Hemolysis impairs hepatic regeneration and functions in sickle cell disease by altering macrophage dynamics

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Introduction: Sickle cell disease (SCD) is characterized by the release of hemoglobin and heme into the circulation, saturation of related plasma scavengers, and heme/iron loading of macrophages. By acting as a damage-associated molecular pattern, free heme drives a pro-inflammatory activation program in macrophages, stimulating cell cytokine production and inducing sterile inflammation in SCD. Overall, this mechanism contributes to the inflammatory landscape and complications typically associated with this disease. In this context, heme/iron-activated Kupffer macrophages (KC) have emerged as key mediators of hepatic inflammation, perpetuating oxidative stress, driving tissue damage, and exacerbating hepatic fibrosis.

While previous studies addressed heme ability to induce inflammatory cytokine production by KCs and alter their functional properties, heme role in hepatic regeneration via macrophage activation remain unexplored. Indeed,

KC-derived inflammatory mediators play a key role in liver regeneration upon tissue damage by stimulating hepatocyte dedifferentiation and proliferation. Here, we asked whether heme-induced chronic cytokine release affects hepatic regeneration and contributes to SCD hepatopathy, and how heme-altered KC population dynamics influence this process.

Methods: Using mouse model of heme overload, SCD, and macrophage depletion or preservation, we investigated the impact of heme on KC dynamics and inflammation, and their implications for liver regeneration in SCD.

Results: KC dynamics were significantly altered in sickle HbS mice, with decreased embryonic (EmKC) and increased monocyte-derived KCs (MoKC), phenotype recapitulated by in vivo heme and iron treatments. HbS EmKCs exhibited apoptosis and impaired self-renewal, evidenced by cell senescence, G0/G1 arrest, and reduced levels of KI67, IL-6R and CSF-1R, critical for proliferation. Interestingly, MoKCs displayed more severe inflammatory skewing than EmKCs in HbS mice, associated with senescence and higher TLR4 levels as well as IL-6 and ROS production, indicating that these cells are the major mediators of heme-driven inflammation. Hx treatment in HbS mice mitigated KC inflammation by both diminishing TLR4 activation and preventing KC dynamics alteration. Ultimately, inflammatory MoKCs in HbS mice were associated with the presence of hepatic regenerative processes, including bile duct hyperplasia and proliferating KI67/Ccnd1^{+} hepatocytes, exhibiting reduced mature (ASGPR,HNF4a,C/EBPa) and increased fetal (SOX9,EpCAM,Taz) markers, features recapitulated by *in vivo* heme treatment. While strategies that increase MokC repopulation exacerbated heme-driven accumulation of fetal-like proliferative hepatocytes, those that preserve EmKCs improved liver regeneration through effective hepatocyte maturation, implicating heme-altered KC dynamics and inflammation in excessive hepatocyte dedifferentiation and loss of adult hepatocyte functions.

Conclusion: Our findings show for the first time that heme alters KC dynamics in SCD via EmKC senescence and selectively drives MoKC activation, leading to immature hepatocyte accumulation, with detrimental consequences for liver regeneration. We propose that targeted therapies aimed at expanding EmKCs or limiting MoKC response likely alleviate hepatic inflammation and ameliorate liver regeneration and functions, with benefit for SCD patients with hepatopathy.

OR71 | SCD-RPA: A point-of-care friendly genetic test for diagnosing SCD from buccal swab samples without extraction

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Introduction: Non-invasive, genetic, point-of-care (POC) testing for sickle cell disease (SCD) is needed for low-resource settings in which the disease is endemic. POC tests have been utilized to improve diagnostic access, but currently available protein-based POC tests have two key limitations we seek to address. First, because they detect proteins not the genetic basis of SCD, they are susceptible to error in recently transfused patients. Thus, children with SCD presenting with anaemia often leave the hospital without a correct diagnosis. Second, they require a blood sample—which can be invasive and requires a medical professional to collect. Prior work in our laboratory developed recombinase polymerase amplification (RPA) primers to selectively amplify the β^{A}-, β^{S}-, and β^{C}-globin alleles. RPA is an isothermal amplification strategy that enables DNA detection at a low temperature (39°C) and is more tolerant to inhibitors than PCR. To capitalize on the inhibitor tolerance of RPA and minimize workflow complexity, we seek to prepare buccal swabs with a simple lysis step followed by dilution – avoiding the concentration and purification steps of traditional DNA extraction. After developing a sample preparation strategy, we optimize a POC friendly sample-to-answer assay, SCD-RPA, and evaluate it with clinical samples.

Methods: We first prepared a number of POC-lysis strategies using chemical, heat, and enzymatic agents and then compared the effectiveness of the strategies with pooled normal volunteer buccal swabs and compared them to a water-only no lysis control condition. We then integrated the sample-to-answer assay utilizing modified dropper bottles to simplify liquid handling, and evaluated the assay with normal-volunteer samples. We then evaluated our SCD assay with banked clinical samples with known SS, SC, AS, and AA β-globin genotypes and additionally compared assay performance to the POC SickleScan test.

Results: NaOH lysis resulted in rapid, consistent amplification (<10 min) of the β^{A} assay with diluted pooled buccal swab from normal volunteers across a range of swab dilutions (Figure 1). This indicates the NaOH lysis results in robust amplification and is suitable for samples with a wide range of cell concentrations. When integrated, the SCD-RPA assay requires only 30 min and five user steps (Figure 2). Next, we utilized banked clinical buccal swab samples to evaluate assay concordance of the SCD-RPA assay with known genotype: SS(6/6), AS (6/6), AA (6/6) and SC (4/6). Further, SickleScan data was available for five of the SS samples and incorrectly identified two as AS—both patients have been transfused within the prior six weeks.

Conclusion: The SCD-RPA assay enables non-invasive, rapid, and user-friendly genetic discrimination of β^{A}, and β^{S} alleles. In patients with a recent history of transfusion, SCD-RPA yields the correct diagnosis, unlike SickleScan. Future work will improve β^{C} detection and evaluate the assay with a larger sample set in Lilongwe, Malawi. This SCD-RPA has significant potential to improve timely diagnosis of SCD in LMIC's.

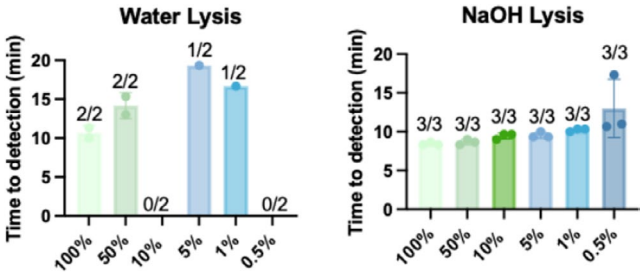

FIGURE 1 Amplification of β^A with decreasing concentration of pooled swab shows improved performance due to greater lysis with sodium hydroxide (NaOH) compared to water.

FIGURE 2 SCD-RPA utilizes a POC friendly workflow and a non-invasive buccal swab sample for rapid detection of SCD.

OR72 | Left ventricular mechanics in pediatric sickle cell disease: Analysis of strain and chamber dimensions

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Introduction: Cardiovascular complications are a major cause of morbidity and mortality in sickle cell disease (SCD), often beginning with subclinical myocardial injury in early life. Traditional echocardiographic measures like ejection fraction are limited in detecting early dysfunction. Speckle-tracking echocardiography (STE), through global longitudinal strain (GLS), offers a more sensitive assessment of myocardial function. While promising, its use in pediatric SCD remains underexplored. This study assesses LV function in children with SCD using GLS, comparing it to conventional indices and exploring associations with genotype, disease complications, hemolysis markers, and disease modifying therapy.
Methods: This retrospective, observational single-center study was conducted at the Children's Heart Center at the American University of Beirut Medical Center between 2015 and 2023. It included pediatric patients with genetically confirmed SCD and age- and sex-matched healthy controls. Clinical data, including demographics, disease complications, lab values, medical therapy, and transfusion history, were extracted from electronic records. Transthoracic echocardiography was performed by three experienced pediatric sonographers using a standardized protocol. LV GLS, systolic and diastolic parameters, transmitral and tissue Doppler indices were assessed. GLS analysis was performed twice by a blinded pediatric cardiologist.
Results: Of 301 echocardiographic studies reviewed, 278 were included, representing 185 participants: 118 pediatric SCD patients (mean age 12.2 years) and 67 matched controls (mean age 11.8 years), with a male-to-female ratio of 1 in both groups. Among SCD patients, 66% had HbSS, 9.3% HbSβ^0-thalassemia, and 17.8% HbSβ^+-thalassemia. Most (83.9%) were on hydroxyurea (mean dose: 20 mg/kg). Compared to controls, SCD patients had significantly lower, but still normal, GLS (–21.5% vs. –22.3%; $p < 0.001$), indicating worse myocardial deformation. They also had significantly higher LV mass index (73.9 vs. 51.8 g/m^2), LV end-diastolic diameter index (40 vs. 35.4 mm/m^2), LV end-systolic diameter (30.6 vs. 27.1 mm), and left atrial volume index (28.5 vs. 16.4 mL/m^2) (all $p < 0.001$). Spectral Doppler showed significantly elevated mitral E velocity (105.8 vs. 89.9 cm/s), E/A ratio (1.9 vs. 1.7), and tricuspid regurgitation velocity (2.2 vs. 2.0 m/s) (all $p < 0.001$). Through one-way ANOVA analysis, GLS did not differ significantly across genotypes ($p = 0.577$), though HbSS patients had larger LA volume and LV mass. Multivariate analysis identified prior stroke ($\beta = 0.9$, $p = 0.048$) and avascular necrosis ($\beta = 1.51$, $p = 0.02$) as predictors of worse GLS, while larger LV end-diastolic diameter index was associated with improved GLS ($\beta = -0.05$, $p < 0.001$). Hemoglobin level, hemolysis markers, and hydroxyurea use were not significantly associated with GLS. Longitudinal follow-up revealed a modest but significant GLS decline (–21.6% to –21.2%) over 3.7 years.
Conclusion: Pediatric patients with SCD exhibit preserved but reduced LV GLS compared to healthy controls, alongside significant cardiac remodeling marked by chamber dilation and diastolic dysfunction. These findings highlight the need for further research to better understand and address cardiovascular complications in this population.

POSTER PRESENTATIONS

PO01 | A five-year retrospective assessment of prenatal diagnosis performed at the Sickle Cell Foundation Nigeria

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Introduction: Persons with sickle cell disorder (SCD) often face significant challenges in caring for their needs,

particularly when they lack knowledge about the condition. Couples at risk of the disorder frequently inquire ways to detect the possibility of having offsprings with sickle cell disorder. Prenatal diagnosis (PND) offers a means to determine the haemoglobin genotype of the fetus, providing families with crucial information to make informed decisions on early management of the condition.

It is a procedure performed first trimester of pregnancy that helps in the early detection and management of genetic disorders such as sickle cell anaemia, providing families at risk an opportunity to make informed decisions regarding their offsprings.

This study is aimed at assessing the frequency and effectiveness of PND performed at Sickle Cell Foundation Nigeria (SCFN) over the last 5 years.

Materials and Methods: A total of 1425 couples, from across Nigeria, were referred for PND to determine fetal haemoglobin genotype. A biodata form was completed by the couples to provide necessary information needed for the pre-PND procedure, and were sorted by conditional formatting using excel. Following pre-PND procedure genetic counselling and blood screening for eligibility, chorionic villus tissue samples were collected trans-abdominally under ultrasound guidance. Fetal DNA was isolated from the tissues and subjected to PCR methods to detect the haemoglobin genotypes.

Result: Our findings revealed that 24% of the couples were from the South-South, 27% from South-East, 38% from South-West, 8% from North-Central, 2% each from North-East and North-West, highlighting the varying degrees of awareness of PND across Nigeria, with the Northern region representing the lowest. The PND of haemoglobinopathies performed on all 1425 CV samples presented HbA (24%), HbAS (49%), HbS (23%), HbAC (1.7%) and HbSC (2.3%). Thirty-four percent of couples whose fetal genotype were HbS opted for termination of pregnancy, while 65% were undecided, but 2% decided to retain, possibly owing to the resulting fetal male gender.

While 29% referral frequency to our centre was attributed to Medical Doctors, the study indicated that 59% of the couples found out that they were at risk before marriage suggesting that despite awareness of their AS incompatibility, they sought PND to determine the risk of SCD. However, 41% of married couples who underwent the procedure depended on the outcome to make informed decisions. This has inadvertently prevented unwarranted termination of the pregnancy and provided avenue for instituting early management routines as best approach to sickle cell disease.

Conclusion: This study has shown that there is generally low awareness among couples-at-risk regarding the role of PND in making informed decisions, for the early diagnosis and management of SCD. Therefore, a unified effort from all stakeholders, both within and beyond the sickle cell community is recommended, to amplify the call for greater awareness and improved access to PND services.

PO02 | Transfusion therapy for sickle cell disease management in Saudi Arabia: Expert clinical practices and recommendations

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Introduction: Saudi Arabia (KSA) has one of the highest prevalence of sickle cell disease (SCD) globally, affecting up to 0.26% of the population.[1,2]

SCD is an inherited haemoglobin (Hb)disorder, resulting in severe disability, reduced quality of life, extensive use of medical resources, increased economic burden, and an increased mortality risk.[3,4] Patients with SCD face numerous acute and chronic complications, including acute chest syndrome (ACS), stroke, painful vaso-occlusive crisis (VOC), multiorgan damage, and an increased risk of infection.[5] Transfusion therapy, alongside hydroxyurea (HU), remains a cornerstone of SCD management, aiming to improve oxygen supply and reduce vaso-occlusion risks.[6] It includes Simple transfusion, manual red blood cell exchange (RBCX), and automated RBCX (arc). Accumulating evidence suggests that aRBCX is rapid and well-tolerated for SCD patients, providing a good control of sickle Hb (HbS) level without increasing viscosity. Importantly, aRBCX reduces iron loading and doesn't increase the alloimmunization risk.[6] However, its use remains limited due to the number of compatible blood units required, venous access, the need for specialized training, and the device's cost.[6]

Despite high SCD prevalence, KSA lacks national guidelines and country-specific plans for effective management strategies.[1,2,7]

To understand the disease landscape, current treatment modalities and explore ways to bridge the gaps in clinical practice for SCD management, Terumo Blood and Cell Technologies (TBCT) medical affairs EMEA department organized an advisory board meeting in March 2024 in KSA.

Methods: Nine local experts, including hematologists and transfusion medicine specialists, discussed local clinical

practice for SCD management and identified key areas of improvement. They also contributed as co-authors to a recently published position paper, sharing the conclusions of this discussion.

Results: Based on their clinical experiences, the panel highlighted the invaluable role of aRBCx in the management of several SCD-related indications, like acute management and prophylaxis of stroke, systemic fat embolism, severe forms of ACS, preoperative management, hematopoietic stem cell transplantation, hepatic crisis, and priapism. However, the discussion also revealed a broader underutilization of aRBCX in the management of pregnant SCD women, despite growing evidence supporting the prophylactic benefits of transfusion exchanges during pregnancy and ASFA recommendations.[8–11] In addition, disparities in clinical management were highlighted, especially regarding the preferred use of HU in some centers. Other gaps identified include a lack of unified national guidelines, local data gaps, access to treatment, specialized training for nurses, lack of equipment like MRI machines and ultrasound-guided venous access. In absence of national recommendations, the experts reported following the international ASFA and ASH guidelines.[11,12]

Conclusion: The advisory panel agreed on the need to nationalize SCD management to improve patient care. A recently published position paper summarizes key next steps identified, including developing national guidelines, creating a national registry, and addressing current challenges through education and training—notably by establishing a national apheresis society.[13] All these priorities are expected to be discussed further soon.

PO03 | A systematic review on nutrition, sickle cell disease, and eating disorders in pediatric populations

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Introduction: Children and adolescents with sickle cell disease (SCD) face complex nutritional and psychological challenges that may predispose them to disordered eating patterns, including clinically significant eating disorders (EDs). Pica has been consistently noted; however, the broader spectrum of eating disorders (EDs) remains underexplored in this population. This review aimed to examine the prevalence, presentation, and impact of EDs among paediatric SCD patients, with a particular focus on nutritional consequences and intervention strategies.

Methods: A systematic review was conducted using five databases (PubMed, Scopus, CINAHL, Cochrane Library, and Web of Science) to identify studies published between 1997 and 2025 examining EDs in children aged 6–18 with SCD. Eligible studies included observational designs, case reports, and qualitative studies that addressed eating behaviours or formal ED diagnoses. The risk of bias was assessed using the Critical Appraisal Skills Programme (CASP) and the Newcastle-Ottawa Scale (NOS). A meta-analysis was performed on data from five studies reporting Pica prevalence using a random-effects model.

Results: Eleven studies met the inclusion criteria, comprising cross-sectional ($n = 6$), retrospective cohort ($n = 3$), and case-based ($n = 2$) designs. Pica was the most frequently reported eating disorder, with a pooled prevalence of 55% (95% CI: 43%–66%) based on five studies. Individual study estimates ranged from 33.9% to 60%, with one study reporting 134 Pica cases among 395 children. Subgroup analysis revealed a prevalence of 56.4% for pagophagia (ice eating) though definitions and diagnostic consistency varied. Meta-analysis showed significant heterogeneity ($I^2 = 95.9\%$) and a prediction interval of 17% to 89%, reflecting the diverse contexts of studies. Pica was significantly associated with iron and zinc deficiencies, low haemoglobin, reduced weight-for-age, and elevated blood lead levels ($p < 0.001$). Additionally, Pica behaviours were correlated with neurodevelopmental disorders in three studies, particularly when children ingested materials such as paper, foam, or fabric. Restrictive eating patterns consistent with ARFID were identified in eight studies. Comorbid psychological symptoms including depression, anxiety, body image concerns, and suicidal ideation were reported in up to 70% of adolescents with disordered eating. Despite the frequency and severity of eating disorder presentations, only one study reported a formal intervention**:** a behavioural case series which demonstrated partial symptom remission. Other studies mentioned micronutrient supplementation or general nutrition advice but lacked structured evaluation or follow-up.

Conclusion: EDs, particularly Pica, are prevalent and clinically significant in children with SCD. Disordered eating contributes to poorer nutritional, haematological, and psychosocial outcomes. Despite this, routine screening and structured interventions are lacking. There is an urgent need for integrated, multidisciplinary care approaches, such as Applied Behaviour Analysis as well as further research, to improve clinical outcomes in this vulnerable population.

PO04 | Education outcomes of children with sickle cell disease in Ghana: A case–control study

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Introduction: Sickle cell disease (SCD) causes both acute and chronic complications that can negatively impact the educational achievement of affected individuals. In Ghana, there is no school-based programs specifically targeting children with SCD, likely due to a lack of local evidence on the relationship between SCD and educational performance. This study aimed to compare the academic outcomes of basic school children with SCD to those of their unaffected classmates.

Methods: This was a case–control study involving basic school children, aged 6–16 years who were screened across 82 schools in the Hohoe Municipality of the Volta Region, Ghana. Cases and control were randomly selected from 3542 children screened for SCD. Cases were matched to controls based on sex, educational level, school and class. Participants were categorised into three educational levels: Kindergarten, Primary, and Junior High School (JHS). The mean annual scores across all academic subjects were calculated and compared using Chi-square in SPSS version 29.0.

Results: A total of 152 participants were included: 57 SCD cases (out of 110 diagnosed) and 95 non-SCD controls (out of 3432 screened). The mean age was 12.8 ± 3.02 years for cases and 12.63 ± 3.10 years for controls ($p = 0.740$). The male-to-female ratio was 1:1.85 among cases and 1:1.5 among controls ($p = 0.539$). Seven participants were in Kindergarten, 71 in Primary, and 75 in JHS. Overall, academic performance was lower among cases compared to controls at all educational levels. In Kindergarten, performance differences across four subjects were not statistically significant. In Primary, among seven subjects, cases scored significantly lower in the verbal subjects: Citizenship Education (58.2% ± 9.7% vs. 63.5% ± 7.9%, $p = 0.012$) and English (57.6% ± 7.8% vs. 62.4% ± 8.5%, $p = 0.021$). In JHS, significant differences were observed in the verbal subjects such as Ghanaian language (59.8% ± 7.3% vs. 63.6% ± 7.4%, $p = 0.036$) and Social Studies (60.7% ± 7.9% vs. 65.4% ± 6.4%, $p = 0.006$), and non-verbal subjects such as: Mathematics (58.7% ± 7.7% vs. 63.2% ± 8.3%, $p = 0.026$) and Information and Communication Technology (59.0% ± 7.9% vs. 62.6% ± 5.8%, $p = 0.035$), all favouring controls.

Conclusion: Children with SCD performed worse academically than their non-SCD peers, with disparities more pronounced at higher educational levels. Early diagnosis, comprehensive management of SCD-related symptoms, and the development of tailored educational support programmes are needed to improve academic outcomes in this vulnerable population.

PO05 | Nutritional status as a risk factor for psychological well-being of adolescents SCD patients in Ghana

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Introduction: Sickle cell disease (SCD) affects approximately 2% of newborns annually. Advances in care, early diagnosis, and good nutrition have improved patients' survival and outcomes. However, poor nutritional governance in low- and middle-income countries contributes to undernutrition and obesity. Although nutrition is known to influence health outcomes, its specific role in SCD, especially, regarding psychological well-being remain largely under-researched. This study investigated the predictors of good psychological well-being among adolescents living with SCD in Ghana.

Methods: Firstly, a total of 98 adolescents aged 13–19, comprising 51 non-SCD and 47 adolescents living with SCD, were administered the Youth Paediatric Symptom Checklist (Y-PSC) and a 14-item nutritional knowledge questionnaire. Secondly, the univariate and multivariate linear regression tests were conducted to determine socio-demographic and clinical factors as predictors of psychological well-being.

Results: The results showed that compared to their non-SCD peers, adolescents with SCD had lower weight measurements [SCD (M (SD) = 44.7 (9.9): Non-SCD (M (SD) = 56.5 (12.0)] and nutritional status (BMI) [SCD (M (SE) = 19.8 (3.41): Non-SCD (M (SE) = 23.7 (3.09)]. Additionally, adolescents with SCD demonstrated lower nutritional knowledge [SCD (M (SE) = 7.8 (0.44): Non-SCD (M (SD) = 9.7 (0.42)], which was positively associated with nutritional status [$B = 2.22$; 95% CI: 0.88, 3.56), $p = 001$]. At the univariate level, compared with non-SCD adolescents, adolescents with SCD had impaired psychological functioning ($B = -6.49$; 95% CI: −11.00, −1.97, $p = 0.005$). Similarly, an increase in nutritional status improved the psychological functioning by 1.54 times ($B = -1.54$; 95% CI: 0.85, 2.24, $p < 0.001$). Conversely sex ($B = -4.17$; 95% CI: −8.85, −0.50, $p = 0.080$), age ($B = -0.49$; 95% CI: −1.67, 0.68, $p = 0.406$), and educational level ($B = -2.06$; 95% CI: −5.94, 1.83, $p = 0.296$) were not significant predictors of adolescents' psychological functioning. Subsequently, in the Multivariate regression analyses, increased nutritional status (BMI) increased the psychological symptoms ($B = 1.41$; 95% CI: 0.55, 2.28, $p = 0.002$).

Conclusion: These findings have significant clinical and policy implications. Integrating nutrition education, psychological support, comprehensive healthcare, and improving the school health program to accommodate adolescents living with chronic conditions, can help improve their overall well-being and quality of life.

PO06 | Summary of natural history and clinical outcomes in sickle cell disease: A collaborative multicenter study

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Background: The Natural History Study in Sickle Cell is a research database set up to establish a research cohort of adults with SCD and to prospectively follow up this cohort to establish detailed natural history data. It is now open at 5 UK sites, both inside and outside London.

Aims:

- To set up a research database of an adult cohort of patients with SCD
- To perform detailed retrospective phenotyping data on entry to cohort
- To collect annual data on clinical and laboratory parameters
- Planned annual data analysis
- Collaboration with multi-centre prospective study with production of annual reports on patient outcomes (pending data sharing agreements)

Methods: Retrospective and prospective database study, natural history cohort.

Results: After 3 years of recruitment there are a total of 697 participants, 409 (58.7%) were female and 288 (41.3%) were male. The age at recruitment ranged from 18 to 81 years, with a mean of 39.0 years (SD = 14.4). Regarding sickle cell genotypes, 459 (65.9%) had HbSS disease, 204 (29.3%) had HbSC disease, 25 (3.6%) had HbSβ^+ thalassaemia, five (0.7%) had HbSβ^0 thalassaemia, and single cases (0.1% each) were observed for HbSLepore, HbSD^{Punjab}, HbSE, and HbSHPFH genotypes.

Regarding ethnicity, 631 of 697 participants (90.5%) self-identified as Black (including Black African, Black African-Caribbean, and Black British). The remaining participants identified as mixed ethnic background (black/white, $n = 4$, 0.5%), Middle Eastern or South Asian ($n = 3$, 0.4%), other mixed backgrounds ($n = 4$, 0.7%), other ethnic groups ($n = 19$, 2.7%), or did not state their ethnicity ($n = 32$, 4.6%). These classifications follow the standard UK ethnicity definitions for self-identified ethnicity (https://www.ethnicity-facts-figures.service.gov.uk/style-guide/ethnic-groups).

A comparison of prevalence of sickle complications in the HbSS and HbSC subgroups can be found in Table 1 and a list of disease modifying therapies taken in Table 2.

TABLE 1 Comparison of sickle complication by sickle genotype.

		N	No	Yes	p-value
Stroke	HbSS	306	275	31	0.079
	HbSC	152	144	8	
Pulmonary hypertension	HbSS	307	246	61	0.007
	HbSC	152	137	15	
Avascular necrosis	HbSS	307	234	73	0.021
	HbSC	152	130	22	
Chronic liver disease (including sickle hepatopathy)	HbSS	303	291	12	0.947
	HbSC	150	145	5	
Chronic kidney disease (including sickle nephropathy)	HbSS	304	252	52	0.448
	HbSC	150	131	19	
Leg ulcers	HbSS	305	280	25	0.027
	HbSC	150	147	3	
Sickle retinopathy	HbSS	257	158	99	<0.001
	HbSC	134	40	94	
Acute chest syndrome	HbSS	297	222	75	<0.001
	HbSC	147	135	12	
Priapism: men only	HbSS	120	84	36	0.039
	HbSC	57	50	7	
Gallstones	HbSS	307	176	131	<0.001
	HbSC	152	131	21	

TABLE 2 Disease modifying therapy by sickle genotype.

		Currently taking	Currently not taking	p-value	Ever taken	Never taken	p-value
Hydroxycarbamide	HbSS	149	158	<0.001	176	92	<0.001
	HbSC	20	130		25	110	
Transfused	HbSS	70	223	<0.001	234	67	<0.001
	HbSC	7	142		61	88	
Hydroxycarbamide and/or Crizanlizumab and/or_Voxelotor and/or_transfusion as disease modifying therapy	HbSS	209	98	<0.001			
	HbSC	26	126				

Conclusion: Our research database presents detailed, longitudinal, real-world data on individuals with sickle cell. This enables researchers to understand the characteristics of sickle cell in a well-managed cohort living in a high-income setting.

PO07 | Bridging the sickle cell disease gap through community-led participatory action cycles in Zambia

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Background: Globally, the burgeoning burden of sickle cell disease (SCD) poses significant health challenges, in Sub-Saharan Africa, which bears over 80% of the disease burden. This is exacerbated by the disparities faced in accessing healthcare for SCD; limited awareness; persistent stigma; delayed diagnosis, and inadequate access to treatment and long-term follow-up care. In many Zambian communities, misconceptions about SCD remain widespread, often resulting in stigma, thus taking a toll on the warriors, caregivers and the entire healthcare system. While significant advances have been made towards SCD, there is still significant bias towards pharmacological interventions while hardly prescribing community led initiatives. To address this, we implemented community-led Participatory Action Cycles (PAC) aimed at increasing awareness among those impacted by SCD. The main objective of the intervention was to increase awareness on Sickle SCD using PAC.

Methods: We implemented PAC between August 2024 and May, 2025. The PAC cycles are iterative process involving planning, action, observation and reflection phases. At the planning phase, the teams identified the root causes of the problems and implement solutions at the action phase. These solutions are observed and evaluated in the observation phase. The final phase is the reflection phase in which the PAC members reflect on what worked or didn't

work and why. The PAC members designed data collection tools and conducted knowledge assessments on SCD using questionnaires and focus group discussions. Outreach programs, including health education and counseling, were provided to churches, maternal and child health (MCH) units, outpatient departments (OPD), schools, warriors and caregivers. Caregivers were recruited in a caregiver support group so that they are given additional psychosocial support. Monthly meetings were held to review the cycles through the implementation research process.

Results: PACs were implemented across 4 selected public sector hospitals in Lusaka (2), Ndola (1) and Kasama (2) districts in Zambia. PAC members used the root cause analysis to identify and prioritize the solutions which included sensitization in churches, schools, wards, MCH, OPD and in the community. Through these activities, a total of 2565 individuals were reached with key messages aimed at raising awareness about SCD. Additionally, four caregiver support groups were established to offer ongoing psychosocial support. Community agents also successfully designed and distributed Information, Education, and Communication (IEC) materials to reinforce key messages. Monitoring and evaluation of these activities revealed meaningful improvements in both knowledge and emotional wellbeing. Caregivers reported feeling more confident in managing Sickle Cell Disease (SCD) at home and appreciated the peer support. One caregiver shared, "Before this group, I felt alone and helpless. Now I understand my child's condition and know I'm not alone."

Another warrior stated, "I used to think SCD was a death sentence, but now I know I can live a full life with the right care and support." Participants consistently emphasized how the interventions had not only improved their understanding of SCD but also strengthened their sense of hope and community.

Conclusion: This study shows how the PAC present an opportunity to raise awareness on SCD and provide support for SCD patients and caregivers in Zambia. Implementation of community-led interventions at scale is recommended as a medium of raising awareness on SCD.

PO08 | Blood transfusion, bone marrow transplant and gene therapy for sickle cell disease: African newspapers' analysis

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Introduction: Blood transfusion, bone marrow transplant and gene therapy are key strategies for managing sickle cell disease (SCD). Moreover, mass media channels such as newspapers are commonly accessed in Africa. However, the extent to which newspapers report the use of blood transfusion, bone marrow transplant and gene therapy for managing SCD in Africa remains unknown. This study aimed to assess the extent to which newspapers in Africa have reported on key topics related to SCD, namely the use of blood transfusion, bone marrow transplant and gene therapy for managing SCD.

Methods: We conducted a systematic content analysis of newspaper articles blood transfusion, bone marrow transplant and gene therapy SCD using two newspaper databases: LexisUni and Newsbank. The search terms were "(sickle cell) AND (disease OR trait OR anaemia OR anemia)". The search strategy was limited to articles published in English until 31 October 2023. We developed an a priori coding framework based on existing literature on media content analyses using a Google Form, and trained two coders to use the coding form. We assess interrater reliability using Cohen's kappa scores, with variables achieving a Kappa score of at least 0.41 (considered to be moderate) being used in the final coding. We used descriptive statistics to analyse key topics and chi-square tests to assess the association between variables, including blood transfusion, bone marrow transplant and gene therapy.

Results: The initial search resulted in a total of 2254 articles in LexisUni and 2467 articles in Newsbank with 1113 meeting the inclusion criteria for full screening, and a total of 236 newspaper articles focusing on blood transfusion, bone marrow transplant, or gene therapy for managing SCD. Of the 236 articles, 63.6%, 46.2% and 9.7% covered bone marrow transplant, blood transfusion, and gene therapy, respectively. The articles were published in 11 African countries, namely Egypt ($n=1$), Zambia ($n=1$), Rwanda ($n=2$), Zimbabwe ($n=4$), Gambia ($n=5$), Ghana ($n=5$), South Africa ($n=8$), Tanzania ($n=13$), Kenya ($n=21$), Uganda ($n=55$), and Nigeria ($n=121$). The articles were published from 2006 to 2023. Most of the articles were predominantly published in June (20.3%), July (13.1%), and August (10.2%). There were statistically significant relationships between month of newspaper publication and mentioning gene therapy ($p=0.007$) but not bone marrow transplant ($p=0.715$) and blood transfusion ($p=0.258$). There were no statistically significant relationships between country of newspaper publication and mentioning gene therapy, bone marrow transplant or blood transfusion.

Conclusion: It was surprising that despite blood transfusion being used more often to manage SCD in Africa when compared with bone marrow transplant and gene therapy, the highest proportion of articles focused on bone marrow transplant. There is a need for increased reporting on the use of blood transfusion for managing SCD to help increase blood donation in Africa. Moreover, increased newspaper reporting on the subject in June indicates that African newspapers cover more stories during the World Sickle Cell Disease Day celebration in June. Researchers and clinicians should engage more with African newspapers throughout the year to help increase media coverage on the topic.

PO09 | RAP-536 ameliorates anemia and vaso-occlusion in experimental model of sickle cell disease

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Introduction: Sickle cell disease (SCD) is a genetic disorder characterized by chronic hemolytic anemia and recurrent vaso-occlusive crises (VOC), causing significant clinical burden. Luspatercept (RAP-536), a ligand trap receptor approved for thalassemia and myelodysplastic syndromes, restores effective erythropoiesis by inhibiting select transforming growth factor-beta (TGF-β) superfamily members including growth differentiation factor 11 (GDF11). This factor has been identified as a key driver of ineffective erythropoiesis in these pathologies. This study evaluated GDF-11 expression in SCD patients and assessed the effects of RAP-536 on anemia and VOC in SCD models, alone or combined with hydroxyurea (HU).

Methods: Plasma GDF-11 levels were measured in SCD patients, healthy donors, and patients with other hemolytic anemias. GDF-11 and pSMAD2 expression were examined in the spleen of Townes HbSS mice via immunohistochemistry. HbSS mice were treated with RAP-536 (1 mg/kg i.p. twice weekly for 8 weeks), alone or with HU (100 mg/kg oral daily). Hematological, biochemical, and histological parameters were measured to assess treatment effects.

Results: SCD patients showed significantly elevated plasma GDF-11 levels (27.7 pg/mL) compared to healthy donors (5.0 pg/mL, $p < 0.01$) and other hemolytic anemias (8.0 pg/mL). HbSS mice showed higher GDF11 expression in the spleen compared to HbAA mice, which correlated with SMAD2 phosphorylation. In HbSS mice, RAP-536 treatment increased red blood cell count and hemoglobin levels, reduced reticulocytes, and improved hemolytic markers including lactate dehydrogenase, bilirubin, plasma free hemoglobin, and free heme. RAP-536 also decreased tissue vascular congestion in liver, lungs, and kidneys during hypoxia-induced vaso occlusive crisis VOC.

Ektacytometry demonstrated that RAP-536 enhanced red blood cell deformability in vivo, indicated by an increased elongation index, correlating with improved oxygen transport. These benefits were independent of fetal hemoglobin (HbF) modulation. RAP-536 significantly reduced blood reactive oxygen species (ROS), potentially lowering VOC incidence and promoting erythropoiesis.

Treatment reduced splenomegaly and promoted erythroid maturation in spleen and bone marrow, with a higher proportion of orthochromatic erythroblasts and reticulocytes (Ter-119$^+$CD71$^-$) relative to basophilic and polychromatic erythroblasts (Ter-119$^+$CD71$^+$). ROS reduction was associated with increased expression of Nrf2 (a key antioxidant regulator) and GATA-1 in erythroid precursors. In a hypoxia/re-oxygenation VOC model, RAP-536's sickling reduction effect was additive to HU.

Conclusion: These pre-clinical results highlight the potential of RAP-536 as a therapeutic agent in SCD by improving ineffective erythropoiesis, reducing hemolysis and ROS, and amelioration of VOC events independently of HbF induction. Ongoing studies address its impact on chronic complications. Findings encourage clinical evaluation of RAP-536 to address anemia and VOC in SCD patients with high unmet needs.

PO10 | Wide deletion at the beta-globin locus explaining severe prenatal anaemia in two sisters

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Introduction: Patients with heterozygous beta-thalassemia do not usually have anaemia in the neonatal or prenatal period, since the main embryonic and foetal haemoglobin (Hb) do not contain beta chains. The LCR (Locus Control Region) is located at the locus β globin of chromosome 11, adjacent to the epsilon gene (ε). The LCR region regulates the expression of the other locus genes (epsilon, gamma, delta and beta).

We present two sisters with a deletion that affects both the HBE gene and the LCR, causing severe prenatal-onset anaemia and subsequently an analytical pattern of classic thalassaemic trait.

Methods: Case 1: 16-year-old girl. Erythematous-violaceous rash, hepatosplenomegaly, anaemia and erythroblastosis detected at birth. A skin biopsy was compatible with extramedullary haematopoiesis. She required two transfusions during his admission. Later referred to the haematologist, her complete blood count (CBC) showed microcytosis and pseudo polyglobulia, suggesting thalassemia trait. Haemoglobin electrophoresis showed no increase in HbA2 or HbF. The molecular study of alpha thalassemia was negative. All subsequent laboratory controls have shown similar CBC. She has been asymptomatic since the first months of life except

for a transitory thick bile and renal foci of extramedullary haematopoiesis followed by paediatric nephrologist.

Case 2: 13-year-old girl. In the 28th week of gestation, hydrops, anaemia and hepatomegaly were detected, so she received two intrauterine transfusions. At birth there is no anaemia, but at one month of life the Hb drops to 6.5 g/dL and she receives a transfusion. Her anaemia improves and from 6 months of age she presents a CBC pattern compatible with thalassaemic trait. As her sister, HbF, HbA2 and the genetic study of alpha thalassemia are normal. Clinically she is completely asymptomatic.

Family history: Non-consanguineous Caucasian parents. The mother has been classified as a thalassaemic trait, as have her father and several maternal cousins. Her haemoglobin electrophoresis and molecular alpha thalassemia study are negative.

Results: Gene sequencing is carried out using the MLPA technique (Multiplex Ligation-dependent Probe Amplification) and a large deletion of 32.3 kb in heterozygosity is detected in the beta globin gene grouping that includes the HBE gene (which codes for the synthesis of epsilon chains) and tthe HS1, HS2, HS3, HS4 and HS5 regions of LCR adjacent locus. The same deletion is found in her sister.

Conclusions: Mutations affecting the ε gene at the beta globin locus will cause decreased synthesis of Gower 1 (ζ2ε2) and Gower 2 (α2ε2) haemoglobins, which are the main ones in early pregnancy. Subsequently, a substitution for Hb Portland (ζ2γ2) and foetal Hb (α2γ2) occurs, so anaemia should no longer be observed at birth.

Mutations in the LCR locus affect the synthesis of the rest of the chains of the beta globin locus, even though these loci are in fact intact. Thus, there is a decrease in the synthesis of gamma, delta and beta chains, a CBC compatible with heterozygous beta thalassaemia is observed but there is no compensatory elevation of HbA2 or HbF.

The presence of a large deletion affecting both the CSF locus and the ε region explains in these patients the coexistence of severe prenatal anaemia and a CBC suggestive of thalassaemic trait with a normal haemoglobin study. The literature review has not shown deletions like to the one described.

PO11 | Cognitive performance evolution in DREPAGREFFE trial comparing transplantation with standard care during 10 year follow-up

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Introduction: In sickle cell anemia (SCA), cognitive impairment is associated with severe anemia, stroke and silent cerebral infarcts (SCI). It remains unclear weather allogeneic stem cell transplantation (alloSCT) is capable of improving long term cognitive performance compared with standard of care (SoC).

Methods: Drepagreffe is a French national trial defined by the random availability of a matched-sibling donor (MSD), comparing alloSCT to SoC in SCA-children undergoing chronic-transfusion for abnormal cerebral velocities (TAMMV ≥200 cm/s). To be enrolled, SCA-children (5–15 years) had to have at least one non-SCA sibling from the same parental couple, with parents agreeing to family HLA-typing, alloSCT if available MSD or continuation of chronic-transfusion for at least one year followed by a switch to hydroxyurea if velocities normalized and there was no stenosis. Sixty-seven SCA-children, seven of whom had history of stroke (four in alloSCT and three in SoC arm) were enrolled (Dec 2010/June 2013).

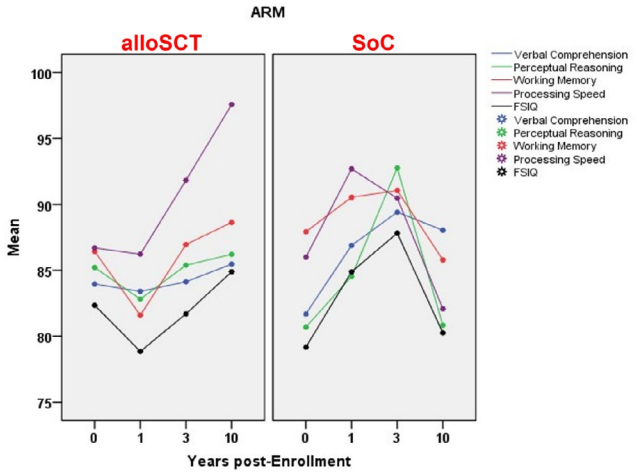
Clinical and biological data, color-Doppler ultrasound, brain MRI/MRA/neck-MRA, cognitive tests and quality of life were assessed at enrollment, 1, 3 and 10 years. The MRI-scores, were obtained by adding up the ischemic lesion scores from left and right sides: 3 (territorial); 2 border zone (cortical and subcortical), 1 (white matter), 1 (basal ganglia infarcts) and 0 if absent on each side. The MRA stenosis-scores, were defined as the weighted sums over the 8 assessed cerebral arteries, as 0 if no stenosis, 1 if mild stenosis (25%–49%), 2 if moderate stenosis (50%–74%), 3 if severe stenosis (75%–99%), and 4 if occlusion. Cognitive testing, included WPPSI-III (3–6 years), WISC-IV and -V (7–16 years) or WAIS-III and -IV (>16 years) scales, depending on the subject age. Cognitive testing was also performed in non SCA-siblings at enrollment, 1 and 3 years averaged across these 3 measures. Indices of Verbal Comprehension (VCI), Perceptual Reasoning (PRI), Working Memory (WMI), Processing Speed (PSI) and Full Scale IQ (FSIQ) are reported.

Results: Of the 67 patients, 32 with MSD were enrolled in alloSCT and 35 with no MSD in SoC arm. At 10 years, all SCA-patients were alive, and no new stroke had occurred.

At enrollment, 64 patients of whom 56 siblings underwent cognitive testing. Stroke-patients ($n=7$) differed strongly from no-stroke patients ($n=57$): mean (SD) VCI:64.9 (20.8) vs. 81.3 (17.0), $p=0.041$, WMI:68.4 (13.9) vs. 86.7 (16.3), $p=0.008$ but not for PRI ($p=0.078$), PSI (0.332) and FSIQ (0.054) while among patients without stroke ($n=57$), no significant difference was found between those with SCI ($n=17$) and those without SCI. However, paired analysis showed strong differences between siblings and stroke-free patients: VCI, $p=0.011$; PSI, $p=0.002$ and FSIQ, $p=0.004$.

At years 1 and 3 there were no significant differences in cognitive performance was observed between both arms.

At year-10, 51 (22 alloSCT, 29 SoC arm) stroke-free patients were tested and significant differences were found in PSI: 98.0 (21.6) in alloSCT vs. 84.4 (14.2) in SoC arms, $p=0.011$. Interestingly, in the alloSCT arm, all cognitive indices deteriored between enrollment and year 1 but gradually improved thereafter whereas in the SoC arm a decline in all indices was observed between year 3 and 10.



