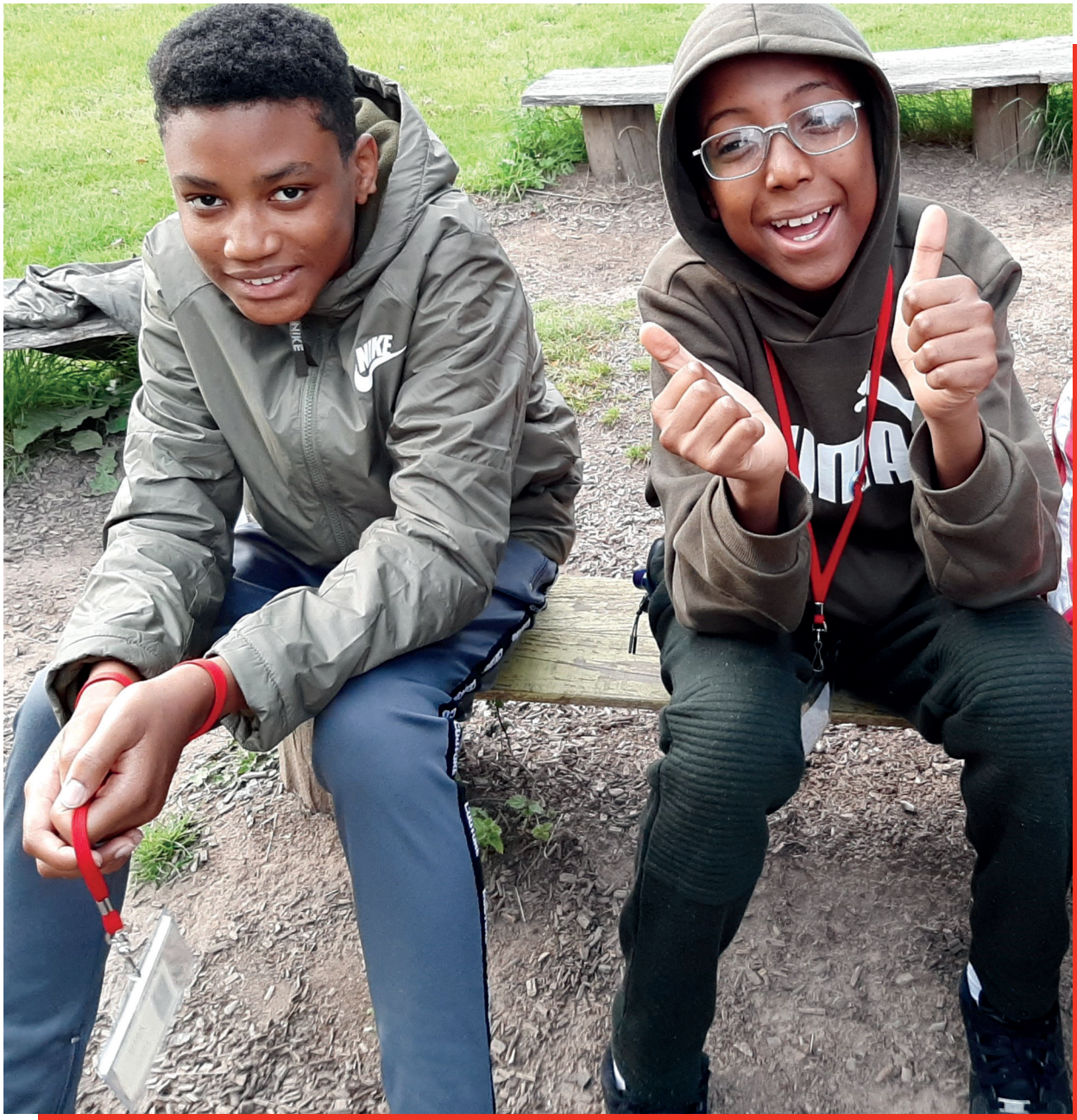
SICKLE CELL SOCIETY

Sickle Cell Disease in Childhood

Standards and Recommendations for Clinical Care

Executive Summary



3rd edition – November 2019

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Please refer to whole document on the Sickle Cell Society website for background information, weblinks and references.