Conclusion: These results showing a long-term improvement in cognitive performance after alloSCT encourage us to recommend alloSCT in the pediatric period to promote better socio-professional integration of SCA-patients.

PO12 | Lung function in children with sickle cell disease

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Introduction: Sickle cell disease (SCD) is a chronic haemoglobinopathy associated with significant multisystemic complications, including progressive pulmonary dysfunction. Pulmonary function tests (PFTs) are vital for monitoring the development and progression of lung disease in this population. This study aimed to evaluate pulmonary function in a paediatric cohort with SCD and to identify clinical and laboratory parameters associated with abnormalities in spirometry and diffusing capacity.
Methods: This retrospective study analysed clinical and laboratory data from 62 children with SCD who underwent PFTs. All patients performed spirometry and were categorised based on results as normal, restrictive lung disease (RLD), or obstructive lung disease (OLD). A subgroup of 39 patients also completed a diffusing capacity of the lungs for carbon monoxide (DLCO) test and were subsequently grouped as having normal or reduced capacity. Statistical comparisons between groups were performed using appropriate non-parametric and categorical tests, including Kruskal–Wallis, Mann–Whitney *U*, and Pearson's chi-squared tests.
Results: Sixty-two patients underwent spirometry, of whom 17 (27.42%) presented abnormal results, with RLD identified in 11 cases (17.74%) and OLD in 6 cases (9.68%). No statistically significant differences were observed among the normal, RLD, and OLD groups for age, baseline haemoglobin, LDH, leucocytes, or the number of prior acute chest syndrome (ACS) episodes. A trend was observed for a higher proportion of males in the abnormal spirometry groups ($p = 0.072$). When evaluating comorbidities, abnormal spirometry showed a borderline association with the presence of cardiovascular disease ($p = 0.066$). In the analysis of the DLCO subgroup ($n = 39$), patients with reduced diffusion capacity were older than those with normal capacity (mean age 13.00 ± 1.93 years vs. 11.48 ± 2.71 years, respectively; $p = 0.037$). No significant differences were detected between the normal and reduced DLCO groups for other variables, including baseline haemoglobin, LDH, leucocytes, or history of ACS episodes.
Conclusion: In this cohort of children with sickle cell disease, older age was the only factor significantly associated with a reduction in carbon monoxide diffusion capacity, suggesting a progressive decline in gas exchange function. While definitive associations with spirometric abnormalities were not found, the data suggest potential trends that may warrant investigation in larger studies. These findings highlight the importance of routine PFTs, and particularly the DLCO measurement, for the early detection and monitoring of pulmonary functional impairment in paediatric patients with SCD.

PO13 | Quality of life in sickle cell: Findings from the UK sickle cell natural history study

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Introduction: The UK Sickle Cell Natural History Study has established a research cohort of adults with Sickle Cell Disease (SCD). Patient-reported measures of quality of life (QoL) are included in the annual data collection, using the Adult Sickle Cell Quality of Life Measurement Information System (ASCQ-Me) and the Patient Reported Outcomes Measurement Information System (PROMIS). The ASCQ-Me is the first QoL measure to be created and validated for adults with SCD. The PROMIS is validated for healthy adults. This sub-study explored associations between demographic (age, sex) and clinical (genotype, treatment type and disease severity) variables and QoL metrics.
Methods: At each annual visit participants were asked to complete four ASCQ-Me measures: Pain Impact, Emotional Impact, Social Impact and Sleep Impact; and two PROMIS measures: Fatigue 4a Adult v1.0 and Cognitive Functioning

8a Adult v2.0. Participants' age, sex, genotype and treatment type were recorded. Disease severity was indexed by metrics including resource utilisation, and a "haemolytic index", determined from a principal components analysis (PCA) of three clinical markers of haemolysis (reticulocyte count, LDH, and total bilirubin levels). Associations between QoL measures and other variables were assessed in SPSS v. 25, using appropriate non-parametric tests as QoL data were non-normally distributed.

Results: 637 patients with SCD completed at least one QoL measure.

Average ASCQ-Me scores were similar to SCD population norms. Average PROMIS scores indicated that our SCD participants reported, on average, higher levels of fatigue and worse cognitive function than the healthy adult population.

On average females reported more problems than males with pain, emotional impact, social impact, fatigue and cognitive functioning (Mann–Whitney *U*-tests, all $p < 0.007$) but not sleep ($p = 0.09$).

On average, the emotional impact and the impact of pain both decreased as age increased (independent samples Kruskal–Wallis test, both $p < 0.05$). There was no evidence of statistically-significant differences between age groups on the other four scales.

There were statistically-significant differences on all QoL measures between the two main genotypes, with HbSS patients reporting, on average, greater negative impact on quality of life compared with HbSC patients (Mann–Whitney *U*-tests, all $p < 0.04$).

Participants on at least one disease-modifying treatment had, on average, significantly worse QoL (more fatigue, worse pain, emotional impact, social impact, sleep impact and cognitive functioning) compared with those not on disease-modifying treatments.

Higher haemolytic index was statistically-significantly associated with worse emotional and sleep impact scores. Higher resource utilisation was statistically-significantly associated with worse scores on all QoL measures.

Conclusion: This study shows the wide-ranging impact of SCD on QoL, and sheds light on important differences including greater negative impact on females compared with males (across all ages, in almost all QoL domains), and a reduction in the impact of pain and emotional impact with increasing age. Associations with clinical characteristics show that participants with a more severe phenotype tend to report greater impact on QoL. Future work will investigate longitudinal changes in QoL metrics and try to predict more precisely those people with SCD who are greatest risk of a negative impact on QoL which could help target psychosocial interventions.

PO14 | Analysis of SCD-related policies in sub-Saharian Africa and Lebanon

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Introduction: The ARISE (African Research and Innovative Initiative for Sickle cell Education: Improving Research Capacity for Service Improvement) project received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No. 824021 to establish staff exchanges (SEs) across Europe, sub-Saharan Africa, Lebanon and the US focused on Sickle Cell Disease diagnosis, treatment and management. One of the project actions focused on mapping healthcare policies and the organisation of centres managing Sickle Cell Disease (SCD) in Nigeria, Kenya, Angola, Zambia, and Lebanon.

Methods: Data collection involved targeted searches for national and international guidelines on SCD management, including diagnosis, treatment, prophylaxis, pregnancy care, and newborn screening (NBS). Data were extracted into structured MS Excel files. Additional searches on PubMed and Google identified pharmacological therapies, laboratory tests, counselling practices, and patient registries. Moreover, six nationwide cross-sectional studies have received ethics approval to map the organisation and offer of services of centres managing SCD in target countries, with surveys assessing blood transfusion, transcranial doppler (TCD) and Magnetic Resonance Imaging (MRI) services.

Results: National and WHO guidelines for SCD and NBS were identified in most of the countries. Nigeria and Kenya have national guidelines aligned with WHO standards, with Kenya also implementing NBS guidelines. No formal policies were identified in Lebanon. An overview of country-applicable guidelines on diagnosis and management of SCD, including topics, was developed. With reference to treatment, access to hydroxyurea (HU), although recommended, remains limited due to cost and availability.

NBS is promising, as it allows early management of the disease, but its implementation faces challenges in scale and funding.

Conclusion: This analysis is part of the ARISE broader effort to advance SCD-related policy, research, training, and awareness in African countries and Lebanon.

ARISE contributed to advancing diagnosis, care standards, and registries, fostering research and collaborative efforts across resource-limited settings. The project fosters ongoing collaboration beyond its formal duration, supporting studies completion and expanded local analysis of policies, treatments, diagnostic services, and registries by the end of 2025.

PO15 | Research and training to address needs of sickle cell disease healthcare professionals: An international experience

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Methods: Throughout the project, the needs for training and skills improvement of health professionals and researchers in the target countries were periodically assessed to adapt the SEs programme and plan next steps. Mixed methods were employed, including electronic surveys, individual interviews with participants, consultation with site leads, and literature analysis. Quantitative and thematic analyses were performed to identify and group preferred topics.
Results: A survey involving 208 potential participants in the ARISE SEs programme from Nigeria, Kenya, Angola, Zambia and Lebanon identified laboratory techniques diagnosis and quality assurance as preference topics (56 respondents, 19.6%), followed by management of the disease and its complications (51 respondents, 17.8%) and clinical and epidemiological research (40 respondents, 14%).
Newborn screening, screening for neurocognitive complications and Transcranial Doppler, genetic counselling and e-health were also relevant topics. Full details are available in Figure 1. These results were in line with what emerged in a prospective cross-sectoral study conducted in Nigeria in 2020 involving 108 healthcare professionals from 4 clinical centres. The study identified SCD prevention & diagnosis, genetic counselling, SCD management & treatments as main training and skills improvement needs.
Additional items were identified in consultation with ARISE site leads and included data infrastructure to enhance data accessibility and quality; mapping of facilities and essential technologies for SCD management; research capacity and expertise for design and conduct of genetic studies (including ethical aspects).
Based on these needs, 183 SEs for a total duration of 454 person-months (mean duration 2.5 months ± 1.9) were organized. 134 researchers from 7 Eu and extra-Eu countries were involved, with a female prevalence (82/134, 61.2%). An overview of training, capacity building and research topics is available in Figure 2 and it is consistent with reported needs: clinical management and laboratory diagnosis and quality assurance were the most common topics (64/183, 35% and 54/183 staff exchanges, 29,5% respectively).
Conclusion: The ARISE project supported staff exchanges across a wide range of themes, aligned with the needs of participants. The impact of the programme will be assessed at three levels: Individual level—focusing on secondees' career progression and professional development; Institutional level—evaluating service readiness and organizational changes; Wider level—assessing contributions to international research collaboration and improvements in SCD management. Efforts are ongoing to secure additional resources to continue activities.

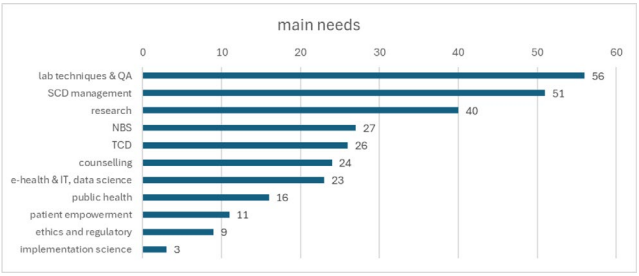

FIGURE 1 Training and skills needs from potential participants in the staff exchange programme.

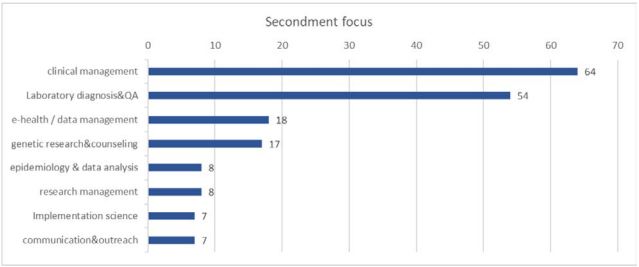

FIGURE 2 Main focus of the staff exchanges performed within the ARISE project.

PO16 | Trialling a telephone monitoring clinic for patients receiving hydroxycarbamide and/or iron chelation therapy

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Introduction: In October 2024, the Specialist Haemoglobinopathy Team at an adult hospital in the North West of England commenced the trial of a telephone monitoring clinic for patients on hydroxycarbamide and/or iron chelation therapy with the aim of improving flexibility for patients and ensuring medication optimisation.
A similar model was trialled by Hollwey (2021) in the paediatric setting and was found to be beneficial in facilitating

improved accuracy of prescription records and structured dose escalation. Several other specialist services within the haematology department at the hospital successfully operate telephone monitoring clinics and it was felt that the model may be beneficial to this patient group.

During the trial, anecdotal evidence suggested that this model was not appropriate for the patient group with many patients not attending for bloods prior to their telephone appointment and many expressing that they prefer face to face review.

An audit was therefore conducted to identify the percentage of patients who did not attend for blood results prior to telephone clinic to justify continuation/discontinuation of the trial.

Methods: Blood forms were sent through the post to patients receiving treatment with hydroxycarbamide and/or iron chelation therapy who had the option to attend phlebotomy clinics at the hospital or within the community. Patients with difficult intravenous access could arrange to attend haematology day ward for blood tests. Patients were then offered a telephone appointment to discuss blood results/symptoms/side effects and to adjust medication dose based on blood results following which a new prescription would be issued. Patients were offered the flexibility to collect prescriptions from the hospital pharmacy any time during the next week.

A retrospective review of clinic lists, and electronic patient records was conducted for all patients scheduled to attend telephone monitoring clinics between October 2024 and January 2025 to identify the following criteria:

- Percentage of patients who did not attend for monitoring bloods prior to telephone clinic
- Percentage of patients who repeatedly did not attend for monitoring bloods prior to telephone clinic
- Percentage of patients who did not answer the telephone

Results: A total of 123 telephone monitoring clinic appointments were reviewed

- 23% patients did not answer the telephone for their monitoring clinic appointments
- 37% of patients did not attend for monitoring bloods prior to telephone monitoring clinics
- 11% patients repeatedly did not attend or attended with no monitoring bloods taken prior to the appointment

Limitations:

- Appointments cancelled by patients were not captured in this audit which represents a missed opportunity to capture data regarding engagement
- Reminder messages were sent for the first 5 weeks of the trial however due to staffing issues, there was no capacity to facilitate this for the entire trial

Conclusion: The results demonstrate a lack of engagement with telephone monitoring clinics within this patient group. The trial was discontinued after 3 months as the team were unable to justify continuing offering telephone monitoring clinics due to poor service utilisation.

Further research could be conducted in the form of patient questionnaires/surveys/interviews to identify the reasons why patients did not engage with telephone monitoring clinics.

PO17 | Transgender and gender diverse care for individuals with sickle cell disease

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Introduction: Sickle Cell Disease (SCD), the most common inherited condition in the United States, is prevalent among African Americans occurring in 1 out of every 365 African American births. The complications associated with SCD include both acute and chronic pain, as well as organ damage. Individuals with SCD who identify as transgender and gender diverse (TGD) encounter unique barriers when seeking healthcare, exacerbating their health challenges.

Methods: The intersection of TGD identities with SCD requires a comprehensive and inclusive approach to healthcare delivery. Moreover, the implication of gender-affirming interventions must be carefully considered, as they may introduce significant risks in the management of SCD. Healthcare providers, particularly nurses, bear an ethical responsibility to deliver respectful, safe, and high-quality care. It is imperative that nurses are well-informed about the specific healthcare needs, risks, and challenges faced by this population.

Results: Individuals who are African American and TGD with SCD often confront discrimination, health-related stigma, and systemic racism during their healthcare experiences, leading to suboptimal care. These systemic challenges contribute to pronounced mental and physical health disparities, including elevated rates of depression and suicide. A considerable number of individuals with SCD may choose to avoid the healthcare system due to a perceived lack of cultural humility among healthcare providers.

Conclusion: This presentation aims to provide a comprehensive overview of the challenges and barriers faced by TGD individuals with SCD, along with evidence-based strategies for improving care. Furthermore, a framework that emphasizes principles of diversity, equity, inclusion, and belonging will be discussed to enhance the healthcare experiences of this rapidly growing population.

PO18 | An interpretative phenomenological analysis of the experience of adults with sickle cell disease receiving HSCT

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Introduction: The provision of psychology support is deemed important for patients undergoing Haematopoietic Stem Cell Transplantation (HSCT), as studies have found a high prevalence of psychological distress is reported. Most research into HSCT have been in relation to haematological malignancies. I reasoned that further research adopting an explicitly psychological focus would be valuable in understanding the lived experiences of adult HSCT recipients with Sickle Cell Disease (SCD) and how they can be supported psychologically through this major life transition.
Methods: Six adults with SCD participated in semi-structured interviews regarding their experience of HSCT. Interviews were transcribed and analysed using Interpretative Phenomenological Analysis (IPA).
Results: The analysis resulted in three Group Experiential Themes: (1) 'Leaving the Inferno'—details how the worsening burden of SCD over time influenced participants in making the decision to proceed with HSCT, despite the risks, with all hoping for a more 'normal life'; (2) 'Travelling through Purgatorio'—documents the challenging experiences participants had, how they coped, and their attitudes towards psychological therapy as a way of supporting them through HSCT; (3) 'Journeying towards Paradiso'—focuses on participants' progress towards the more 'normal' life they had hoped for after HSCT and ongoing adjustment to life without SCD. Crystal Park's Meaning-Making model was selected as a theory that could help in understanding the way in which participants' beliefs and goals developed through a life lived with SCD guided their interpretation of their HSCT experience.
Conclusion: Psychological therapies that can facilitate the process of meaning-making would appear potentially helpful in supporting people with SCD through HSCT and adjusting to life afterwards. The importance of making therapy culturally sensitive is emphasised, with African Psychology being a strengths-based approach that may be particularly relevant. Finally, a relational approach to supporting people with SCD through HSCT at the level of the healthcare system as a whole is argued for, extending the principles of Trauma-Informed Care towards building genuine trust with recipients who may have experienced health and race-based stigma and discrimination.

PO19 | Hospital-based newborn screening for sickle cell disease in Luanda, Angola

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Introduction: Sickle cell disease (SCD) is a severe monogenic recessive disorder with an estimated mortality rate of 50%–90% by age five if left undiagnosed. Early diagnosis is critical to reducing mortality and morbidity in affected children; however, it remains largely unavailable in Sub-Saharan Africa, where disease prevalence is highest. The Lancet Haematology Commission strongly recommends that all children worldwide be screened for SCD by 2025.
The aim of this presentation is to share the results from implementing newborn screening for Sickle Cell Disease at Hospital Materno-Infantil Dr. Manuel Pedro Anzacot de Menezes, Angola.
Methods: From June 2023 to December 2024, all children born or vaccinated at Hospital Materno-Infantil Dr. Manuel Pedro Anzacot de Menezes, Angola, who had parental consent, were screened for SCD. Blood was collected by heel prick test, and hemoglobin electrophoresis was performed by Isoelectric Focusing (IEF) in the equipment Migele (acquired with the support of Revvity and Arise project). All SS results were confirmed by PCR-RFLP, and other hemoglobin variants were sequenced.
Results: A total of 13 256 samples were collected and analysed by IEF. Results indicate a prevalence of 1.4% SS (183) and 20,2% of carriers (2681). Other hemoglobin variants were identified in 44 children, and included E, C and B-talassemia, and other variants in alfa genes. Of all the diagnosed children, medical services could only contact 167 parents, and only 131 children started periodic medical follow-up consultations and prophylactic treatments. Two of these children are already deceased. Thirty-six parents refused follow-up.
Conclusion: These results align with existing estimates of the high prevalence of Sickle Cell Disease in Angola and underscore the critical importance of newborn screening programs to reduce the substantial under-five mortality and morbidity associated with the disease. Furthermore, the notably high refusal rate for attending medical consultations highlights the urgent need to complement screening efforts with robust investments in community health education and literacy, ensuring families understand the importance of follow-up care and treatment.
This study has been conducted within the African Research and Innovative initiative for Sickle cell Education (ARISE) that has received funding from the European Union's Horizon 2020 research and innovation program under the Marie

Skłodowska-Curie grant agreement No 824021. This project also has the financial support IPL/IDI&CA2024/GenFalci_ESTeSL and of FCT/MCTES H&TRC UIDB/05608/2020 and UIDP/05608/2020.

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PO20 | Interleukin-1β modulates erythroid development and iron distribution in a murine model of sickle cell disease

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Introduction: Sickle cell disease (SCD) is a hereditary haemoglobinopathy typified by chronic haemolytic anaemia, recurrent vaso-occlusive crises, and progressive multi-organ damage. A hallmark of SCD is the sustained pro-inflammatory state, associated with elevated circulating levels of cytokines, such as IL-1β and IL-6. Increasing evidence indicates that ineffective erythropoiesis, characterized by impaired maturation of erythroid progenitors, may contribute to SCD-related anaemia. This dysfunction is driven by a hostile bone marrow environment, due to chronic inflammation and oxidative stress. IL-1β, in particular, has been shown to impair haematopoietic stem and progenitor cell (HSPC) function, suppress erythropoiesis, and disrupt iron homeostasis. Here, we investigated whether IL-1β modulates erythroid lineage development in the bone marrow and spleen and whether it alters iron distribution, thereby contributing to ineffective erythropoiesis and chronic anaemia in SCD.

Methods: Wild-type C57BL/6 (WT) mice received daily intraperitoneal injections of recombinant IL-1β at low (1 ng/mouse) or medium (5 ng/mouse) doses for 15 days. Additionally, homozygous Townes SCD mice (HbSS) and hemizygous control mice (HbAS) were treated with anti-IL-1β antibody (100 ng/animal, intraperitoneally) once a week for three weeks. Reticulocyte counts and erythroid cell populations were analysed in peripheral blood, bone marrow samples, and the spleen by flow cytometry. Erythroid cell populations were identified by flow cytometry using the TER119 and CD71 surface markers, including early progenitors ($TER119^{-}CD71^{+}$), differentiating erythroblasts ($TER119^{+}CD71^{+}$), and late erythroid cells ($TER119^{high}$). Serum IL-6 levels were measured by ELISA. Liver sections were stained with Prussian blue to assess iron and haemosiderin deposition.

Results: WT C57BL/6 mice treated with low or medium doses of recombinant IL-1β for 15 days exhibited dose-dependent effects on erythroid cell development. Low-dose IL-1β reduced blood $CD71^{+}$ reticulocytes and $TER119^{+}$ erythroid cells in the bone marrow, accompanied by an accumulation of early progenitors ($TER119^{-}CD71^{+}$), increased frequencies of proerythroblasts (ProE, defined as $CD71^{high}TER119^{intermediate}$ cells) and less mature erythroblast (EryA, gated $CD71^{high}TER119^{high}$ FSC^{high}) populations. The most mature erythroblast subset (EryC, gated $CD71^{low}TER119^{high}$ FSC^{low}) was also decreased, suggesting impaired erythroid maturation in the bone marrow. In contrast, medium-dose IL-1β decreased splenic ProE and increased mature erythroid cells ($TER119^{+}$, $TER119^{high}$), while reducing EryB ($CD71^{high}TER119^{high}$ FSC^{low} subset) at low dose only. Serum IL-6 levels and hepatic iron deposits remained unchanged across treatments. In the Townes SCD model, HbSS mice displayed elevated leukocyte, reticulocyte and platelet counts, increased IL-6 levels, and disrupted erythropoietic profiles marked by the expansion of ProE, $TER119^{+}CD71^{+}$, and $TER119^{-}CD71^{+}$ populations in the bone marrow, and increased EryA and EryB with decreased EryC in the spleen. Liver sections showed increased haemosiderin deposition. Notably, anti-IL-1β therapy significantly reduced haemosiderin in the livers of HbSS SCD mice.

Conclusion: Together, these findings indicate that IL-1β alters erythroid differentiation in a dose-specific manner, and that IL-1β could represent a potential target for mitigating inflammatory and erythropoietic dysregulation in SCD.

PO21 | The prevalence and characteristics of pica in children with sickle cell disease

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Background: Sickle cell disease (SCD) is a hereditary red blood cell disorder in which pica—ingestion of non-food substances for over a month at an atypical age (>2 years)—is often encountered. Reports on the prevalence of pica and its characteristics among children with SCD are limited. Therefore, this study aims to determine the prevalence of pica in paediatric patients with SCD and to describe the clinical characteristics of children with SCD and pica.

Methods: A retrospective cross-sectional study was conducted using electronic health records of children aged 3–18 years with a confirmed diagnosis of sickle cell disease

(any genotype) attending the Sickle Cell Comprehensive Care Centre of the Erasmus Medical Centre—Sophia's Children Hospital between October 1st 2023, and October 1st 2024, for their annual follow-up visit. Data on patient characteristics, pica behaviour, and laboratory measurements were collected.

Results: Of 112 children attending the outpatient clinic, 96 were eligible for inclusion. At the time of their visit, 25 (26.0%) patients reported having pica currently, and 55 (57.3%) patients had a history of pica. Most consumed substances included paper, sponge, and fabric. Mean age was 8.80 years (SD: 4.23) in the current pica group (72.0% HbSS, 52.0% female) and 10.14 years (SD: 4.54) in the no current pica group (54.9% HbSS, 49.3% female). Children with current or past pica more often had a HbSS/HbSβ^0 genotype (72.0% vs. 54.9%) compared to those who never had pica ($p = 0.041$). Pica was not found to be associated with haemoglobin concentration, iron levels or other clinical characteristics.

Conclusion: This study demonstrates that pica is highly prevalent among children with sickle cell disease, highlighting the need for routine screening and caregiver education. Although the HbSS and HbSβ^0 genotypes are linked to an increased risk of pica, other clinical predictors appear to be absent. Therefore, further research—particularly into psychological and social factors—is essential to better understand why individuals with sickle cell disease are especially prone to developing pica.

PO22 | The economic and clinical impact of aRBCX to manage sickle cell disease in the UK

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Introduction: This study estimated the lifetime clinical and economic impact of paediatric- or adult-initiated automated versus manual red blood cell exchange (aRBCX vs. mRBCX) in two populations (paediatrics initiated aged five and adults initiated mean age 38) with sickle cell disease (SCD). The target population comprises adult and paediatric patients at high risk of clinical complications who are ineligible for, refractory to, or unwilling to undergo hydroxyurea therapy, characterized by a significant risk of severe clinical complications.

Methods: A patient-level simulation model was developed to estimate lifetime quality adjusted life year (QALY) and UK specific healthcare cost outcomes for aRBCX compared to mRBCX. Model parameters, including clinical efficacy, mortality, health-related quality of life (HRQoL) were identified from the peer reviewed literature. Clinical expert opinion informed model parameters and assumptions. Costs were sourced from national databases and published literature and inflated to 2022/23 where necessary.

Monte Carlo simulations were employed to capture variability in patient characteristics, calculate iron overload, clinical events, and survival rates. Baseline characteristics and event probabilities were modelled over a lifetime and since clinical events were not mutually exclusive, a patient's history of clinical events, particularly vaso-occlusive crises (VOCs), influenced subsequent events and mortality rates.

Costs and benefits were discounted by 3.5% as per NICE guidelines. Second-order probabilistic sensitivity analysis was performed for 1000 individuals' lifetimes over 500 iterations. Key outcomes included clinical event frequency, healthcare resource utilization, and associated costs.

Results: Overall, aRBCX is cost-saving for both adult-initiated and paediatric-initiated individuals. Key drivers of cost-savings for both populations are the reduction of months spent on chelation therapy, the reduction in the number of DMTs, and a reduction in acute events.

Among the paediatric-initiated population, aRBCX led to a £112 811 reduction in cost per patient (17.4%) and a QALY gain of 0.29. Disease-modifying transfusions (DMTs) were reduced by 49.1% (283 vs. 557), emergency transfusions by 19% (101 vs. 125), and chelation duration by 93.0% (5 vs. 68 months). The frequency of VOCs decreased by 20.3% (91 vs. 114), with corresponding cost reductions of 21.0% for VOC management and over 94% for chelation therapy.

In the adult-initiated population, aRBCX reduced total costs by £61.85 per patient (a 11.1% decrease) and yielded an additional 0.24 QALYs, driven by better clinical outcomes and reduced resource use. DMTs declined by 49.1% (149 vs. 293), emergency transfusions by 19.2% (56 vs. 69), and chelation duration by 87% (5 vs. 37 months). VOCs decreased by 20.3% (51 vs. 63). These gains translated into £18 433 (21%) in VOC-related savings and £9785 (81%) in chelation cost reductions per patient.

aRBCX is cost-effective in 100.0% of probabilistic sensitivity analysis iterations for both populations, illustrating the results are robust.

Conclusion: aRBCX allows for increased success in achieving clinical targets versus mRBCX, leading to improved control of SCD, fewer exchange procedures, fewer clinical events, and less time on chelation therapy versus mRBCX. There is potential for large cost-savings, allowing funds, hospital beds, and staff time to be redistributed.

PO23 | Engagement with national cancer screening programmes in adults with sickle Cell Disease in England

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Introduction: The life expectancy and overall health of patients with sickle cell disease (SCD) is improving due

to significant improvements in specialist medical care. Older patients with SCD are equally susceptible to age-related comorbidities commonly observed in the general population, independent of their underlying haematological condition. Individuals living with SCD may be at risk of underutilising primary healthcare screening programs, partly due to confirmation bias, whereby new or atypical symptoms are prematurely attributed to their underlying condition by both patients and healthcare providers, leading to inadequate investigation and potential diagnostic oversight. Additionally, there may be a mistaken assumption that the specialist annual review comprehensively addresses all aspects of a patient's health, potentially leading to gaps in routine preventative care and general health screening.

King's College Hospital NHS Foundation Trust has initiated a comprehensive service review project, titled *Ageing Well with Sickle Cell*, aimed at identifying gaps and unmet needs in the care of adults living with SCD. As part of the service review, attention was directed towards taking part in screening for preventable cancers, prompted by reports from the United States indicating alarmingly low engagement rates among individuals with sickle cell disease

Methods: The departmental Governance Committee approved the audit. Patient records were selected from the King's College Hospital cohort in accordance with entries recorded in the National Haemoglobinopathy Registry. We included all patients from the boroughs Lambeth, Southwark and Lewisham whose GPs were connected to the London Care Record (LCR). The LCR is a secure digital system that allows healthcare professionals across London to access patient information from different organisations in one place. Subsequently, patient records were reviewed in accordance with the National Public Health Screening Programme Guidelines to assess evidence of screening invitations and documented attendance.

- Breast cancer screening in female patients aged 50–74 who were invited to and attended mammography
- Bowel cancer screening in patients aged 55–74 with evidence of Faecal Immunochemical Test (FIT) completion
- Cervical cancer screening in female patients with a cervix, aged 24.5–64, with evidence of attendance

Data was collected between September 2024 and January 2025.

Results:

Malignancy	Eligible patients in cohort	Invited for screening	Attended for screening	National non-SCD coverage**	London non-SCD coverage**
Breast cancer	63	38 (60.3%)	25 (39.7%) (66% of invitations)	66.4%	55.9%
Bowel cancer	77	67 (87.0%)	49 (63.6%) (73% of invitations)	67.6%	58.0%
Cervical cancer	117	101 (86.3%)	101 (86.3%)	68.8%	61.6%

**Data represent either 2022/23 or 2023/24.

Conclusion: Overall, participation in the national cancer early detection programmes among the cohort was comparable to the average uptake across London; however, breast cancer screening coverage was lower, both in terms of the proportion of individuals invited and the subsequent attendance following invitation. Data must be interpreted in the context that information from the national screening programmes was documented correctly in the patients' GP records.

PO24 | Co-designing support strategies for parents during the first year following their child's sickle cell diagnosis

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Introduction: Newborn Screening (NBS) in the United Kingdom (UK) allows for presymptomatic identification and early initiation of treatment for babies affected by genetic or congenital conditions including sickle cell disease (SCD). UK standards state a trained healthcare professional should deliver all NBS positive results for SCD to parents face-to-face before 28 days of age. But communication and information provision following a positive NBS for SCD is variable and does not always meet parental needs. Babies with SCD should enter the care of a specialist haemoglobinopathy centre by 90 days of age. High levels of morbidity and early mortality are evident for those with SCD that are not followed and managed optimally. Ongoing support for families can be difficult; fear, distress, and perceived stigma may prevent parents from engaging with healthcare services. We sought to co-design a support strategy for parents during the first 12 months following their child's SCD diagnosis to encourage early engagement with health services.

Methods: Experience-based Co-Design (EBCD) principles guided study design. Parents and professionals were purposefully recruited according to predefined inclusion/exclusion criteria. Semi-structured interviews were conducted with parents and professionals to explore experiences of parental support during the first year following a child's SCD diagnosis. Following this, co-design meetings were held online with parents and professionals who had been interviewed.

Interview data were analysed thematically to inform co-design. Co-design sessions were content analysed to enable development of an animation describing support needs of parents during the first 12 months following their child's SCD diagnosis. Ethical approval was granted by the University Ethics committee (LRS/DP-23/24-41719) and

London City and East Research Ethics Proportionate Review Committee (24/PR/0663).

Results: A total of 18 parents (17 mothers and one father) were interviewed; 17 were carriers (genotype AS), and one mother had sickle cell disease (genotype SS). Parents were recruited via social media ($n = 9$) and two NHS Trusts ($n = 9$), one on London and one in the Northwest of England. Children ($n = 18$), who were the focus of the interview, ranged in age from 6 to 36 months (median 19.5 months). Twelve had the Hb SS genotype and 6 had the Hb SC genotype. Twelve professionals were interviewed who were recruited from two NHS Trusts one in London ($n = 6$) and one in the Northwest of England ($n = 2$), social media ($n = 3$) and via a professional network ($n = 1$).

Five themes from the interviews were used to draft the content of the animation. Two mixed co-design meetings were held with parents and professionals who had taken part in interviews to finalise the content, aesthetic and functional characteristics of the animation. Co-design meetings were facilitated by Nifty Fox Creative. Four parents volunteered to voiceover the animation. A final version of the animation was presented to parent and professionals during a celebration event.

Conclusion: The project demonstrates the value of using a co-design approach with parents and professionals to provide tailored support for parents during the first year following a SCD diagnosis. The resulting animation offers a parent-informed resource to encourage early engagement with healthcare services and address parental emotional and information needs.

PO25 | Patient advocacy in sickle cell research

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Introduction: In the UK, between 12 000 and 15 000 people live with sickle cell,[1] and around 300 babies are born with the condition each year.[2] The condition causes red blood cells to become rigid and sickle-shaped, leading to blockages in blood vessels that can obstruct blood flow and cause extremely painful episodes called sickle cell crises.[3]

Despite how widespread sickle cell is and the severe health impacts it has for affected individuals, it continues to be overlooked in research. Key reasons for this include historical underfunding,[4] racial bias in healthcare systems[5–7] and according to the landmark No One's Listening report, a lack of political and institutional prioritisation.[8] The 2021 report described low awareness of sickle cell amongst healthcare professionals and negative attitudes towards sickle cell patients as factors leading to the "failings in providing joined-up sickle cell care". Urgent changes in the approach to sickle cell care and research were declared.

These findings reinforce what has long been known by the sickle cell community: (1) that investment in sickle cell research is well behind other genetic conditions, contributing to a lack of effective treatments,[9] and (2) the research that has been conducted has often been shaped without the input of the sickle cell community. This gap between researchers and the people affected by sickle cell means that research may fail to reflect the real needs and lived experiences of those it aims to serve.

An added layer to this issue is that sickle cell primarily affects people of Black African and Black Caribbean descent[10]—groups that already experience some of the worst health outcomes across many conditions.[11,12] Excluding these voices from research is not just an oversight. It is a serious matter of health equity.

Without meaningful involvement from the sickle cell community, research may overlook ways to improve care for a group that has long been underserved.

Methods: Recognising this urgent need for a more inclusive, equitable approach to sickle cell research, King's Health Partners and Genomics England launched a collaborative initiative, placing the lived experience of sickle cell patients and carers at the centre. The initiative brought together two patient advocacy groups—the *Kings Health Partners Sickle Cell of Excellence Patient/Carer Group* and the *Genomics England Sickle Cell Patient Voice Group*, both made up of people either living with sickle cell or caring for someone who does. The aim was to co-produce guidance for researchers and institutions on how to work with patient advocacy groups and to define what meaningful, high-quality engagement looks like in practice.

King's Health Partners (KHP) Sickle Cell Centre of Excellence (SCCOE) Patient/Carer group

- The Patient/Carer Group was established in 2024 to contribute to and support the KHP Haematology Sickle Cell Centre of Excellence (collaboration between researchers and doctors across Guy's and St Thomas', King's College Hospital and King's College London). The aim of the SCCOE is excellence in SC education and training, research, and clinical collaboration with patients and carers at the centre.
- The SCCOE is ideally placed to implement the recommendations from this advocacy project. Together we are advocating for more money in SC research and increased awareness of the limited treatment options for this devastating condition.

Patient and carer advocacy groups play a vital role in healthcare and research by representing the voices of people living with a health condition. In the context of sickle cell, patient advocacy groups act as essential intermediaries and bring immense value to the research process by serving as trusted voices for the sickle cell community. They are uniquely

positioned to provide researchers with insight into what matters most to patients, what barriers they face, and what should be considered when designing research studies.

How we worked together

This guidance was created through a series of four two-h discussions with members from the *Kings Health Partners Sickle Cell Centre of Excellence Patient/Carer Group* and the *Genomics England Sickle Cell Patient Voice Group*. Each

session was guided by key questions designed to help people reflect on the reality of living with or caring for someone with sickle cell, as well as the experience of being invited to take part in research studies.

Discussions were open, honest, and full of valuable insights. People spoke about what made them feel genuinely included, as well as experiences that left them feeling like "just another data point". They also shared thoughtful suggestions on how those experiences could be improved, offering practical ideas to help researchers build stronger relationships with sickle cell patient groups and better engage with the wider sickle cell community.

Genomics England Sickle Cell Patient Voice Group

- The Genomics England Patient Voice Group was set up in November 2022 as part of the Diverse Data Initiative, an ambitious programme of work within Genomics England (GEL) aiming to tackle underrepresentation within health data with the goal of supporting equitable outcomes of genomic medicine for all.
- The group was set up so that people with lived experience in the areas that GEL's Diverse Data program were working could contribute by advising GEL about how we went about our research, and to give us feedback about how participant groups were experiencing our program.
- The group has provided valuable support to GEL in enhancing its understanding of sickle cell, offering insightful feedback across a wide range of initiatives. These included reviewing and advising on the Genomics England Sickle Cell webpages, the Improving Black Health Outcomes (IBHO) BioResource Patient Information Sheet, and their sickle cell questionnaire. Additionally, the group has contributed innovative project ideas and collaborated with partners, drawing upon their lived experience and subject-matter expertise. Their involvement has ensured that the voices and perspectives of those with lived experience have been meaningfully integrated throughout the project.

Although the main goal was to create guidance for researchers and institutions, the process evolved into something much more than that. It provided a safe space for peer support and created a meaningful opportunity for learning and sharing between the two groups.

Results: Together, the patient advocacy groups brought with them community-based insights and highlighted the importance of shifting research culture from one that extracts data to one that empowers participation. The shared understanding of patient advocacy groups as critical partners in research set the tone for the conversations, with the consensus that collaboration of this kinds leads to research that is relevant, ethical, and beneficial for both researchers and participants. Throughout the discussions, we explored the importance of researchers engaging meaningfully with advocacy groups from the outset of studies to ensure that they understand the key challenges involved in recruiting people with sickle cell, adopt culturally sensitive approaches, and embody the right attitudes needed to build trust. These conversations drew on the groups' personal experiences and formed the foundation of a rich and thoughtful process.

The outcome of the discussions has been grouped into five themes that describe key areas where group members felt patient advocacy groups can offer valuable insight to researchers throughout the research process. Each theme we identified includes key reflections

from the patient groups on what researchers need to know when working with people affected by sickle cell, along with practical, patient-informed solutions.

Conclusion: This work has been essential in highlighting the critical and influential role of patient advocacy groups in research. While the guidance reported here is grounded in the context of sickle cell, the core principle of community collaboration is relevant across health conditions and research disciplines.

Sickle cell patient advocacy groups are invaluable in helping researchers and institutions design more inclusive, ethical, and patient-centred approaches. Drawing on their own lived experience, patient advocacy groups offer insights that go beyond clinical knowledge, enabling researchers to better understand the realities of living with sickle cell.

Their involvement helps ensure that communication with patients is effective, respectful, and grounded in empathy—key elements for building trust and fostering meaningful collaboration. They can also help researchers and institutions understand the importance of demonstrating credibility and creating accessible opportunities for engagement.

Importantly, sickle cell patient advocacy groups play a crucial role in guiding research design to be culturally competent and to avoid them reinforcing existing disparities. Their input can help shape research protocols so that they are both ethically sound and responsive to the needs of the community.

This approach moves research away from a top-down model towards a truly collaborative process. To uphold ethical standards and ensure that sickle cell research is relevant and impactful, it is vital that researchers and institutions engage sickle cell patient advocacy groups as equal partners from the outset.

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PO26 | Assessing clinician knowledge and confidence in managing patients with thalassaemia in a low prevalence setting

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Introduction: The South West of England (SW) is the largest region in England, spanning over 23 000 square kilometres. It is also a low prevalence area for thalassaemia, with only 70 patients registered to the SW on the National Haemoglobinopathy Registry. Most patients are primarily under the care of the single Specialist Haemoglobinopathy Team in the region, with much smaller numbers under the care of one of the eight Local Haemoglobinopathy Teams (LHT).

This large region with low prevalence offers unique challenges in gaining practical skills of managing patients with thalassaemia, along with difficulties in delivering educational sessions to clinicians who need it. To assess the knowledge and confidence of clinicians in the region we carried out surveys to further characterise the regional need.

Methods: Clinicians within the SW were identified from previously established databases used by the SW Haemoglobinopathy Coordinating Centre. Two surveys were developed—one for clinicians in general practice (GP survey), and one for staff members involved in LHTs including consultant haematologists and specialist nurses (LHT survey). These surveys were distributed by email.

Results: In total there were thirty responses to the surveys (12 responses to GP survey, 18 responses to LHT survey), encompassing a range of clinicians across the entire SW region.

When asked how confident they feel in managing patients with haemoglobinopathies including thalassaemia, the GP survey revealed that the respondents measured their confidence at a mean of 3/10 (range 1–6/10). 92% of respondents had not had any formal education on haemoglobinopathies in the past 3 years. 100% would find further education helpful.

The LHT survey showed that 72% of respondents encounter patients with thalassaemia once every 3 months or less frequently. The mean self-reported confidence in managing chronic complications of thalassaemia was 4.5/10 (range 1–9/10) and for acute complications was 4/10 (range 1–9/10). Respondents were on average slightly more confident with managing iron chelation, with a mean of 5/10 (range 1–10/10). 67% of participants had one or two educational activities dedicated to thalassaemia in the last year and 33% had none.

Conclusion: These survey results highlight a large unmet need within clinicians in the South West. Provision of high-quality education on thalassaemia in low prevalence areas is critical to ensure that clinicians maintain a high level of confidence when they see patients with thalassaemia.

Following on from this, we are in the process of arranging a full educational day on thalassaemia along with The Red Cell Network. We plan on repeating the survey following the education day to assess the impact of this intervention. We also plan to link to thalassaemia teaching resources on our website which should increase the accessibility to thalassaemia related education for clinicians in our region. We would encourage other regions to complete similar surveys with their LHTs and regional GP practices to assess learning needs and confidence levels across the region.

PO27 | QIP on improving clinical outcomes for sickle cell patients by using the ACT NOW acronym

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Introduction: Sickle cell disease (SCD) is a serious chronic inherited haemoglobinopathy in which acute vaso-occlusion from the abnormal red cells results in painful crisis and potentially life-threatening complications. It affects over 17 000 people in England.

Patients with SCD frequently report delays in pain management, lack of compassion and substandard care during crisis. In response to the recommendations outlined in the No One's Listening report, the ACT NOW acronym which outlines key steps in emergency care was co-created by clinical experts and patients to improve sickle cell crisis management.

Our aim is to enhance awareness and knowledge among doctors in the Emergency Department and Medical Clerking team in managing sickle cell crisis, with the goal of improving patient care quality and improving clinician confidence through the introduction of the ACT NOW acronym. Although SCD is relatively common across the UK, Derriford Hospital—which serves Plymouth and the surrounding area—has only 14 SCD patients. This lack of opportunity for practical experience makes it important to improve education and awareness among staff at our hospital to ensure better care for patients presenting with painful crisis.

Methods: An initial survey of 37 doctors was conducted, followed by a re-survey involving 32 doctors from the Emergency Department and medical clerking team. Interventions included dissemination of ACT NOW educational cards (with QR codes to access further information), teaching sessions, posters across departments, and creating easy access to the material via the hospital intranet. Follow-up data were collected after 5 months of interventions.

Results: Most survey respondents (70%) reported rarely or never managing patients with SCD. Key clinical outcomes showed that awareness of timely administration of analgesia within 30 min of initial presentation improved from 94% to 96%, knowledge of pain reassessment every 30 min improved from 43% to 71%, and awareness of the correct supplementary oxygen threshold improved from 24% to 65%. Most participants (87.5%) recognised infection as a potential trigger for painful crisis, but cold exposure was less well recognised (71.8%). Confidence with managing sickle cell crisis was similar in the pre- and post-survey (pre 30% "somewhat" or "very confident", post 28%).

Conclusion: A focused educational intervention using the ACT NOW acronym effectively improved knowledge in managing sickle cell crisis.

81% of respondents found the ACT NOW acronym helpful, reporting improved clinical knowledge in sickle cell crisis management. Additionally, 100% of respondents indicated that the introduction of an electronic prescription order set would further enhance care quality and consistency. A key barrier encountered was high staff turnover and variability in rota schedules which may impact the sustainability of our interventions. To address this challenge, we plan to implement scheduled teaching sessions on an annual basis, aiming to embed them into routine training and promote long-term sustainability.

We identified that confidence did not increase between the pre- and post-survey. This reflects the fact that although educational interventions are helpful to improve knowledge, confidence must be built through clinical experience. Placements in high prevalence areas for emergency department staff in low prevalence areas could be a possible idea for future improvement.

PO28 | Trainee-led service improvement—Developing our south west haemoglobinopathy coordinating centre

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Introduction: Haemoglobinopathy Coordinating Centres (HCC) were established in 2019 as part of NHS England's development of Specialist Haemoglobinopathy Services which aim to standardise care for haemoglobinopathy patients. The South West of England faces a unique challenge in that the HCC covers a very large geographical area (covering around 23 000 km^2) with a low prevalence of haemoglobinopathy patients (around 400 patients between adults and paediatrics). Many of the local haemoglobinopathy teams (LHTs) across the region have very small patient numbers, meaning that it can be challenging to build local expertise and their service. In September 2024, the HCC employed a registrar-level Haemoglobinopathy Quality Improvement (QI) Fellow (full time 40 h per week) for one year to attempt to overcome some of these challenges. This role has allowed the haematology specialist registrar to become involved in regional leadership, service improvement and innovation.

Methods: Baseline data was collected from LHT clinicians by carrying out Teams interviews using a structured questionnaire. Changes were implemented using QI methodology where possible.

Results: LHT clinician interviews revealed a lack of dedicated time and resources for haemoglobinopathy patients. Only 25% of sites have a named haemoglobinopathy CNS and dedicated haemoglobinopathy clinic. 25% of sites provide haemoglobinopathy education within their department, but 0% of sites provide education outside of the haematology department. 62.5% of sites have a local acute management guideline. 100% of LHTs felt they would benefit from easier access to SHT guidelines.

Based on the results of LHT interviews, multiple changes were introduced. Virtual annual review clinics with the specialist team and LHT were established across five sites to reduce the patient's need to travel long distances whilst also receiving specialist input. We increased the reach of patient and public involvement events to also include regional patients, meaning that those across the region would have improved access to research. A network website was set up to allow for universal access to up-to-date guidelines for treating teams across the region without requiring log-in details to view them. An audit programme was developed, including devising ways to involve LHTs in audit and quality improvement (eight mandatory audits based on UKFHD Quality Standards v5.1, specialised services quality dashboards and care standards). Lastly, we have rolled out a dedicated haemoglobinopathy educational programme with pre-recorded sessions, online training packages, in-person training days and recruitment of a regional practice education facilitator. Teaching sessions have been provided to over 350 clinicians in the region to date.

Further areas for quality improvement have been identified including joint specialty clinics and nurse-led hydroxycarbamide clinics.

Conclusion: The development of this quality improvement fellow post provided benefits for both the regional service and the trainee. Other regions could consider introducing similar roles to provide an excellent opportunity for career development for the trainee, and service improvement for the HCC. Creating new posts such as this increase interest in haemoglobinopathy and build into the future sustainability of the service by training junior colleagues to become specialists in the field.

PO29 | Overcoming inequalities in access to specialist haemoglobinopathy care across the south west of England

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Introduction: The South West is the largest region in England, spanning over 23 000 square kilometres. There are 440 haemoglobinopathy patients registered in this region on the National Haemoglobinopathy Registry (NHR). 110 patients (25%) are primarily cared for by 8 local haemoglobinopathy teams (LHTs) in the region.
In October 2024, our data showed that only 5 (4.5%) of patients had an annual review with the Specialist Haemoglobinopathy Team (SHT) either locally or elsewhere. This represents a significant unmet need within the regional patients who do not have equivalent access to care as those located near the SHT.
We aimed to identify the costs (financial and time burden) associated with different types of appointments including online, face-to-face (F2F) hybrid (patient at LHT with local clinician, SHT joining on Teams) or fully in person at SHT site for patients across the region. We used this information along with other factors (clinician preference, LHT opinion, patient feedback and other practical considerations) to decide how to provide specialist annual reviews to patients across the South West.
Methods: The financial cost and time burden associated with the different appointment options was assessed using online tools including mileage calculators, train/bus fare websites, hospital parking charges and average pay as you go data costs.
Patient and LHT clinician opinion was sought through structured interviews conducted over Microsoft Teams. Following the pilot clinic period, patient feedback was obtained with an online survey.
Results: The average cost and travel time associated with each type of appointment was:

- **Online meeting**—£6.11 for 1GB pay as you go data. No travel time
- **F2F hybrid in LHT**—bus £6.43, car with parking £6.84—likely 30–45 min travel time
- In person at SHT
  - Train £44.73 (range £10.30–£103) average travel time 1 h 10
  - Car £29.65 (range £8.60–£57.18) average travel time 1 h 45.

In patient interviews, we found that patients would value SHT input and preferred having a formal annual review once per year. Patients would like the option of choosing the type of appointment that they have but would prefer not to need to travel.
The SHT clinician attending the LHT for in person annual reviews was also felt to be challenging and unsustainable due to the significant time burden associated with travelling to the LHT sites.
As of 21st May 2025, nine patients have been reviewed in joint clinics and 11 patients are scheduled for upcoming appointments. This represents 18% of regional patients.
Conclusion: There are significant financial and time burdens associated with attending the SHT for in person annual review in the South West of England—with travel from LHTs costing up to £103 and taking up to 3 h each way to travel. We have addressed this by setting up virtual annual review clinics, giving each LHT the option to run either hybrid F2F or online clinics.
We have completed a pilot period of joint regional annual reviews with excellent feedback and satisfaction. Patients explained that they found the appointments easy to attend and were highly satisfied with the input from the SHT. LHT clinicians found it useful to be able to address complexities of the cases within the clinic appointment.
We are now in the process of setting up a sustainable model for joint annual review clinics going forward with the aim of establishing joint annual review with the SHT for 100% of patients in the region.

PO30 | Trouble in the air: A case of aspergilloma in a child with sickle cell disease

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Introduction: Sickle cell disease is a systemic condition often complicated by respiratory issues such as acute chest syndrome, asthma, pulmonary hypertension and restrictive lung disease. The chronic inflammatory milieu increases patients' vulnerability to infections, which may trigger vaso-occlusive crises. Fungal infections in sickle cell disease are rarely reported.
Results: An 8-year-old boy with sickle cell disease, was admitted to our department for cholangitis associated with a viral illness, which responded to intravenous antibiotic therapy with ceftazidime and metronidazole. During this episode, hydroxycarbamide was suspended. Until that point, therapy had effectively controlled the disease without the need for exchange transfusions.
A chest X-ray performed on admission revealed an opacity in the right lung apex. CT imaging showed a cavitary, air-filled lesion with a thick contrast-enhancing wall and associated ipsilateral lymphadenopathy. Both the Quantiferon and Mantoux tests were negative, and there was no family history of tuberculosis or recent travel.
Bronchoalveolar lavage (BAL) tested positive for *Aspergillus fumigatus*, while testing was negative for Mycobacterium (PCR, microscopy, and culture), *Pneumocystis jirovecii*, Galactomannan antigen, and Candida mannan. The serum beta-D-glucan test was positive. Based on the imaging

findings and microbiological results, a diagnosis of pulmonary aspergilloma was made.

Voriconazole therapy (14 mg/kg/day; initially intravenous, then oral) was started with close clinical, biochemical, and electrocardiographic monitoring. After 2 months of well-tolerated treatment, follow-up chest CT showed thinning of the cavity wall, which no longer enhanced with contrast, and resolution of lymphadenopathy. BAL and serum beta-D-glucan tests were negative. Antifungal therapy was continued for a total of 12 weeks.

To avoid confounding potential signs of hepatic toxicity, Hydroxycarbamide was reintroduced after 2 months of well-tolerated antifungal treatment.

Conclusions: *Aspergillus* infections are typically seen in immunocompromised patients and are associated with significant morbidity and mortality. Although our patient is immunocompetent, his underlying condition involves chronic inflammation and increased susceptibility to infections. Additionally, he had been receiving hydroxycarbamide, a cytoreductive drug that may lower leukocyte counts.

To our knowledge, this is the first reported case of pulmonary aspergilloma in a paediatric sickle cell patient with no prior history of acute chest syndrome or significant pulmonary infections.

Evidence in the literature is limited and asymptomatic aspergillomas in immunocompetent individuals may sometimes be managed conservatively with radiologic follow-up. In this case, given the patient's underlying hematologic condition, antifungal therapy was initiated and led to clear clinical and radiological improvement. Treatment was continued for 12 weeks, consistent with recommendations for invasive aspergillosis, although no standard minimum duration is currently defined for isolated aspergilloma.

An open question remains regarding the origin of the pneumatocele colonized by *Aspergillus*, and the most appropriate management of the residual cavity.

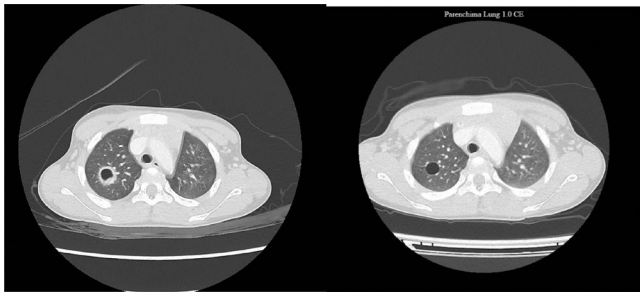

FIGURE 1 Left: baseline CT scan showing a cavity with contrast-enhancing walls. Right: follow-up scan after 2 months of therapy.

PO31 | Understanding sickle cell disease: Knowledge and educational needs of rural–urban communities in Kaduna, Northern Nigeria

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Introduction: Sickle cell disease (SCD) presents a significant public health challenge in Nigeria, particularly in Kaduna State, where the sickle cell trait prevalence is estimated at 20%–25%. Despite this burden, many affected individuals and caregivers lack knowledge and access to specialized information, thus; delayed treatment and increased morbidity. This study aimed at understanding knowledge level of SCD, identify available and preferred educational materials and information sources in rural-urban communities.

Methods: A short empirical study was conducted, involving 60 adult SCD patients and caregivers (29 rural, 31 urban) from Gubuchi (rural) and Samaru (urban) communities in Kaduna State. Data were collected using questionnaire, employing purposive sampling for participant selection. Mean, frequency and percentage analyses were undertaken using Statistical Package for Social Sciences software version 25 and Microsoft Excel, 2016.

Results: Demographically, rural participants were predominantly caregivers (75.9%), married (69.0%), and had lower education levels (37.9% secondary, 31.0% religious). Urban participants were more of patients (51.6%) and caregivers (48.4%), predominantly single (51.6%), and highly educated (96.8% tertiary). The majority 75.9% of rural and 96.8% of urban participants correctly identified SCD as an inherited blood disorder. In terms of cure, 51.7% of rural and 61.3% of urban respondents correctly stated SCD is not curable, a notable proportion still believed it could be (rural: 31.0%; urban: 25.8%). Pain and Fever were consistently recognized as common symptoms in both settings.

Regarding educational materials, 75.9% of rural and 90.3% of urban participants reported receiving them, primarily from hospitals. Print materials (brochures/leaflets) were widely received, but urban areas had greater access to online resources and videos. Short videos (4.6 $\bar{x}$) were highly preferred in rural areas, while print materials (4.5 $\bar{x}$) were most preferred in urban areas. Rural communities largely preferred local languages (58.6%), whereas urban communities favored English (64.5%). Major barrier to access is lack of awareness of material location (rural: 4.3 $\bar{x}$; urban: 3.9 $\bar{x}$), low literacy levels in rural areas (3.9 $\bar{x}$).

Conclusion: Significant disparities in SCD knowledge and educational resources access exist between rural and urban communities in Kaduna State. Basic understanding of SCD is fair, misconceptions persist, especially rurally. Therefore, effective interventions require culturally and linguistically sensitive materials, favoring short videos and local languages in rural areas, and online resources and English in

urban. Addressing awareness gaps, literacy and proactive distribution by healthcare providers is key to improved SCD management and quality of life among affected populations.

PO32 | Health by stealth: Improving awareness, engagement and wellbeing for families living with red cell disorders

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Introduction: Children and young people (CYP) with SCD are often marginalised and impacted by social determinants of health including disparities in healthcare access. Pain episodes, hospital attendances, poor access to care and racism are some factors that affect quality of life in SCD.
We describe a program employed by The Red Cell Network to improve engagement and enhance holistic care for CYP with red cell disorders. Quality improvement methodologies were employed to ensure continuous improvements. By collaborating with a professional health coach with lived experience of SCD CYP/parents benefitted from personalised and peer support to improve well-being.
Methods: Via two community events and a holistic wellbeing online course we were able to improve access to information using a "health by stealth" approach. An initial fun event was planned, co-created with CYP/parents, in collaboration with community and third sector partners.
The first event (June 2022) was hosted at Tottenham Hotspur Football Club. Alongside health information were a range of activities including DJ, celebrities, B-Positive choir and games. Benefits included peer support for parents, expert panel Q&A, health promotion stalls; including dental health, research and SCD information. Feedback was collated via in-person and online forms and interviews. In response to feedback a second event at London Zoo in October 2024 included CYP with thalassaemia/rare anaemias.
Alongside, a virtual wellbeing program was designed and delivered. Initially for adults it was co-created with the health coach. Six weekly sessions covered mental well-being, physical health management strategies, and community-building activities. Feedback highlighted barriers to access and consistent engagement. Timings were adjusted and participants offered a WhatsApp group to facilitate engagement.
Following incorporation of this feedback a four-week course ran on Saturday mornings for people with SCD with WhatsApp support. Participants reported feeling 'very confident' about applying what they had learned into daily life. They were also 'very likely' to recommend the program to a friend. An amended course for parents/carers was designed running for 4 weeks on Saturday mornings. Whilst numbers were small those that attended valued the opportunity to take time for themselves as carers.
Results: 123 adults and 153 CYP attended the event at Spurs in 2022. Key themes emerging from feedback included the need for greater community support, improved accessibility to healthcare resources and professionals, and more frequent engagement opportunities outside of clinical environments. 104 CYP and parents/carers attended the second event at London Zoo in October 2024. 21 people have gone through the wellbeing courses.
Parents reported time pressures associated with caring for ill children made consistent attendance difficult. Suggestions of 'drop-in' sessions are being considered to address this issue.
Conclusion: The findings highlight the accessibility and importance of culturally tailored, community-based approaches in addressing health inequalities and improving engagement for CYP with inherited blood disorders. While more work is needed to improve uptake of the wellbeing course, this initiative demonstrates the value that can be gained from being part of a strong support network and supporting well-being through non-medical interventions.

PO33 | The 'αO2-PRBCThal' trial on the use of Hemanext One® for blood transfusion support in thalassemia

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Introduction: Patients with transfusion dependent thalassemia (TDT) are regularly transfused every 2–4 weeks. Red blood cells (RBCs) storage processing aims to preserve the RBCs' properties. Long-term storage leads to donor-dependent biochemical and morphological changes in RBCs, collectively termed as "storage lesions". The HEMANEXT ONE RBC Processing and Storage system limits oxygen, which fuels oxidative damage, aiming in preserving high quality RBCs over longer storage time. HEMANEXT ONE has not been studied in chronically transfused individuals. The aim of our study is to investigate whether RBCs' storage under hypoxic conditions with the HEMANEXT ONE method is at least non-inferior to standard methods in providing transfusion support to TDT patients.

Methods: The trial will include adult patients followed at the Thalassemia Units either of the First Department of PediatricsNKUA or at the LAIKON General Hospital. Patients need to fulfil the following criteria: (i) documented diagnosis of β-TDT defined as receiving ≥6 RBC units/24 weeks and no transfusion-free period for ≥42 days during 24 weeks, (ii) available transfusion history for at least 6 months (iii) chelation and other chronic therapies at a stable dose, all for at least 6 months prior to enrollment.
The study aims to assess changes in the transfusion burden, the degree of hemolysis and the presence of metabolic disturbances. The Primary Endpoint is defined as changes from baseline in RBC transfusion burden, with changes differing at >20% (corresponding to at least 1 unit/24weeks) from baseline being considered significant. The treatment phase consists of six months, during which the patient will receive PRBC prepared by HEMANEXT ONE methodology and this will be compared to a period of receiving RBCs stored by standard methods.
The study follows a sample verification analysis that provided evidence for the high quality of RBC's stored with the HEMANEXT ONE method.
Results: Two sites in Greece will participate in the trial and the targeted enrollment is 30 evaluable patients. Enrolment is expected to be completed by Q4, 2025.
Conclusions: Overall, hypoxic storage seems to offer advantages in mitigating oxidative stress, without promoting RBC lysis. The 'αO2-PRBCThal' trial may provide evidence that the HEMANEXT ONE RBC storage method is both safe and able to provide transfusion support to TDT patients without increasing the transfusion burden, the degree of hemolysis and the metabolic disturbances.

PO34 | Beyond cardiac mortality: The distinct pathway of hepatocellular carcinoma in hemoglobinopathies

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Introduction: Hepatocellular carcinoma (HCC) is responsible for the rising mortality rate in hemoglobinopathies, especially thalassemia. Even though, heart failure or other complications are major contributing factors to overall mortality HCC exhibits a unique clinical profile. The present study defined HCC-related mortality risk and compared it to other fatal events in Greek patients with hemoglobinopathies.
Methods: Three national hemoglobinopathy medical facilities evaluated 99 deaths from 2012 to 2023. Thirteen patients (13.1%) died from HCC. Demographic, clinical, endocrine, virological, iron-related, and pharmacological aspects of 86 non-HCC fatalities were compared. Multivariate logistic regression, chi-squared tests, and *t*-tests were used.
Results: Hepatocellular carcinoma (HCC) resulted in 13 of the 99 total deaths (13.1%), while heart failure represented the most common cause, with 46 deaths (46.5%), followed by 40 deaths (40.4%) due to various other causes, such as infections, malignancies, cerebrovascular disease, renal failure, and thrombotic events. Although HCC was less prevalent than heart failure, it revealed a considerably distinct clinical and epidemiological profile. In contrast to heart failure and the broader category of deaths classified as other causes, which affected patients across all genotypes—including thalassemia major, thalassemia intermedia, HbSS, HbS/β-thalassemia, HbH disease, and δβ-thalassemia—HCC-related mortality occurred almost exclusively in patients with thalassemia. Specifically, 8 of the 13 hepatocellular carcinoma (HCC) deaths (61.5%) occurred in patients with thalassemia major, 4 (30.8%) in thalassemia intermedia, and 1 (7.7%) in a patient with sickle cell anemia (HbSS). Notably, no cases of hepatocellular carcinoma (HCC) were observed among patients with HbS/β-thalassemia, despite their high prevalence in the total mortality population (33.3%).
The mean age at death did not differ significantly among groups (53.9 ± 8.96 years for HCC, 55.0 ± 12.99 for non-HCC deaths). However, HCC deaths were strongly associated with specific clinical features. HCV infection was present in 92.3% of HCC cases, compared to only 18.2% in non-HCC deaths ($p < 0.001$). Notably, hypogonadism was observed in 81.8% of HCC patients versus 27.8% of others ($p < 0.001$), and splenectomy had been performed in 84.6% of HCC patients, significantly higher than the 43% in non-HCC deaths ($p = 0.005$). In terms of iron burden and treatment exposure, patients with HCC had received iron chelation therapy for significantly longer periods (mean duration 36.3 ± 15.1 years) compared to non-HCC patients (21.7 ± 16.6 years, $p = 0.007$), although ferritin and LIC values at the time of death did not differ significantly between groups. Hydroxyurea use was significantly lower among HCC patients (10% vs. 49.4%, $p = 0.018$), while testosterone replacement therapy was more frequently observed (50% vs. 30.9%), with no statistical significance.
Conclusions: HCC in patients with hemoglobinopathies follows a specific pathogenic pathway, manifesting primarily in thalassemi syndromes. It is characterized by a strong correlation with chronic HCV infection, endocrine dysfunction (particularly hypogonadism), prior splenectomy and prolonged exposure to iron chelation. Its clinical presentation contrasts significantly with the typical presentation of other complications and its genetic profile is not consistent with that of other genetic profiles in the medical literature.

PO35 | Reduced six minute walk distance is associated with end organ damage in sickle cell disease

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Introduction: Dyspnea and reduced exercise capacity is common in adults with sickle cell disease (SCD); the etiology is often multi-factorial. Six minute walk testing (6MWT) is easy to perform and allows for assessment of exercise capacity and ambulatory oximetry. We hypothesized that patients with SCD and end organ dysfunction will have lower 6MWT distances and higher frequency of oxygen desaturations than those without end organ dysfunction. We used the baseline clinical data from the STERIO-SCD prospective, randomized placebo-controlled Phase 1–2 clinical trial of riociguat[1] for treatment of high-risk patients with SCD to investigate this hypothesis.

Methods: Data were obtained as part of the multi-center STERIO-SCD clinical trial. Eligible patients were 18 years or older with SCD confirmed by hemoglobin (Hb) electrophoresis or HPLC fractionation (all SCD genotypes), and at least one of the following high risk criteria (HRC): (1) elevated systolic blood pressure ≥130 mmHg on at least 2 occasions, (2) an elevated tricuspid regurgitant jet velocity (TRV >2.9 m/s) or (3) proteinuria. 6MWT with oximetry on room air was performed utilizing standard protocols. In this descriptive analysis, we characterized baseline clinical values in the cohort by computing means and standard deviations or counts and proportions for continuous and categorical variables, respectively. These summary statistics were computed for the full cohort and separately for patient subgroups defined by the number of HRC the patients met.

Results: 114 patients were enrolled in STERIO-SCD; the mean age was 43.1 ± 12.0 years, 51.8% were female and 71.1% had HbSS disease. The mean Hb for the cohort was 9.2 ± 1.9 g/dL; 45.3% had Stage 1 hypertension, 14.7% had an elevated TRV and 35.1% had proteinurea. 75 (65.8%) had one high risk criteria (HRC), 35 (30.7%) had two and four (3.5%) had three. The overall cohort had a mean 6MW distance of 396.6 ± 145.3 m and was reduced compared to the non-SCD population (normal 400–700 m depending on age, sex and height). Larger number of HRC criteria met were descriptively associated with shorter 6MW distance and lower post-6MWT oxygen saturations (Table 1).

Conclusion: Patients with sickle cell disease and systemic hypertension, an elevated TRV and/or proteinurea reflective of end-organ damage exhibit lower exercise capacity and ambulatory oxygen saturations. Lower exercise capacity and hypoxemia corresponds with greater degree of organ dysfunction. This suggests that end organ disease limits functional capacity in patients with SCD and that 6MWT is a way of identifying higher risk patients.

TABLE 1 Six minute test walk distances and post six minute walk oxygen saturations*

Number of high risk criteria	1	2	3
Six minute walk distance (m)	416.7 ± 158.6	359.8 ± 92.6	328.0 ± 197.1
Oxygen saturation post-6MWT (%)	96.6 ± 3.5	96.5 ± 3.7	88.0 ± 11.1

* Data presented as mean ± standard deviation. 6MWT: Six minute walk test

PO36 | Access to curative therapies for sickle cell disease

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Introduction: Sickle cell disease (SCD) is an inherited blood disorder that results in hemolysis and intermittent episodes of vaso-occlusion, which can progress to severe organ involvement. It is a lifelong illness and associated with significant morbidity and early mortality. Given the disease burden, curative therapies with bone marrow transplantation (BMT) have been considered, particularly in patients with severe disease in childhood. However, there are still significant limitations including a limited donor pool. In December of 2023, the FDA approved two new gene modification therapies to help address this gap. These transformative therapies offer the opportunity to overcome the donor barriers and represent a potential breakthrough in SCD treatment. In this study we aimed to determine how the patients in our clinics have approached these new therapies with their treatment teams. We examined potential barriers patients may face when considering such transformative therapies.

Methods: We conducted a retrospective IRB-approved observational study at the Levine Cancer Institute and Wake Forest School of Medicine. Using our patient databases, we identified patients with SCD seen from December 8th, 2023 to May 31st, 2024 who had discussed BMT and gene modification therapies with their clinical teams. We extracted demographic and clinical information as well as medical and socioeconomic barriers to curative therapies and analyzed these data with descriptive statistics. Continuous variables are reported as means, medians and ranges while categorical variables are

reported as frequencies and percentages. Fisher's exact test was utilized for categorical variables, and the Wilcoxon rank-sum test was utilized for continuous variables.

Results: Of 999 patients identified, 379 (37.9%) had discussed BMT and gene therapy with their clinical teams. Patients who discussed transformative therapies were significantly younger than those who did not (median age 13 vs. 27 years, $p < 0.0001$). Patients with the SS and $S\beta^0$ genotypes were significantly more likely to have discussed these therapies than those with other genotypes (80.7% vs. 58.1%, $p < 0.0001$). The majority of patients (78.9%, 296 of 375) who discussed transformative therapies with their clinical teams were interested in further discussions. Only 12.8% were candidates for BMT based on the availability of matched sibling donors. Additionally, 14.4% of patients expressed concerns about potential organ dysfunction and whether their organs could tolerate the chemotherapy required for BMT or gene modification therapy. Other commonly identified barriers were limited social support (23.5%), financial concerns (12.2%), and adherence to treatment (29.3%).

Conclusion: Our data indicate that a substantial proportion of patients with SCD receiving care at our institutions are interested in curative therapies. However, both medical and socioeconomic barriers limit eligibility and access. Notably, lack of a matched sibling donor and concerns about organ tolerance to high doses of chemotherapy are major limiting factors. Particularly alloimmunization, renal function, and management of iron overload will be key for future success. Additionally, socioeconomic concerns also remain as key barriers to access. These insights underscore the need for targeted patient education, enhanced resource allocation, and systemic efforts to reduce disparities and expand access to BMT and gene therapy for patient with SCD.

PO37 | Congenital erythrocytosis caused by hemoglobin San Diego: A case report and review of the literature

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Introduction: It is well known that high oxygen (O_2) affinity hemoglobin (Hb) variants may be related with hereditary erythrocytosis. Hb San Diego, first described in 1974, is caused by a β-globin chain substitution (Val109 → Met), which shifts the O_2 dissociation curve to the left, reducing O_2 delivery and therefore stimulating erythropoiesis. The causative HBB gene variant derives from a base substitution (GTG>ATG) in CD109 (HBB:c.328G>A). A case of congenital erythrocytosis caused by Hb San Diego is reported.

Methods: A case of hemoglobin San Diego related erythrocytosis is reported, based on data from the patient's medical records. Molecular diagnosis was performed by Sanger Sequencing.

A search in PubMed identified 19 publications on hemoglobin San Diego, dated from 1974 to 2020 and a brief review is provided.

Results: A male, non-smoking patient of Japanese and Greek descent had been referred to a hematology outpatient clinic at the age of 28, after cholecystectomy, due to persistent erythrocytosis. CBC: Hb 18.7 g/dL, Hct 56%. WBC 7580/μL, ANC 3700/μL, lymphocyte count 1200/μL, PLTs 235 000/μL, LDH 195 U/L (within normal ranges).

The patient reported asymptomatic hematocrit elevation from the age of 15. Family history was negative for erythrocytosis. Imaging studies (abdominal ultrasound) revealed hepatic steatosis without splenomegaly. Erythropoietin (EPO) levels were within normal range. Molecular testing for JAK2 V617F and exon 12 mutations was negative. Two consecutive bone marrow biopsies reported no features of polycythemia vera and cytogenetics were normal. EPO receptor gene testing was negative. Sleep apnea study revealed apnea episodes of mild severity without significant O_2 desaturation.

The patient was administered clopidogrel per os and underwent phlebotomies every 1–2 months, maintaining Hb around 15.8 g/dL and Hct 51%. No thrombotic events were recorded and brain CT was negative for ischemic findings. The patient was finally referred for further investigation to an expertise center for hemoglobinopathies. HPLC electrophoresis did not detect a pathologic Hb variant, but molecular testing identified Hb San Diego variant in heterozygous state.

Since the proper diagnosis was made, clopidogrel and phlebotomies were discontinued.

Hb San Diego has been reported in North America, Europe, Asia and Middle East. Most cases were asymptomatic and identified during routine testing or thrombosis workup. Common findings included:

- Hb 17.5 – 21 g/dL, Hct >55%
- Normal WBC and PLT and EPO levels
- Low P_{50} values (15–18 mmHg)
- Absence of splenomegaly or myeloproliferative features

Cases with compound heterozygosity (e.g., with HbS or β-thalassemia), lead to more complex phenotypes. Management is generally conservative unless symptoms or thrombotic events have occurred.

Conclusion: Our patient presents a typical clinical course: early-onset erythrocytosis, absence of thrombotic events, and a benign hematologic profile, all attributable to a congenital, high O_2 affinity Hb variant.

Proper diagnosis is essential to avoid inappropriate management (phlebotomy or cytoreductive therapy), in asymptomatic patients with erythrocytosis. In cases where polycythemia vera has been excluded, further diagnostic

work-up for congenital erythrocytosis is required. Molecular testing of globin genes should be encouraged since some high O_2 affinity Hb variants are not detectable in HPLC. Family screening is also advised given autosomal dominant inheritance.

PO38 | Sickle cell disease in Greece: A different landscape; the experience of a center of expertise

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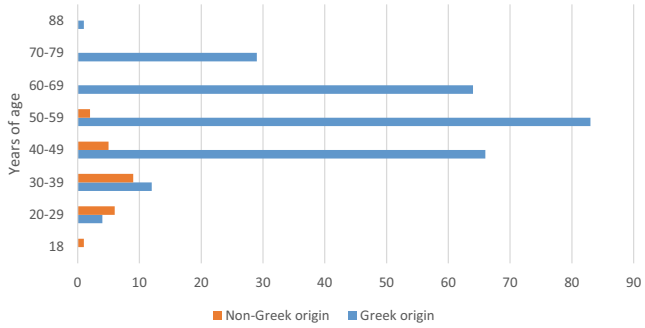
Introduction: Sickle cell disease (SCD), the most common inherited blood disorder worldwide, poses a significant global health burden, that has been unrecognised until recently. The impact on the physical and psychological health of patients (pts) as well as economic and social consequences are as big as the differences in management among different healthcare systems across the globe. In Greece the estimated frequency of SC trait (SCT) is 1%–2% and the expected annual birth rate has been estimated at 66 per 100 000 births. The total number of SCD pts in the country was 1032 in a national registry, last updated in 2015.
The aim of this study is to depict the management of sickle cell in Greece, including prevention and treatment.
Methods: The structure and the strategies implemented by a public Prevention Network that covers the whole country are presented and the results are evaluated for a 10-year period. Carrier screening is performed by established methods (full blood count, HPLC, sickling test). Molecular diagnosis is based on traditional diagnostic methods and is performed centrally, in the laboratory of the Coordinating Center of the Network.
A Clinical Department of the Coordinating Center is dedicated to SCD treatment and data on management and are also reviewed.
Results: The Prevention Network for hemoglobinopathies, introduced decades ago, consists of 14 Prevention Units for carrier screening across the country, especially in areas with high frequency of heterozygosity, and is coordinated by a Reference Centre located in the capital of the country. Common diagnostic algorithms are applied in all Units and when couples of parents at risk of having an affected baby are identified genetic counselling is offered, including prenatal diagnosis options.
From 2014 until 2023 129 817 individuals were screened for hemoglobinopathies and 1776 SCD carriers and 12 035 β-thalassemia carriers were identified. The frequency of SCT raised from 1% in 2014 to 1.9% in 2023, and it was higher in big cities. In the same period 1593 prenatal fetal diagnostic samples were analyzed for severe forms of thalassemia and SCD. Parents of the fetuses were mainly of Greek origin, but also of foreign/immigrant origin, including Albania (highest percentage 5.7%, 2022), Sub-Saharan Africa (highest percentage 2.5%, 2022), Balkans, Middle East, Asia, and Latin America (<2.5% annually). Prenatal fetal diagnostic testing identified 63 cases of SCD during this decade. Annual affected SCD births in Greece are steadily <5 during this period.

Figure 1: Number of patients per age group, distributed according to Greek or non-Greek origin



In the Clinical Unit of the Coordinating Center 282 SCD pts are followed. The majority of pts (185/282, 66%) are on hydroxyurea (HU) treatment only, whereas 45/282 (16%) are on HU and regular transfusions, 14/282 (5%) on regular transfusions only and 38 (14%) receive no disease modifying treatment. The number of patients per decade of age and origin is shown in Figure 1. The majority of pts (63.5%) are ≥50 years old. Most pts younger than 30 years are immigrants of non-Greek origin.
Conclusions: Prevention strategies targeting new affected births can reduce the burden of SCD at a national level. Younger SCD patients are mainly of non-Greek origin. Optimal treatment has significantly prolonged survival in SCD. Combined prevention and treatment strategies and equal access to public health services, free of charge, a core element of rare disease management, results in disease burden amelioration both in native and immigrant populations.

PO39 | Evaluating manual and automated RBC exchange in pediatric sickle cell disease: A Portuguese multicenter study

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Introduction: Sickle cell disease (SCD) encompasses a group of rare structural hemoglobinopathies characterized by the presence of hemoglobin S in homozygosity or compound

heterozygosity with other variants. Despite advances in care, no treatment is fully effective in preventing or managing SCD complications. Automated red blood cell exchange (RBCX) removes abnormal erythrocytes and replaces them with donor cells, returning non-erythrocyte components to the patient. While both manual and automated exchanges are theoretically iron-neutral, manual exchange often leads to iron overload due to technical limitations, necessitating chelation therapy. Automated RBCX is believed to avoid this complication. However, comparative data on manual versus automated RBCX in Portuguese patients is scarce.

Methods: This is a retrospective and prospective multicenter study conducted across four sickle cell treatment hospitals in the Lisbon area. Data will be collected from pediatric and adult patients undergoing manual or automated RBCX for the prevention or treatment of SCD complications. Retrospective data will cover January 2015 to September 2024, and prospective data will be collected from October 2024 to September 2025. Data include demographics, diagnosis, treatment indication, technical and hematological parameters, vascular access type, adverse events, and clinical outcomes. Data will be anonymized and stored in Excel® databases per center. Statistical analysis will be performed using SPSS® Version 29. Cost-effectiveness will also be assessed.

Results: Data collection is ongoing. Preliminary findings will compare the clinical outcomes, safety, and iron overload profiles between manual and automated RBCX. The study aims to identify differences in adverse events, transfusion efficiency, and the need for iron chelation therapy. Cost-effectiveness will also be analyzed.

Conclusion: This study will provide valuable insights into the comparative effectiveness of manual versus automated RBCX in a large cohort of portuguese SCD patients. It is expected to support clinical decision-making and optimize transfusion strategies, potentially reducing iron overload and improving patient outcomes.

PO40 | Patient and public, involvement and engagement (PPIE) in the HALO study: Strengthening research through co-design

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Introduction: Incorporating Patient and Public, Involvement and Engagement (PPIE) is widely acknowledged as an essential part of research. However, the literature lacks clear evidence on the impact of PPIE contributions and the application of underpinning frameworks.

The Haematology Lived Experience and Outcomes (HALO) study involves a north of England patient reported survey and data linkage for people in England diagnosed in childhood with, sickle cell disease, beta thalassemia and two common childhood cancers. The data linkage will use routinely collected national data sources while the survey will provide patient reports of their experiences and quality of life. There will be an option to link both to provide a more comprehensive picture.

The study aims to understand better the longer-term impacts of these conditions across health, education and quality of life. This information can be used to identify and address unmet needs, inform policy and support counselling of future generations.

Methods: The HALO study is guided by a co-design framework, fostering meaningful collaboration with PPIE contributors. This partnership has been integral to developing the patient survey (including cognitive testing), refining participant facing materials, addressing concerns about data linkage, and co-producing outreach materials such as the HALO study video and social media vignettes. Regular engagement continues online and in-person meetings, ensuring iterative feedback through discussions and email correspondence. Contributors are reimbursed following National Institute for Health and Care Research (NIHR) PPIE payment guidelines, recognising their invaluable expertise and lived experience.

Results: Active engagement from individuals with lived experience significantly enriched the study. These insights have enhanced cultural awareness, strengthened messaging, and identified potential barriers to participation and survey completion. Furthermore, PPIE perspectives have illuminated concerns regarding data linkage and consent. As a result, study design and participant resources have been improved for greater accessibility and clarity. By prioritising PPIE, HALO successfully amplifies the voices of communities, such as those affected by sickle cell disease and beta thalassemia, whose perspectives have historically been underrepresented.

Conclusion: The HALO study PPIE contributors report a sense of being heard, valued, and confident in their role within the research team, while researchers gained deeper appreciation of PPIE's transformative impact on study design and development. These insights will serve as a foundation for future research, promoting inclusive and equitable methodologies. Proposed next steps include expanding PPIE membership to engage seldom heard groups and so integrate PPIE earlier in grant applications and study design phases to further enhance the quality of studies and increase opportunities for public contributors.

PO41 | Risks and benefits of transfusion in sickle cell disease patients: A challenging balance

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Introduction: Red blood cell (RBC) transfusion, either on demand or as part of a prophylactic transfusion program, mitigates Sickle Cell Disease (SCD) severity by reducing circulating HbS and improving oxygen delivery. Nevertheless, chronic transfusional support carries significant risks including a high alloimmunization rate in SCD patients.

The aim of this study was to evaluate SCD patients followed at our institution between January 2000 and April 2025 regarding sociodemographic and immunohematological data, main SCD complications, transfusion regimen, prevalence of alloimmunization and identified alloantibodies.

Methods: Patients demographic data (age, sex, race, genotype), transfusion regimen (prophylactic or on demand transfusion support, simple versus exchange transfusion, on an acute or chronic context), patients' acute and chronic complications, alloimmunization rate and identified antibodies were collected from clinical and laboratory records. Patients initially diagnosed with SCD but subsequently followed at other institutions were excluded.

Results: 33 patients (18 female/15 male), aged between 1 and 60 years (55% adults, 45% paediatric patients), mostly of African descent (91%) and homozygous for Hb SS (91%) were evaluated. All of them had at least one acute complication requiring hospitalization during their lifetime (Figure 1) and all adult patients had at least one chronic complication related to SCD (Figure 2) during the period covered by this study, although the great majority (94%, $n=31$) was being treated with hydroxyurea. 73% of patients ($n=24$) exclusively received on-demand transfusion support during acute crisis. Nine patients (27%) were included in a regular prophylactic transfusion program: 4 paediatric patients in monthly exchange transfusion program for stroke prevention and 5 adult patients on a monthly simple transfusion regimen.

We observed a 24% ($n=8$) alloimmunization prevalence (Table 1), with anti-E being the most frequently identified alloantibody ($n=4$). One patient had a hyperhemolytic crisis after transfusion. No other transfusion reactions were observed.

Conclusion: The number of SCD patients has significantly increased in Europe in recent years due to migration flows. The significant rate of hospitalization due to infections and vaso-occlusive events, along with the prevalence of chronic pain, cardiac and neurologic impairment, emphasizes the need for a multidisciplinary approach. Simple or exchange transfusion is a first-line treatment in the management of acute events and in the primary and secondary prevention of ischemic stroke. However, transfusion is associated with acute and chronic complications, which reinforces the implementation of appropriate protocols to minimize transfusion risk and optimize outcomes.

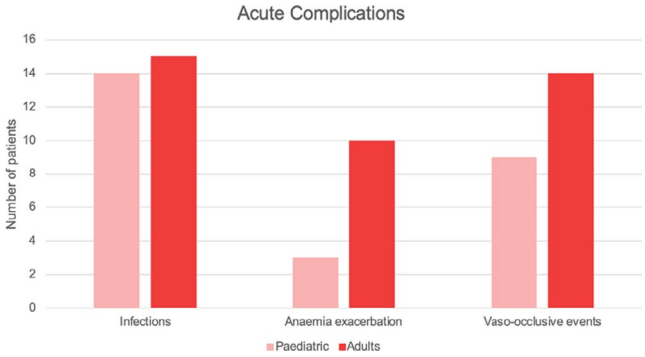

FIGURE 1 Acute complications.

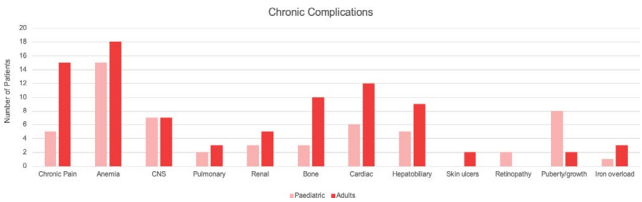

FIGURE 2 Chronic complications.