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Abbreviations

A&E	Accident and Emergency
CAMHS	Child and adolescent mental health services
GP	General practitioner
Hb	Haemoglobin
HCC	Haemoglobinopathy coordinating centre
HPFH	Hereditary persistence of fetal haemoglobin
LHT	Local haemoglobinopathy team
MDSAS	Medical Data Services and Solutions
MRI	Magnetic resonance imaging
NHR	National haemoglobinopathy registry
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
PHE	Public Health England
PICU	Paediatric intensive care unit
PPV	Polysaccharide pneumococcal vaccine
RCPCH	Royal College of Paediatrics and Child Health
SATs	Standard attainment tests
SCD	Sickle cell disease
SHT	Specialist haemoglobinopathy team
TCD	Transcranial Doppler
UKAS	UK accreditation service

Aims of this document

These recommendations have been written to support clinicians and to ensure that every infant has access to the same quality of care wherever they live. They are written for paediatricians, haematologists, specialist nurses and psychologists, and for those responsible for monitoring outcomes i.e. hospital trusts, commissioning authorities and peer-review services.

The document is not intended to provide extensive clinical guidance for the management of acute complications. It outlines a model of care for children with sickle cell disease (SCD) who have been identified through the newborn screening programme. It extends from newborns until transition into adult care– which is usually between 16 and 18 years. It will also have relevance for the care of children who may have missed out on newborn screening before the programme was introduced, or who have come from abroad and been diagnosed after the newborn period. It is based on a consensus of clinicians with experience in the UK, Jamaica and the USA.

Conditions to be treated

SCD denotes all genotypes containing at least one sickle gene in which HbS makes up at least half the haemoglobin (Hb) present. In addition to sickle cell anaemia (this will be referred to as HbSS in future in this document), there are other compound heterozygous conditions that occur in the UK. Conditions to be treated include:

Haemoglobin SS (sickle cell anaemia)

Haemoglobin SC

Haemoglobin SD^{Punjab}

Haemoglobin SE

Haemoglobin S/β thalassaemia (β+, β^0, δβ and Lepore)

Haemoglobin SO^{Arab}.

Changes to this edition

Specific revisions to be noted include:

- The standards are defined in line with Public Health England guidance and Metric Definition Sets that inform the Specialised Services Quality Dashboard commissioned by NHS England to aid consistent monitoring.
- Where relevant, standards conform or refer to other related standards e.g. the newborn screening programme, transcranial Doppler (TCD) screening.

- New standards include the coverage of children offered hydroxycarbamide (previously known as hydroxyurea) therapy, coverage of children on the national haemoglobinopathy registry (NHR) and the number of children having an annual review.
- Links have been provided for all other standards in order for the most up-to-date version to be available at all times.
- The recommendations on cerebrovascular disease, preoperative transfusion and hydroxycarbamide therapy have been updated.
- The section on delivery of healthcare has been expanded to acknowledge the effect that socioeconomic determinants have on health.
- A new information technology system for referring infants from newborn screening into treatment is introduced.

Basis of recommendations

Recommendations are based on evidence, which may have been obtained by

- randomised controlled trials
- good clinical studies
- clinical opinion based on expertise.

Examples of a strong evidence base in the management of HbSS and HbS/β^0 thalassaemia include the use of prophylactic penicillin in children, routine TCD screening to identify children who might be at risk of stroke and prescription of hydroxycarbamide to reduce the frequency of painful episodes and acute chest syndrome.

Grading of recommendations

For the recommendations, the letter in brackets following the recommendation refers to its grading, as based on the US Agency for Health Care Research and Quality recommendations.

A	Requires at least one randomised trial as part of the body of literature of overall good quality and consistency addressing the specific recommendations
B	Requires availability of well-conducted clinical studies, but no randomised clinical trials, on the topic of the recommendations
C	Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality

Standards in this document

The standards are linked to the strong recommendations and provide a mechanism by which laboratory, nursing and medical care can be assessed across the country. Some standards are already in use through the NHS Sickle Cell and Thalassaemia Screening Programme or have been agreed by NHS England in the specialist commissioning dashboard. Some are already part of the quality standards agreed by the UK Forum for Haemoglobin Disorders in collaboration with the West Midlands Quality review service.

Grouping of recommendations

The recommendations have been divided into the following sections:

- Organisation of care (community- and hospital-based care)
- Pathway of care (from newborn screening to transition to adult care)
- Ongoing issues (often managed at home/in the community)
- Chronic complications (usually requiring hospital care)
- Acute complications (usually requiring urgent inpatient care)
- Elective surgery and perioperative care
- Specific treatments.