Table 1. Identified alloantibodies

PATIENTS	ALLOANTIBODIES
1	Anti-Fy^a, Anti-S, Anti-C, Anti-E
2	Anti-s
3	Anti-K, Anti-E
4	Anti-E, Anti-Fy^a
5	Anti-C
6	Anti-E, Anti-S, Anti-Jk^b
7	Anti-C^w, Anti-Le^b
8	Anti-M

PO42 | Improving sickle cell disease care: The power of public–private partnership in high-burden counties in Kenya

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Introduction: Over recent years, there has been a lot of investment from the private sector, through the public sector, into sickle cell disease (SCD) care. This is through improvement of different aspects of care such as capacity building of healthcare providers (HCPs), community health promoters (CHPs) and newborn screening programs. According to the Sickle Pan-African Research Consortium (SPARCo), facilities—depending on level—should have certain standards of care to promote improved patient outcomes. In Kenya, through a privately sponsored project, the Ministry of Health has been able to implement capacity building of HCPs and CHPs, assess readiness of facilities to provide care, and pilot infant screening programs.
Objectives: To build the capacity of health care workers (HCWs) and CHPs on SCD management.
To conduct clinical, laboratory, and pharmacy assessment of facilities in high-burdened regions.
To screen and evaluate the prevalence of SCD and sickle cell trait (SCT) among newborns and infants using a POC test in four pilot Kenyan counties.
Methods: A curriculum for training HCWs on SCD was developed by subject matter experts with a simplified version drafted for CHPs.
The HCW training happened as a 1-day workshop, whereas, the CHPs were trained for half a day. Both teams were subjected to a pre-training and a post-training test.
We assessed two main public facilities in each county offering SCD using a semi-structured questionnaire to assess their readiness to offer SCD care.
Four SCD high-burden counties in the country were chosen to pilot the infant screening activities.
Results: A total of 705 HCWs (43% males, 57% females) were trained. Different cadres were represented. Participants were drawn from different level of institutions. The mean score for the pre training test was 9.7 (48%) while the one for the post training test was 15.9 (76%).
A total of 754 CHPs (31% males, 69% females) were trained. Their pre-test average was 7.21, the post-test average was 8.8. 50% of the facilities had pediatricians, 71.4% had either a family physician, or an internist, and all of them had medical officers. 50% had dedicated SCD clinic days and databases or registers.
All the 14 facilities do a complete blood count. 85.7% of the laboratories do a sickling test, 57.1% have a peripheral blood film, 21.4% have a point-of-care test, and 21.4% do confirmatory testing. Only 7.1% had a newborn screening program.
57.1% had hydroxyurea, 57.1% had Pen V, and none had the booster (pneumococcal and meningococcal) vaccines stocked up. Another 21.4% did not have either of the 3 commodities. Notably, 64.3% of the facilities experienced stock-outs.
A total of 2983 newborns and infants were screened. Out of this, 27 (0.9%) were diagnosed to have SCD, whereas 252 (8.4%) were diagnosed to have SCT. Of the 27 positive screened cases, only 5 (18.5%) have since been enrolled into clinic follow-up.
Conclusion: There was noted immediate improvement in knowledge by the trainees. Health facilities should prioritize stocking SCD products as their availability is crucial in providing optimal care. In resource-constraint set-ups, establishing regular follow-up of patients could prove troublesome despite early diagnosis. Therefore, government inclusion and resource allocation is recommended to ensure sustainability of these projects initiated by public-private partnerships.

PO43 | Correlation between volumetric capnography and 6-minute walk test in sickle cell disease

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Introduction: Due to complications arising from sickle cell disease (SCD), particularly chronic pain, many patients experience movement limitations. Low back pain, avascular necrosis of the femoral head, and leg ulcers are examples of clinical manifestations that may impair ambulation in these individuals. Consequently, the application of the 6-minute walk test (6MWT) may be compromised. However, volumetric capnography (VCap), a highly sensitive test for assessing pulmonary function, requires minimal physical effort, unlike the 6MWT. Thus, the aim of this study was to evaluate whether the distance covered in the 6MWT correlates with VCap.
Methods: The study was approved by the Ethics Committee of the University of Campinas (UNICAMP). Participants with a confirmed diagnosis of sickle cell disease (SCD) were recruited from the Hemoglobinopathies Outpatient Clinic at the Hematology and Transfusion Medicine Center of UNICAMP. Eligible participants had to be in a clinically stable condition, meaning free from complications that could interfere with the performance of the VCap and the 6MWT. Smokers and individuals with cardiac, pulmonary, or musculoskeletal diseases unrelated to the progression of SCD were excluded. All participants first underwent VCap, followed by the 6MWT. Descriptive statistics were used, with continuous variables presented as median and range (minimum–maximum). Spearman's correlation analysis was performed to assess associations between the distance covered in the 6MWT and the volumetric capnography (VCap) variables.
Results: The study included 30 patients: 14 females and 16 males. Among them, 17 had HbSS, 9 had HbSC, 2 had HbSβ^0, and 2 had HbSβ$^+$ genotypes. The median age was 44.5 years

(range: 28–64), and the median body mass index was 22.7 kg/m^2 (range: 16.4–32.4). Regarding the distance covered in the 6MWT, the median was 450.5 m (range: 295.0–566.0). A significant correlation was found between the 6MWT and the following VCap variables: alveolar min volume (MValv), 4.79 mL (2.28–8.53; $R = 0.410$, $p = 0.024$); anatomical dead space (VDaw), 116.8 mL (78.6–182.4; $R = 0.543$, $p = 0.001$); carbon dioxide production (VCO_2), 144.7 mL/min (64.2–246.8; $R = 0.470$, $p = 0.008$); inspiratory tidal volume (Vi), 418.1 mL (244.5–1194.4; $R = 0.370$, $p = 0.044$); peak expiratory flow (PEF), 19.3 L/min (10.3–38.9; $R = 0.426$, $p = 0.018$); and peak inspiratory flow (PIF), 26.8 L/min (12.8–34.9; $R = 0.470$, $p = 0.008$). There was no significant correlation between the other VCap variables, and the distance covered in the 6MWT.

Conclusion: The results of this study demonstrate a significant correlation between the distance covered in the 6MWT and the VCap variables in patients with sickle cell disease. Therefore, this correlation suggests that VCap may serve as an alternative or complementary method to assess functional exercise capacity in these individuals, especially when physical limitations make the 6MWT less feasible. However, additional studies including a larger number of patients with SCD may be necessary to further validate these findings.

PO44 | Impact of diaphragmatic breathing training on inspiratory muscle strength and ventilation in sickle cell disease

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Introduction: Sickle cell disease (SCD) is associated with a wide range of acute and chronic complications affecting several end-organs, including the heart, liver, lungs, and kidneys. Respiratory manifestations are an important cause of morbidity and mortality in this population. Dyspnea and exercise intolerance frequently occur due to both pulmonary involvement and the intrinsic characteristics of the disease. Diaphragmatic breathing (DB) has been shown to improve these symptoms in patients with asthma and chronic obstructive pulmonary disease. However, its effects remain poorly studied in individuals with SCD. This study, therefore, aimed to investigate the impact of DB on patients living with SCD.

Methods: Participants were recruited from the Hemoglobinopathies Outpatient Clinic of the Hematology and Transfusion Medicine Center at the UNICAMP and were randomized into two groups: Control Group (CG) and Intervention Group (IG). Both groups underwent an initial and a final assessment, with a 12-week interval between them. These assessments included volumetric capnography (VCap), the Modified Medical Research Council (mMRC) dyspnea scale, measurements of maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP), and the 6-minute walk test (6MWT). The IG was instructed to perform DB at home in three sets of 20 repetitions per day, five days a week. Participants were provided with a notepad to log the date and time of each DB session, along with any reasons for missed sessions. IG participants were contacted weekly via a smartphone messaging application (app) to ensure adherence and proper execution of the exercise at home. Additionally, they were required to submit a smartphone-recorded video of one DB session through the app each week. CG participants were contacted weekly to avoid bias from exclusive IG follow-up. Comparison between groups was performed using the Mann-Whitney and Fisher's exact tests. Within-group comparisons of DB effects were performed using Wilcoxon's Sign Rank Test.

Results: Thirty patients participated in the study (CG = 14; IG = 16). There were no significant differences between the groups in terms of sex ($p = 0.081$), age ($p = 0.802$), body mass index ($p = 0.417$), or genotype severity ($p = 0.706$). The genotype distribution was as follows: in the CG, eight had HbSS, four had HbSC, and two had HbSβ^+; in the IG, nine had HbSS, five had HbSC, and two had HbSβ^0. In the within-group analysis, the IG showed significant improvements ($p \leq 0.05$) in maximal inspiratory pressure (MIP; $p = 0.002$), as well as in certain variables measured by volumetric capnography (VCap), including inspiratory tidal volume ($p = 0.050$) and the Tobin index ($p = 0.029$). Variables such as expiratory tidal volume ($p = 0.093$) and expiratory time ($p = 0.073$), along with the remaining VCap parameters, did not show statistically significant changes. No significant differences were observed between groups in any of the assessed variables. The CG showed no significant changes in any of the comparisons.

Conclusion: Diaphragmatic breathing is a simple exercise to perform and may improve respiratory mechanics, leading to increased inspiratory muscle strength and pulmonary ventilation in patients with SCD. Increasing the number of sets may enhance the training effect and potentially improve respiratory parameters more consistently, particularly those related to inspiratory strength and ventilation variables assessed by VCap.

PO45 | Optimising automated red cell exchange transfusion for sickle cell adult patients at Manchester Royal Infirmary

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Introduction: Sickle cell disease (SCD) is a hereditary blood disorder characterised by the production of abnormal haemoglobin S, resulting in sickled red blood cells (RBCs) that obstruct microvasculature, causing complications such as acute chest syndrome, stroke, and vaso-occlusive crises (VOC). Automated red cell exchange transfusion (ARCET) is an established treatment for both acute and chronic management, offering benefits such as reduced iron overload. In high-risk patients, including those with a history of stroke or frequent hospitalisations, regular ARCET is employed to prevent disease-related complications. However, inconsistent adherence to ARCET protocols can lead to over-transfusion, excess blood use, and resource strain. At the Manchester Royal Infirmary's Haematology Day Care Unit, new ARCET practices were implemented to optimise transfusion volumes, reduce overuse of blood products, and ensure appropriate post-transfusion haemoglobin S (HbS) targets. This audit aimed to assess the impact of the updated practices on blood unit usage, HbS control, and adherence to national transfusion standards.

Methods: A retrospective audit was conducted on patients undergoing regular ARCET, using the Spectra Optia™ automated device (Terumo BCT) from October 2024 to March 2025. Data were extracted from the hospital's electronic system (HIVE/EPIC), including transfusion records, HbS levels, indications, and frequency of procedures. Key metrics included the number of RBC units transfused, pre- and post-transfusion HbS percentages, and alignment with UK transfusion guidelines. Data analysis was performed using R (version 4.2.2). Of 37 patients reviewed, 13 were excluded due to incomplete data. Two periods were compared: pre-review (October–December 2024) and post-review (January–March 2025).

Results: Patients presenting with recurrent VOCs (19.6%), stroke (14.3%), and acute chest syndrome (12.5%), were the most common transfusion recipients. Post-review implementation showed a 16% reduction in RBC units transfused, decreasing from 520 to 437 units. Distribution of post-transfusion HbS improved, with most patients achieving target HbS levels of 10%–20% both pre- and post-review (79.7% vs. 74.5%, respectively), despite an increase in baseline pre-transfusion HbS in the latter group (>30% HbS; 82.8% pre-review vs. 92.7% post-review). However, a proportion of patients continued to fall short of the <30% HbS target after transfusion (14.1% pre-review vs. 12.7% post-review). Frequency of transfusions also shifted, with fewer patients receiving ARCET every 5–6 weeks (60% pre-review vs. 44.4% post-review) and more patients receiving transfusions at extended intervals (7–12 weeks; 24% pre-review vs. 39.6% post-review), reflecting improved resource use.

Conclusion: Revised ARCET practices reduced RBC usage without compromising HbS control in most patients, indicating improved resource use and adherence. However, some patients exceeded the 30% HbS threshold, partly due to an NHS Blood and Transplant 'amber alert' (restricts blood usage due to shortages) causing relaxation of targets to 50% HbS in some cases. This underscores the need for better monitoring, individualised care plans, and continued education. The short, retrospective timeframe may have limited statistical findings. Future audits will extend the analysis period and include prospective data. Wider adoption across NHS services may yield similar benefits and warrants further investigation.

PO46 | Translating research into practice: Implementing the LEARNER SCD pregnancy study in Angola

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Introduction: Pregnancy in Sickle Cell Disease (SCD), a severe genetic condition highly prevalent in Sub-Saharan Africa, is usually associated with an increase in severe outcomes. Not only do the common symptoms of the disease, such as severe anemia and vaso-occclusive crises, tend to exacerbate, but also the risk of eclampsia, pre-eclampsia, maternal and fetal death, intrauterine growth restrictions, and low birth weight is higher. Medical surveillance during pregnancy is essential, and also, the search for prophylactic and affordable measures is an urgent need, especially in Low- and Middle-income countries with high prevalence of this disease.

The use of daily low-dose aspirin is considered safe in pregnant women with SCD and is recommended after 12 weeks of gestational age by the British Society of Hematology for those at severe risk of pre-eclampsia. The LEARNER clinical study (NCT06417411) aims to evaluate the effects of daily low-dose aspirin in SCD pregnancy, comparing its impact on severe outcomes if this prophylactic and affordable medication is started in the first or the second trimester.

Methods: This study aims to recruit 450 pregnant women with a confirmed SCD diagnosis in multiple maternity and infant hospitals in Luanda, Angola. Consenting patients will be assigned to the first (weeks 6–13) or second (weeks 14–27) trimester groups according to their gestational age, as confirmed by ultrasound. Participants will start daily low-dose aspirin and will do regular follow-up appointments till 6 weeks postpartum. Aspirin will be interrupted at week 36, delivery time, or earlier if decided by the clinical team.

Results: Recruitment started in March 2024, after ethical and regulatory approvals (Parecer no. 52/CEMS/2023, and 99/ARMED/MINSA/2024). In 15 months, 113 women were enrolled in the study, 57 in the first trimester and 56 in the second trimester. To date, 271 severe events, 3 associated with the medication, 9 cases of pre-eclampsia/eclampsia, 36 preterm deliveries, 5 miscarriages, 1 perinatal death, and 4 maternal deaths were registered.

Conclusion: The current sample size is too small to draw statistically significant conclusions about the efficacy of starting low-dose daily aspirin earlier in pregnancy. Although the project has been promoted in hospitals and health centers through the media, in newspapers, and on television, to increase the participation in the study, the number of enrolled patients is below the expected, as most pregnant women tend to seek hospital care only during the later stages of pregnancy. It is urgent to invest in health literacy and SCD education in Angola and increase patients' awareness of the need to do prenatal and follow-up consultations during pregnancy for the prevention of pregnancy-associated complications in women with SCD.

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PO47 | Longitudinal analysis of sleep-disordered breathing and cognitive outcomes in children living with sickle cell anaemia

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Introduction: Sleep-disordered breathing (SDB) is a common complication for children living with sickle cell anaemia (SCA). SDB disrupts breathing at night, leading to a lower nocturnal oxygen supply, increased sympathetic activity and intermittent hypoxia, which can be observed as obstructive sleep apnoea (OSA) through polysomnography (PSG), an overnight study that measures breathing patterns, sleep time, oxygen levels and other physiological measures. Reduced oxygen delivery leads to multiorgan complications, including neurological sequelae such as stroke, silent cerebral infarction and cognitive dysfunction. Children with SCA often exhibit cognitive deficits including slowed processing speed, attention deficits, and problems with executive function. These challenges can impact academic performance, employability, and overall quality of life.

Up to 40% of children living with SCA experience OSA, with 43% of those children showing signs of severe OSA (OSA index >5 events/h). In the general population, compromised cerebral oxygen delivery may contribute to cognitive and executive dysfunction. However, very few studies have investigated the association between SDB and cognition in individuals living with SCA.

This study investigated the longitudinal change in polysomnographic outcomes and the association with cognitive functions in children living with SCA. We hypothesised that (a) PSG outcomes would worsen over time and (b) PSG outcomes would predict lower cognitive performance.

Methods: Data from the Sleep Asthma Cohort (SAC 1, 2 and 3) included participants living with SCA (aged 4–18 years) who were initially recruited between 2006 and 2009, with follow-up studies conducted through until 2019. PSG indices, i.e., obstructive apnoea hypopnoea index (OAHI-number of obstructive apnoea and hypopnea events per hour), central apnoea index (CAI-number of times breathing stops without obstruction), mean overnight oxygen saturation and total sleep time were assessed over two visits. Cognitive testing at visit 3 (2016–2019) included age appropriate Weschler Intelligence Scales and the Delis Kaplan Executive Function System (D-KEFS) as well as the Behaviour rating inventory of Executive Function (BRIEF-2) self and parent rated questionnaire.

Results: Ninety-two participants (91 HbSS, 1HbSβ) completed a PSG at Visit 1 and 56 participants returned for Visit 2, 40 of whom returned for the Visit 3 cognitive assessment; mean ages for each visit were 9.9 (3.8), 14.7 (3.69), and 17.7 (4.64) years, respectively. Total sleep time significantly decreased between the two visits, while overall PSG indices remained stable. Mean overnight oxygen saturation at Visit 1 significantly predicted working memory at Visit 3. In addition, CAI at Visit 2 was associated with lower scores on the verbal comprehension index and self or caregiver-reported measures of executive function.

Conclusions: PSG indices did not change significantly over time; however, PSG assessment in clinical practice for those living with SCA may be beneficial, especially within the context of sickle pathology where other comorbidities, such as acute chest syndrome, change in body weight, and nasal congestion may impact the severity of SDB. Overnight oxygen saturation levels and central apnoea influence cognitive outcomes for children living with SCA. These results suggest integration of sleep assessments into routine care of individuals living with SCA.

Fig. 1a

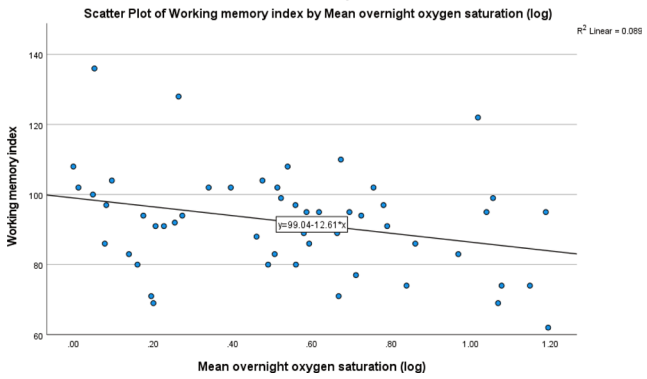


Fig. 1b

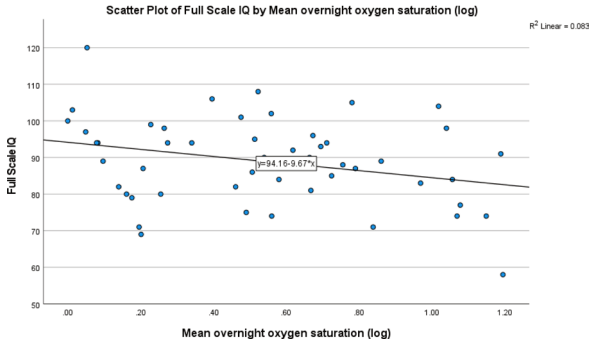


Figure 2a

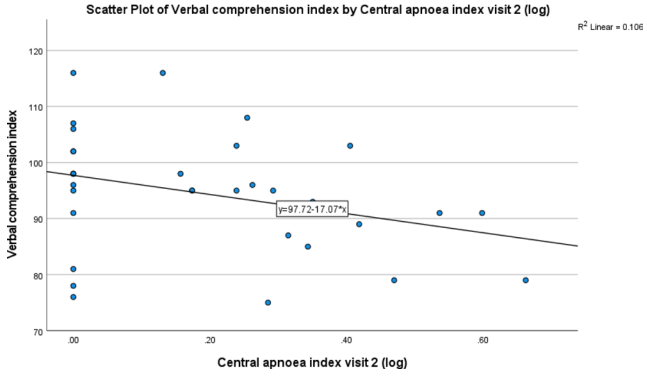


Figure 2b

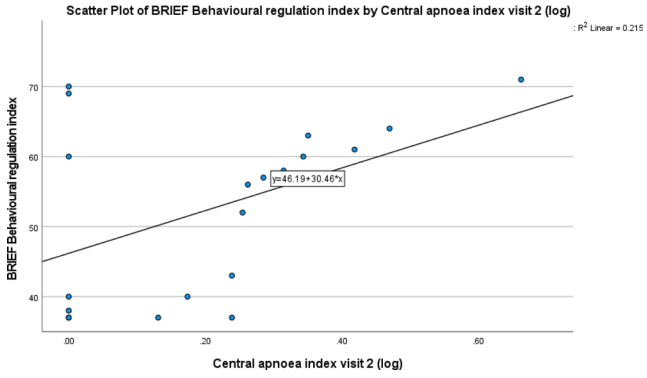
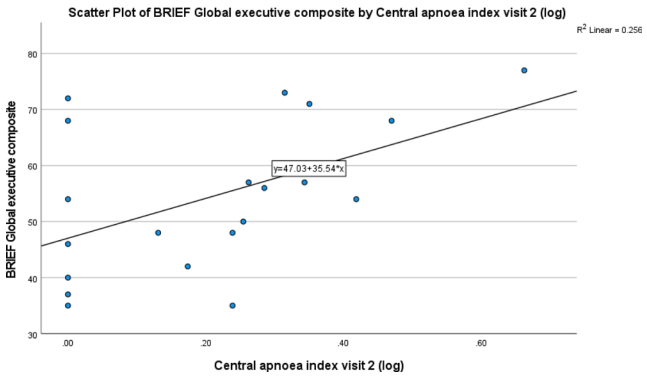


Figure 2c



PO48 | Distribution of hemoglobinopathies in the Elbasan Region and the importance of their early diagnosis treatment

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Introduction: Hemoglobinopathies are inherited hemoglobin disorders that represent a significant health challenge in Albania, especially in the coastal and southern areas of the country. Scientific studies have identified a high prevalence of beta-thalassemia, sickle cell disease (sickle cell disease), and other hemoglobin variants in the Albanian population.

Purpose: The purpose of our study is to determine the main types of hemoglobinopathies in the Elbasan district and their distribution based on age, gender, time period and geographical extent.

Methodology: Our study is of a retrospective descriptive type and the data were obtained from the files of the regional hospital of the Elbasan district. Patient data were analyzed based on age group, gender, time period and geographical area. The study covers the period 2020–2024.

Conclusions:

1. The age group most affected by the disease was over 65 years old (48.72%), followed by the age groups 55–64 years old (13.13%) and 45–54 years old (12.17%).
2. Women were affected more than men, with 125 cases (52.9%), compared to men with 111 cases (47.03%).
3. The year with the most cases was 2023, with specifically 57 cases (24.15%), and followed by 2024 with 48 cases (20.33%).
4. Urban areas were more affected than rural areas, (56% vs. 44%).

Recommendations:

1. Due to the high prevalence of hemoglobinopathies in Albania, it is important to implement national screening and health education programs.
2. Early identification of carriers and provision of genetic counseling can help prevent the birth of children with severe forms of these disorders.
3. Furthermore, improving treatments and care for existing patients will contribute to improving their quality of life.

Keywords: hemoglobinopathies, screening, gender, age group, period of time

PO49 | "Fit to sit"? Surfacing hidden consequences of emergency department overcrowding on sickle cell crisis care

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Introduction: Challenges in delivering emergency care for people experiencing sickle cell crises (SCC) are longstanding. However, overcrowding in UK hospitals has accelerated, largely driven by delays in transferring patients from emergency departments (EDs) to wards. Increasingly, people experiencing SCC, who would once have been placed in ED beds, are now classified as "fit to sit" and cared for in chairs instead. This shift has consequences—largely unexamined—for people experiencing SCC and ED clinicians.
Methods: This paper draws on data from the EPOC4 study (Exploring Practices of Care during Sickle Cell Crises), an 18-month ethnographic case study conducted across three hospitals in East London. A patient advisory group of three individuals living with SCD provide guidance throughout. The fieldwork involved over 200 h of participant observation in clinical settings, 41 in-depth interviews with people living with sickle cell disease and healthcare professionals, and a 6-month series of longitudinal research visits with four individuals living with the condition. Biographical narrative interviews were analysed using the Listening Guide method. The broader dataset was examined through ethnographic analysis.
Results: The practice of managing patients in ED chairs during crisis episodes affects multiple dimensions of care:
For people experiencing crises:

- Sitting exacerbates pain, particularly with crises affecting back, hips, or legs.
- Many people experience loss of dignity. This includes:
  - exposure of intimate areas
  - receiving opioid injections in front of other patients
  - experiencing vomiting or drowsiness in crowded public spaces.
- Basic interventions like oxygen and IV fluids become harder to administer and are offered less consistently.
- Prolonged ED stays (often exceeding 24 h) before hospital admission increase exposure to a chaotic environment during episodes of intense suffering. These experiences influence peoples' decisions to present to hospital and when to go home, and can prolong length of stay.
- Some conclude that their suffering is underappreciated and not taken seriously enough.

For hospital staff:

- ED staff experience moral injury when they feel complicit in suffering arising out of experiencing a sickle cell crisis in an uncomfortable metal chair because beds are unavailable.
- Opportunities for nurses to provide holistic care and build therapeutic relationships are constrained. No longer able to enact care by providing jugs of water or adjusting a bed, the nursing role centres on administering medications.
- Specialist haematology reviews in ED often occur in public areas, reducing the quality of clinical history and examination, and compromising confidentiality

Both people with sickle cell and staff actively develop strategies to work around these constraints. These include sharing informal knowledge about triage processes, modifying chairs for comfort, advocating for timely access to beds, and sustained communication between emergency clinicians and patient advocacy groups.
Conclusion: This study illustrates how ED overcrowding enacts a form of unacknowledged rationing that shapes the delivery of care during SCC. It highlights the consequences of these systemic pressures to people living with sickle cell and ED clinicians. Nevertheless, both groups have developed adaptive strategies aimed at making "good enough" care possible within an overwhelmed healthcare system.

PO50 | Homozygous HBB promoter variant with MEFV carrier status: A pediatric case of iron overload

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Introduction: Regulatory pathogenic variants in the *HBB* gene are associated with β+-thalassemia alleles, often resulting in a milder clinical phenotype due to residual beta-globin chain production. We present a complex pediatric case with nearly a decade of inconclusive diagnostics, MRI-confirmed hepatic/splenic iron overload, a limited transfusion history, and genetic findings suggestive of β+-thalassemia allele.

Methods: A 9-year-old male born at 37 weeks of gestation to non-consanguineous parents with intrauterine growth retardation (birth weight: 1550 g, length: 41 cm) was referred for genetic investigation due to persistent microcytic, hypochromic anemia, hyperferritinemia, elevated transaminases, significantly increased haemoglobin F level (69.2%) according to haemoglobin electrophoresis results. MRI demonstrated hemosiderosis of the liver and spleen, and hepatosplenomegaly was noted. Liver biopsy confirmed hemosiderosis, Scheuer Grade 1. Serial ferritin values ranged from 929 to 1147 ng/mL over 1 month, with normal transferrin saturation. The patient has received a total of four blood transfusions throughout his life. Genetic analysis of specific point mutations in *HFE* and *UGT1A1* upon suspicion of hemochromatosis and Gilbert's syndrome were negative. The patient was referred for large-scale testing and evaluation of possible atypical thalassemia. Whole Genome Sequencing (WGS) was performed using the Twist TruSeq NanoDNA Kit on the Illumina NovaSeqX platform, according to laboratory protocols.

Results: WGS analyses identified a pathogenic variant in the *HBB* promoter region: NM_000518.5:c.-80T>A, detected in apparent homozygosity. This variant has been previously described in patients of Middle Eastern origin, but not in European population. In addition, the patient was found to carry a heterozygous pathogenic variant in *MEFV*: c.2080A>G, *p*.(Met694Val), associated with Familial Mediterranean Fever, though the child exhibited no overt inflammatory episodes. Segregation of family members is currently in progress.

Conclusion: The presence of a homozygous promoter variant, combined with iron overload, suggests ineffective erythropoiesis and confirm the clinical diagnosis of thalassemia. The *HBB* c.-80T>A variant is known to not fully disrupt the *HBB* gene, but to reduce transcriptional activity, resulting in milder and atypical presentation. The co-occurrence of an *MEFV* variant may contribute to iron dysregulation through low-grade inflammation. This case illustrates the importance of early genomic diagnostics to resolve the complexity posed long-year clinical diagnosis finding for thalassemia and emphasizes the importance of comprehensive molecular follow-up of affected and unaffected family members. It underscores the need to consider promoter mutations in unexplained pediatric hemosiderosis in the absence classical thalassemia mutations.

PO51 | Intelligence outcome in children with sickle cell disease: A systematic meta-analyses and meta-regression

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Introduction: Sickle cell disease (SCD) is the most common hereditary haemoglobinopathy affecting haemoglobin synthesis, leading to a wide range of irreversible complications, including stroke and silent cerebral infarcts (SCI). The impact of SCD on the developing brain poses a threat to intelligence functioning in children. Previous meta-analyses revealed intelligence impairment associated with SCD but were limited to specific intelligence measures and groups (i.e. only studies included with confirmed MRI information or matched control groups) and did not address determinants for adverse intelligence outcome among children with SCD. Therefore, this study aims to provide a comprehensive meta-analysis of all reported intelligence outcomes in children with SCD and to perform a meta-regression to determine risk and protective factors.

Methods: MEDLINE, Embase, and PsycINFO were searched for relevant studies until January 31, 2024. Research articles with original data were included if they reported on children diagnosed with SCD aged ≤18 years and full-scale IQ scores obtained using any standardized measure of IQ. Meta-analytic effect sizes (Cohen's *d*) were calculated for differences in IQ scores between children with SCD and control groups or normative data. Meta-regression was used to investigate the association between demographic and clinical risk factors and full-scale IQ effect sizes.

Results: A total of 90 articles published between 1963 and 2023 were included, encompassing data of 5719 children with SCD and 914 matched controls. The results revealed a large effect size of SCD for FSIQ ($d = -0.81$, $p < 0.001$), indicating that children with SCD have lower intelligence (equating to −12 IQ points). This finding was consistent in a sensitivity analysis restricted to studies including control groups matched for demographic variables (−10.5 IQ points, $d = -0.7$, $p < 0.001$). Further analysis into aspects of intelligence (i.e. verbal comprehension, working memory, and processing speed) showed similar results, with effect sizes ranging between −0.9 SD to −0.6 SD, translating to −13.5 to −9 IQ points. Meta-regression analyses revealed that lower

foetal Hb (%) levels were associated with poorer FSIQ scores ($B = 0.06$, $p < 0.05$), as were stroke diagnosis ($B = -0.009$, $p \leq 0.01$) and chronic transfusion treatment ($B = -0.008$, $p < 0.005$). No other significant relationships were observed.
Conclusion: This meta-analysis and meta-regression provides robust evidence of intelligence impairment in children with SCD. The findings reveal a significant and large diffuse impact of SCD on intelligence outcome in children, including both fluid (problem-solving abilities) and crystallized (accumulated knowledge and skills) aspects of intelligence. The observed impairments may crucially impact other developmental domains of functioning, such as behavioural, emotional, social, and academic functioning. These results underscore the profound impact of sickle cell disease on intelligence during childhood, emphasizing the need for early and routine neurocognitive monitoring, along with timely and targeted interventions to improve outcomes.

PO52 | Effectiveness of hydroxyurea in Sudanese children with severe sickle cell anemia

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Introduction: Sickle cell disease (SCD) is a genetic, multisystem disorder marked by acute illness and progressive organ damage, with sickle cell anaemia (SCA) being its most common form. Complications include painful crises, anemia, infections, and chronic organ dysfunction, leading to a reduced life quality and expectancy. Globally, an estimated 300 000 children are born with SCD annually, with 80% in Africa, where under-5 mortalities range from 50% to 90%. The prevalence of SCD in Sudan ranges from approximately 0.8% in central regions to as high as 30.4% in certain western areas. Hydroxyurea (HU), initially a chemotherapy agent, emerged in the 1990s as a promising pharmacologic therapy for SCA. It primarily increases fetal haemoglobin (HbF) levels, inhibits HbS polymerisation, and reduces chronic inflammation. HU is absorbed orally and excreted via hepatic and renal pathways. Hydroxyurea is an effective treatment for sickle cell anemia, with generally mild side effects. But few studies have assessed its effectiveness in Sudanese children. This study aimed to study the role of hydroxyurea in severe sickle cell anaemia among young SCD patients in Sudan.
Methods: This was a descriptive cross-sectional, hospital-based study conducted from June 2022 to December 2022 at Jaafar Ibn Ouf Referral Pediatric Hospital in Khartoum, Sudan. The study population included all children aged 1 to 15 years with severe sickle cell anemia (SCA) who were receiving hydroxyurea (HU) therapy. Data were collected using a structured data collection sheet, which was completed through direct interviews with caregivers, clinical evaluations of the patients, and review of their medical test results. Verbal consent was obtained from the caregivers prior to data collection. Statistical analysis was performed using SPSS version 26, and a p-value of less than 0.05 was considered statistically significant.
Results: A total of 285 children with severe SCA on hydroxyurea were enrolled over six months. The majority (66.3%) were aged 11–15 years, with a slight female predominance (51.2%). The median weight was 25 kg (IQR: 19–30 kg). Most participants (87.5%) were vaccinated, while 50% received Penicillin V and 22% were MCV vaccinated. The majority (62.5%) had used hydroxyurea for over two years. Reported improvements included decreased admission rates (58.7%), reduced blood transfusions (34.8%), and fewer painful episodes (17.5%). However, 32.5% of children experienced no improvement. Significant improvements were observed in hematological parameters, liver enzymes, and renal function ($p < 0.0001$). No significant relationship was found between hydroxyurea administration and platelet counts ($p = 0.047$). Highly significant association between the duration of hydroxyurea administration and the improvement in SCD severity ($p < 0.0001$).
Conclusion: This study demonstrates that hydroxyurea therapy in Sudanese children aged 1 to 15 years with sickle cell anemia has beneficial effects on various clinical and laboratory parameters, including a reduction in hospital admissions and blood transfusion requirements, alongside improvements in hematological, hepatic, and renal markers. While significant improvements were observed in most patients, a notable proportion showed no clinical improvement, indicating the need for further research into individual responses and optimization of treatment strategies.

PO53 | Developing consensus guidelines for screening, diagnosis, and management of sickle cell retinopathy: Global Delphi study

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Background: Sickle Cell Retinopathy (SCR) is a potentially blinding complication of Sickle Cell Disease (SCD) caused by vaso-occlusion and subsequent chronic retinal ischaemia. It is especially common in individuals with HbSC and HbSβ-thalassaemia genotypes.[1,2] SCR progresses from non-proliferative to proliferative stages, with the latter posing sight threatening complications such as neovascularisation, vitreous haemorrhage and tractional retinal detachment. While SCR can be asymptomatic even in advanced stages, it remains under-recognised in routine SCD clinical care. There is currently no global consensus on when to screen, which diagnostic tools to use, or the most effective treatment approach. The SCR.net applies a 'Decolonising Healthcare' framework that addresses this gap by incorporating equity into research and centering on the experiences of people living with SCD.[3]

Aim: To develop consensus-based guidelines for the screening, diagnosis, and management of SCR using a global Delphi process co-designed with clinicians, people living with SCD, carers, and policy makers.

Methods: A modified Delphi study is being conducted via Qualtrics, consisting of 2 to 3 rounds of anonymised online surveys. We aim to recruit 250 to 300 participants globally, including ophthalmologists, haematologists, nurses, public health professionals, traditional medicine practitioners, policymakers, individuals with SCD, and caregivers from the Global South and North. Round 1 will capture both open-ended and structured responses; later rounds will refine statements and utilise the Likert-scales to build consensus. Consensus is defined as ≥70% agreement across domains such as screening eligibility, diagnostic methods and management options.

Ethics: This study has ethical approval from Lagos University Teaching Hospital Health Research Ethics Committee (Ref: ADM/DSCST/HREC/APP/7443). Informed consent, secure data handling, and participant confidentiality and anonymity will be maintained throughout. All participants will receive a detailed information sheet and will be required to provide informed consent.

Next Steps: The Delphi study will be launched at key regional and international meetings, including the African Retinal Society (ARS) in Zimbabwe and the Ophthalmological Society of the West Indies (OSWI) in Jamaica in July 2025. An additional rollout will be done at the ASCAT conference in October 2025. We will also disseminate the study through professional societies, networks and community groups to ensure widespread engagement. The ASCAT conference provides a strategic opportunity to raise awareness of SCR and encourage meaningful participation.

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PO54 | Iron regulation markers in haemoglobin-S variants: Hepcidin, ferritin/serum iron levels in Port Harcourt, Nigeria

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Introduction: In sickle cell disease patients, chronic inflammation, infections, and medications can impact iron levels and potentially influence prognosis. The monitoring of Hepcidin, ferritin, and other iron values is of great clinical utility in haemoglobin-S variant disorders in our locality as most patients, particularly sickle cell disease are recipients of multiple transfusion and are at risk of iron overload. This cross-sectional study assessed levels of Hepcidin, Ferritin and Serum Iron in haemoglobin-S variants steady state patients and controls.

Materials and Methods: Eighty (80) consenting participants, twenty (20) each having HbSS, HbSC, HbAS and control haemoglobin A (HbAA) between 5 and 60 years, were recruited for the study. Three milliliters of venous blood were collected by venipuncture after administering structured questionnaire and the plasma analyzed by ELISA technique for hepcidin, ferritin, serum iron, TIBC and UIBC. Data obtained were analyzed using descriptive statistical tools (ANOVA, Turkey's multiple comparison test and student *t*-test—results were considered significant at $p < 0.05$).

Results: Hepcidin was highest in HbSC (22.92 ± 4.22 ng/mL) and HbSS (16.14 ± 6.26 ng/mL). Ferritin level was high in HbSS (244.75 ± 160.34 ng/mL) and HbSC (242.70 ± 212.84 ng/mL). Serum iron was significantly decreased in HbSS (54.90 ± 16.95 μg/dL) and HbSC (69.85 ± 35.37 μg/dL) compared to other groups. There was no statistically significant difference in hepcidin, ferritin, serum iron, TIBC, and UIBC levels when compared across the studied groups based on sex. However, a statistically significant higher value for serum iron level in females (62.50 ± 15.50μg/dl) compared to males (47.30 ± 15.42 μg/dL) in the HbSS group was observed.

Conclusion: The study revealed that there is an elevated level of hepcidin, ferritin in HbSC and HbSS subjects with concomitant decreased in serum iron level in same subjects compared with HbAA and HbAS. TIBC and UIBC are highest in HbSS subjects, followed by HbSC, HbAS, and HbAA. Gender influences serum iron levels but not hepcidin, ferritin, TIBC, or UIBC. Elevated hepcidin and ferritin levels in HbSS and HbSC, driven by macrophage activity, can serve as indirect markers for inflammation, anaemia, and iron sequestration in hemoglobin-S disorders.

PO55 | Mortality in stillbirths and under-five children with sickle cell hemoglobinopathy identified through population-based post-mortem study

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Introduction: Child mortality from sickle cell disease (SCD) in sub-Saharan Africa is presumed high but remains poorly quantified. Sierra Leone has among the highest child mortality rates globally, yet the contribution of SCD to premature mortality is unclear. This gap delays interventions and policy prioritization. This study presents baseline data on stillbirths and under-five mortality associated with SCD in Sierra Leone, using findings from a population-based post-mortem surveillance program.
Methods: The Sierra Leone site of the Child Health and Mortality Prevention Surveillance (CHAMPS) program conducts ongoing multi-site surveillance to determine causes of death (CoD) in children under five. CHAMPS uses minimally invasive tissue sampling (MITS), a validated alternative to complete diagnostic autopsy, and more reliable than verbal autopsy (VA). Hemoglobinopathy genotypes were determined in deceased children via two point-of-care tests (SickleSCAN and Gazelle). CoDs were classified as underlying, immediate, or comorbid, and stratified by age, gender, and sickle cell genotype across two sites. Verbal autopsies were analyzed for insights into care-seeking behaviors and health literacy.
Results: Between 2023 and 2024, we analyzed 911 under-five deaths. Hemoglobin genotypes were AA (594), AS (283), SS (28), and others (6). Site-based case totals were 203 and 708. Age at death included: stillbirths (241, 24.2%), <24 h (72, 6.2%), 1–6 days (148, 14.5%), 7–27 days (58, 5.1%), and 1–5 years (232, 29.1%). Male and female deaths were 505 (55.9%) and 406 (44.1%), respectively. Among children with SCD, malaria and anemia were identified as immediate or contributing causes in 24 and 4 cases, respectively. Infectious agents commonly associated with death ($n = 248$) included Plasmodium falciparum, Streptococcus pneumoniae, and Klebsiella pneumoniae. SCD was identified as the underlying CoD in three cases. Verbal autopsy data suggested that many deaths were potentially preventable with better resources and timely clinical care.
Discussion: The burden of mortality among children with SCD in Sierra Leone is disproportionately high. These findings emphasize the urgent need for targeted wellness programs and early interventions to reduce morbidity and mortality. The methods used here may serve as a model for estimating SCD-related mortality in other sub-Saharan African countries and inform public health policy for child survival.

PO56 | 9-Month of hydroxyurea reduces albuminuria in children with sickle cell disease in the DR Congo

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Introduction: To evaluate albuminuria and glomerular filtration after 9 months of treatment with HydroxyUrea (HU) in a population of children followed for early sicklanemic nephropathy.
Methods: Open clinical trial including children with sickle cell disease under the age of 18 years followed for early sicklanemic nephropathy (glomerular hyperfiltration = HFG and/or microalbuminuria). A mean dose of 20 mg/kg/day of HU was administered to each child with clinical and biological controls every trimester. HFG (new Schwartz formula) was defined by a rate >140 mL/min/1.73 m^2; albuminuria by the albuminuria/creatininuria ratio (ACR) in mg/g. The Wilcoxon and Mac Nemar tests were used to compare the results at admission and at the nineth month of treatment.
Results: Our study included 30 children (mean age 8.9 ± 4.1 years; 40% boys) whose average fetal hemoglobin level increased from 10 ± 7.4 to 18.8 ± 4.9% and the average number of blood transfusions decreased from 7.4 ± 6.7 to 0.1 ± 0.3 bags per month ($p < 0.001$) and the number of CVOs from 1.8 ± 1.1 to 0.2 ± 0.4/month ($p < 0.03$). We noted a frequency of HFG which dropped from 30% to 2.3%. Mean albuminuria increased from 122.5 ± 16.3 to 30 ± 2.4 mg/g.
Conclusions: HU improved the progression of sicklanemic nephropathy. The mechanism of action explaining this result seems to be explained by the improvement of blood rheology.

PO57 | Early sickle cell nephropathy and risk variants of APOL1 genes in Congolese children (DRC)

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Introduction: Microalbuminuria and hyperfiltration, early markers of Sickle cell nephropathy (SCN) have been reported to be associated with apolipoprotein L-1 (*APOL1*) high risk genotypes (HRG) in African Americans. This association has not yet been assessed in Congolese Sickle cell disease (SCD) children. Therefore, the aim of the present study was to assess the association between *APOL1* high risk genotypes and early markers of kidney disease in SCD children living in the Democratic Republic of Congo (DRC).

Methods: In this cross-sectional study, we have investigated 266 SCD children from two centers (CMMASS in Kinshasa $n = 101$and Saint Luc Hospital at Kisantu/Bas Kongo $n = 165$) that give a comprehensive care to SCD patients. *APOL1* high-risk genotype (HRG) was defined by the presence of two risk variants (G1/G1, G2/G2 or G1/G2) and low-risk genotype (LRG) by the presence of 1 or zero (G1/G0, G2/G0 or G0/G0). Elevated albuminuria and hyperfiltration, as the main outcomes of the study, were defined by urinary albumin/creatinine ratio (ACR) ≥30 mg/g and estimated glomerular filtration ratio (eGFR) >130 mL/min per 1.73 m^2 for females and >140 mL/min per 1.73 m^2 for males, respectively. Logistic regression analysis was used to assess the relationship between *APOL1* high-risk genotypes and early sickle cell nephropathy.

Results: Of the 266 SCD children enrolled, 51(19.2%) and 83(31.2%) of them presented with abnormal albuminuria and hyperfiltration, respectively. *APOL1* HRG was observed in 17 (6.5%) patients with the compound heterozygous G1/G2 as the most frequent genotype. *APOL1* HRG was strongly, significantly and independently associated with both abnormal albuminuria (aOR 10.14; 95% IC 2.22–1.63; $p = 0.003$) and hyperfiltration (aOR 15.66; 95% IC 2.98–22.25; $p = 0.001$).

Conclusion: The present study has shown that nearly seven out of one hundred SCD children bear a high risk *APOL*1 genotype that is strongly and significantly associated with early markers of kidney disease.

PO58 | Pulmonary hypertension in SCD: Prevalence and associated factors in adults ≥30

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Introduction: Sickle cell disease is an autosomal recessive genetic disorder caused by a mutation in codon 6 of the β-globin gene. Pulmonary hypertension (PH) associated with sickle cell disease is a progressive and potentially fatal complication, occurring in 2%–5% of cases, and confers significant morbidity with a prevalence exceeding 30% in echocardiography-based studies.

Objective: This study aimed to evaluate the prevalence of PH and its associated factors in adult sickle cell patients aged ≥30 years in Senegal.

Materials and Methods: This was a cross-sectional, descriptive, and analytical study conducted over 6 months (March 15, 2024, to September 15, 2024) among sickle cell patients aged ≥30 years followed at the Clinical Hematology Department of the National Blood Transfusion Center in Dakar.

Results: We enrolled 118 patients with major sickle cell syndrome. The prevalence of PH was 30.5% (36/118). The mean age was 43 ± 10 years, with a female predominance (66.7%). The SS phenotype was present in 91.6%, and severe anemia in 55.5% ($p = 0.029$). Exertional dyspnea was observed in 20 patients (55.5%), with a mean hemoglobin level of 7.8 ± 1.9 g/dL. On electrocardiography (ECG), left atrial hypertrophy was detected in 38.9% and left ventricular hypertrophy in 69.4%. The most common repolarization abnormalities involved T-waves, with negative T-waves in 9 cases and prolonged QT segments in 2 cases. Echocardiography revealed left atrial dilation in 30 patients (83.3%). The mean indexed cardiac output was 3.8 ± 0.86 L/min/m^2, with hyperdynamic cardiac output in 41.7% of PH patients ($p = 0.01$). Systolic dysfunction (LVEF Simpson Biplane <50%) was observed in only five patients (13.9%, $p = 0.01$). Left ventricular hypertrophy was present in 16 patients (44.4%). PH correlated with age ($p = 0.036$), anemia ($p = 0.035$), nephropathy ($p = 0.01$), frequency of acute chest syndrome (>3 episodes/year, $p = 0.01$), and signs of right heart failure such as pulmonary B2 sound ($p = 0.03$) and hepatojugular reflux ($p = 0.002$). No correlation was found between PH and hemolysis markers. PH was significantly associated with ECG findings of left atrial hypertrophy ($p = 0.025$) and left ventricular hypertrophy ($p = 0.03$), as well as echocardiographic left atrial dilation ($p = 0.03$) and left ventricular dilation ($p = 0.003$).

Conclusion: PH is common in adult sickle cell patients. Our findings suggest that ECG and echocardiography parameters may aid in early PH screening; however, cardiac catheterization remains the gold standard for confirmation. Screening for PH should be prioritized to improve quality of life and life expectancy in this population.

PO59 | Health system reforms in Kenya: Implications of the 2023 insurance act for sickle cell management

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Introduction: Kenya's 2023 Social Health Insurance Act (SHIA) redefined the national health financing framework by replacing the National Health Insurance Fund (NHIF) with the Social Health Authority (SHA) and introducing three new pooled funds: the Primary Healthcare Fund (PHCF), the Social Health Insurance Fund (SHIF), and the Emergency, Chronic and Critical Illness Fund (ECCIF). These reforms aim to reduce out-of-pocket spending, enhance risk pooling, and expand access to essential services. For individuals with sickle cell disease (SCD), a high-burden, chronic condition in Kenya, these changes present critical opportunities and challenges in accessing comprehensive and

high-cost interventions, such as automated red cell exchange (aRBCX). This analysis critically assesses the implications of SHIA for the financing, accessibility, and benefit design of SCD-related services, with a particular focus on haematological coverage and cost-containment mechanisms.

Methods: A policy analysis was conducted based on SHA legislation, fund-specific guidelines, and reimbursement schedules. Key elements reviewed included criteria for therapeutic procedures, cost ceilings, frequency limits, and coverage of SCD services across care levels.

Results: Financial contributions structure: SHIF introduced an income-based contribution model at 2.75% of gross salary, replacing the NHIF's fixed KES 1700 ceiling.

- *Provider-level reforms*: Reforms in provider empanelment and primary care gatekeeping are anticipated to increase system efficiency and mitigate inappropriate referrals, while potentially standardising care quality between public and private facilities.
- *Outpatient diagnostic coverage*: SHIF provides coverage for essential diagnostic laboratory investigations, including full blood counts and hemoglobinopathy screening, for SCD at a tariff of KES 6800 per visit, with a limit of one visit per year.
- *Inpatient care services*: SCD inpatient care is covered under SHIF with tariffs ranging from KES 3360 (Level 4) to KES 4480 (Level 6), capped at 180 days per household per year.
- *Medical imaging and diagnostics*: Under SHIF, imaging is reimbursed between KES 3500 and KES 11 000, depending on modality. However, a cap of two imaging sessions per modality per household annually fails to align with clinical needs for SCD management, such as quarterly TCD scans for high-risk pediatric patients.
- *Therapeutic apheresis*: aRBCX is included in the SHIF Hematology and Oncology Package at KES 70 000 per session, limited to three sessions annually and subject to a shared KES 400 000/year cap. While its inclusion marks a key progress in aligning coverage with SCD care standards, the lack of a dedicated sub-limit may constrain access for patients requiring higher treatment frequency. Ring-fencing apheresis funding could support more sustainable and equitable access.
- *ECCIF*: Although designed for critical care, ECCIF does not explicitly include chronic SCD interventions, limiting its relevance for this population.

Conclusion: SHIA redefines coverage for chronic and rare conditions in Kenya. Including high-cost SCD care in a prepayment scheme is a step toward UHC. To maximize impact, reforms must improve benefit depth, align service caps with clinical needs, and ensure adequate funding. Real-world data and cost-effectiveness assessments should guide future benefit revisions. Safeguarding budgets for rare diseases is key to achieving equitable and sustainable access to quality care.

PO60 | Evaluation of RBC exchange practices in managing sickle cell disease across gulf hospitals

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Introduction: Red blood cell exchange (RBCX) has become a key therapeutic modality in managing patients with sickle cell disease (SCD), enabling the removal of abnormal erythrocytes and improving clinical outcomes. Automated exchange offers better HbS control, less iron overload, and greater efficiency particularly in high-volume settings.This study aims to evaluate current RBCX practices in selected hospitals across the Gulf region, focusing on both elective and emergency exchange procedures, as well as their clinical indications.

Methods: A cross-sectional study was conducted in 2024 to evaluate red blood cell (RBC) exchange practices in the management of sickle cell disease (SCD) across selected hospitals in the Gulf region. A structured questionnaire was developed, reviewed, validated and distributed to healthcare professionals via WhatsApp. The survey assessed the availability of RBCX, procedure types (manual vs. automated), frequency, settings, institutional guidelines, and team responsibilities.

Results: A total of 94 healthcare professionals from 53 hospitals participated across the Gulf region, 86 (91.5%) were from saudi arabia and 8 (8.5%) from different city around gulf region. Of these, 88 (93.6%) reported that red blood cell (RBC) exchange is performed at their institutions. Among these, 29 (33%) relied on manual exchange, 25 (28.4%) employed automated exchange, and 34 (38.6%) utilized both methods.

In terms of frequency, 41 respondents (46.6%) reported performing 5–15 RBC exchange procedures per month, 35 (39.8%) reported fewer than 5, and 12 (13.6%) reported more than 15 procedures per month.

Emergency RBCX was most commonly performed in Intensive care units (90.9%), followed by wards (40.9%), High dependency units (23.9%), and ERs (10.2%).

Elective procedures were primarily conducted in day care units (40.9%), Intensive care units under regular admission (30.7%), and inpatient wards (26.1%).

Institutional guidelines for RBC exchange in sickle cell disease were reported by 63 participants (71.6%), while 25 (28.4%) lacked standardized protocols. Among the six centers not offering RBC exchange, main barriers included insufficient resources (66.7%), lack of institutional support

(66.7%), unclear processes or guidelines (50%), and limited staff experience (16.7%).
Additionally, Role clarity was reported by 78 respondents (88.6%), with physicians overseeing initiation and clinical decisions, nurses managing patient preparation and monitoring, and laboratory staff handling machine operation and blood coordination.
Conclusion: Red blood cell exchange is widely practiced for the management of sickle cell disease across hospitals in the Gulf region, though notable variability exists in procedural approaches and infrastructure Expanding access to automated exchange especially in busy centers could substantially make a real difference in patient care. To get there, we need to address practical barriers like limited equipment, staffing challenges, and the lack of clear institutional guidelines. These findings highlight the need for regional collaboration and development of standardized protocol to optimize outcomes and to improve care quality.
Keywords: sickle cell disease, red blood cell exchange, automated exchange, manual exchange, Gulf region, transfusion practices, haematological outcomes.

PO61 | RBC transfusion to treat or prevent complications in SCD: An overview of cochrane reviews

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Introduction: Sickle cell disease (SCD) is a severe inherited disorder that can cause pain, end-organ damage, and premature death. Red blood cell (RBC) transfusions are regularly used to treat SCD complications or as part of long-term transfusion programs to prevent complications.
We aimed to summarize the evidence from Cochrane Reviews on the effectiveness and safety of RBC transfusions versus no transfusion; or restrictive versus liberal transfusion strategies, for treating or preventing complications in people with SCD.
Methods: We included Cochrane Reviews of randomized or quasi-randomized controlled that addressed RBC transfusions as an intervention for SCD complications. The quality of included reviews were assessed using AMSTAR and the quality of outcome evidence was evaluated using GRADE.
Results: We included 16 Cochrane Reviews, of which five involved RBC transfusion interventions. Only four reviews included usable data with all evidence coming from nine trials involving 1502 participants.
Short-term RBC transfusions versus standard care: In people undergoing low- to medium-risk surgery, RBC transfusions may reduce the risk of ACS in individuals with African haplotypes. There was little or no difference for other outcomes.
Long-term RBC transfusions versus standard care: In children and adolescents at high risk of stroke, long-term RBC transfusions probably reduce stroke risk and may reduce the risks of acute chest syndrome, painful crises, and silent cerebral infarct. Long-term transfusions may increase the risk of iron overload but had little effect on transfusion reactions.
Long-term RBC transfusions versus transfusions to treat complications (pregnancy): Long-term RBC transfusions may reduce painful crises but had little or no effect on other outcomes.
RBC transfusions versus hydroxyurea: Hydroxyurea with phlebotomy may increase the risk of painful crises compared to RBC transfusions. For stroke prevention, the evidence was very low quality.
Restrictive versus liberal transfusion strategies: In people undergoing surgery (e.g., cholecystectomy), there was little or no difference in outcomes.
While the reviews were all of high methodological quality (AMSTAR), the quality of evidence for individual outcomes was often low or very low due to risk of bias, indirectness, and imprecision (GRADE).
Conclusion: RBC transfusions prevent stroke in children and adolescents at high risk of stroke and may reduce the risk of SCI, ACS and painful crises. There is a lack of high-quality evidence for adults with SCD. Additionally, reporting of other outcomes, including patient-centred outcomes such as quality of life, remains limited. Further high-quality RCTs are needed to strengthen the evidence base for transfusion practices in SCD.

PO62 | Understanding resource barriers to accessing curative therapy for sickle cell disease

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Introduction: Gene therapy for sickle cell disease (SCD) offers a compelling opportunity to cure a highly morbid disease that affects 100 000 Americans. However, the intensive time and resource demands of gene therapy combined with disproportionate rates of poverty and disparities in healthcare access experienced by patients with SCD raise concerns that a large proportion of patients with SCD will be unable to access this curative therapy. Identifying patient and family-perceived resource barriers to accessing SCD gene therapy is essential to guide the development of supportive care interventions to ensure equitable access.
Methods: This is a cross-sectional, single-center, mixed methods study of children with a diagnosis of SCD age 2 to <18 years who have established care at a large, quaternary care children's hospital. Foreign national patients and patients with history of prior bone marrow transplant or

gene therapy were excluded. Parents/guardians completed a quantitative survey with the following domains: socio-demographics, household structure, household material hardship (HMH—food, housing, utility, or transportation insecurity), household income, and participation in governmental means-tested programs. The survey also included a hypothetical curative therapy scenario—modeled on gene therapy—to assess family-perceived ability to access such a treatment.

Results: Study accrual is ongoing with $n = 80$ enrolled of a target $N = 100$ participants. Among 85 eligible parents approached, 80 (94%) consented to participate, of whom 76 (95%) have taken the survey. Cohort characteristics include children who are parent-identified as Black (63%) or Hispanic (21%), publicly insured (67%), and living in a single-parent household (51%). Parents report a median household income of $50 000 (range $0–315 000); and 65% ($n = 40$) of households are low-income (<200% Federal Poverty Level). Forty-five (59%) parents report HMH in at least one domain, including food insecurity (42%), utility insecurity (42%), housing insecurity (41%) and transportation insecurity (17%). HMH was reported in the context of frequent participation in means-tested programs—including 40% of parents who reported utilizing the Supplemental Nutrition Assistance Program (SNAP), 23% Special Supplemental Nutrition Program for Women, Infants, and Children (WIC), 23% subsidized housing assistance, and 17% energy assistance programs.

Currently, 64% of parents have difficulty in obtaining routine SCD care for their child; they reported challenges with time off work (41%) and transportation (14%) as the biggest barriers. Only 42% of parents thought they would be able to obtain the hypothetical curative SCD therapy with their current resources and social support. Transportation (24%), housing support (21%), and work coverage (20%) were cited as the most helpful proposed resource supports.

Conclusion: Preliminary data demonstrate the feasibility and acceptability of evaluating family-perceived barriers to curative therapy among families of children with SCD. Initial findings show that families of children with SCD face strikingly high resource needs and a majority report they would have difficulty in accessing gene therapy. Ongoing qualitative interviews will provide deeper insight into these challenges and guide the development of targeted health equity interventions to reduce barriers to access.

PO63 | Fixel-based analysis of cerebral white matter diffusion magnetic resonance imaging data in sickle cell anaemia

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Introduction: White matter damage, linked to neurocognitive challenges, in sickle cell anaemia (SCA) has been shown, when analysing dMRI data using tract-based-spatial statistics (TBSS), to be widespread. However TBSS is prone to errors in regions of complex geometry and crossing fibres. Fixel-based analysis (FBA) is a novel diffusion MRI analysis technique that aims to model and hence investigate the properties of the separate fibre bundles within a voxel, therefore overcoming the errors associated with crossing fibre populations.

Methods: The aim was to use fibre-specific metrics of white matter integrity to investigate the changes in white-matter fibre bundles within SCA compared to healthy controls and whether this relates to cognitive outcomes. FBA was applied to a cohort of participants with SCA ($n = 101$) and healthy controls ($n = 44$) between the ages of 8 and 30 years. Healthy controls were age and race matched. The fibre metrics investigated were fibre cross-section (FC), fibre density (FD) and fibre density and cross-section (FDC).

Results: No widespread statistical significant difference in FC, FD or FDC between participants with SCA and controls was found in this analysis, suggesting that there is no widespread difference in white matter microstructure as measured by FBA between these two groups. No significant widespread correlation was identified with processing speed index (PSI) an indicator of cognition. Age was found to be significantly positivity correlated with FC and FDC in widespread white matter in both patients with SCD and healthy controls. Fibre cross-section in this cohort increased with age between the ages of 8 and 30 years. The significant fixels were mostly located in the frontal and temporal lobes. Many of the regions that were related with age in both groups were found to include the corpus callosum. There is a suggestion of divergence in FC between SCD and controls as age increases. Mean FC is higher for healthy controls than patients with SCD, suggesting that the size of the white matter fibres is larger for controls at age 30 years.

Conclusion: Despite no widespread differences in the fibre metrics found between patients with SCA and healthy controls, developmental associations between age and fibre-cross section were found to be widespread. The indication of higher FC in healthy controls suggests that WM development in SCA may be reduced by the exposure to constant hypoxia. This study may have been limited by the cohort size, which may have left the fixel-based analysis underpowered. Also, multiple comparisons correction in FBA is stronger than in TBSS as there are usually more fixels than voxels and FBA is not limited to the WM skeleton, as in TBSS, increasing the amount of white matter included in the analysis.

PO64 | Analysis of the pilot study of the International Hemoglobinopathy Research Network (INHERENT)

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Introduction: Hemoglobinopathies, including sickle cell disease (SCD) and thalassemia syndromes, represent the commonest monogenic diseases. Although their pathogenesis is well established, the diverse clinical manifestations and their varying degree of severity are less understood and are partly influenced by genetic modifiers. Despite the identification and characterization of genetic modifiers by previous studies, these are, as yet, insufficient to guide treatment recommendations or stratify patients reliably. The International Hemoglobinopathy Research Network (INHERENT) investigates the role of genetic modifiers in hemoglobinopathies, with the aim to identify and validate further disease modifiers. This pilot study tested the operational feasibility of the INHERENT study across different geographic and healthcare settings and identified and addressed challenges in performing a large, multi-ethnic genome-wide association study (GWAS).

Methods: The following steps of the study implementation have been tested: (a) obtaining local bioethics approval on the basis of the applicable local legal framework, (b) patient enrolment, written informed consent, and data collection using a common case report form (CRF), (c) sample collection and shipment, (d) genotyping of globin genes, (e) centralized GWAS experiments, and (f) statistical analysis. The completeness of the collected dataset was also assessed.

Results: The pilot study enrolled 1044 patients from 15 centres spanning 8 countries, namely Angola, Cyprus (2), Denmark, DR Congo, Greece (3), Malaysia (3), Nigeria (3), and the USA. Additional 13 centres have obtained a bioethics approval, but have not initiated patient enrolment yet. The distribution by disease group is 42.2% SCD and 57.8% thalassemia patients, while the median age is 28 years (mean: 31.1), with 69.6% adult and 30.4% pediatric patients. Data completeness (affirming presence, absence, or not enough data) of key parameters related to medical complications is approximately 85%, while the range of completeness for laboratory parameters was wide, with a maximum at 80%. Notably, a higher rate of cardiac/pulmonary, kidney/liver, endocrinological and bone complications is observed in adult thalassemia patients, while a higher rate of pain-related and acute anemia complications are observed in pediatric SCD patients.

Biological material for 768 of the patients was shared centrally, and GWAS experiments have been performed using the Illumina GSA SNP array.

Key challenges identified in the pilot study include:

a. the unavailability of key phenotypic data in routine clinical practice in several countries, particularly when the tests are not covered by insurance
b. the need for a more detailed standardization and simplification of the INHERENT CRF to ensure uniform and consistent collection of data across participating centers
c. the unavailability, limited access or high costs of molecular diagnosis services in some countries
d. varying levels of knowledge and technical skills in laboratory work across centers
e. challenges related to the storage, quality and shipping of biological material in some countries

Conclusion: The pilot study tested common standards developed within INHERENT and enabled early identification of key challenges associated with the execution of a large, multi-ethnic study for hemoglobinopathies. The

pilot is pivotal for scaling up the INHERENT GWAS across the entire network, enabling the study of a hemoglobinopathy population of unprecedented size and diversity.

PO65 | Hospital utilisation in sickle cell disorders: A two-year audit of frequent and prolonged inpatient admissions

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Introduction: Sickle cell disorders are complex multisystem conditions that significantly impact quality of life. Individuals can experience acute vaso-occlusive crises, chronic pain, end-organ damage, and early mortality. These complications often lead to frequent hospital presentations and prolonged inpatient stays, disrupting daily life, increasing risk of hospital-acquired complications such as infection and acute chest syndrome, and placing substantial burden on healthcare systems. Understanding factors contributing to frequent admissions and extended hospitalisation is essential to develop strategies that mitigate these effects.
This audit explores common factors among individuals with sickle cell disorders who experienced frequent admissions and prolonged hospital stays at a single Specialist Haemoglobinopathy Team centre between 2022 and 2024 and compares findings to a previous audit in 2015–2018.
Methods: Patients with frequent admissions (>5 inpatient admissions per year) and/or prolonged admissions (hospitalisation >20 consecutive days) were identified via electronic patient records. Relevant demographic, clinical, and psychosocial data were extracted and analysed.
Results: In total, 355 and 435 admissions lasting ≥1 day were recorded for patients with sickle cell disorders in 2022–2023 and 2023–2024 (average stays: 4.63 vs. 5.09 days). 19 patients were included in this audit with mean ages comparable across years (42.8 vs. 43.5 years; range: 14–77). Co-morbidities were common, including depression, chronic kidney disease, and biliary calculi. Most patients (79%, $n = 15$) were receiving disease-modifying therapies (hydroxycarbamide, red cell exchange transfusions, or both). In 2022–2023, two patients had >5 admissions compared with 9 in 2023–2024 (mean admissions: 8.5 vs. 8.22). Mean ages were 28.5 and 33.3 years. Two patients had >5 admissions in both years due to painful crises compounded by poor mental health. Four patients each year had inpatient stays >20 days (range: 21–119). Mean ages were 50 and 66.5 years. Prolonged admissions were commonly initiated by vaso-occlusive crises, then complicated by other factors during hospitalisation. Two patients required ITU admission. During both audit periods, psychology support uptake was high (47.4%, $n = 9$), due to low mood, social or housing needs. Two patients were under mental health services for major or chronic depression. Compared to the 2015–2018 audit, similar numbers of patients had frequent or prolonged admissions.
Conclusion: Patients with frequent admissions often required increased psychological support, likely influenced by the cumulative burden of physical, social, and psychological symptoms related to sickle cell disorder. Those with prolonged admissions tended to be older and had greater needs for social and community services. Both audits revealed persistent themes: significant co-morbidities, high reliance on psychological and community mental health services, and complex social needs including housing and financial instability. These highlight the complex biopsychosocial needs of individuals with sickle cell disorders and support development of integrated, long-term psychological and social care interventions, as is currently being piloted in Southeast London with an enhanced community project. The growing population of complex older patients with sickle disorders requires research into their unmet needs, which is being explored locally with the Ageing Well with Sickle Cell initiative.

PO66 | An integrative pica intervention for children with sickle cell anaemia

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Introduction: 34%–60% of Sickle Cell patients experience pica (Hackworth & Williams, 2003).
A transdiagnostic intervention pathway was developed to support the paediatric Sickle Cell patients, promote sustainability of therapeutic gains, and reduce re-referrals for pica psychology support. This innovative approach formed the basis of a feasibility study, explored treatment efficacy and contributed an answer to the pica 'why' question.
Feasibility in this study addressed four areas regarding patients' access to the 'Pica Intervention Pathway': *Acceptability*; *Demand, Implementation* and *Adaptation*.
The pathway consists of three main stages: (1) Clinical Assessment, (2) Home-Based Intervention and (3) Direct Parent-Patient Intervention. It utilised transdiagnostic approaches of Systemic Psychotherapy, Dialectical Behaviour Therapy (DBT) and parent focused Emotion Coaching.
Methods: Patients referred by clinicians for support were included in the study. Two quantitative questions were explored.

1. Is Pica in this Sickle Cell (Hb SS) patient group related to an emotional wellbeing difficulty (e.g. anxiety or depression), sensory processing need or underlying neurodevelopmental disorder (NDD) of which emotional dysregulation is a feature?
2. Would patients' Revised Children's Anxiety & Depression Scale (RCADS) data indicate intervention efficacy in reducing self-reported anxiety/depression and overall emotional dysregulation?

One qualitative question was explored: *What were patients' and their family's experiences of this intervention?* which was answered through qualitative interviews with four patients/families who completed treatment.

Results: From Dec 2023 to April 2025, 42% (14/33) of paediatric Sickle Cell Anaemia referrals were for pica support. Ten patients started and five completed the intervention; with a 50:50 gender ratio. Two cohorts of patients accessed the intervention.

Results: *Quantitative Question 1*: Clinical assessment (including functional analysis) found pica was associated with an internalised emotional dysregulation problem across the patient group.

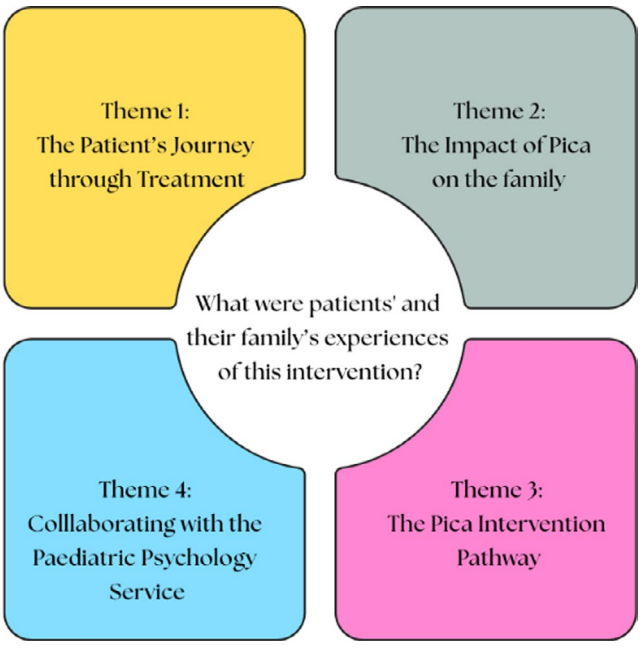
All five patients had sensory difficulties, and three patients were found to have a likely undiagnosed neurodevelopmental disorder (NDD).

Results: Quantitative Question 2: In Cohort 1, there was an approximate 32%–39% drop in self-reported anxiety ratings; and 5%–32% drop in self-reported depression ratings. There was a similar trend with the Cohort 2 patient group.

Qualitative Results: Interpretative Phenomenological Analysis (IPA) (Smith, Flowers & Larkin, 2022) was used to interpret patient/family intervention experiences, and analysis elicited four 'Group Experiential Themes' related to intervention *acceptability* illustrated in the figure below.

Conclusion: This feasibility study suggests promising acceptability findings based on the mixed-methods data interpretation. The continuation of the intervention will shape ongoing formulation concerning this patient group and the pica phenomenon.

Clinical formulation suggests that clinicians and families must be aware of the presence of social factors (e.g. school/academic experiences, parenting styles, racism) as contributors to pica behaviour for this patient group. Additionally,



the presence of potential neurodevelopmental disorders (NDDs) in this patient group has been suggested. The remaining feasibility criteria is addressed in the figure below.

PO67 | Survival of patients with congenital red blood cell disorders: A Danish register based analysis

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Introduction: Congenital red blood cell (RBC) disorders are the most common genetic disorders worldwide, including haemoglobin disorders such as sickle cell disease and alpha and beta thalassemia, which are a large contributor to childhood mortality in in low resource countries where these disorders are prevalent. Congenital RBC disorders are becoming more common in Denmark and other European countries due to migration. Denmark has complete and reliable nationwide routinely collected registers, providing opportunities to examine the status of patients with RBC disorders, and compare with matched unaffected individuals.

Methods: We identified all congenital RBC patients registered in the National Patient Register and the Danish Red Blood Cell Center's laboratory database from 1st January 1980 to 31st December 2021. Patients were diagnosed using an algorithm based on laboratory verified hemoglobin phenotype or ICD10

diagnosis codes, and included genetic carriers, by which analyses were stratified. Diagnoses were grouped:

- Alpha thalassemia
- Beta thalassemia
- Sickle cell disease
- Hereditary spherocytosis
- Other congenital disorders (including G6PD deficiency)
- Poorly defined disorders

Two comparator populations were identified in the Danish civil registration system, with up to 40 comparators per patient, matched on:

- Age and sex
- Age, sex and world region of origin

Individuals were followed from date of diagnosis until death, emigration, or end of study (31st December 2021), whichever occurred first.
Kaplan–Meier estimators were used to describe survival, and hazard ratios were estimated with Cox regression analyses.
Results: The following populations were identified:

- 5378 congenital RBC disorder patients:
  - Alpha thalassemia $n = 152$
  - Beta thalassemia $n = 386$
  - Sickle cell disease $n = 292$
  - Hereditary spherocytosis $n = 1476$
  - Other congenital disorders $n = 737$
  - Poorly defined $n = 2335$
- 8213 genetic carriers
- 313 655 age-sex matched comparators
- 170 673 age-sex-origin matched comparators

A total of 4 991 252 years at risk for patients, carriers and comparators was observed with a median follow-up time of 7.6 years [IQR: 3.6, 14.3].
Median age at diagnosis for patients was 36.3 years [IQR: 7.3, 66.2]. Women were overrepresented in alpha, beta thalassemia and sickle cell disease groups (55%, 60% and 58%, respectively). Overall, survival for congenital RBC patients was impacted. Adjusted hazard ratios [95% CI] for death for congenital RBC patients compared to age-sex matched comparators: alpha thalassemia 1.3 [0.7, 2.5], beta thalassemia 2.8 [2.1, 3.6], sickle cell disease 3.0 [2.1, 4.3]. Five year survival for congenital RBC patients was 78%, carriers 98%, age-sex comparators 95% and age-sex-origin matched comparators 92%.
Conclusion: Survival is impacted by congenital RBC disorders in Denmark. The observed reduction survival of congenital RBC disorder patients relative to comparison groups may represent a lower bound for true survival differences due to unobservables. Results may be impacted by healthy migrant effect describing the hypothesis that the healthiest individuals with enough resources and the ability to migrate from their home country, are likely to have better health status than native residents in a new country. Patients had relatively high median ages at diagnosis which may reflect migration rather than an original diagnosis. No clear impact of genetic carrier status was observed.

PO68 | From multiprofessional to interprofessional: Rethinking how we teach haemoglobinopathy management

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Introduction: The management of Sickle Cell Disorder (SCD) requires effective collaboration between diverse professionals. Traditional medical education tends to separate professional groups, limiting learners' understanding of others' roles and reducing confidence in interprofessional collaboration. Interprofessional education is widely recognised as an effective strategy for improving care in other chronic diseases. A notable gap remains in the literature specific to interprofessional education in SCD, despite the condition's inherently multidisciplinary management involving coordinated decision-making across medical, nursing, pharmacy, laboratory, and psychosocial teams to deliver high-quality, holistic care (Fox et al., 2018).
Methods: We designed a case-based interprofessional teaching session as part of a haematology education day. Participants included medical students, foundation and early-career doctors, nurses, pharmacists, advanced nurse practitioners, clinical nurse specialists and biomedical scientists. The case focussed on sickle cell crisis and was designed to reflect a real-world clinical scenario, incorporating authentic laboratory data, psychosocial complexity, and key safety considerations, including the risk of alloimmunisation. Facilitators were briefed to encourage participants to teach and learn from one another, drawing on Vygotsky's concept of the "more knowledgeable other" (Vygotsky, 1978). Pre- and post-session questionnaires evaluated changes in participants' confidence, attitudes, and understanding of interprofessional roles in haemoglobinopathy care. Responses were collected using a 5-point Likert scale (1 = Strongly Disagree, 5 = Strongly Agree), supplemented by free-text responses exploring moments of perceived learning from other professionals.
Results: 40 individuals participated in the session; 40 completed the pre-course questionnaire and 29 completed the post-course evaluation. Mean scores improved across all interprofessional learning domains. The most notable increases in: (1) understanding the competencies of other professionals (3.75 → 4.38, Δ + 0.63); (2) confidence in interprofessional communication (3.93 → 4.45, Δ + 0.52); and (3) awareness of how others complement their own role (3.98 → 4.48, Δ + 0.51). Free text responses indicated a better understanding of roles (particularly laboratory and pharmacy), and recognition of the value of shared responsibility in SCD care. Participants highlighted peer-to-peer teaching as a meaningful part of their learning.

Conclusion: Interprofessional, case-based teaching meaningfully improves learners' understanding of roles, communication, and collaboration in sickle cell care, addressing a critical gap in traditional haemoglobinopathy education and supporting safer, more integrated patient care. This approach moves beyond learning "with" others to learning from and about them, aligning with priorities for integrated care and patient safety (WHO, 2010).

PO69 | Red cell exchange in transfusion-dependent thalassaemia: A case series from three UK centres

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Introduction: Red cell exchange (RCE) is widely employed in the management of sickle cell disorder, offering a reduced risk of iron accumulation compared to standard top-up transfusions while concurrently lowering sickle haemoglobin levels (Stussi et al., 2019; Berdoukas et al., 1986). In thalassaemia syndromes, iron overload arises due to chronic transfusion requirements and ineffective erythropoiesis. Although chelation therapy remains the standard approach to iron burden management, its efficacy may be compromised by intolerance, toxicity, or suboptimal adherence (Musallam et al., 2025). This study presents a case series of three adult patients with transfusion-dependent thalassaemia for whom RCE was utilised primarily as a strategy to mitigate iron overload.
Methods: Three patients from separate UK centres with transfusion-dependent β-thalassaemia (β^0/β^0, β^+/β^0, E/β^0) underwent RCE due to limitations in chelation therapy. We reviewed transfusion regimens, chelation history, iron parameters (serum ferritin, liver iron concentration (LIC), cardiac T2*), chelation side effects and outcomes before and after RCE.
Results: Patient 1 (Female, 52, South Asian): β^+/β^0 genotype, transfusion-dependent since infancy. Due to significant chelator toxicity (optic neuritis, renal impairment, arthritis), manual RCE every three weeks (3 units) was commenced and tolerated well, with occasional vasovagal episodes. Over 18 months of RCE, there has been an improvement in iron load (ferritin 4252 to 3822 ng/mL; LIC 12.1 to 5.8 mg/g/dw). Cardiac T2* has declined slightly (32.5 to 25.7 ms) but remained within an acceptable range. Alloantibodies (Anti Bg(a), Anti Kp(a)) were present prior to initiating RCE, with no new alloantibody formation. RCE continues alongside low-dose chelation with deferiprone and deferasirox.
Patient 2 (Male, 59, Turkish): β^0/β^0 genotype, transfusion dependent since infancy. Due to poor adherence to chelation (desferrioxamine), automated RCE was commenced every 7 weeks with 8 units and tolerated well. Over 18 years of RCE, ferritin has remained stable (latest 768 ng/mL); LIC and cardiac T2* have not been assessable due to scan intolerance. There has been no new alloantibody formation. RCE is ongoing, with low-dose deferasirox.
Patient 3 (Female, 56, South Asian): E/β^0 genotype, transfusion dependent since adolescence. Due to severe intolerance to all standard chelators (angioedema, systemic pain, fevers), manual RCE was commenced every 6 weeks (3 units in, 2 units out) and tolerated well. Over 12 years, there has been a significant improvement in iron load: ferritin reduced from 3971 to 288 ng/mL; LIC from 24.2 to 8.9 mg/g/dw; cardiac T2* from 29 to 37 ms. There has been no new alloantibody formation. RCE was discontinued and she now receives top-up transfusions with low-dose desferrioxamine, which she is able to tolerate.
Conclusion: RCE can be an effective and safe iron removal strategy in transfusion-dependent thalassaemia patients who are unable to tolerate or adhere to chelation. In selected individuals, it offers a means of achieving iron reduction with minimal side effects. These cases illustrate varied indications and outcomes of RCE in thalassaemia and highlight its potential as a useful adjunct or alternative to chelation therapy. Further prospective studies are warranted to define optimal protocols, patient selection, cost-effectiveness, and the impact on these regimens on the control of the ineffective erythropoiesis.

PO70 | Physician-reported patient population overview in sickle cell disease: A multinational, real-world survey

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Introduction: Sickle cell disease (SCD) is an inherited blood disorder caused by a β-globin gene mutation producing sickle Hb (HbS). This causes red blood cell sickling, leading to hemolysis, anemia, vaso-occlusive crises (VOCs), and cumulative organ damage. Limited evidence is available through global physician-reported patient clinical data. We aimed to describe the clinical characteristics, healthcare resource utilization and treatment in SCD populations across multiple regions.
Methods: Data were evaluated from the Adelphi Real World SCD Disease Specific Programme, a cross-sectional survey with retrospective data collection in Brazil, EU5 (France, Germany, Italy, Spain, the United Kingdom), India, Kingdom of Saudi Arabia (KSA), and the United States (US) from August 2024 to April 2025. Physicians reported patient data, via a Patient Record Form, on demographics, clinical characteristics, hospitalizations and treatment. Patients who had received a bone marrow transplant, gene therapy, or voxelotor were excluded from this descriptive analysis.

Results: Overall, 306 physicians reported data on 2191 patients (Brazil: $n=233$; EU5: $n=1100$; India: $n=258$; KSA: $n=251$; US: $n=349$). Mean (standard deviation; SD) patient age was 26.7 (12.8) years, 55.1% were male, and 48.6% were Black, African American, or Caribbean.

Overall, 65.1% of patients had HbSS genotype (Brazil: 61.3%; EU5: 63.1%; India: 69.8%%; KSA: 72.2%; US: 65.5%). Mean (SD) number of VOCs in the past 12 months was 1.9 (2.0) with 49.8% of patients experiencing ≥2 VOCs (Brazil: 50.6%; EU5: 43.0%; India: 57.8%; KSA: 80.9%; US: 42.7%). Mean (SD) hemoglobin level was 9.6 (1.5) g/dL (Brazil: 9.3 (1.5); EU5: 9.9 (1.5); India: 9.3 (1.6); KSA: 9.1 (1.5); US: 9.6 (1.5)). Iron overload through most recent ferritin levels of >1000 ng/mL were reported in 2.6% of patients (Brazil: 7.1%; EU5: 2.1%; India: 0.0%; KSA: 5.7%; US: 0.0%). Overall, 47.4% of SCD patients were diagnosed with comorbidities, anxiety (25.7%) and depression (10.2%) were the most widely reported.

Excluding routine visits for treatment or blood transfusions, mean (SD) overall number of hospitalizations was 1.3 (1.9) in the past 12 months (Brazil: 0.8 (1.0); EU5: 0.8 (1.6); India: 1.8 (1.7); KSA: 3.4 (2.6); US: 0.9 (1.3)). Of these hospitalizations, the mean (SD) number of hospitalizations specifically for VOCs was 2.0 (1.6) (Brazil: 1.4 (0.7); EU5: 1.7 (1.3); India: 1.9 (1.2); KSA: 3.2 (2.1); US: 1.8 (1.3)).

Hydroxyurea was the most widely prescribed medication for SCD (74.0%; Brazil: 70.9%; EU5: 72.4%; India: 96.5%; KSA: 87.7%; US: 53.9%). In the US only, SCD modifying treatments including Crizanlizumab (34.1%) and L-glutamine (11.7%), were more commonly prescribed than in other countries, due to access. Overall, 73.8% of patients had received a blood transfusion in the past 12 months (Brazil: 78.6%; EU5: 74.0%; India: 80.2%; KSA: 81.2%; US: 59.3%). Mean (SD) number of transfusions was 2.6 (3.4) (Brazil: 2.9 (5.0); EU5: 3.1 (3.3); India: 2.0 (2.9); KSA: 2.4 (3.1); US: 1.3 (1.7)). Overall, 24.3% of patients were receiving chronic transfusions at survey completion (Brazil: 21.6%; EU5: 30.3%; India: 23.3%; KSA: 29.6%; US: 5.2%).

Conclusion: Despite the high use of SCD treatment and blood transfusions, people with SCD still experience pain crises, low hemoglobin levels, elevated ferritin levels, comorbidities, and hospitalizations. More treatment options and improved access to comprehensive SCD care may reduce the rate of SCD complications and acute care utilization.

PO71 | The frequency of alloimmunization in patients with sickle cell disease: Risk factors and outcomes

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Introduction: Sickle cell disease (SCD) is a prevalent hemoglobinopathy in Oman, with an estimated prevalence of 0.2%, making it relatively common among genetic disorders. Blood transfusions are essential for managing severe complications of SCD, but repeated transfusions can lead to red blood cell (RBC) alloimmunization. This complicates transfusion therapy and patient care. Understanding the frequency, associated risk factors, and outcomes of alloimmunization in SCD patients is vital to develop targeted prevention strategies suitable for this population.

Methods: This retrospective cohort study included 421 SCD patients with a positive antibody screen who attended Sultan Qaboos University Hospital (SQUH) between 2006 and 2024. Clinical, laboratory, and transfusion-related data were extracted from the hospital's patient information system. Data were analyzed using IBM SPSS version 23. Descriptive statistics summarized patient characteristics and alloimmunization prevalence. Associations between alloantibody presence and clinical outcomes were examined using chi-squared tests. A $p<0.05$ was considered statistically significant.

Results: The alloimmunization rate among transfused SCD patients at SQUH was 6.39%. Of the 421 patients with a positive antibody screen, 334 had specific alloantibodies identified. Females comprised 58% of the cohort, males 42%. The median age was 35 years (range 1–79), with most patients having the HbSS genotype. The most frequently identified alloantibodies were Anti-E (31.4%) and Anti-K (22.6%).

Risk factor analysis showed higher alloimmunization rates in females. Splenic status data revealed that 36% of patients had undergone splenectomy or were autosplenectomized. Age at first transfusion was available for 124 patients, with 21.7% receiving their first transfusion at ≤5 years. Additionally, 47% of patients had received transfusions outside SQUH.

Among the cohort, 44 patients developed transfusion reactions: 11 experienced delayed hemolytic reactions, 7 had acute hemolytic reactions, and the rest developed non-hemolytic reactions. Anti-E was the most common alloantibody detected in patients with transfusion reactions.

Conclusion: Alloimmunization is a notable complication among SCD patients receiving transfusions. Anti-E and Anti-K were the most common alloantibodies identified. A significant proportion of patients received transfusions outside the primary care setting, where extended antigen matching may have been lacking. The occurrence of both hemolytic and non-hemolytic transfusion reactions emphasizes the need for enhanced transfusion protocols, including extended antigen matching and centralized transfusion monitoring, to minimize alloimmunization and improve patient outcomes.

PO72 | Fetal hemoglobin's effect on malaria in African sickle cell patients: A thematic regional analysis

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Background: Malaria and Sickle Cell Disease (SCD) are two of the most pressing health challenges across sub-Saharan Africa, often intersecting in both geographic distribution and clinical burden. While the sickle cell trait is known to

confer partial protection against malaria, the role of elevated fetal hemoglobin (HbF) levels in modifying malaria infectivity and disease outcomes among individuals with SCD remains underexplored. This thematic analysis investigates the relationship between HbF levels and malaria susceptibility in African populations affected by SCD, within the broader context of the regional disease burden and emerging therapeutic perspectives.

Methodology: This analysis synthesizes data from peer-reviewed studies, regional health surveillance reports, and hospital-based records published between 2000 and 2024. Using a thematic framework, patterns were identified regarding malaria incidence, severity, and hospitalization among SCD patients with varying HbF levels. Studies were selected based on inclusion of HbF quantification, confirmed SCD genotypes, and documented malaria outcomes. Key themes such as age-related HbF expression, antimalarial intervention coverage, and hemoglobinopathies were examined to contextualize findings within regional healthcare dynamics.