These are followed by the eight standards, which cover:

- reporting of newborn screen-positive results to parents
- timely follow-up, diagnosis and treatment of newborn infants with a positive screening result
- timeliness of penicillin prophylaxis
- coverage of pneumococcal immunisation
- coverage of TCD scanning
- offer of/treatment with hydroxycarbamide
- registration on the NHR
- performance of an annual review.

Recommendations

Organisation of care – community

- There should be a network of care based on local community care, including GPs, the local sickle cell and thalassaemia centre (if available), health visitors, voluntary sector and school nurses, with links to the relevant haemoglobinopathy teams. (C)
- Parents should be put in touch with local and national voluntary organisations and local sickle cell and thalassaemia centres. (C)

- GP and community nurses should be kept informed about patients on a regular basis. (C)
- There should be community paediatric services to coordinate the community needs of the child and to liaise with child and adolescent mental health services (CAMHS), local authority services and the voluntary sector as needed. (C)
- Local authority services (including education and social services) should be aware of the specific needs of children with SCD and their families. (C)
- Any child with a deterioration in cognitive functioning should be assessed by an educational psychologist or clinical/neuropsychologist. (C)
- CAMHS should be aware of the specific emotional and learning needs of children with SCD and their families. (C)
- Parents need to know how to access welfare benefits. (C)

Organisation of care – hospital

- Organisation of care at the local haemoglobinopathy team (LHT) and specialist haemoglobinopathy team (SHT) levels should be in line with the findings of the specialist review. (C)
- The LHT and SHT should work closely with the HCC. (C)
- There should be a named paediatrician responsible for follow-up in the LHT. (C)
- There should be a named paediatrician and/or paediatric haematologist in the SHT. (C)
- There should be access to nurses experienced in caring for children with SCD. (C)
- There should be access to clinical psychology services. (C)

Pathway of care (from newborn screening to transition to adult care)

a) Initial identification

- Newborn screening laboratory scientists and clinicians responsible for the care of screen-positive infants must use Public Health England (PHE)'s Newborn Outcomes System to refer screen-positive infants from screening into treatment services (C)
- All parents/carers of infants where SCD is suspected via the newborn screening programme should be given the result by the time the child has reached 28 days. **See Standard 1**. This should be done in a culturally sensitive manner, respecting the parents' dignity and individuality. An interpreter should be provided where necessary. (C)
- The result should be communicated to the family GP and health visitor as soon as it is received by the specialist nurse counsellor, or named healthcare professional. (C)

- Newborn infants with a positive screening result should be seen at a paediatric clinic to confirm the screening result or be discharged having been found to have a clinically insignificant result by ≤90 days of age. (C)
- Penicillin prophylaxis should be offered to all children with SCD (A) and should be initiated by 90 days of age. (C) **See Standard 3**.
- Appropriate written information about the condition should be provided for carers. (C)
- Parents should be given the opportunity to have genetic counselling, especially if they did not take up this option before their child was born. (C)

b) Confirmation of diagnosis

- A blood sample to confirm the screening result should be taken at or before the first sickle cell clinic visit and sent to a laboratory accredited by UKAS to carry out haemoglobinopathy testing. (C)
- DNA analysis should be requested in cases where the diagnosis is unclear. (C)
- Penicillin prophylaxis should be started while waiting for confirmation of the final diagnosis. (C)

c) Outpatient care

(i) Organisation of follow-up

- An infant screened as having a possible significant haemoglobinopathy through the newborn screening programme should be seen in a designated sickle cell clinic by 90 days of age. (C) **See Standard 2**.
- At the first visit the family should meet with a doctor and/or nurse experienced in the management of SCD who can give them accurate information and advice. (C)
- The parents should be encouraged to consent to their child being entered on to the NHR. (C) **See Standard 7**.
- Confirmation of the diagnosis, date of first clinic attendance and date of starting prophylactic penicillin should be returned to Medical Data Services and Solutions (MDSAS) electronically. (C)
- There should be regular communication between the SHT, the LHT, primary care and the community nursing teams. (C)
- There should be a policy for monitoring attendance in clinic and for following up those families who fail to attend. This should include documentation of children who have moved to another area. (C)
- There should be ongoing support for the family and promotion of management of straightforward illness, including uncomplicated pain, at home. (C)
- There should be access to specialist assessment and treatment when required. (C)

- Every child should be reviewed at least once a year by the SHT; this may be by direct consultation, in an outreach clinic or within a multidisciplinary team setting as appropriate. (C)
- Every outpatient visit should provide an opportunity for ongoing education of the child and family. (C)