Results/Lessons Learnt: Findings across multiple African regions suggest a consistent association between elevated HbF levels and reduced malaria infectivity among individuals with SCD. Patients with higher HbF concentrations exhibited fewer clinical episodes, decreased symptom severity, and improved recovery outcomes. The protective role of HbF appears to be mediated by enhanced red cell stability and reduced parasite propagation. However, variations in healthcare access, co-morbidities, and prophylactic measures influenced outcomes across different settings. These disparities underscore the importance of considering genetic and systemic factors in malaria control efforts among SCD populations.

Recommendations: This analysis underscores the potential of elevated HbF as a mitigating factor in malaria morbidity among patients with SCD. There is a growing need to integrate HbF-boosting therapies into public health strategies in malaria-endemic regions. Enhancing early diagnosis, supporting hydroxyurea access, and investing in community-level education could contribute significantly to dual disease management. Future policies must recognize the intersection of genetics and infectious diseases to foster more equitable, data-driven interventions across Africa.

PO73 | Regional treatment perceptions among people with sickle cell disease and their caregivers: LISTEN survey findings

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Introduction: People with sickle cell disease (PwSCD) experience pain episodes, fatigue and multi-organ complications. There is a paucity of data on awareness among PwSCD and their caregivers (CGs) about symptomatic and disease-specific treatment methods for SCD.

Aim: This regional analysis of the global LISTEN survey identified PwSCD and CGs perceptions of treatment methods and satisfaction rates for SCD.

Methods: LISTEN was a quantitative survey conducted between 06-Oct-2022 and 22-Aug-2023 in 17 countries. Eligible participants were from diverse regional groups: Sub-Saharan Africa (SSA), Europe (EUR), Latin America (LATAM), Middle East and North Africa (MENA) and South-Asia (SA). PwSCD aged ≥18-years and CGs must care for an SCD patient and be involved in making decisions around SCD treatment for PwSCD in their care, rated the importance of factors (grouped into five main categories) on a Likert scale.

Results: PwSCD ($n = 891$) and CGs ($n = 163$) responded about treatment types and satisfaction, while 562 PwSCD and 103 CGs responded about SCD-specific treatment. Across all regions, the percentage of PwSCD who received treatment to reduce or alleviate SCD symptoms varied between 60% and 82% with the highest reported in SA (82%) and the lowest in Europe (60%). However, pain management treatment was more consistent between regions (62%–69%). The use of regular blood transfusions and antibiotics varied across regions, with the highest usage reported in MENA (44%) and Europe (43%), respectively. Fewer than a quarter of PwSCD from SSA (15%) and MENA (13%) were unaware of the treatment. The majority (78%–95%) of PwSCD were on hydroxycarbamide/hydroxyurea (HU) for SCD specific treatment across all regions, with the lowest reported in SA (78%). PwSCD reported low satisfaction with SCD treatment (36%–60%) across all regions, with the least satisfaction in SA (36%). CGs of PwSCD reported variable rates of awareness of SCD specific treatment (55%–95%) and treatment for pain (0%–91%), with 39%–85% satisfaction rates.

Conclusion: A varied landscape of treatment models and satisfaction levels among PwSCD and their CGs were observed. While treatment for pain was consistent across all regions, treatment to alleviate/reduce SCD specific symptoms varied from 60% to 82%, highlighting, perhaps, different disease phenotypes, treatment patterns or access to therapy. High treatment dissatisfaction rates indicate a need for region-specific approaches to care that utilise innovative therapies or access to additional disease-modifying therapies.

PO74 | Is unilateral arm cannulation equally effective in removing haemoglobin S as bilateral arm cannulation?

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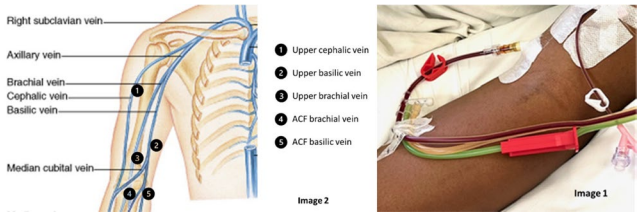
Introduction: Establishing peripheral venous access (VA) for automated red blood cell exchange (RBCEx) is

conventionally achieved by inserting cannulas in both arms (bilateral). This practice is due to concern that dual cannulation in one arm (unilateral) may be less efficient, as there is a risk of immediate re-circulation of the patient's processed blood back into the extracorporeal circuit.

Our center has adopted a unilateral arm cannulation (ULAC) method intended to minimize blood recirculation and be as effective in removing Haemoglobin S (HbS) as bilateral arm cannulation (BLAC). This study compared cannulation techniques to test the null hypothesis that ULCA for RBCEx is as effective as BLAC in removing HbS.

Methods: Data was prospectively collected during consecutive procedures. The removal efficiency (RE) of HbS was calculated using pre and post procedural HbS percentage (HbS%). Data was collected from 14th January to 3rd June 2025. Procedures were excluded if the Fraction of Remaining Cells (FRCs) was <30% or >40%. Only procedures undertaken with peripheral veins were included. Ultrasound was used to assist all vein cannulations. The average RE percentage for each cannulation method was compared using the unpaired *t* test.

The return cannula was sited 'upstream' (more proximal to the heart) from the inlet cannula in the ULAC method to minimalize the risk of blood recirculation. Different vein tributaries were used for the return and inlet cannulae (e.g. cephalic and basilic). The return cannula was sited in the upper cephalic vein at the level of the mid bicep muscle. The inlet cannula was sited in either the antecubital fossa (AFC) or upper basilic or brachial veins (see Images 1 and 2).



Any vein suitable for cannulation was used in the bilateral arm method.

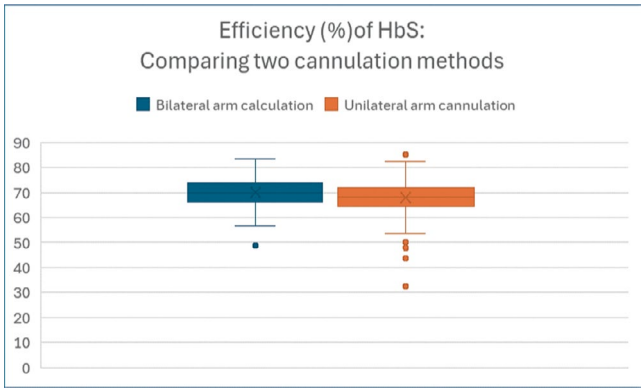
Results: 550 procedures were undertaken. 59 procedures were excluded either because the pre and/or post HbS% results were not available (no. 18) or the FRCs was <30% or >40% (no. 37). The pre HbS% blood sample was tested 0 to 5 days prior to the RBCEx (87.5% ≤2 days).

Table 1.

Method	Total	HbS% removal efficiency		
		Range	Average	Median
ULAC	404	32.59% to 85.23%	68.03%	68.22%
BLAC	91	48.89% to 83.40%	70.11%	69.88%

Statistical analysis demonstrated that the ULAC is actually less efficient in removing HbS ($p \leq 0.0034$, 95% confidence interval (−3.4650 to −0.6926) when compared to the BLAC. Although the median RE was similar, there were more outliers in the unilateral arm technique (no. 5) (see Graph 1).

GRAPH 1



Conclusion: These results conflict with the null hypothesis, since a significant difference between the two methods has been demonstrated. Results were skewed by the 5 outliers in the ULAC. Two of these patients have been changed to the BLAC method due to recurring low RE.

Minor vein networks between the main vein branches, may occasionally exist, that allows a proportion of the blood being returned via the return cannula to be recirculated into a relatively closely located inlet cannula. It is important to review the efficiency results of each procedure to identify such individuals.

The ULAC method was used considerably more often in this study as it is favoured by many patients. Prospective data will be collected to obtain a larger data set.

PO75 | Constipation in children with sickle cell disease in Sultan Qaboos University Hospital: Management and outcome

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Introduction: Sickle cell disease (SCD) is considered the most common blood disorder in the world, with a high prevalence in Oman compared to the other Gulf countries. The main symptoms in patients with SCD are painful episodes or vaso-occlusive crises (VOCs) in different body regions.

Constipation might negatively affect the quality of life of SCD patients and increase the frequency of VOCs. The

current research aims to compare the outcome of the treatment of constipation and its relation to the reduction of VOCs. We also reported the different management types of constipation in SCD patients and their efficacy.
Methods: We collected data of 299 patients with SCD who had undergone abdominal X-rays in Sultan Qaboos University Hospital (SQUH), Muscat, Oman, from April 2007 to November 2024 through the Electronic Patient Records (EPR) and found to have markedly loaded colon. We counted the average number of VOCs for each patient per year before the treatment of constipation and then for one year after effective resolution of constipation.
Results: Most of the caregivers and older children (72%) denied a history of chronic constipation before the abdominal X-ray was taken. The medical treatment of constipation included phosphate enemas, movicol, and lactulose. Lactulose was the most frequently used laxative, in 68.9%, and physiotherapy was the least used method, which was used only in 8% of the patients. Moreover, laxatives and physiotherapy were able to reduce the number of VOCs/year after treating the constipation. Although physiotherapy to treat constipation was the least commonly used, it resulted in the greatest reduction in the median of VOC/year from 4.5 to 2.
Conclusion: Constipation is a common finding in children with SCD. Treatment of constipation, whether through medications or physiotherapy, is associated with a reduction in the rate of VOCs. Clinicians looking after children with SCD should be aware of chronic constipation as one of the precipitating factors of vaso-occlusive crises in children with SCD.

PO76 | Applying co-design throughout the research cycle; co-designing a research proposal with adults with sickle cell

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Introduction: There is a lack of literature to guide healthcare providers on feasible, acceptable and effective non-pharmacological pain self-management strategies for adults with SCD. Clinical data from a single site in England suggests that a sickle cell specific pain management programme is acceptable and may positively impact pain related outcomes and hospital utilisation. However, there are challenges with recruitment and equitable delivery. Recognising these challenges, we utilised co-design principles to develop a research proposal informed by existing evidence and knowledge provided by adults with sickle cell and healthcare professionals. We suggest that utilising co-design principles during research development supports research that is meaningful and relevant to those who care about it most.
Methods: *Phase 1.* A core patient-partnership group, including three females with lived experience of sickle cell, was established. Three depth discussions were facilitated by a clinical academic. Meeting summaries were shared with themes linked to accompanying quotes. Guided by the summaries, the project group proposed six fundamental elements of a sickle cell self-management intervention, illustrated in a co-designed resource [Figure 1].
Phase 2. The clinical academic met eleven people with sickle cell with no previous involvement in the project. The co-designed resource was used to spark conversation. Feedback on the resource lead to further refinement, and members used it as a foundation for broader discussions. Through these conversations, and conversations with healthcare professionals, the project group gained clarity on aspects of the proposal related to acceptability and feasibility, including:

- Pain self-management research was identified as a research priority.
- Development of an intervention suitable for multi-professional delivery, for equitable care, was valued.
- Members favoured resources focused on patient narratives and real-life experiences.
- Members supported development of digital resources.
- Features of Experience Based Co-Design were perceived as helpful to ensure the experiences of people with sickle cell would be heard within the project.

Phase 3. The clinical academic drafted a proposal incorporating feedback from the groups. The draft was refined and finalised by the project partners.
Results: We demonstrated that incorporating co-design principles throughout the research cycle is achievable with investment of time and resources. Building relationships and developing trust is key. Critical actions include:

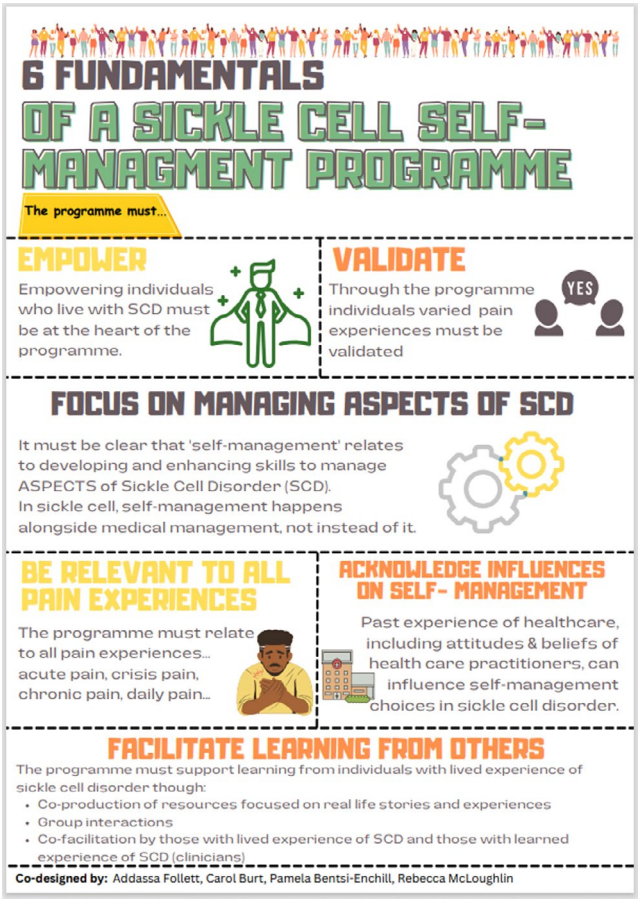
- Planning for multiple meetings with key partners to build relationships.
- Acquiring adequate funds to remunerate individuals in recognition of their time and input.
- Providing feedback on suggestions or insights incorporated into the project plan and ideas that aren't included.

Involving individuals with different types of knowledge in the development of our research proposal brought multiple benefits:

- New and different perspectives were gained.
- Insights into areas of complexity facilitated decision-making.
- Confirmation that the project focused on a priority area.

Conclusion: Incorporating co-design principles is possible during the development of sickle cell research proposals, with adequate commitment and resources. Utilising co-design approaches can support research that is meaningful and acceptable to people who live with sickle cell who the research impacts most.

Figure 1:



PO77 | Perceptions and knowledge gaps regarding artificial intelligence among hematology professionals: Where do we stand?

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Introduction: Preliminary evidence of Artificial Intelligence (AI) introduction in healthcare shows strong potential in enhancing patient outcomes. In hematology, applications are emerging rapidly. To support successful AI integration into health care systems, it is crucial to assess healthcare professionals' (HCPs) understanding of basic AI concepts, as well as their attitudes and expectations regarding its clinical application.

Methods: It was administered a cross-sectional validated survey which covered demographics, work setting, AI-related knowledge, research involvement, perceived impact, implementation barriers, concerns, and clinical phases where AI could offer value. It targeted all healthcare professionals and researchers part of the European hematology community via ERN-EuroBloodNet and HELIOS, and was distributed through the EU Survey Platform between January and June 2025. Participation required electronic informed consent and complied with GDPR regulations.

Results: Preliminary analysis included 73 participants from 25 countries across four continents: Europe (79.5%), Asia (11%), Africa (8.2%), and America (1.4%). Most worked in teaching hospitals (74%). Of the sample, 64.4% were involved in clinical practice and research, while 35.6% were exclusively researchers. Physicians comprised 49.3%—predominantly senior attendings (69.4%)—with the rest being nurses, biologists, and other HCPs. Educationally, 24.3% had an MSc and 56.8% held a PhD.

Regarding AI knowledge, 74% correctly pointed to the definition of "Machine Learning (ML)," though 38.4% were unsure, and 22.5% of those confident answered incorrectly. For "Deep Learning (DL)," 57.5% chose correctly, yet 47.9% were unsure, and 37% of confident respondents answered incorrectly. While 56.2% were familiar with "Big Data," only 31.5% identified their core characteristics (Volume, Variety, Velocity).

AI tool usage was reported by 71.2%: 28.8% used one, 30.1% used two to four, and 12.3% used more than four. Tools included ChatGPT-like applications for data handling, natural language processing, and predictive models for diagnosis, prognosis, and patient safety. Big Data sources cited were wearable devices, genomics, multi-omics, and electronic health records.

A substantial 76.7% had read at least one AI-related hematology publication, and 37% were actively involved in AI projects. The perceived impact of AI was highly positive: 94.6% believed it would improve both patient outcomes and their field. However, key implementation barriers included lack of skills/knowledge, limited funding, and restricted data access. Main concerns were privacy (61.6%), bias and fairness (60.3%), and accountability.

Conclusion: While there is strong enthusiasm for AI in hematology, notable gaps in foundational knowledge exist. Many healthcare professionals struggle with correctly defining key AI terms, sometimes overestimating their understanding. As AI tools become increasingly embedded in clinical practice, their successful implementation will require focused training to prevent misuse and minimize bias. This transition may be challenging for both professionals and patients, highlighting the need for

a structured and gradual approach. Supporting healthcare professionals through tailored educational opportunities will enhance critical thinking and decision-making capacity, easing the shift and reducing risks associated with rushed or incorrect implementation. A deliberate, inclusive strategy is essential to ensure that AI integration makes a meaningful and sustainable impact during this pivotal period of technological transformation.

PO78 | A needs assessment approach to define educational priorities for hemoglobinopathy care: Insights from HELIOS COST action

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Introduction: Effective management of hemoglobinopathies requires specialized knowledge and collaboration among healthcare professionals (HCPs). With an increasing number of patients needing specialized care across Europe, there is an urgent need to train the next generation of HCPs to improve patient outcomes and quality of life. This study aimed to map the expertise and educational priorities of trainees and mentors involved in hemoglobinopathy care and research within the European COST Action HELIOS, a global network of over 220 individuals from 33 countries, endorsed by ERN-EuroBloodNet.

Methods: A cross-sectional online survey covering multidisciplinary aspects of hemoglobinopathy diagnosis, management, and treatment was co-designed by researchers coming from different backgrounds (nursing, bioscience, internal medicine and pediatrics). The survey codesign was preceded by a targeted literature review that identified key topics, which were refined through final expert consensus involving professionals from multiple countries. The survey assessed availability and area of expertise of potential mentors, possible training activities, alongside trainees' educational priorities. It was then conducted among HELIOS participants from September 2024 to January 2025. Responses were analyzed using descriptive statistics and comparative analyses to assess variations in training needs across regions, age groups, and professional roles.

Results: A total of 76 HELIOS participants from 27 countries responded in the initial release of the survey. Most respondents were aged 30–49 (78%) and held PhDs (78.3%), primarily working in teaching hospitals (52%) or research institutes (30.7%). Physicians were the largest group (39.5%), with 13 other professional roles represented. A majority (66%) were interested in receiving training, including 18 mentors who also sought to advance their knowledge in specific areas such as multidisciplinary management, psychosocial care, and palliative care. Mentor expertise focused on molecular pathophysiology (50%) and diagnosis (43.3%), with gaps in implementation science, ethics, pain management, and patient monitoring (all ~20%). Underrepresented areas included hematopoietic cell transplantation, palliative care, and interprofessional models (all ≤14%). Trainees prioritized diagnosis (86%), research (84%), ethics (80%), and emerging areas such as AI (91%), although rated all survey topics as important, expressing at least 44% interest for each topic. No significant regional or age differences were observed.

Conclusion: The survey reveals expertise in molecular pathophysiology and evidence-based screening and diagnosis, but highlights gaps in comprehensive patient management, palliative care, and psychosocial aspects. These gaps align with high trainee demand, reflecting the growing complexity of hemoglobinopathy management. Remarkably, trainees expressed significant interest across all surveyed topics, with each garnering at least 40% interest. This broad enthusiasm, coupled with mentors' interest in receiving additional training in specific areas, underscores the current lack of a well-rounded and systematic educational approach. To address these needs effectively, adopting a participatory needs assessment approach in selecting topics and implementing diverse educational strategies (e.g., hands-on workshops, mentorship programs, journal clubs) is a key aspect to ensure the creation of both rigorous and relevant training. Such a program will be designed by HELIOS to keep pace with the changing landscape of hemoglobinopathy care, to equip emerging specialists with the diverse skill set required for delivering comprehensive, patient-focused care.

PO79 | Systematic review of carotid intima-media thickness in beta-thalassemia: comparative analysis and biomarker relationships

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Introduction: Premature atherosclerosis is a significant cardiovascular complication in beta-thalassemia. Carotid intima-media thickness (CIMT) serves as a non-invasive marker of subclinical atherosclerosis and is increasingly used in clinical and research settings. Numerous studies have evaluated CIMT in beta-thalassemia patients and its association with disease-related biomarkers, yet findings remain inconsistent. This systematic review aims to assess differences in CIMT between beta-thalassemia patients and healthy individuals and explore its correlation with key biomarkers.

Methods: A systematic review was conducted following PRISMA guidelines. Databases searched included PubMed, Web of Science, ScienceDirect, and the WHO Virtual Health Library. Observational studies reporting CIMT values in beta-thalassemia patients versus healthy controls, or its correlation with biomarkers, were included. Analyses were performed to calculate standardized mean differences (SMD) and pooled correlation coefficients using random-effects models. Risk of bias was assessed using Joanna Briggs Institute tools, and publication bias was evaluated using funnel plots, Egger's, and Begg's tests.

Results: Twenty-six studies with 1236 patients were included. Analysis showed significantly higher CIMT values in patients with beta-thalassemia major (SMD = 1.50, 95% CI: 0.929–2.075, $p < 0.001$) and intermedia (SMD = 1.50, 95% CI: 0.243–2.751, $p = 0.019$) compared to healthy controls. CIMT in beta-thalassemia major was positively correlated with disease duration ($r = 0.669$, $p = 0.011$), patient age ($r = 0.385$, $p = 0.048$), serum ferritin ($r = 0.319$, $p = 0.004$), and total cholesterol ($r = 0.353$, $p = 0.047$). No significant correlations were found with BMI, hemoglobin, or LDL.

Conclusion: Beta-thalassemia, particularly major and intermedia types, is associated with increased CIMT, indicating elevated risk for subclinical atherosclerosis and cardiovascular complications. CIMT also correlates with several clinical and biochemical markers, underscoring its value as a tool for risk assessment in these patients. Regular cardiovascular monitoring should be integrated into the clinical care of beta-thalassemia patients.

PO80 | The patient journey—Prioritising awareness of sickle cell disease early in medical training

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Introduction: Despite considerable progress in specialist led care for patients with sickle cell disease (SCD), the management of acute crises by non-specialists remains substandard. This can lead to patient frustration, avoidance or delays presenting to hospital and sometimes even death. The 2021 all party parliamentary report 'No-one's listening[1]' identified serious failings in care to patients with SCD, including poor training of non-specialist clinicians and perceived medical racism.

To raise awareness early on in medical training, our team of medical education fellows developed a training session for pre-clinical medical students as part of their 'Transition to Clinical Practice' module.

Methods: We designed an interactive small-group training session for medical students, entitled '24 h in A&E: the journey of a sickle cell patient.' The 120-min session aimed to meet the identified learning gap and link to module objectives.

We 'followed' a fictional patient journey from home, via A&E to the inpatient ward and later discharge planning. Themes covered included: best practice for pain management; warning signs of deterioration (including an acute chest crisis), and barriers to optimal care, including hesitancy to request analgesia for fear of being stigmatised as 'drug seeking.'

A range of learning modalities were used, including video clips of patient experiences produced by King's Health Partners.

88 students completed the training session on 3 separate dates in May 2025. Quantitative and qualitative data was collected via anonymous online surveys prior to and immediately after completing the session.

Results: Pre and post session survey average scores were compared. Student perception of their knowledge about SCD pathophysiology increased from 15.4% ('a great deal') to 34.3%. Those who knew 'a little/unsure,' decreased from 25.9% to 14.9%.

Stated awareness of SCD being a public health concern increased from 60.3% to 91.4% post session. A minority of students did not think sickle cell disease was a public health concern (14%) before the session, but this had further decreased to 4.5% after the teaching.

When asked about life threatening SCD complications, perceived knowledge had improved in several conditions: stroke (54% to 69%), acute chest syndrome (29.9% to 61.3%) and renal failure (46.5% to 61.7%).

The qualitative responses highlighted that a focus on patient experience can be powerful. One student commented that 'I really enjoyed some of the videos—they were informative and engaging at the same time,' The simulated patient journey was appreciated, with one student thanking the educators for 'explaining… extra medical and clinical information, it was super interesting and made it feel like we were on the wards.'

Conclusion: There is a considerable evidence base which supports the aim of our session: that non-specialist SCD education needs improvement[2,3]. This small-scale study is the first of its kind to demonstrate that an educational intervention of the patient experience can influence short term baseline knowledge and beliefs around SCD in a medical student cohort. It is the opinion of the authors that haematologists/medical educators should play a pivotal role in promoting early awareness around 'failings of care[1]' in this historically stigmatised patient group.

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PO81 | Understanding the relational dimensions of supporting young migrants with sickle cell disease in England

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Introduction: Sickle cell disease (SCD) is the most common genetic blood disorder in the UK, disproportionately affecting people of Black African and Afro-Caribbean descent. As the UK becomes more diverse due to global migration, an increasing number of children and young people (CYP) with SCD come from migrant backgrounds. These CYP face intersecting challenges, such as language barriers, insecure immigration status, housing instability, and discrimination, which complicate access to timely, appropriate healthcare.[1] Although national guidelines promote comprehensive, integrated SCD care, service delivery remains inconsistent and often inadequate, particularly outside specialist settings. The 2021 *No One's Listening* report[2] revealed 'serious care failings', including racism, underinvestment, and poor experiences in A&E and general wards. Consequently, migrant CYP with SCD are seeking care in a context where SCD care is far from ideal, placing further strain on a system that struggles to accommodate diversity and difference. Yet, little is known about how service providers, namely healthcare professionals and third-sector organisations, perceive and address the needs of migrant CYP with SCD.

Methods: Drawing on Tronto's relational theory of care,[3,4] we explored how service providers support migrant CYP SCD, and how systemic, social, and spatial relationships shape their care practices. We conducted semi-structured interviews with 15 healthcare professionals (including haematologists, general practitioners, nurses, psychologists and social workers) and 10 staff from SCD-focused third-sector organisations across England. Interviews were audio-recorded and transcribed, which were analysed using constructivist grounded theory, employing line-by-line coding, constant comparison, and theoretical categorisation, in collaboration with a Public and Patient Involvement advisory group comprising four young migrants living with SCD in England.

Results: Service providers identified five relational barriers, shaped by the intersection of migration, chronic illness, and social precarity, which were often difficult to disentangle: (1) Personal vulnerabilities stemming from educational disruption and financial hardship; (2) Systemic and cultural barriers, including language issues and xenophobia; (3) Partial or precarious citizenship, where immigration status undermined care access and trust in services; (4) diagnostic and screening gaps that delayed or prevent access to appropriate care; and (5) geographies of care, reflecting stark spatial inequalities in care delivery. Despite these challenges, providers, particularly those with lived experience of migration and/or SCD, offered crucial relational care: guiding families through systems, advocating for support, and building networks. Yet this care was often ad hoc, relying on individual commitment and discretion rather than systemic strategy.

Conclusion: Healthcare for a diverse, marginalised SCD population cannot be fully understood and effectively delivered through biomedical or policy frameworks alone. For young migrants with SCD, providers were navigating and bridging gaps in care provision, often with creativity and personal resolve. While this responsiveness is commendable, it raises pressing, urgent moral questions about sustainability in the absence of structural reform. Current care arrangements often fail to ensure continuity, rendering care effectively discretionary. Using a relational lens, the study exposes how broader social inequalities and interdependencies shape care. In addition to practical measures such as integrated service pathways, improved screening, culturally sensitive training, and policies that decouple healthcare access from immigration status, we argue for a fundamental shift in how SCD is conceptualised: as a shared socially constructed process rather than an individual clinical encounter or transaction.

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PO82 | Improving ophthalmologic screening in pediatric and young adult patients living with sickle cell disease

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Introduction: Individuals living with sickle cell disease (SCD) are at increased risk for ophthalmologic issues including retinopathy (damage to blood vessels in the retina), retinal thinning and macular ischemia. Annual screening is recommended beginning at 10 years of age for all genotypes. As of 6/30/23, only 42.4% (216/509) of our patients aged 10–21 years had received a screening exam in the preceding 2 years. The documentation was inconsistent as exams were performed by many different ophthalmology providers, including physicians and optometrists, as well as providers outside of our hospital system. It was noted that some patients under age 10 years had been seen by ophthalmology and noted to have findings related to their SCD raising the question of whether we should be screening at a younger age.
Methods: Our institution initiated quality improvement (QI) and research efforts to:

- Increase screening rates for patients 10 years of age and older through use of a population health tool to identify those due for screening, use of a scheduler to help arrange the appts, coupling the appts with hematology clinic visits when possible, and regular meetings with ophthalmology colleagues to address barriers.
- Standardize exam components to ensure the screening was comprehensive and documentation consistent for ease of data collection. Exam records from outside institutions were reviewed to ensure they met the above standards.
- Review records of patients under age 10 who had been evaluated by ophthalmology.

Results

- Screening rates in patients aged 10–21 years increased from 42.4% on 6/30/23 to 73.5% (363/494 patients) on 5/31/25.
- Ophthalmology colleagues standardized the exam and documentation which consists of a dilated fundoscopic exam (including macula, vessels and periphery) with fundus photography and/or fluorescein angiography where indicated. The exam also includes optical coherence tomography (OCT) in all patients to evaluate for retinal thinning and macular ischemia/infarct. If retinopathy is present, it is staged (non-proliferative—stage I/II or proliferative—stage III/IV/V). The new template was piloted with a single provider from 5/1/24 to 5/31/25 in 100% of visits (216 encounters in 167 patients).
- Seventy patients under age 10 had one or more eye exams; 18.6% (13/70) had findings related to their SCD (retinal artery occlusion, stage I/II retinopathy, and/or macular thinning/ischemia). Findings were noted in patients of different genotypes (SS, SC and S beta + thalassemia) age 5 to 9 years.

Conclusions:

- QI efforts were effective at increasing rates of ophthalmologic screening in individuals living with SCD from 42.4% to 73.5%. Issues identified were treated promptly to reduce the possibility of vision impairment. Ongoing efforts are focused on sustaining the new workflows to ensure the screening rates remain robust.
- 100% percentage of ophthalmology visits in the pilot successfully used the new template. Next steps will incorporate the use of this template with all providers in the department so that screening is comprehensive and consistent, and data can be easily abstracted.
- Ophthalmologic findings related to SCD were noted in 18.6% of the 70 patients screened under age 10. Indications for the visits varied, and further evaluation of this cohort is ongoing to ascertain whether it would be beneficial to broaden current screening guidelines.

PO83 | HEROES: Educating and empowering the next generation of healthcare professionals in sickle cell disease management

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Introduction: Globally, ~8 million people live with sickle cell disease (SCD), the majority in Africa, the Middle East and India, where high mortality rates, patient burden and significant healthcare disparities persist. Limited disease awareness, diagnostic difficulties, and persistent racial and socioeconomic disparities contribute to inequities in quality and access to care. This underserved community needs empowered haematologists to advance evidence-based SCD care, addressing a significant gap in patient care and treatment outcomes. The HEROES programme aims to empower the next generation of haematologists to drive change, tackle healthcare inequalities and use a holistic approach to transform SCD care.

Methods: A non-promotional, educational scientific programme, initiated in 2024, with live webinars and a 3-day face-to-face (F2F) meeting, composed of plenary presentations, small group discussions and interactive workshops led by international and regional experts, was implemented. An agenda, driven by insights gathered from a patient, was designed to address global unmet needs, regional challenges and patient concerns. Agenda topics included paediatric-to-adult transition, implicit bias towards individuals living with SCD and the pathway to becoming an SCD specialist. Delegates were selected by an expert panel based on region-specific criteria for each meeting and the ability to impact future patient care. Delegates' pre- and post-meeting knowledge and awareness of SCD were assessed using surveys.
Results: Ninety-one delegates from 14 countries attended HEROES F2F in Türkiye, Tanzania and India, pre-meeting webinars and ongoing webinar series. A pain animation developed in collaboration with people with SCD highlighted challenges in the patient journey and the debilitating and invisible nature of pain that patients experience. Pre- to post-meeting survey results showed a positive effect; SCD knowledge and awareness of the day-to-day reality for patients increased from an average of 7.1 to 9.0/10 and 7.0 to 9.1/10, respectively. Average healthcare professional (HCP) confidence levels increased for SCD diagnosis (7.9 to 9.5), care (7.2 to 9.1), supporting paediatric-to-adult transition (6.3 to 8.8) and treating multiorgan complications (6.8 to 8.7). A paired *t*-test showed that delegates awareness and confidence in treating SCD significantly improved ($p < 0.0001$). Programme relevance to clinical practice was rated as 9.5/10 on average, with an overall quality of 9.7/10. Delegates from the Türkiye and Tanzania F2F meetings made a total of 149 pledges aligned with the Lancet Haematology Commission's 'Global Strategies to Improve Outcomes in Sickle Cell Disease'. Pledges addressed the following: epidemiology (12), screening and prevention (43), established and emerging therapies (53), cellular therapies (5), and training and education (36). Within 3 months after the meetings, delegate pledge updates included launching multidisciplinary teams and adolescence transition clinics (8), education and training on SCD and SCD management (7), proposals for mobile healthcare centres in remote areas (1) and securing a mentor (2).
Conclusion: The HEROES programme successfully educated and empowered HCPs in a neglected disease area. HEROES will continue to expand its support of HCP education, fulfilling one of the Lancet Commission's strategies by delivering improved equity and outcomes, and providing the care that people with SCD deserve.

PO84 | Hydroxyurea use reduces pulmonary hypertension prevalence and TRV severity in pediatric sickle cell disease

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Introduction: Pulmonary hypertension (PH) affects up to one-third of children with sickle cell anaemia (SCA) and significantly worsens long-term outcomes. Hydroxyurea (HU) therapy ameliorates several pathophysiological mechanisms such as haemolysis, inflammation, and vaso-occlusion; but its overall association with both PH prevalence and echocardiographic severity (as measured by tricuspid regurgitant velocity, TRV) in paediatric SCA populations has not been fully characterized.
Objective: To determine whether HU use is associated with a lower prevalence of PH and a shift toward milder TRV elevations, and to compare key laboratory markers of haemolysis and inflammation between HU-treated and untreated children.
Methods: We enrolled 242 children with SCA aged 2–17 years at Jos University Teaching Hospital, including 121 who had received HU for at least six months and 121 age and sex matched controls. All participants underwent standardized Doppler echocardiography, with PH defined as TRV ≥2.5 m/s. TRV elevations were categorized as mild (2.5–2.9 m/s) or moderate–severe (≥3.0 m/s). Laboratory indices measured included haematocrit, total white blood cell count, platelet count, and serum lactate dehydrogenase (LDH). PH prevalence and TRV severity distributions were compared using χ^2 tests; laboratory differences were assessed by Mann–Whitney *U* test. A two-tailed $p < 0.05$ denoted statistical significance.
Results: PH prevalence was 26.4% (32/121) in the HU group versus 52.1% (63/121) in controls ($p < 0.0001$). Among those with PH, mild TRV elevations occurred in 12.4% (15/121) of HU-treated versus 30.6% (37/121) of controls, and moderate–severe elevations in 14.0% (17/121) versus 21.5% (26/121; $p = 0.02$ for overall severity distribution). HU-treated children also showed significantly lower median LDH (323 vs. 363 IU/L; $p = 0.001$), total white blood cell count (9.3 vs. 13.5 $\times 10^9$/L; $p < 0.0001$), and platelet count (350 vs. 390 $\times 10^9$/L; $p = 0.019$), alongside higher haematocrit (25.8% vs. 23.2%; $p < 0.0001$).
Conclusion: Hydroxyurea therapy in paediatric SCA patients is associated with a 50% reduction in PH prevalence and a shift toward less severe TRV elevations, accompanied by improved laboratory markers of haemolysis and

inflammation. These findings support early HU initiation as part of comprehensive strategies to prevent and attenuate PH in children with SCA.

Keywords: sickle cell anaemia, pulmonary hypertension, hydroxyurea, tricuspid regurgitant velocity, lactate dehydrogenase; pediatric echocardiography.

PO85 | Genetic determinants of total haemoglobin level in individuals with sickle cell disease

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Introduction: Total haemoglobin level is a readily measurable, clinically relevant trait that reflects the anaemia burden and disease severity in individuals with sickle cell disease (SCD). To gain insights into the genetic determinants of haemoglobin concentration, which can reveal new pathways influencing disease outcomes beyond foetal haemoglobin.

Methods: We performed a genome-wide association study of haemoglobin level in 1339 individuals with SCD, comprising 967 individuals from Nigeria and 372 individuals of Caribbean or West African descent in England (South-East London sickle gene bank). Using a linear mixed model to account for population structure as implemented in GCTA (Genome-wide Complex Trait Analysis software, version 1.91.7), we adjusted for sex, age, and haemoglobin phenotypes. GCTA was also used for genome-wide SNP-heritability estimate, while a step-wise conditional analysis was carried out using conditional and joint analysis in GCTA (GCTA-COJO).

Results: The median haemoglobin concentration of the two cohorts was 8 (ranging from 3.6 to 15.9) g/dL. We identified evidence of association with haemoglobin concentration at eight genome-wide significant and suggestive loci, including two known foetal haemogobin loci: *BCL11A* (rs1896296, $p = 4.92 \times 10^{-9}$, $\beta = 0.26$) on chromosome 2 and *HBS1L-MYB* (rs66650371, $p = 6.89 \times 10^{-7}$, $\beta = 0.50$) on chromosome 6. The genome-wide SNP heritability estimate for haemoglobin concentration in these cohorts was 0.53. A stepwise conditional analysis on chromosome 2 revealed an independent signal at rs1836202, a variant absent in non-African populations, suggesting the presence of an additional, distinct genetic signal influencing haemoglobin concentration.

Conclusions: These findings highlight both shared and ancestry-specific genetic influences on haemoglobin concentration in individuals with SCD. Understanding these genetic contributions could uncover novel biological pathways and support efforts to stratify disease risk in SCD.

PO86 | Equity in genomics: Engaging with the sickle cell community

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Introduction: Sickle cell disease (SCD) is a genetic condition that disproportionately affects people of African and Caribbean descent. Despite recent advances in genomics and the promise of curative treatments such as gene therapy, individuals with SCD remain underrepresented in genomic research. This is shaped by a legacy of structural racism, historical marginalisation, and a lack of meaningful community engagement. Questions of trust, relevance, and inclusion are central. This research explores how individuals and communities affected by SCD in the UK understand genomics, engage with research opportunities, and navigate the ethical and structural challenges that shape participation.

Methods: A qualitative study, grounded in community-based participatory research (CBPR) approaches, was conducted using in-depth interviews and focus groups with three key groups: individuals (18–29 years old) living with SCD, healthcare professionals, and wider community members (family and advocates). An advisory group was also consulted before and during data collection. Data were analysed thematically using both inductive and deductive coding, informed by principles of community-based research and bioethical reflection.

Results: Four major themes were identified: (1) lived experiences of SCD shaped by systemic inequalities; (2) perceptions of genomics as both a hopeful and unfamiliar terrain; (3) barriers to research participation including mistrust, structural inequality, and poor communication; and (4) facilitators of engagement such as community knowledge, cultural relevance, and equitable partnerships. Across all groups, trust emerged as a central and cross-cutting issue, underpinned by past experiences and shaped by the way research is conducted and communicated.

Conclusion: These findings will inform an upcoming community workshop designed to co-produce a framework for ethical engagement in genomic research with SCD-affected communities. Addressing inequities in genomic research requires moving beyond inclusion as recruitment. It demands an ethics of engagement grounded in care and reciprocity that is led by the community. By centring lived experience and embedding community voices in the research process, this study contributes to reimagining how SCD communities can be equitably involved in shaping the future of genomic research.

PO87 | Implications of Oxidative stress in patients with sickle cell disease who received multiple blood transfusions

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Purpose: Despite the increasing use of transfusion therapy in managing sickle cell disease (SCD), there has been limited investigation into the effects of multiple transfusions on oxidative stress markers in these individuals. The study aimed to determine the oxidative stress parameters of patients with sickle cell disease attending Asokoro General Hospital, Maitama Districts Hospital, Wuse General Hospital in Abuja, Nigeria.
Methods: Blood specimens were collected from 100 Hb SS participants (50 steady state and 50 crises) who had received more than three episodes of transfusion, and 50 Hb AA participants who had never received blood transfusion (control).The oxidative stress biomarkers were determined using Enzyme-Linked Immunosorbent Assay techniques.
Results: The result obtained showed that superoxide dismutase (SOD) and catalasewere significantly lower, while malondialdehyde was significantly higher ($p < 0.05$) in sickle cell subjects in crisis and steady state compared to the control group, and significantly lower ($p < 0.05$) in subjects in crisis compared to subjects in steady state. Furthermore, SOD was significantly ($p < 0.05$) higher in female subjects in both steady state and crisis compared to male subjects. There was no statistically significant difference in other oxidative parameters studied with respect to gender and age ($p > 0.05$).
Conclusion: In conclusion, the lower antioxidant activity in SCD subjects compared to control, and in VOC compared with steady state subjects confirms the increased oxidant activity in sickle cell anemia which is worsened during periods of crises. These findings suggest that patients with SCA have increased lipid peroxidation in addition to an imbalance in their pro-oxidant and antioxidant states.
Keywords: sickle cell disease, oxidative stress, antioxidant, lipid peroxidation, transfusion.

PO88 | Sickle cell awareness and diagnosis in Ghana: Impact of the Okyenhene's medical caravan community initiative

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Introduction: Sickle cell disease (SCD) is the most common inherited blood disorder in sub-Saharan Africa, accounting for approximately 80% of the global burden. In Ghana, an estimated 16 200 of the 900 000 annual births are affected by SCD, contributing significantly to childhood morbidity and mortality. Despite this, newborn screening (NBS) remains limited, and awareness is hindered by stigma, misinformation, and spiritual beliefs. The West African Genetic Medicine Centre (WAGMC), University of Ghana, collaborates with traditional leaders to deliver community-based outreach programmes targeting genetic disorders. In 2024, WAGMC partnered with the Okyenhene, the Paramount Chief of Akyem Abuakwa in the Eastern region of Ghana, during his 25th anniversary celebrations to implement his Medical Caravan (OMC). This initiative aimed to reduce health disparities by offering free screening and education on SCD, cancers, and sensory and dental impairments.
Objectives: This case study from the OMC illustrates its impact on community-based genetic screening, SCD awareness, diagnosis, and prevention. It explores how culturally sensitive outreach can bridge healthcare gaps and empower families with knowledge for informed decision-making.
Case Study: A mother attended the OMC at Kyebi seeking care for her daughter's hearing difficulties. Unexpectedly, her two younger daughters (aged 8 and 13 years) were diagnosed with SCD (HbSC), while her eldest daughter (aged 16 years) and the mother herself were identified as carriers with HbAS and HbAC traits respectively. The family's genetic profile revealed that the mother had children with two different partners and was planning future pregnancies with a third. Notably, the 8-year-old had been asymptomatic, while the 13-year-old had experienced frequent pain crises since infancy, previously attributed by her grandmother to "Ahututuo," the local Twi term for SCD. Despite multiple hospital visits, no formal diagnosis had been made until the OMC intervention.
Results: This mother expressed deep appreciation for the screening, which clarified her daughters' health conditions and provided actionable guidance on disease management,

including hydration and malaria prevention. She also recognised the importance of genotype testing before future pregnancies. Her eldest daughter acknowledged the value of understanding genetic inheritance and committed to genotype screening before marriage. The 13-year-old expressed relief at finally receiving a diagnosis and learning how to manage her condition.

Conclusion: The use of point-of-care Sickle SCAN® testing enabled immediate diagnosis and counselling, demonstrating the effectiveness of integrating genetic services into community health initiatives. The OMC's holistic approach combining diagnostics, education, and culturally grounded engagement, enhanced community participation and reduced stigma. This case underscores the transformative potential of community engagement and genetic screening in improving early detection, promoting informed reproductive choices, and addressing healthcare inequities. The success of the OMC supports the expansion of NBS and premarital genetic counselling as vital strategies for SCD management in Ghana and similar settings.

PO89 | Help mom, I'm in pain

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Introduction: Pain attacks in children with sickle cell disease that are unexpected and severe require rapid and adequate pain relief that starts in the home situation. Pain attacks affect the daily lives of children and parents. Parents of these children often have a Ghanaian background. Because these parents often come from the lower socio-economic classes, it seems more difficult to teach self-management to their children. A standard pain treatment plan issued and explained by the paediatric sickle cell team appears to be carried out suboptimally at home. The team has too little knowledge about parents' experiences with dealing with pain and treatment plan.

Methods: It is a qualitative research design for which nine semi-structured interviews were conducted with parents of Ghanaian descent with a child with sickle cell disease. Thematic analysis was used in analysis.

Results: Parents name the following themes that influence dealing with pain in the home situation. On the emotional level, feelings of stress, fear and anxiety are experienced. Based on sociocultural aspects, massage and prayer are interventions that parents want to perform for their children. The confidence in the pain medication and the advice of the team give direction to action. Parents want to have knowledge of how to deal with the pain properly with a personal treatment plan because that gives guidance in the event of a sudden crise.

Conclusion: The research shows that Ghanaian sociocultural aspects play a role in dealing with pain, so there seems to be a need to integrate this into a personal pain treatment plan, so that children of Ghanaian parents with sickle cell disease will be treated faster and more adequately in the future.

PO90 | Healthcare utilization and clinical burden of sickle cell disease in a Portuguese emergency department

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Introduction: Sickle cell disease (SCD) is a rare hemoglobinopathy with limited epidemiological data in Portugal. Recent national screening initiatives have identified an incidence of approximately 1:17 000, with higher prevalence in certain regions. Clinical management predominantly focuses on addressing vaso-occlusive crisis, which often lead to emergency department visits. This study aims to characterize patterns of emergency care use, clinical presentations and patient outcomes in a Portuguese hospital setting.

Methods: This retrospective observational study reviewed SCD-related emergency visits to the General Emergency Department of a district hospital from January 2021 to December 2023. Patients aged ≥18 years with SS, Sβ, or SC genotypes were included. Collected data included demographic variables, triage categories, waiting times, length of stay, diagnoses, treatments administered, and readmissions rates. Descriptive statistics and correlation analyses were conducted.

Results: A total of 264 episodes from 93 patients (mean age: 30 years; 61% male) were analyzed, with an average of 2.8 visits per patient. The most frequent triage complaints were limb pain (81 episodes) and back pain (74 episodes), primarily associated with severe pain discriminators. The majority of patients were triaged as very urgent (65.2%) or urgent (27.3%), with a mean waiting time of 58 min. Patients remained in the emergency department for an average of 13 h, and the admission rate was 45.8%. The main diagnosis was vaso-occlusive crisis (89.8%), treated primarily with tramadol, pethidine, NSAIDs, and morphine. Readmission within 72 h was low (6 episodes).

Conclusions: SCD patients frequently seek emergency care for vaso-occlusive crisis, with prolonged stays exceeding durations reported in previous studies. The severity of presentations, triage priorities, and treatment patterns reflect the high clinical burden in this population. These findings underscore the need for tailored management protocols adapted to local healthcare settings in order to improve patient care and optimize resource use.

PO91 | Use of phlebotomy in sickle cell disease: Results of a multinational EuroBloodNet survey

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Introduction: Sickle cell disease (SCD) is a severe and highly complex disorder characterised by vaso-occlusion episodes

(VOE) and chronic haemolytic anaemia. Besides chronic organ damage, patients experience acute and severe complications such as painful VOE and the life threatening acute chest syndrome. Treatment of SCD is limited, especially in patients without or low level of haemolysis. Phlebotomy is used in hereditary haemochromatosis to reduce iron overload. Retrospective studies have demonstrated its beneficial effects in HbSC disease (HbSC) and homozygosity for haemoglobin S (HbSS) by decreasing blood viscosity and inducing iron deficiency. The later has been shown to be beneficial in pre-clinical studies in mice by lowering intracellular haemoglobin concentration, thereby reducing sickling tendency. Despite the fact there are no randomized controlled trials performed to evaluate the efficacy of phlebotomy in SCD, several national guidelines in Europe suggest its use. Our study aims to understand the use of phlebotomy in disease management of SCD.

Methods: A survey was sent via the ERN-EuroBloodNet network to its members. Answers were collected from May to July 2024. The data collected concerned the use of phlebotomy in different SCD genotypes, the impact of total haemoglobin (Hb) level and it's use in relation to occurrence of SCD-related complications.

Results: Thirty answers were collected from 9 member states all over the European Union. Seven answers were excluded (Greece $n=2$; Italy $n=4$, and Czechia $n=1$), due the use of phlebotomy exclusively as part of an exchange transfusion procedure. The remaining 23 centers (from 7 EU countries) represented a paediatric population of 2455 children and 5852 adults.

In 7/23 of these SCD centers a phlebotomy protocol was available. The majority of these centers (17/23; 74%) use both episodic phlebotomy and phlebotomy programs. Some centers only use episodic phlebotomy (3/23) or phlebotomy programs (2/23).

If a patient presents with an acute SCD-related complication and a high Hb level, most centers will perform phlebotomy in HbSC (20/23), HbSS/HbSBeta° thalassaemia (15/23, or HbSβ$^+$ thalassaemia(15/23). Nevertheless, there is little consensus about the Hb cut-off level to starting phlebotomy except in HbSC symptomatic patients were the majority of caregivers start phlebotomy when Hb exceeds 11 g/dL. (Fig.1)

Most frequently mentioned indications for phlebotomy are especially situations where hyperviscosity is a prominent factor of pathophysiology, such as recurrent VOE, priapism and retinopathy. There was no consensus on the target Hb level to achieve after phlebotomy which were reported from 8.0 to 11.0 g/dL for all SCD genotypes.

The majority of the centers don't use phlebotomy in asymptomatic patients with a high Hb level (Fig. 1).

Conclusion: In almost all member states included in this study, phlebotomy is frequently used in symptomatic patients with SCD, in particular in HbSC. There is no consensus on the Hb cut-off level to initiate phlebotomy, and more discrepancies between caregivers upon its use in HbSS/HbSβ^0, and HbSβ$^+$. Future studies, including randomised controlled trials, are warranted to assess the efficacy and safety of phlebotomy in SCD.

Figure 1. Reported haemoglobin cut-offs (g/dL) for initiation of phlebotomy in SCD

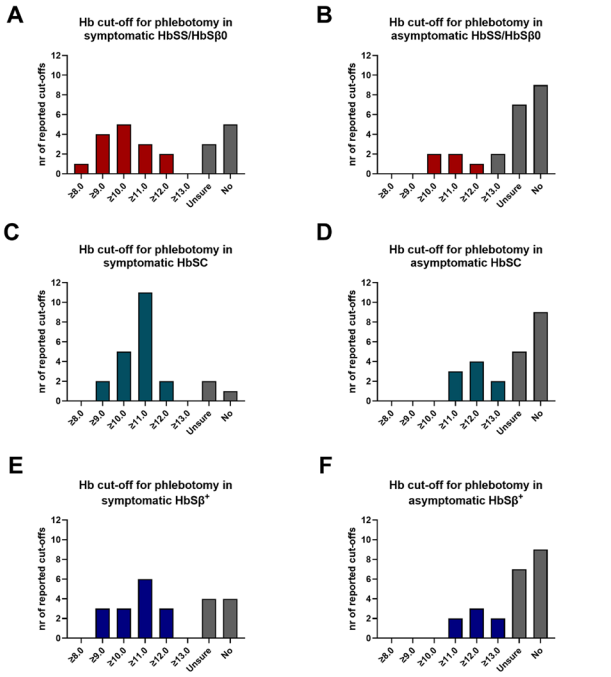

Figure 1. Reported haemoglobin cut-offs (g/dL) for initiation of phlebotomy in SCD. *Panel A, C and E show hemoglobin (Hb) levels at which caregivers initiate phlebotomy in symptomatic patients (HbSS/HbSβ^0 red bars, HbSC turquoise bars, HbSβ+ blue bars) . Panel B, D and F show hemoglobin (Hb) levels at which caregivers initiate phlebotomy in asymptomatic patients.*

PO92 | SCD recommendations in the EU: A EuroBloodNet review of national implementation, gaps, and research priorities

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Introduction: Sickle cell disease (SCD) care across the European Union (EU) is marked by significant variability in the availability and content of national clinical practice guidelines and clinical decision-making tools. While some countries have recently updated national documents, others lack any formal ones. This heterogeneity contributes to disparities in clinical management and outcomes for individuals living with SCD. The ERN-EuroBloodNet original initiative represents the first systematic comparative analysis of national SCD recommendations in Europe. By identifying evidence gaps, and areas of agreement and disagreement within the recommendations, this project supports coordinated research efforts aimed at promoting health equity across EU member states. The initiative is supported by the ERN Guidelines project (Tender Nº SANTE/2018/B3/030). Methodological support is provided by the Canary Islands Health Service Evaluation Unit and its research foundation (SESCS/FIISC).

Methods: Initially, ERN-EuroBloodNet and SCD experts coordinating national recommendations on SCD were identified and invited to join the initiative. The Expert Panel included 14 members from 8 EU countries, who collected available national documents. In parallel, SESCS/FIISC conducted a systematic search to identify additional relevant documents (e.g., consensus statements, expert recommendations) through databases and repositories including PubMed, TripDatabase, ECRI Guidelines Trust, Orphanet, EURORDIS, and NORD.

Documents were selected based on the following criteria: focus on SCD, national scope, origin from an EU country or the United Kingdom, publication within the last 10 years, relevance to the objectives of the task; and in any language.

The methodological quality of preselected documents was assessed using the AGREE II instrument. Any document in national language was translated into English.

Results: After the selection process, 33 documents were selected for comparative analysis. The Expert Panel identified 20 key topics: newborn screening, follow-up, penicillin prophylaxis, vaccination, fever treatment, painful vaso-occlusive crisis management, splenic sequestration and splenectomy, acute chest syndrome management, stroke management, TCD/MRI, priapism, renal function, cardiomyopathy, pre-surgery management, analgesia in acute and chronic settings, pregnancy, hydroxyurea, blood transfusion, hematopoietic stem cell transplantation and transition of care.

Experts were assigned to review specific topics according to their expertise and applied to the adult and pediatric domains where appropriate.

For each topic, priority questions were identified for which the recommendations and their level of evidence were obtained. This comparative analysis was summarized in comparative tables and is currently being drafted.

Conclusion: In addition to the standards of care identified, the divergences and knowledge gaps will make it possible to define targeted and collaborative research projects. They will support the development of harmonized and evidence-based clinical policies across Europe like for clinical registries. Additionally, creating an English-language repository of national recommendations on the ERN-EuroBloodNet website will provide a valuable resource, promoting equity in care across the EU.

PO93 | The importance of external quality assessment (EQA) in the laboratory diagnosis of haemoglobinopathies

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Introduction: UKNEQAS Haematology provides a comprehensive range of external quality assessment (EQA) programmes designed to support the quality assurance needs of laboratories in the UK and internationally. Three specialist EQA programmes assess the proficiency of laboratories offering haemoglobinopathy testing. Accurate laboratory diagnosis of hemoglobinopathies is vital, especially for patients requiring antenatal risk assessment and prenatal diagnosis.

Methods: To evaluate the proficiency of haematology laboratories, UKNEQAS distributes specimens which simulate a range of haemoglobinopathy case profiles, from carrier and disease states to "normal" or healthy cases. These specimens represent adults, children and newborns, and are derived from human blood obtained a range of sources, including NHS Blood and Transplant and commercial suppliers. Depending on the programme, the survey material may be supplied as whole blood, dried blood spots or DNA.

At the time of writing, the UKNEQAS haemoglobinopathy EQA programmes serve approximately 400 laboratories across the UK, Ireland and internationally. The Abnormal Haemoglobins (AH) programme which evaluates the proficiency of adult haemoglobinopathy screening laboratories has approximately 350 participants. The Newborn Sickle Screening (NH) programme, for specialist laboratories that provide a screening service for newborn babies using dried blood spot cards, has approximately 60 participants. The DNA Diagnostics for Haemoglobinopathies (DN) Programme, for laboratories that offer genotyping of the alpha and beta globin genes, has approximately 50 participants.

Results: A data review of the AH programme analysed 15 years worth of distributions. The AH programme issues six surveys annually, which each contain three specimens of adult blood. Between 2010 and 2024 a total of 270 specimens were distributed to UK and non-UK laboratories for haemoglobinopathy proficiency testing. These included a range of cases such as alpha-thalassaemia, beta-thalassaemia and sickle cell carriers, other Hb variant carriers (e.g. Hb C, Hb E, Hb D-Punjab, etc.) and raised Hb F. Annual targets are set for each of these case scenarios and in general the targets are consistently met. However, the target for beta thalassemia carriers (2 cases per year) was only met six times in the 15 year period. This shortfall is primarily due to limited availability of suitable beta thalassaemia carrier donors.

A key focus of the AH programme is to test the proficiency of haemoglobinopathy screening methods to accurately detect

and quantify the Hb A2, Hb F and Hb S fractions. In order to achieve this, UK NEQAS must send out specimens that contain these fractions at varying levels. Of the 270 specimens distributed, 87 (32%) contained Hb S, 51 (19%) had a raised Hb F and only 18 (7%) had a raised Hb A2. The low frequency of raised Hb A2 specimens highlights the challenge of sourcing beta-thalassaemia carrier donor blood.

Conclusion: This data review reflects a successful period for UKNEQAS in delivering a wide range of haemoglobinopathy cases for laboratory proficiency testing. However, a notable shortfall remains in the provision of beta thalassaemia carrier specimens. To effectively assess laboratory performance in the accurate measurement of Hb A2, the number of raised Hb A2 specimens being distributed must increase. UKNEQAS is actively working to recruit more beta thalassaemia carriers willing to donate blood for use in EQA services.

PO94 | Management of vaso-occlusive episodes of sickle cell disease in a district general paediatric emergency department

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Introduction: South London has the highest concentration of people with sickle cell disease (SCD) in the UK, the majority from Black ethnic backgrounds. Lack of awareness and stigmatizing attitudes amongst health care professionals towards people with SCD can contribute to failures in care. Acute vaso-occlusive episodes (VOE) of SCD require prompt assessment and management, often with opiate-based analgesia, to reduce the risk of morbidity and mortality. The aim of this project is for all children with acute VOE of SCD presenting to a district general Emergency Department (ED) to be assessed and managed within thirty min of booking and have a re-assessment of their pain thirty min after receiving adequate analgesia.

Methods: Patients coded to have HbSC/HbSS attending ED were identified by the hospital attendance report generator. The online patient record system, Cerner, was interrogated. Inclusion criteria were age equal to or less than 16 years, pain as a presenting complaint, and a diagnosis of acute VOE of SCD. Adequate analgesia was defined by the local SCD pain guideline based on pain score or description of pain. Baseline data was collected from April-June 2024 and audited against National Institute for Health and Care Excellence (NICE) 2014 Quality Standards 1–3 (QS58) which are summarised by the following statements:

a. Patients to have a clinical assessment within 30 min of booking into ED
b. Patients to have a documented initial pain score
c. Patients to have an assessment of their pain within 30 min of booking into ED
d. Patients to receive adequate analgesia within 30 min of booking into ED
e. Patients to have a documented re-assessment of pain at thirty min after analgesia

Quality Statement	Baseline median (%)	Post intervention median (%)
a) Clinical assessment	74	96
b) Initial pain score	60	100
c) Pain assessment	62	62
d) Adequate analgesia	36	36
e) Re-assessment of pain	32	66

Plan-Do-Study-Act cycles were completed monthly between November-April 2025. Interventions included multidisciplinary teaching on SCD, presentation at local clinical governance meetings, resident doctors teaching on induction to paediatrics, creation of a 'pain in SCD' patient information leaflet accessed by QR code posters in ED, and distribution of the leaflet at triage. The aim of the leaflet was to empower families to speak up about their SCD pain management.

Results: There were statistically significant changes in the post intervention data for statements a), b) and e), demonstrated by a shift of six data points above the baseline median on respective run charts ($p < 0.05$). There were no statistically significant changes in statements c) or d). Post intervention medians were calculated for (a), (b) and (e), as shown by the table:

Conclusion: This project showed a statistically significant improvement in timely clinical assessments, documentation of initial pain score, and re-assessment of pain after analgesia, which is recommended by NICE to improve the care of patients with acute VOE of SCD. Further work is needed to improve assessment of pain and timely analgesia. It was noted that some patients were given simple analgesia only if not taken prior to triage, despite reported high pain scores, which could delay receiving opiate-based analgesia and prolong episodes of pain. Updated Royal College of Emergency Medicine SCD guidance recommends offering analgesia within fifteen min, which will likely pose a challenge to busy ED departments.

PO95 | Exploring clinical practice and perceptions of hydroxyurea for pregnant women with sickle cell disease

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Introduction: The treatment of sickle cell disease during pregnancy is limited to blood transfusion, as hydroxyurea, the drug given to treat sickle patients, has been shown to

have teratogenic effects in studies performed in animals in the 1960s. However, these studies used doses significantly higher than relative human doses, and case studies have raised few concerns over the use of hydroxyurea in pregnancy since then. Therefore, we are gathering perspectives from healthcare professionals involved in managing sickle cell disease during pregnancy.

Methods: We conducted a cross-sectional study using a self-administered online survey to gather insights from healthcare professionals involved in managing sickle cell disease (SCD) during pregnancy. Participants included haematologists, maternal-fetal medicine specialists, obstetricians, specialist sickle cell nurses, and obstetric medicine physicians.

The survey, created using established best practices for questionnaire design, was published via the Qualtrics platform on the 8th April 2025. Participation was limited to professionals who confirmed that they care for pregnant patients with SCD through a screening question. The study was approved by King's College London's Research Ethics Management Application System (REMAS), and no external funding was received.

Most questions were closed-ended, with space for free-text input in some sections. The survey focused on clinical decisions and concerns related to hydroxyurea use during pregnancy, particularly whether and when to stop the medication, if it should be continued during assisted reproductive treatments, and under what clinical circumstances it might be restarted or continued during pregnancy. These scenarios included patients with frequent vaso-occlusive crises, severe acute chest syndrome, limited transfusion options, or complex antibody profiles, focusing on cases where clinical decisions may differ due to limited formal guidance.

To ensure clarity and relevance, the questionnaire was piloted with clinicians experienced in managing SCD in pregnancy, and revisions were made based on their feedback. We used a multi-channel approach to reach potential respondents, including email, social media, and professional meetings. We also collaborated with organisations such as the British Society of Haematology, American Society of Hematology, Society for Maternal-Fetal Medicine, and Canadian Hemoglobinopathy Association to help distribute the survey. Participation was anonymous unless respondents chose to share identifying information.

Results: We hope to present the results of the survey at the next meeting.

Conclusion: In our findings, we hope to highlight the spectrum of clinical approaches to the management of hydroxyurea during pregnancy in patients with sickle cell disease, reflecting both the complexity of individual cases and the lack of unified, evidence-based guidelines. Once fully collected, these insights will hopefully stimulate collaborative discussion and future studies that will support safer, more consistent care for pregnant individuals living with sickle cell disease.

PO96 | Morbimortality SCD with recurrent VOC and TDT >12 years in Spain. Waiting for gene therapy

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Introduction: Patients with transfusion-dependent thalassaemia (TDT) and sickle cell disease (SCD) with recurrent vasoocclusive crises (VOC) have a high rate of severe complications and mortality. Current treatments do not address their underlying cause or completely resolve their clinical manifestations. Pending the introduction of gene therapy in Spain, there is a paucity of papers that have studied the specific characteristics of these patient groups in our country.

Methods: Observational, descriptive, multicentre and retrospective study (from 2013 to 31 December 2021), in ≥12 years and: SCD genotype SS/Sβ+/Sβ0 with recurrent VOC (≥2/year for 2 years), or TDT. Index date was considered the date of the second VOC in the second year in SCD, and the date of registration in REHem-AR in TDT.

Our aim was to describe their demographic characteristics, specific complications, treatments and mortality.

Results: 47 SCD. Median age at diagnosis 2 years (0.0–17), at index date 11 years (5.0–36), 53% male. 77% SS, 13% Sβ0 and 11% Sβ+.

Median annual VOC at index date 2.67 (2.0–7.0), most frequent painful crisis (100%), acute chest syndrome (60%) and priapism or splenic sequestration (4.3%), with median incidence rate 18.4, 0.2 and 0.01 cases/total follow-up time,

respectively. 12.8% had cerebral vasculopathy (arterial stenosis, Moya-moya), 3 patients (6.4%) had alterations in transcranial Doppler ultrasound, 1 patient had cerebrovascular accident.
91% were on or received hydroxycarbamide, median duration 5.6 years (4.7–8.4); 6.7% splenectomised; 12.7% were on or received chronic transfusion regimen, deferasirox as the most commonly used chelator (21%).
One patient died at 17 years in 2021, mortality incidence rate 0.35.
44 TDT. Median age at diagnosis 1.2 years (0.5–2.2), at index date 13 years (12.0–34.0), 55% male. 48% 11.5% alloimmunised. Ferric haemosiderosis (75%), cardiac haemosiderosis (55%), hepatobiliary derived complications (70.5%), and endocrinopathies (25%) were the most frequent complications; incidence rate 3.7, 5.2 and 5.7 cases/total follow-up time, respectively. 8 patients (18%) had heart disease, incidence rate 1.2; 4 patients (9%) had deep vein thrombosis. No patient had a stroke.
14% were on or received hydroxycarbamide. 42 patients (95%) were receiving or had received chelation therapy, deferasirox (89%) most commonly used drug. 59% splenectomised.
2 patients died, median age 32 years (27.2–36.7) in 2017 and 2021, mortality incidence rate 4.3 cases/total time.
Conclusion: The results from these patients improve our understanding of their needs. Future studies could focus on patients with the same characteristics but <12 years or with a chronic transfusion regimen, who may also benefit from gene therapy.

PO97 | Cognitive abilities of hydroxyurea treated, untreated sickle cell disease children with normal controls of India

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Background: Cognitive impairments are a well-documented complication in children with sickle cell disease (SCD), potentially impacting academic performance and daily functioning. While hydroxyurea (HU) therapy is routinely administered to reduce SCD-related complications, its effect on neurocognitive outcomes remains uncertain. Regional disparities in healthcare and educational infrastructure may further influence cognitive development. This study aims to assess cognitive profiles among HU-treated and untreated children with SCD compared to healthy controls in two Indian states—Assam and Karnataka.
Methods: A cross-sectional study was conducted involving pediatric participants from Assam and Karnataka, grouped into: HU-treated children with SCD (Treated), untreated children with SCD (Untreated), and age-matched healthy controls (Control). Cognitive functioning was evaluated using the Wechsler Intelligence Scale for Children–Fifth Edition (WISC–V), which measures six indices: Verbal Comprehension Index (VCI), Visual Spatial Index (VSI), Fluid Reasoning Index (FRI), Working Memory Index (WMI), Processing Speed Index (PSI), and Full Scale IQ (FSIQ). Group and regional differences were analyzed using two-way analysis of variance (ANOVA).
Results: Participants from Karnataka scored significantly higher on most WISC–V indices than those from Assam. Within Karnataka, healthy controls outperformed both SCD groups in VCI, FRI, PSI, and FSIQ, with HU-treated children showing intermediate performance. Several group differences reached statistical significance in Karnataka. In contrast, scores across all groups in Assam were uniformly lower, with minimal or non-significant group-level variation.
Conclusion: Both geographic location and treatment status influenced cognitive outcomes in children with SCD. Participants from Karnataka, especially healthy controls, demonstrated superior cognitive performance compared to those from Assam. Hydroxyurea therapy was associated with better cognitive scores relative to no treatment, although both SCD groups lagged behind controls. These findings underscore the critical role of regional context and treatment access in shaping neurodevelopmental trajectories and highlight the need for targeted interventions tailored to specific populations.
Keywords: sickle cell disease, hydroxyurea, cognitive ability, full scale IQ.

PO98 | Role of liver biopsy in adult TDT undergoing gene therapy or HSCT

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Introduction: Liver assessment is a crucial component of assessment as part of haemopoietic stem cell transplantation and gene therapy work up in Transfusion Dependent Thalassaemia. Advance liver disease, a history of cirrhosis or the presence of bridging fibrosis are exclusion criteria as they increase the risk of transplant related mortality and veno-occlusive disease. There is currently no established pathway for adult patients with Transfusion Dependent Thalassaemia. We report our experience with liver assessment in patients undergoing gene therapy or matched related donor transplantation with non-invasive methods using ARFI elastography and transient elastography. Liver biopsy is the reference standard, but it is an invasive method.
Methods: All patients being worked up for gene therapy or matched related HSCT have a detailed liver assessment with a review of documentation of current and previous MRI Liver Iron assessment results, ferritin, virology testing including hepatitis A, B, and C looking for active or chronic hepatitis. They also get a blood test to look at ALT, Conjugated bilirubin, AST, and PT to look for advance liver disease.
They all then have non-invasive testing with a fibroscan. This is either ARFI elastography and/or transient elastography. Those

with an abnormal fibroscan results or a significant liver history go on to have a liver biopsy. In the initial few patients, some of them had an MRI liver when the fibroscan was abnormal.

Results: Eight patients were evaluated with age ranging from 17 to 37 years. The mean age was 25 years. 5 were men and 3 were women. Five out of 8 patients had a recommendation for liver biopsy. 3 patients had a normal fibroscan results and proceeded to apheresis. Four out of 8 patients had an abnormal fibroscan results ranging from 6.5 kPa to 8.6 kPa suggesting a fibrosis stage score of at least F2. The fifth patient is planned for a liver biopsy despite a normal fibroscan result given the significant history previous prolonged liver iron loading and hepatitis C. He is due for a matched sibling donor haemopoietic stem cell transplantation. All cases were discussed at the UK National Haemoglobinopathy Panel or cellular therapy group. All patients had a normal ALT, AST, split bilirubin, and PT.

2 out of the 5 patients had liver biopsies reported and confirmed there is no evidence of bridging fibrosis or advance liver disease. Both patients have progressed and have had their stem cells collected for gene therapy treatment. 2 more patients have completed their liver biopsy and are awaiting final report before apheresis slots are booked. The fifth patient is awaiting a liver biopsy date.

Conclusion: Liver biopsy has a role to play in the decision making process when fibroscan results are abnormal. The 2 patients are eligible based on liver biopsy results. Patients who have had a significant history of poor iron control, those with a history of poor documentation of iron control and in patients who have additional risk factors for developing liver fibrosis or cirrhosis can benefit from a liver biopsy. Patients and clinicians felt more confident with results of the biopsy as it gave a better risk assessment of venoocclusive disease when fibroscan results were abnormal or the history suggested they were higher risk for gene therapy or stem cell transplantation. As we gather more experience in treating adult patients, this pathway will continue to develop and improve.

PO99 | Outcome of hydroxycarbamide use in children and adults with sickle cell anaemia in Jos, Nigeria

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The treatment of sickle cell anaemia (SCA) with Hydroxycarbamide (HU) has been shown to result in significant lowering of the rate of vaso-occlusive crisis (VOC), acute chest syndrome, stroke, blood transfusions, and hospitalization. The benefits and safety of HU in patients with SCA spans across infants to adulthood in Africa.

HU is underutilized in low and middle income countries, especially in Sub-Saharan Africa in spite of its efficacy in the reduction of morbidity and mortality. Reasons for the low uptake of HU include, misconceptions related to drug safety and the cost of drug and associated laboratory monitoring, unpredictable hospital pharmacy stocks and availability of different drug strength are also relevant.This study is an appraisal of the outcome of HU use on clinico-haematological parameters of a cohort of subjects with SCA, following one year of treatment with HU at a single centre in north central Nigeria to review the impact on their wellbeing.

Methodology: Bingham University Teaching Hospital Jos is a Missionary/Private organisation. Hydroxycarbamide was recently introduced free of charge to the Sickle Cell Clinic by the SCORE Charity Foundation, United Kingdom. The rapid uptake of Hu led to the increase in the number of our patients from 40 to 149 within 1 year.

This was a retrospective study undertaken at Bingham University Teaching Hospital, Jos. Data of patients attending SCA clinic who were on a fixed dose of 20mg/kg of HU for 1 year were analysed. Assessed variables included biodata, pre- and post-treatment haematological and cliniical parameters. Ethical approval was obtained from the Research and Ethics Committee of Bingham University Teaching Hospital.

Results: The cohort comprised 149 patients aged 1–34 years, with a male-to-female ratio of 1:1.1. Among the 81 patients who experienced greater or equal to three vaso-occlusive crisis episodes at baseline, 69 remained in that category following treatment, while 12 transitioned to the ≤2-episode group. A similar shift was observed in hospital admissions and blood transfusion.

An increase in mean haemoglobin concentration was observed, rising from 8.5 ± 1.6 g/dL at baseline to 9.1 ± 1.1 g/dl following treatment. The mean absolute neutrophil count declined from 5563.9 ± 4525.3/mm^3 to 2584.2 ± 1537.63/mm^3. Similarly, the median platelet count decreased from 390.0×10^9/L (IQR: 255.0–454.5) to 322.0×10^9/L (IQR: 268.0–408.3).

Conclusion: The study showed improvement in the wellbeing of children and adults with SCA following the use of hydoxycarbamide. There is an urgent need to improve access, affordability, and consistent availability of HU to promote its widespread use among children and adults with SCA in low- and middle-income countries.

PO100 | Imaging transcranial Doppler, effective tool for the prevention of stroke in children with SCD: Meta-analysis

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Introduction: Sickle cell disease (SCD) is a chronic condition that is characterized by vaso-occlusion, recurrent anaemia, end-organ damage, and cerebrovascular disease. One of the most severe and disabling complication of sickle cell disease is stroke. Transcranial Doppler Ultrasound (non-imaging; TCDni) can be used to measure cerebral blood flow velocity (CBFV) in the middle cerebral artery (MCA) and other intracranial arteries secondary to raised CBF or arterial narrowing. This has been standard of care for at least 25 years and an endpoint in observational studies and clinical trials. However, the lack of adequately trained personnel and equipment has brought about the use of Imaging Transcranial Doppler (TCDi) as an alternative. Guidelines for TCDi recommend not using angle correction as TCDni does not but it is then essential to focus on obtaining the optimal velocity along the vessel.This systematic review aims to evaluate the use of TCDi as an effective tool for the evaluation and prevention of stroke in children with SCD and to compare it with TCDni.
Methods: We searched for relevant papers published between 1970 and 2025 in PUBMED, MEDLINE, EMBASE and GOOGLE SCHOLAR. The studies were included if participants with SCD were between the ages 2 and 18 years and if they were screened for stroke using TCDi and TCDni with data comparing the two modalities. Reviews, case series, case studies, editorials and conference proceedings were excluded. Duplicates were removed and the titles were screened for relevance by two authors, with full papers retrieved where it was agreed that the paper was relevant. Each study was assessed using the Appraisal Skills Programme Case Control Checklist.
Results: A total of 630 articles were retrieved. After removal of duplicates and review of titles and abstracts, 12 comparative studies were included, 7 of which presented mean % difference between TCDni and TCDi in 561 patients with values between −4.26 and −19%. 36 (6%) patients from 4 studies had abnormal TCDni with time-averaged mean of the maximum velocity (TAMMV) in the MCA >200 cm/s. For TCDi, angle correction was not an option in one study, was not considered in nine studies, and was reported as giving velocities closer to the TCDni in two, including one from Nigeria reporting 26 children with SCD and abnormal TCD. The studies were all moderate to low-quality.
Conclusion: TCDi may be an effective tool for the evaluation and prevention of stroke in children with SCD. However, not all studies included abnormal TCD and there are a number of manufacturers so that more data comparing TCDi with and without angle correction with TCDni are needed. In the meantime it may be prudent to compare TCDi with TCDni for quality assurance on a site. Follow-up studies should be undertaken using TCDi and TCD to standardize the cut-off point for high-risk of clinical stroke.

PO101 | Bridging the gap: Perspectives of transitioning adolescents with sickle cell Disease

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Introduction: Transitioning adolescents with sickle cell disease (SCD) from paediatric to adult healthcare requires more than a change in service, it demands a holistic and patient-centred approach. We explored the lived experiences of young people navigating this transition to identify psychological, structural, and service-related barriers and facilitators impacting continuity of care and outcomes. We also analysed practical aspects of how transition care is delivered across West London Haemoglobinopathy Coordinating Centre (HCC).
Methods: A pilot focus group was conducted with two young adults with SCD who had transitioned to adult services. Using semi-structured discussions, we explored perceptions of transition, emotional readiness, healthcare professional interactions, and system-level experiences. Data were thematically analysed to extract key insights. A survey of health care professionals across the West London HCC is also underway to assess provision of transitional care.
Results: Participants described transition as a critical and challenging phase, with increasing responsibilities whilst developing independence from parental support. The young people highlighted the loss of trusted paediatric relationships and lack of individualised attention in adult services, contributing to feelings of isolation and anxiety. Knowledge disparities among healthcare professionals, particularly outside London, were a recurring concern. The inpatient experience often involved mistrust, stigmatisation e.g. assumption of drug-seeking behaviour, and a perceived lack of empathy in emergency and non-specialist settings, echoing reports from other multicentre qualitative studies (Renedo et al., 2020). While some positive elements were noted, such as consistent and supportive nursing staff in haematology day units, participants highlighted the need for clearer transition pathways, better psychological preparation, and improved awareness and understanding among non-specialist staff. Service improvements such as; group transition events—providing the opportunities to tour the adult service, meet fellow patients and members of the adult haemoglobinopathy MDT and the introduction of a peer mentorship programme, have

helped address some of these concerns. However, further work is required to move towards better equality in adolescent transition care across the HCC.

Conclusions: This qualitative study highlights the psychological and systemic hurdles faced by adolescents with SCD transitioning to adult care. It emphasises the importance of structured, empathetic, and collaborative transition frameworks that empower young patients, maintain continuity, and improve outcomes. These findings advocate for targeted education for adult healthcare providers, incorporation of youth voices in service design, and the need for enhanced public health awareness and overall improved visibility of SCD.

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PO102 | SCD mission in India: Progress and updates

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Health Services and Outcomes Research including Psychology

SCD Mission in India: Progress and updates: Sickle cell disease has a prevalence of 8.75% (trait) in India. The MoHFW Tribal Health Expert Committee report has listed sickle cell disease as one of the 10 special and most common problems in Tribal Heath that affect the tribal people disproportionately, thus making this an important intervention. Ministry of Health under NHM initiated the work on hemoglobinopathies (Thalassemia and Sickle Cell Disease) in 2014 and in 2016 wherein comprehensive guidelines on prevention and management of Haemoglobinopathies were released and provision of funds towards screening and management of Sickle cell disease were made.

Seeing the burden of disease, it was envisaged to have a separate scheme/Mission to detect, manage, prevent and generate awareness for SCD through a convergence model. For this a joint meeting with Ministry of Tribal affairs, women & child development, Department of Science and technology and Ministry of social justice was held to draw the strategic road map for SCD which address the issues in a holistic manner.

Aim of Mission: Its target was to eliminate sickle cell disease, as a public health problem in India before 2047. To address the urgent need to control and manage SCD in India's population, the Government of India launched the National Sickle Cell Anaemia Elimination Mission in year 1 July 2023, at shadol, a tribal area in central India with significant funding for large-scale measures to control sickle cell disorders in India.

The Mission had a focus on screening, creating awareness and genetic counselling, strengthening diagnostic laboratory services along with management and treatment facilities. It also had a mandate to establish linkages across different levels of care, such as, community engagement, collaboration and partnerships with existing Government platforms like RBSK (Rastriya Bal Swasthya Karyakram) and PMSMA (Pradhan Mantri Suraksha Matritva Abhiyan) to create awareness and screening. It also planned to collaborate with e-raktkosh for blood transfusion etc and facilitate research as development of POCT for sickle cell disease and Gene therapy.

Progress and Update: Awarenes creation in 26 tribal languages and 12 regional languages has led the programme to percolate down to the last mile. Newborn screening, has been established in 12 states while antenatal screening and adolscent screening has been initiated in all the 17 identifies states. With this India has been able to achieve the screening of 57 million, and detected 16 millioin trait and 200 thousand disease.Timely initiation of preventive care, such as penicillin prophylaxis and vaccinations,in these sujects has significantly reduced the frequency and severity of infections up to 25% in patients with sickle cell diserase. Similarly,making available access to medications upto PHC level like hydroxyurea, liquid hydoxurea for neonates as part of this mission has reduced sickle and pain crises up to 27%.

Conclusion: In essence,by facilitating robust access to testing, diagnosis, treatment, and ongoing patient care, the Mission has ensured better health to individuals with SCD ultimately improving their health outcomes and reducing their disease associated suffering and mental agony. In the coming years, India hopes to emerge as one of the big suppliers of POCT for sickle cell disease detection and HU. Also, for research going on gene therapy, India may very soon see the light of gene therapy for SCD patients in near future.

PO103 | Improving Black health outcomes—Creating an impactful and diverse research resource

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Introduction: Individuals of Black ancestry are underrepresented in large genome wide association study data sets such, with as little as 2% representation. But people of Black ancestry are known to have increased genetic diversity compared to other populations. Such disparity limits the ability to extrapolate meaningful findings from genomic data that can be applied to populations of African ancestry; this has implications for the understanding of prognosis and effective treatments for affected individuals.

NIHR BioResource has established Improving Black Health Outcomes (IBHO) to begin addressing this imbalance,

aiming to create a resource that can be used to investigate health questions of importance to UK Black communities.
As part of this, the BioResource is collaborating with Genomics England to recruit sickle cell patients, both children and adults, collect information and generate genomic data to provide a world-leading research resource where the most pertinent questions about this challenging condition can begin to be answered.
Methods: The IBHO BioResource invites individuals from Black ethnic backgrounds, and those living with sickle cell, to participate in research aimed at improving our understanding of how these conditions might develop and specifically affect those from Black communities.
People with sickle cell are invited to join the study via their clinical care team and recruitment activity happens at their appointment or a time convenient to them. Joining IBHO involves providing consent to the BioResource, and the option of joining Genomic England's National Genomic Research Library.
Participants provide samples when joining which are used to generate genomic data (short-read and long-read whole genome sequencing); clinical teams provide phenotype data regarding medical history and treatments and participants provide their own report of their experience of sickle cell including chronic pain, medication and blood transfusions.
All participants in the BioResource consent to being contacted about further research studies and clinical trials.
IBHO has been designed and developed with individuals with lived experience and community groups.
Results: In the first year of recruitment over 2500 participants have been recruited to IBHO and more than 1000 are people with sickle cell. Genomic data is already being generated for those who have joined the project and there have been several enquiries from research groups about using the data held by IBHO to undertake research projects.
There are key research areas identified as requiring attention in sickle cell and IBHO has the power to help advance knowledge in these areas. By including children young people and adults in IBHO there will be opportunity to study how the disease progresses over time and improve care at every stage of life. The ability to recontact participants in IBHO means that there is an efficient way of identifying and inviting people with sickle cell to take part in studies and clinical trials that can lead to more, and better, treatment options. Participant data from the BioResource has already contributed to the development of the NHS England Blood Group Genotyping Programme.
Conclusion: By pairing extensive clinical and self-reported health and lifestyle data with genomic data IBHO BioResource can power research that will shape future healthcare strategies and interventions tailored to meet the needs of people with sickle cell.

PO104 | Beyond the crisis: Tracking vaso-occlusive crisis recovery through patient-reported experiences and wearable data insights

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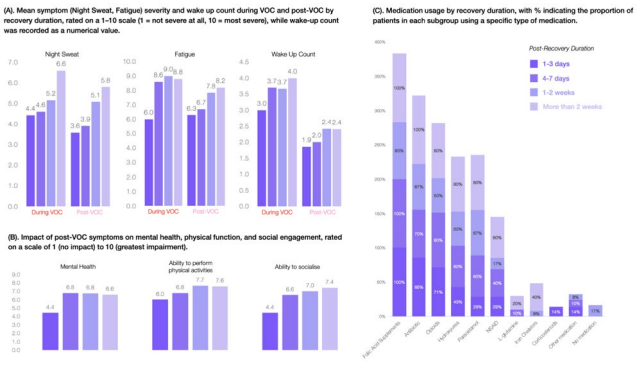
Introduction: Sickle cell disease (SCD) is characterised by recurrent vaso-occlusive crises (VOCs) with long-lasting effects that extend beyond acute pain episodes. This work sought to investigate the burden of sleep-related symptoms pre- and post-VOCs, in order to better understand the factors affecting post-VOC recovery and longer-term outcomes.
Methods: Between February 2024 and February 2025, data were collected from 34 individuals with SCD in the UK through a digital survey and wearable devices. Symptom severity (1 = least, 10 = most), sleep disturbances, fatigue, and medication use were recorded during VOCs and the recovery period, recorded and assessed as a numerical value, and linear regression was applied to wearable data ($p < 0.05$) to explore associations with symptom burden and recovery duration.
Results: Across participants (74% female; median (range) age 37.5 (18–60) years), 76% were HbSS and 24% HbSC genotypes. Recovery durations varied, 21% recovering in 1–3 days, 32% in 4–7 days, 35% in 1–2 weeks, and 12% required more than 2 weeks. Most participants (85%) reported experiencing the same post-VOC symptoms each time, 47% with consistent severity linked to VOC cause ($n = 2$) or symptom intensity ($n = 2$). Similarly, 68% reported consistent recovery durations, impacted by VOC severity ($n = 1$) or pain location ($n = 2$).
Patients with prolonged recovery reported more severe night sweats both during VOCs and recovery (Figure 1A), and those recovering over ≥1 week had the highest levels of fatigue and disrupted sleep. Additional sleep concerns included difficulty falling asleep (21%) and anxiety during sleep (9%). Beyond physical symptoms, symptom burden included reduced mental health and ability to socialise in those requiring ≥4 days for recovery (Figure 1B).



Wearable data indicated lower light sleep and higher deep sleep during VOCs and the first week post-VOC among those with longer recovery durations. Light sleep and night SpO_2 in turn negatively correlated with pain scores, while higher deep sleep and lower sleep heart rate were linked to lower pain severity ($p < 0.05$). Opioid use was associated with higher light sleep, SpO_2, ECG bpm, activity levels, and sleep HR ($p < 0.05$). However, five participants reported worsened recovery symptoms from opioids, including insomnia, digestive issues, and fatigue.

Of the 12 participants who used medications specifically for post-VOC recovery, 9 noted symptom improvement. Four found supplements (vitamins/electrolytes) beneficial in managing fatigue and sleep disturbance (Figure 1C).

Conclusion: This work highlights that post-VOC recovery in SCD is highly individualised, with extended recovery times linked to increased symptom severity, disrupted sleep, and greater impacts on mental and physical wellbeing during VOCs and the post-VOC period. Furthermore, this appeared to be associated with the highest usage rates across all medication types and a subsequent higher disease burden and medication reliance during recovery management, with low or inconsistent effectiveness. Wearable insights provided new understanding of how sleep physiology changed during recovery, particularly in those taking opioids, who in some cases reported worsening symptoms and side effects. Despite high medication use, recovery support remains inconsistent, emphasising the need for more targeted approaches to help individuals return to baseline health after a VOC.

PO105 | Growth status of a UK paediatric sickle cell cohort in the era of disease-modifying therapies

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Introduction: Children with sickle cell disease (SCD) have historically been reported to be at risk for impaired growth, but recent studies also highlight rising obesity rates in UK and US SCD cohorts. We aimed to provide real-life data on the growth patterns (height and BMI) of children with SCD managed at a UK centre serving a high-prevalence area with high uptake rates of Disease Modifying Therapy (DMT), and to explore the influence of demographic and clinical factors on these growth parameters.

Methodology: Retrospective observational study of all patients in our paediatric SCD cohort. Serial anthropometric and clinical data were extracted from electronic patient records, and statistical analysis to compare pre- and post-DMT growth parameters was performed using SPSS. *z*-scores for height and BMI were calculated using UK-WHO growth charts.

Results: Our cohort included 150 patients (female 51%, mean age 9.1 ± 4.7 years, range 0.3–16.7 years). Only 3.3% of patients were classified as underweight (BMI <5th percentile), whereas 23% were categorized as overweight (BMI >85th percentile), and 11% as obese (BMI >95th percentile). Female patients were more likely to fall into the overweight category, and patients with HbSC genotype had a higher mean BMI *z*-score compared to those with HbSS (0.62 vs. 0.28, $p = 0.035$). A significant positive correlation was observed between BMI z-scores and Hb levels ($p = 0.02$), but not with other clinical factors such as age, hospitalization rates, age at diagnosis, or use of DMT. Only 4% of patients were categorized as having short stature (height <3rd percentile). A statistically significant increase in height z-scores was noted one year after initiation of DMT ($p < 0.001$). Subgroup analysis of different types of DMT also highlighted significant improvement in height z-scores separately with hydroxycarbamide and as well as regular transfusions.

Conclusion: Children with SCD in our UK cohort exhibit growth and obesity rates comparable to the general paediatric population. Female patients and those with HbSC genotype appear to be at higher risk for overweight status. Disease-modifying therapies, including hydroxycarbamide and regular transfusions, have a positive impact on growth, particularly on height. Further longitudinal studies are needed to evaluate the long-term growth patterns of children with SCD in the era of disease-modifying treatments, as well as to assess the risk factors and consequences of obesity in this population and inform targeted preventive strategies.

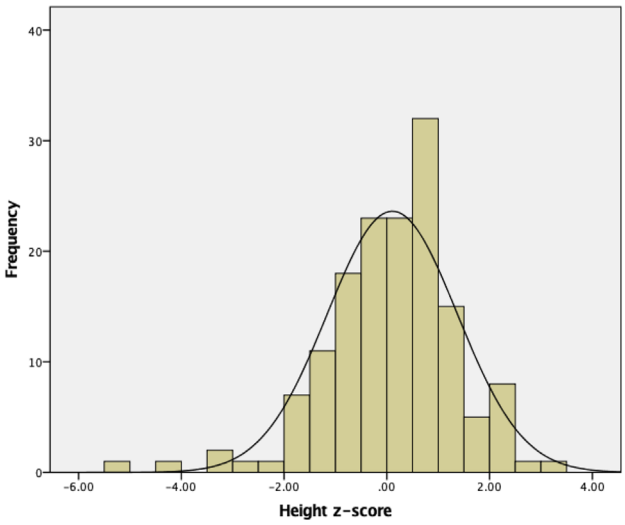
TABLE 1 Comparison of clinical characteristics across weight categories

	BMI <85th centile	BMI >85th centile	p Value
Female	53 (46%)	24 (71%)	0.011
Mean age	9.4 ± 4.6	7.9 ± 4.9	0.09
HbSS	77 (68%)	21 (66%)	NS
HbSC	37 (32%)	11 (34%)	
Mean annual hospitalisations	0.35	0.32	NS
Steady State Hb (g/dL)	95 ± 16	100 ± 15	NS
Hb F (%)	10.9 ± 10	14.3 ± 12.7	NS
Retics	164 ± 86	166 ± 85	NS

TABLE 2 Comparison of height and weight parameters before and after DMT.

	Before DMT	1-year post DMT	p value
Height z-score	0.0227 ± 1.11	0.376 ± 0.99	<0.0001
BMI z-score	0.344 ± 1.09	0.516 ± 1.1	0.2
% Underweight	5.2%	1.8%	0.81
% Short stature	7.7%	0%	0.001

Figure 1: Distribution of patients by height z-scores



PO106 | Transcranial Doppler velocities in Nairobi children with sickle cell disease

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Introduction: Sickle cell disease (SCD) is the most common inherited hemoglobinopathy and has the most significant burden in Sub-Saharan Africa. Sickle cell disease increases the likelihood of stroke, with approximately 10% of children and adolescents experiencing a stroke before reaching 20 years of age.

Children with SCD have a stroke lifetime risk of 25%–30% and a peak incidence at 7 years of age. Transcranial Doppler (TCD) ultrasonography aids in identifying children with SCD who are at an increased risk of stroke, thereby enabling effective primary stroke prevention measures. Evidence recommends annual trans-cranial Doppler ultrasound (TCD) to screen for risk of stroke in children aged 2–16 years. Recent studies in sub-Saharan Africa have reported much lower prevalence of velocities greater than 200 cm/s in the context of similar incidence of stroke as in the USA and Europe.

Methods: The main outcome primarily focuses on cerebral blood flow velocity (CBFv) measurements obtained through TCD imaging to determine the prevalence of abnormal CBFv measurements in children with SCD. TCD has been performed to measure the highest time-averaged mean of maximum velocity (TAMMV) primarily in major vessels, specifically the middle cerebral artery (MCA). The STATA statistical software package has been used for data analysis. Ethical approval for this study has been obtained from the Research Ethics Committee of Gertrude's Children's Hospital and the Aga Khan University, Nairobi Institutional Scientific and Ethics Review Committee (ISERC).

We undertook a retrospective study of CBFv in children with SCD presenting to the SCD clinics across two sites: Gertrude's Children's Hospital and Uhai Neema Hospital, in Nairobi. TCD had been undertaken in consecutive patients who were referred, applying standard protocols to perform the test. We also documented the occurrence of stroke in these children.

Results: We retrieved data for 85 children; they were of median age 8 (IQR 4–12) years, and 42% ($n = 36$) were females. The left CBFv measurements was of average 102 (IQR 94–111) cm/S; and the right CBFv was 104 (IQR 96, 110) cm/S. Only 1 child had left CBFv >200cm/S. Four had conditional left CBFv (>175 cm/S). Four had right ≤CBFv 50 cm/S and 6 had left CBFv ≤50 cm/S. Six had suffered stroke; and in 5 of them, we were not able to insonate the corresponding MCA after the stroke happened.

Conclusion: The cerebral blood flow velocity (CBFv) measurements observed in our cohort of children with sickle cell disease (SCD) in Nairobi show a similar profile to those reported in other African settings. These findings highlight the need to re-examine CBFv reference values for children with SCD residing in sub-Saharan Africa, correlating also with their Hb levels. Further research involving both children with and without SCD will be essential to generate locally relevant data and determine whether the currently established transcranial Doppler (TCD) thresholds are appropriate for this population.

PO107 | Feasibility of hydroxyurea for sickle cell disease in Nairobi's informal settlements: A retrospective study

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Introduction: Sickle cell disease (SCD) is one of the most prevalent monogenic disorders in sub-Saharan Africa, associated with significant morbidity and mortality, particularly among children. Acute and chronic complications, including vaso-occlusive crises (VOCs), infections, and organ damage,

influence quality of life and reduce survival. Hydroxyurea (HU) has been shown to reduce VOC frequency, improve hematologic parameters, and reduce disease-related complications, but data on its use in low-resource, urban African settings remain limited. This study aimed to assess the feasibility, clinical impact, and safety profile of Hydroxyurea use among SCD patients attending a dedicated clinic within the informal settlements of Nairobi, Kenya.

Methods: We conducted a retrospective cohort analysis of 2206 clinical visits from 328 children and adolescents with SCD managed in two dedicated SCD clinics in Nairobi between March 2019 and March 2021. Patients were categorized based on HU use. Clinical outcomes, including rates of VOCs, infections, and major complications, were compared between HU users and non-users. Linear mixed-effects models assessed HU's impact on hematological parameters, while competing-risk Cox regression models estimated the risk of clinical events. HU dosing patterns and tolerability were also examined.

Results: HU use was associated with a lower incidence of VOCs (19.6 vs. 24.7 per 10 person-years) and infections (11.3 vs. 12.4 per 10 person-years) compared to non-users. Adjusted analyses demonstrated that HU significantly increased hemoglobin levels by +0.36 g/dL (95% CI: 0.19–0.53) and mean corpuscular volume (MCV) by +3.47 fL (95% CI: 2.20–4.73). The hazard ratio for VOC occurrence was 0.82 (95% CI: 0.66–1.02) and for infections 0.72 (95% CI: 0.55–0.95), suggesting a protective effect of HU, while no significant association was found for major complications (HR 1.39, 95% CI: 0.40–4.78). Notably, lower HU doses (<20 mg/kg/day) achieved comparable reductions in VOC risk to higher doses (20–25 mg/kg/day) and were associated with a lower risk of infections and major complications.

Conclusion: HU proved to be a feasible and beneficial intervention in this low-resource, urban setting, significantly reducing the incidence of infections and VOCs in children and adolescents with SCD. While the risk of major complications remained low across both groups, long-term, prospective studies are needed to fully establish HU's safety and optimal dosing strategies in similar contexts, particularly where socio-economic factors and healthcare access may affect treatment adherence and outcomes.

Moreover, this study underscores a broader public health gap: the lack of comprehensive epidemiological data on SCD in Kenya. For the future, we propose piloting an electronic national register for SCD patients, developed in collaboration with key stakeholders including the Ministry of Health, academic and clinical partners. This would be a critical tool to monitor disease prevalence, patient prognosis, health status, and access to care across the country. It would also support health system planning, inform policy development, and facilitate targeted research and clinical interventions. Improved understanding of the national burden of SCD is essential to guide the design of effective, context-specific strategies to improve outcomes for individuals living with SCD in Kenya.

PO108 | Raven's matrices as a cognitive screening tool for children with SCD: A Nairobi pilot study

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Introduction: Sickle cell disease (SCD) is the leading cause of childhood stroke worldwide and the most common inherited disorder in Sub-Saharan Africa. Cognitive deficits, linked to silent cerebral infarcts and anaemia, are frequent in children living with SCD. Raven's Progressive Matrices (RPM), widely used in Sub-Saharan Africa, have shown value in detecting cognitive issues in SCD patients. This study investigates the association between RPM scores, haemoglobin (Hb) levels, speech delay, and stroke, using the RPM first and the second updated editions.

Methods: In this pilot study, 33 children and young adults were tested with RPM first edition at Ruaraka Uhai Neema Hospital (May 2024–Feb 2025). Another 25 SCD patients were assessed with Raven's 2 (Mar–May 2025). RPM scores were combined with clinical history (speech delay, stroke, epilepsy) and lab data (recent and median Hb over 12–24 months). Descriptive statistics, scatter plots, and box plots were used. Associations between RPM scores and Hb were tested using Spearman's correlation.

Results: In the first group of 33 patients, the median age was 11 years (range: 5–36), and most were male (76%). 5 had a pre-existing major complication (4 strokes, 1 epilepsy due to birth asphyxia), and 3 reported speech delay. Median and last haemoglobin (Hb) levels showed moderate correlations with RPM scores, with Pearson coefficients of 0.50 (95% CI: 0.19–0.72) and 0.43 (95% CI: 0.10–0.67), respectively. RPM scores were lower in those with major complications (median = 25.0 vs. 52.5) and in patients with speech delay (median = 36.0 vs. 51.5).

In the second group of 25 patients tested with Raven's 2, 56% were male. Ages ranged from 5 to 29 years (mean = 12.64, median = 13). Three patients reported a previous stroke. Scatter plot analysis suggested a positive relationship between median Hb levels and Raven's 2 scores: higher Hb levels were generally associated with higher scores. Box plots showed lower Raven's 2 scores among SCD patients with complications (median = 67.0) versus those without (median = 91.0), and in patients with cognitive delay (median = 47.0) versus those without (median = 91.0).

Spearman's rank correlation revealed a weak, non-significant positive relationship between Raven's 2 scores and both last visit Hb levels ($p = 0.324$, $p = 0.115$) and median Hb levels ($p = 0.260$, $p = 0.210$).

Conclusion: Standardized cognitive screening tools like RPM can guide early preventive interventions for SCD patients in Sub-Saharan Africa, where imaging and TCD access is limited. Our findings align with existing research showing lower cognitive performance in SCD patients, particularly those with cerebrovascular complications or anaemia. Future research should include control groups and cross-cohort comparisons (e.g., with other European or African data) to explore genetic, socio-economic, and environmental factors affecting cognition in SCD. Longitudinal studies with repeated assessments would clarify how cognitive decline relates to silent and overt strokes, improving targeted interventions. RPM remains a practical, informative tool in these settings, offering valuable insights into neurocognitive risks in paediatric and adolescent SCD populations.

PO109 | Outcomes from a transition care model for adolescents with sickle cell disease in Nairobi

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Introduction: Adolescents and young adults living with Sickle Cell Disease (SCD) face significant challenges as they transition from pediatric to adult care services, particularly in resource-constrained settings. In Nairobi's informal settlements, barriers include weak health system infrastructure, limited disease awareness, poor self-management capacity, and a lack of tailored transition protocols. In response, a Self-Management Program (SMP) was piloted to strengthen health system readiness, empower adolescents, and develop a structured transition of care protocol.
Methods: The SMP was implemented at Ruaraka Uhai Neema Hospital (RUNH) between January and December 2023, in collaboration with local and international partners. The intervention combined health workforce training, peer-led teen clinics, patient education, support groups, and the development of a draft Transition of Care Protocol. Four Training-of-Trainers (ToT) sessions were conducted, engaging 15 healthcare professionals. A multi-disciplinary team comprising doctors, nurses, counsellors, and peer educators was formed. The program enrolled 69 adolescents aged 13–18 years, surpassing the initial target of 60. Eight dedicated Teen Clinics were held, achieving a total of 205 visits.
Results: The programme proved highly effective in boosting adolescent engagement and self-management. ToT sessions achieved measurable knowledge improvements, with a 20% gain in one training, and pre- and post-tests confirmed knowledge retention. Teen Clinics provided a safe, adolescent-friendly space for consultations, health education, and peer interaction, averaging 26 patients per clinic. Patients reported improved disease knowledge, emotional awareness, and clinic attendance. Patient diaries, group health talks, and peer-led sessions fostered greater confidence and participation in care decisions. The piloted protocol standardized key practices for transition of care and improved service continuity. Efficiency was enhanced through the use of existing institutional infrastructure, the involvement of community health promoters (CHPs), and peer educators in community mobilization. A partial co-payment model encouraged patient ownership while preserving access.
Impacts included improved health-seeking behaviors, stronger caregiver and adolescent engagement, and early signs of proactive self-care. Adolescents showed increased confidence in managing their condition and navigating health services. Capacity was built among local health staff through training and mentorship. Challenges around financial sustainability remain, with opportunities identified for income-generating activities.
Conclusion: This pilot project demonstrated the feasibility and value of a structured adolescent-centered model for SCD in Nairobi's informal settlements. Transition of care is an increasingly urgent issue in resource-limited settings, as early diagnosis, and improved care enable more children with SCD to survive into adulthood. Recommendations include expanding the age range from 18 to 25 years, enhancing adherence monitoring through digital tools, and strengthening community partnerships. Additional priorities involve equipping clinics for moderate emergencies, integrating mental health services, and scaling the Transition of Care nationwide. Long-term outcome tracking and mid-term evaluations are essential to refine care models and promote sustainable, locally-led health services for young people living with SCD.

PO110 | Prevalence, acceptability and feasibility of newborn screening for sickle cell disease in western Kenya

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Introduction: Majority of children with Sickle Cell Disease (SCD) in Sub-Saharan Africa will die before celebrating their 5th birthday if no intervention is provided. The World Health Organization (WHO) recommends newborn screening

(NBS) as one of the early interventions to reduce morbidity and mortality associated with SCD. NBS programs for SCD have however not been implemented in Kenya posing a challenge in comprehensive care for children with SCD. This study aimed to assess the acceptability and feasibility of newborn screening for SCD and SCT (Sickle Cell Trait) among parents/caregivers of newborns and health care providers at Webuye County Hospital and to determine the prevalence of SCD and SCT among the newborns.

Methods: Cross-sectional study conducted with newborns, their caregivers, and healthcare providers at Webuye County Hospital. After consent was given, interviewer-guided questionnaires were administered to participants. NBS was performed using hemotype SC screening kits.

Results: A total of 639 newborns were enrolled in the study at a median age of 14 h (IQR 6–18 h) and 50.7% were males. The mean birthweight was 3061.7 grams, and their mothers had a mean age of 25.7 years. Among caregivers, 79.7% were aware of SCD, only 42.7% knew that SCD is acquired genetically, and 55.7% were not aware of how a SCD diagnosis is made. Only 5 (0.8%) of infants had ever tested for SCD with Hb AA results. Acceptability of newborn screening was high at 99.4% (95% CI 98.7%–99.8%). The prevalence of SCD was 1.3% (95% CI 0.5–2.2%) and SCT at 8.8% (95% CI 6.5–11.2%).

Conclusion: Acceptability of NBS for SCD among caregivers is high. The prevalence of SCD and SCT is high in Western Kenya. There is need to scale up NBS programs in high burden SCD counties for early diagnosis and linkage to comprehensive care.

PO111 | The H-PRIME trial: Hydroxyurea-pragmatic reduction in mortality and economic burden

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[1]KEMRI-Wellcome Trust Research Programme, Kenya, Kilifi, Kenya, [2]Mbale Clinical Research Institute, Mbale, Uganda, [3]Imperial College London, London, UK, [4]Central Public Health Laboratory, Kampala, Uganda, [5]MRC Clinical Trials Unit at University College London, London, UK, [6]Cincinnati Children's Hospital, Cincinnati, USA

Introduction: Sickle cell disease (SCD) is a major cause of ill health and premature death in Africa. Malaria, anaemia, and bacterial infections are all major contributing factors. Too few trials have investigated optimum management approaches within the region.

Methods: Hydroxyurea-Pragmatic Reduction In Mortality and Economic burden (H-PRIME: ISRCTN15724013) is a large, pragmatic, 2×2×2 factorially randomised trial investigating three separate therapeutic interventions. 1800 children aged 1–10 years attending SCD clinics at four sites in Eastern Uganda are being randomized to: (1) hydroxyurea, administered at either a higher dose (median 25 mg, range 15–30 mg/kg/day) or a lower dose (median 10 mg, range 6–13 mg/kg/day), prescribed pragmatically using a 1000 mg scored tablet which can be divided into quarters, dosed using the same weight-bands either daily or three times a week, and with clinically-guided rather than routine laboratory monitoring; (2) enhanced malaria chemoprophylaxis with weekly doses of dihydroartemisinin-piperaquine versus monthly doses of sulfadoxine-pyrimethamine (standard of care); and (3) enhanced antibacterial prophylaxis with daily cotrimoxazole at all ages versus twice daily penicillin V until 5 years of age (standard of care). All children will be followed until 48 months after the first randomisation. The primary endpoints will be mortality for the hydroxyurea randomisation, malaria-associated hospital admission for the antimalarial randomisation, and all-cause hospital admission for the antimicrobial randomisation. Secondary outcomes will include the incidence of SCD-specific complications, the receipt of blood transfusions, haemoglobin and fetal haemoglobin concentrations, Grade 3/4 liver function/creatinine test results, and serious adverse events. The economic costs and benefits of the three interventions will also be compared.

Results: The first participant was recruited to H-PRIME on 16th January 2024. Recruitment will be completed by July 2025. The rationale for the trial and the baseline characteristics of trial participants will be presented.

Conclusion: The management of SCD in Africa is largely based on guidelines developed in high-income, resource-rich countries where resources are more limited and, for numerous reasons, the clinical epidemiology of the SCD is very different. H-PRIME will produce data that will inform best practice for the management of SCD in Africa in the future.

PO112 | Investigating the role of complement activation in sickle cell disease

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Introduction: Sickle cell disease (SCD) is a hereditary haemoglobin disorder characterised by the production of an abnormal haemoglobin S, leading to chronic haemolytic anaemia, recurrent vaso-occlusive episodes, organ dysfunction, and premature mortality. Inflammation is central to the pathophysiology of SCD, with increasing recognition of the complement system as a key mediator. Haemolysis

releases free haem, which activates the alternative complement pathway, contributing to endothelial injury, leukocyte adhesion, and thrombo-inflammation. While complement activation has been observed in paediatric SCD populations, data in adults—particularly stratified by genotype, phenotype, sex, and treatment status—remains limited.

Aim: This pilot study investigates the relationship between complement activation and clinical phenotype, genotype, sex, and disease-modifying therapy in an adult SCD cohort, with a view to identifying potential biomarkers and therapeutic targets.

Methods: Following ethics approval, adult SCD patients (≥18 years) of all genotypes were recruited from Hammersmith Hospital. Plasma samples were collected during routine outpatient reviews or prior to routine red cell exchange. Complement activation markers C3a, C5a, and sC5b-9 were quantified using ELISA. Clinical data—including genotype, sex, disease-modifying therapy (DMT), and disease severity (mild/moderate/severe based on disease complications)—were extracted from patient records. Statistical analysis included parametric and non-parametric tests based on data distribution, and correlations between complement levels and clinical variables were assessed.

Results: Preliminary findings revealed significantly elevated sC5b-9 levels in patients with mild/moderate disease compared to those with severe phenotypes ($p = 0.02$), potentially reflecting modulation by DMT in the latter group where most patients were receiving regular exchange transfusions. Female patients demonstrated significantly higher C5a levels than males ($p = 0.01$), indicating possible sex-related differences in complement activation. No significant differences in complement activation based on age (18–39 vs. 40–69) or DMT status alone. There was also no statistically significant difference in complement markers observed between genotypes, although the HbSC subgroup was underrepresented. When examining complement fragmentation patterns by phenotype, although not reaching statistical significance, results showed segregation with lower sC5b-9 and C5a levels in the HbSC group.

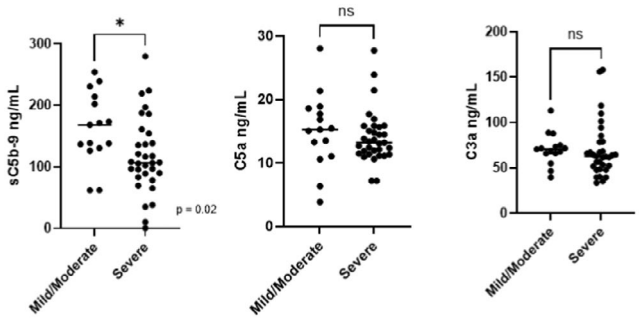

FIGURE 1 Complement activation markers in mild/moderate vs. severe disease.

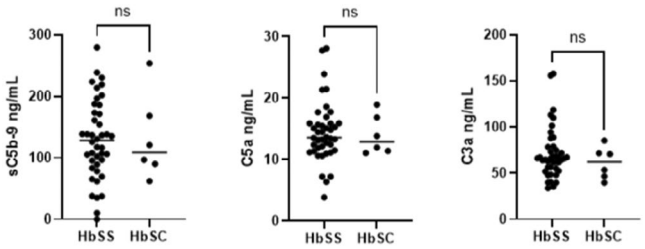

FIGURE 2 Complement activation markers in HbSS vs. HbSC individuals.

Conclusion: This represents one of the first studies examining complement activation in an adult SCD cohort stratified by multiple clinical factors. Results highlight potential sex-specific differences and suggest DMT may modulate complement activity. C5a and sC5b-9 may serve as biomarkers of inflammatory burden, though interpretation must consider treatment status. Limited genotype diversity in this cohort underlines the need for larger, more representative studies which must also include those patients with severe phenotype not receiving DMT. These findings advance our understanding of alternative pathway involvement in SCD and may inform the utility of complement fragmentation patterns as prognostic biomarkers.

PO113 | Understanding hydroxycarbamide use in sickle cell: Perspectives from patients and healthcare professionals

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Introduction: Hydroxycarbamide (HC) represents the primary disease-modifying therapy for sickle cell disorder (SCD), demonstrating significant efficacy in reducing pain crises, hospitalisations, and mortality. Despite strong evidence supporting its benefits, uptake remains suboptimal globally, with complex patient and healthcare provider factors influencing utilisation. Understanding the multifaceted barriers and motivations affecting HC use is essential for developing targeted implementation strategies. The current literature lacks comprehensive exploration of both patient and healthcare professional perspectives within the same study framework. Therefore, our study aims to gather preliminary data to understand barriers to hydroxycarbamide use in SCD from patients' and healthcare professionals' perspectives.

Methods: We will conduct a co-produced mixed-methods pilot study, employing qualitative focus group discussions and quantitative survey questionnaire, to explore HC use among people with SCD and healthcare professionals. The Patient and Public Involvement (PPI) advisory group will include six patient representatives who will guide research objectives and co-produce the survey and focus groups. A steering committee of three stakeholders (clinical nurse specialist, consultant haematologist, and patient organisation representative) will work in parallel. Two focus groups will be conducted: one with SCD patients ($n = 7$, aged ≥18 years, with mixed HC experience) and another with healthcare professionals ($n = 7$, with minimum 2 years SCD experience; haematologists, nurses, GPs, and pharmacists). Co-produced surveys will be developed through iterative collaboration. Focus groups will last 90–120 min with thematic moderation and audio recording. Qualitative data will undergo inductive thematic analysis using framework approach with dual coding. Quantitative survey data will be analysed using descriptive statistics and integrated with qualitative findings through triangulation methodology.

Results: We anticipate diverse participants representing varied HC experiences and professional backgrounds. Focus group discussions may reveal complex interplay between patient knowledge, healthcare communication, systemic barriers, and individual decision-making processes affecting HC utilisation. The PPI framework aims to provide effective patient-centred research priorities and culturally appropriate data collection methods.

Conclusion: This pilot study aims to demonstrate feasibility and value of co-produced patient engagement in mixed-methods research for understanding implementation challenges in SCD care. Integration of patient and healthcare professional perspectives is likely to reveal multilevel factors influencing HC use, from individual beliefs to systemic healthcare delivery issues.

Patient-driven collaborative research from project conception: The pilot will be co-patient-led with the PPI group to ensure research relevance and patient-centred outcomes while providing methodological insights for larger-scale implementation studies. Findings will inform evidence-based recommendations for improving HC uptake through targeted interventions addressing identified barriers at patient, provider, and system levels.

PO114 | Study design: A phase 2, randomized, placebo-controlled, dose-finding trial of tebapivat in sickle cell disease

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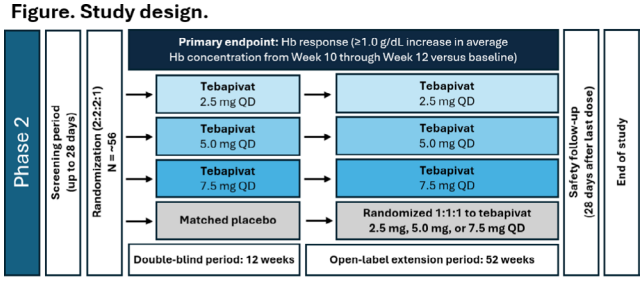
Introduction: Sickle cell disease (SCD) is an inherited blood disorder characterized by the production of sickle hemoglobin (Hb), leading to stiff, distorted, crescent-shaped red blood cells (RBCs) that cause blood flow obstruction, vaso-occlusion, and pain. Sickle RBCs have a reduced life span, leading to hemolytic anemia and fatigue. Activation of the RBC-specific form of pyruvate kinase (PKR), a key enzyme in RBC metabolism accounting for 50% of adenosine triphosphate (ATP) production, improves membrane integrity and deformability of RBCs in SCD. PK activation decreases levels of 2,3-diphosphoglycerate (DPG) and inhibits the polymerization of sickle Hb in its deoxygenated state, thus reducing RBC sickling. Tebapivat is an activator of the PKR and PKM2 isoforms of PK that is being investigated as a potential therapy for SCD. In a Phase 1 study in adult patients with SCD (NCT04536792), oral tebapivat at doses of 2 mg or 5 mg once daily (QD) for 28 days was well tolerated and led to increased levels of Hb and ATP, decreased levels of 2,3-DPG, and improvements in markers of hemolysis

Figure. Study design.



Hb, hemoglobin; QD, once daily

and erythropoiesis. Based on these results, a Phase 2 study of tebapivat in patients with SCD was designed.

Methods: To report the study design of a Phase 2, double-blind, randomized, placebo-controlled, dose-finding trial evaluating the efficacy and safety of tebapivat in adult patients with SCD (NCT06924970). In the 12-week double-blind period, approximately 56 patients will be randomized 2:2:2:1 to receive tebapivat 2.5 mg QD, 5.0 mg QD, 7.5 mg QD, or matched placebo (Figure). Patients who complete the double-blind period will be eligible to enter the 52-week open-label extension period: those receiving tebapivat will continue treatment at the same dose; those receiving placebo will be randomized 1:1:1 to receive tebapivat 2.5, 5.0, or 7.5 mg QD. Key inclusion criteria include age ≥16 years, confirmed diagnosis of SCD, Hb concentration of 5.5–10.5 g/dL based on the average of ≥2 readings during the screening period, and written informed consent. If patients are receiving hydroxyurea (HU), the dose must be stable for ≥90 days before randomization. Key exclusion criteria include receiving regularly scheduled RBC transfusions, >10 sickle cell pain crises (SCPCs) in the 12 months before providing informed consent, hospitalization for an SCPC or other vaso-occlusive event in the 14 days before randomization/providing informed consent, platelet count below the lower limit of normal (per local laboratory) or <150 000/L during screening or platelet transfusion within 28 days of randomization/providing informed consent, severe kidney disease or hepatobiliary disorders, receiving hematopoietic stimulating agents or disease-modifying therapy (other than HU) in the 90 days before randomization, and prior gene therapy or bone marrow or stem cell transplantation. The primary endpoint is Hb response (defined as a ≥1.0 g/dL increase in average Hb concentration from Week 10 through Week 12 compared with baseline). Secondary endpoints include the average change from Week 10 through Week 12 compared with baseline in Hb concentration, markers of hemolysis and erythropoiesis, and patient-reported measures of fatigue and pain, pharmacokinetics and pharmacodynamics, and safety assessments.

Results: Enrollment is planned to start in June 2025.

Conclusion: This Phase 2 study will investigate the efficacy and safety of tebapivat compared with placebo in patients with SCD.

PO115 | Outcomes of newborn screening for sickle cell disease: A systematic review of follow-up and survival

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Introduction: Newborn screening for sickle cell disease (SCD) has been established in the USA, UK and Europe for more than 40 years and more recently has been introduced in other regions, including Africa and India. In this systematic review, we present available data on follow-up and outcomes.

Methods: Medline, Embase and Global Health databases were searched using terms including 'newborn' or 'neonat*' and 'sickle' and 'outcome' or 'death' or 'stroke'. Language is currently restricted to English. Duplicates were removed and the results were reviewed by two authors, initially looking at titles, then abstracts, then full manuscripts.

Results: 475 studies were retrieved, of which 43 were reviewed in detail. Two were excluded as the main period of recruitment occurred prior to 1983, 12 were excluded as they were abstracts from conference proceedings only, two were excluded as they did not include clinical outcomes of interest, 3 because the subject was the effect or prevention of specific infections, e.g. COVID-19 or pneumococcus, 5 which only focussed on specific outcomes, e.g. splenic sequestration, vaso-occlusion, retinopathy or stroke and two because they were reviews. Of the 17 included studies 1 was from the USA, 1 from Canada, 2 from the UK, 6 from continental Europe (3 from Belgium, 1 each from France, Spain and the Netherlands), 5 from India, 1 from the middle East and 1 from Haiti. A total of 5963 of the 6347 babies diagnosed with SCD in these cohorts (94%) were followed up for up to 22 years or until death, i.e. these data refer to childhood. Forty-three children from 11 studies developed severe infection, typically secondary to Pneumococcus. Reported survival ranged between 94.5 and 100% (13 studies), with stroke-free survival 90.7%–99.8% (9 studies). Abnormal transcranial Doppler was documented in 3.2 to 10.4% of patients who were screened (4 studies) but difficulties in implementation were described in several cohorts.

Discussion: This review examines global progress in newborn screening (NBS) for SCD, highlighting its expansion beyond high-resource settings and demonstrating a high follow-up rate (94%) across 17 cohorts. Early diagnosis through NBS improves childhood survival, thanks to interventions like penicillin prophylaxis, immunisations, and parental education. However, variability in stroke-free survival and limited access to transcranial Doppler (TCD) screening reveal ongoing challenges. Gaps in infrastructure, specialist care, and data collection—especially in sub-Saharan Africa—undermine program effectiveness. The lack of standardised outcome reporting further limits comparisons. Overall, NBS is lifesaving, but global implementation and evaluation need strengthening.

Conclusion: Newborn screening (NBS) for SCD saves lives. Survival rates >94% show the power of early diagnosis and intervention. Stroke-free survival is high, but depends on access to follow-up care, including TCD screening.

Implementation challenges persist especially in low-resource settings with gaps in follow-up and access to care. Underreporting from high-burden regions limits our understanding of global program effectiveness.

Recommendation

- Strengthen Follow-Up Care
- Standardize Outcome Reporting
- Invest in Research in High-Burden Areas
- Expand Access to TCD Screening
- Integrate NBS into National Health Systems

PO116 | Bridging the gap: Designing transition pathways for adolescents with sickle cell disease

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Introduction: Sickle cell disease (SCD) is a chronic, inherited blood disorder affecting millions globally, with the highest burden in sub-Saharan Africa. Improved pediatric care has led to increased survival into adolescence, but healthcare systems now face the challenge of supporting adolescents as they transit to adult services. Poorly managed transitions are linked to loss of follow-up, psychosocial distress, reduced treatment adherence, and increased hospitalisation. Despite these risks, structured transition pathways are often lacking in low- and middle-income countries. Adolescents navigating this process frequently report confusion, fear, and difficulty in adjustment to unfamiliar adult care environments. This study aims to explore the lived experiences of young people with SCD and their healthcare providers, and to co-design a digital solution—specifically, a mobile application—that supports continuity of care, emotional readiness, and independent disease management during this critical transition.
Methods: This qualitative study adopts a design-thinking approach to engage two primary participant groups: (1) adolescents and young adults (aged 15–25) living with SCD who are preparing for or have recently transitioned to adult care; and (2) healthcare providers from both pediatric and adult care systems. In-depth, semi-structured interviews will be conducted to explore experiences, emotional challenges, communication gaps, and service expectations. Thematic analysis will be used to identify barriers and opportunities for support. Findings will directly inform the co-design of a mobile application with core functionalities such as personalized transition timelines, peer stories, appointment tracking, and care team messaging. A rapid iteration cycle, including participatory feedback from youth and clinicians, will guide refinement of the app prototype to ensure cultural relevance and usability.
Results: Preliminary desk research and stakeholder consultations have revealed three core challenges in current transition practices: (1) fragmented communication between pediatric and adult care teams; (2) emotional resistance among adolescents, particularly fear of losing trusted providers; and (3) inadequate orientation and youth engagement strategies in adult care services. These insights emphasize the need for a youth-centered, culturally grounded tool to bridge the transition gap. Although formal data collection is ongoing, early feedback supports the feasibility and desirability of a mobile app that can offer continuity, clarity, and emotional support during the transition phase.
Conclusion: As survival into adulthood becomes more common for individuals living with SCD, transition care represents an urgent, yet underdeveloped, priority in many health systems. This study contributes a participatory, early-stage framework for improving transition experiences through a co-designed mobile application. By centering the voices of adolescents and clinicians, the project seeks to develop a tool that is context-sensitive, empowering, and scalable. The next phase will involve finalizing the app prototype and pilot testing it within care settings, with the goal of improving health outcomes and autonomy for adolescents with SCD.

PO117 | Optimising red cell exchange in sickle cell disease through personalised protocol review

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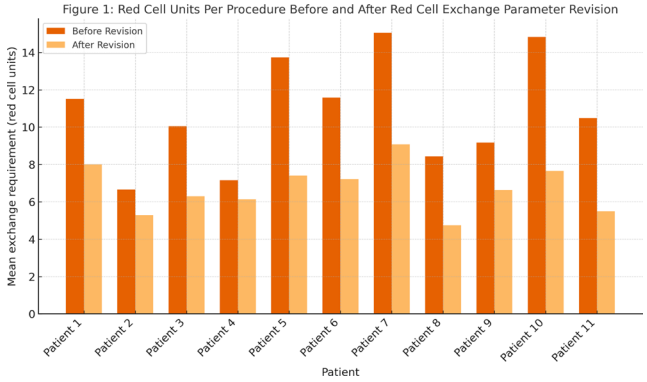
[1]*Department of Haematology, Cambridge University Hospitals NHS Trust, Cambridge, UK,* [2]*Medical Affairs, UK-EMEA, Terumo BCT, UK*

Introduction: Automated red cell exchange (aRBCX) is the preferred transfusion method for patients with sickle cell disease (SCD) on chronic transfusion programmes. Its goals are to reduce HbS%, avoid iron overload, and control complications such as stroke, while avoiding increased blood viscosity. NICE recommends the Spectra Optia ™ Apheresis Systems (Terumo Blood and Cell Technologies, Lakewood, CO).
At our centre, a high rate of adverse events during aRBCX raised concerns. An internal audit benchmarket against national and manufacturer guidelines revealed inconsistent review of exchange parameters and frequent red cell overuse.
Methods: Of 13 patients undergoing regular aRBCX at CUH, 11 were included in this audit (2 were excluded: one due to intermittent exchange, the other due to prolonged treatment gaps). Data from a 12-month period (2023–2024) were collected. Standards were drawn from 2016 British Journal of Haematology guidelines, recommending a pre-exchange HbS ideally below 30%, post-exchange Hct ≤30%–33%, and individually tailored targets for post-HbS.
Following audit findings, all treatment protocols were reviewed in collaboration with Terumo. Revised, individualised exchange settings were agreed with patients during multidisciplinary consultations involving clinical psychology.
Results: Among the 11 patients, one exceeded 50% HbS on a single occasion, and five did not meet the recommended post-exchange Hct limits. Six patients had experienced adverse effects including fainting, nausea, and fatigue, with two requiring hospital readmissions.

Following the change, the mean number of red cell units per procedure was reduced from 10.78 to 6.72, a mean reduction of 4.06 units (range 1.02–7.18) (Figure 1). The mean post-exchange Hct reduced from 33.43% ± 3.39% to 30.70% ± 2.85%, in line with safety recommendations. Despite reduced transfusion volumes, mean post-exchange HbS increased from 7.66% ± 1.89% to 18.50% ± 4.19% remaining clinically acceptable. Mean pre-exchange HbS rose modestly, from 36.38% ± 10.92% to 42.78% ± 9.81%.

Figure 1: Red Cell Units Per Procedure Before and After Red Cell Exchange Parameter Revision



Only two patients continued to experience fainting post-intervention. No new or worsening clinical complications were reported. One patient required two additional top-up transfusions, one discontinued aRBCX citing psychological factors, and one died from unrelated causes as shown in Figure 2.

Figure 2: Summary of Adverse Events Before and After Red Cell Exchange Parameter Revision

Adverse Event	Before Revision	After Revision
readmission to hospital	2	0
Fainting	4	2
Exhaustion	1	0
Nausea	1	0
Top-up transfusion	0	1 (2 times)

These results demonstrate that effective suppression of HbS and safe Hct levels can be achieved using significantly fewer red cell units. This supports the practice of individualised targets over fixed transfusion thresholds and suggests that previous over-transfusion contributed to adverse outcomes.

Conclusion: This audit-led intervention confirms that personalised aRBCX protocols can safely reduce red cell usage while maintaining clinical effectiveness. National and manufacturer guidelines offered a strong foundation, but clinical judgement and regular multidisciplinary review were essential in tailoring care. Treatment plans should be adjusted based on trends in HbS suppression, haematocrit, adverse effects, and clinical course—including pain episodes and hospitalisation. Our findings reflect the experience reported by Tsitsikas et al. (2021), who similarly reduced red cell use through protocol refinement. Continued monitoring of long-term outcomes will ensure sustained benefit and support ongoing optimisation of transfusion practice in SCD.

PO118 | Impact of a patient co-developed e-learning module for HCPs in a tertiary hospital in London

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Introduction: Sickle cell disease (SCD) is the most common genetic blood disorder in the UK, affecting approximately 17 500 individuals. The South East region has the highest concentration of individuals living with SCD.

The 2021 parliamentary "No one is listening" report commissioned by the Sickle Cell Society, found multiple issues with care, including sub-standard care, low awareness amongst health care professionals (HCPs), and negative attitudes towards patients.

We recognised need for an accessible educational tool aimed at multidisciplinary HCPs caring for patients with SCD. The Sickle Centre of Excellence, within Kings Health Partners, funded a patient co-produced online learning module for SCD, it has been well received in our Trusts and is now hosted by the NHS on the national e-learning for health website Acute Sickle Tool. It's an interactive module combining patient videos with clinical guidance, focuses on acute presentations in SCD, such as pain crisis, outlines principles of initial management and appropriate escalation. It also addresses the impact of health-related stigma.

Over 1100 clinical staff at our Trust have completed the tool in the year since launch, we undertook a survey to assess its impact on knowledge and attitudes.

Methods: A seven-question online survey was distributed to HCPs in our Trust, who had completed the module and those who hadn't. Information was collected on clinical roles and awareness of the module, completion status, questions also assessed knowledge of SCD and pain management.

Results: Ffity-six staff, age range 16–65 years, filled in the survey, 38 (67.9%) had completed the module, 18 (32%) had not. 71% of module completers were nurses, 12 (67%) of the 18 non-completers were doctors and only 50% of non-completers were aware of the training module.

Nearly all respondents in both groups were involved in the care of patients with SCD (97% of completers; 94% of non-completers).

89% of both groups were aware of National Institutes Clinical excellence (NICE) guidance that analgesia should be given within 30 for patients with SCD presenting with pain, 11% of non-completers (11%) selected 1 h, 3(8%) of completers chose 1 h, and 1 chose 4 h.

Beliefs about opioid-seeking behavior differed: 56% of non-completers of module non-completers believed it was a concern, versus 26% of completers.

Both groups were aware of the importance of alerting the SCD team of all SCD inpatient episodes (97% of completers, 94% of non-completers).

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Discussion: The survey results highlighted a need to raise awareness of the module among staff within our Trust, half our non-completers were not aware of it.

The module appears to have been effective in improving awareness and shaping more informed attitudes among HCPs, with completers of the module demonstrating a lower tendency to associate patient pain management with opioid-seeking behavior.

We are in a high prevalence region for SCD, so it is unsurprising HCPs report involvement with SCD patients, and had some knowledge about SCD. However, the survey highlighted despite this awareness, there remained misconceptions amongst HCPs who had not received specific sickle training about SCD patients and analgesia use.

This highlight the value of targeted education in enhancing knowledge, reducing stigma and bias in the care of patients with SCD.

Patient videos developed by KHP Haematology are also freely available on youtube, QRcodes will be shared to access the links on presentation.