(ii) Education about sickle cell disease

- There should be a systematic approach to education, which will vary at different ages. (C)
- Parents and carers should be made aware of the symptoms and signs associated with severe and life-threatening complications and know where to take their child if these occur. (C)

d) Inpatient care

- A care pathway should be in place in the local unit (LHT) for assessment of the child in accident and emergency (A&E) and for transfer to a designated ward if admission is necessary. (C)
- Protocols should be available to cover the management of all acute sickle cell complications. These should include worsening anaemia, febrile episodes, severe acute pain, acute neurological complications, acute chest syndrome and priapism. (C)
- A designated consultant paediatrician and/or paediatric haematologist, with a named deputy, should be responsible for the management of all children in the LHT and SHT. Junior doctors involved in assessment and treatment of acute sickle admissions should be made aware of acute complications and the local treatment protocols through regular education/training sessions. (C)
- Communication and transfer to a specified PICU should be readily available according to an agreed procedure. (C)
- There should be an accessible hospital transition policy in place and the introduction of a key support worker, with the aim to start preparation and planning at an early age e.g. 13–14 years. (C)

e) Transition

- A detailed review should be carried out at 15–16 years to assess the patient's knowledge of their condition and treatment concordance, understanding about SCD management, concerns about healthcare in an adult setting, emotional readiness for transition, self-efficacy and general readiness to transfer. (C)
- A transition or adolescent clinic should be available to allow the adolescent to meet the adult sickle cell team and for a formal review and handover to take place. (C)
- Adult and paediatric protocols for managing complications, in particular painful episodes, should correspond as much as possible. (C)

Ongoing issues

a) Prevention of infection

- Twice-daily penicillin prophylaxis or alternative should be prescribed by 90 days of age and continued throughout childhood. (A) **See Standard 3**.
- Local negotiation should be carried out between hospital, GPs and pharmacies to ensure a reasonable length of prescription to encourage compliance. (C)
- Reasons for parents not giving their children penicillin should be explored and addressed as fully as possible. (C)
- Immunisation against pneumococcal infection should include Prevenar 13 and PPV according to national schedules. (C) **See Standard 4**.
- Two doses of MenACWY should be given in either the first or second year of life. (C)
- A robust local policy should be in place to ensure that children receive PPV (in hospital or primary care) and this information should be recorded and shared between primary and secondary care. (C)
- Annual influenza immunisation should be offered. (C)
- When appropriate, malaria prophylaxis should be strongly recommended and current guidance sought for the area of travel. (C)
- Parents should discuss with their medical team before their child travels by plane. (C)

b) Management of pain at home

- Parents/carers and older children should be given clear guidance on how to assess and manage pain at home, including the type and dose of analgesia to be used for different levels of pain intensity, and when to seek medical advice. (C)
- Parents/carers should be informed about non-pharmacological therapies for pain, such as massage. Children should be encouraged to use psychological coping strategies, including distraction techniques such as games, computers and television. (C)
- Children should be encouraged to identify and avoid factors that regularly trigger acute pain, such as exposure to cold or windy weather, excessive physical activity and dehydration. This information should also be passed on to the school by a competent healthcare professional. (C)
- Hydroxycarbamide should be recommended to children getting significant episodes of pain at home. (C)

c) Nutrition and growth

- Height and weight should be measured at each visit and plotted on appropriate growth centile charts. (C)
- Referral to a dietitian should be made to consider extra caloric input if the child is hospitalised for frequent or long periods. (C)

- Zinc supplementation should be considered if growth is impaired. (B)
- Advice should be given on avoiding vitamin D deficiency, and vitamin D deficiency should be treated. (C)
- Children with delayed growth should be reassured if there is evidence of delayed skeletal maturation; however, they should be referred to a paediatric endocrinologist if there are no physical signs of puberty at 14 years in a girl and 14.5 years in a boy. (C)
- Pica can usually be managed with explanation; a referral to a clinical psychologist is recommended if the pica is part of a more generalised eating disorder. (C)

d) Nocturnal enuresis

- If nocturnal enuresis is present over the age of 6 years, this should be documented and parents should be given information and advice on treatment, including avoidance of drinking at night time. (C)
- If the history is suggestive of sleep-disordered breathing, this should be documented, overnight oxygen saturations should be measured and a referral made for an ear, nose and throat (ENT) opinion. (C)
- Desmopressin therapy should be considered in those children who do not respond to routine advice and management. (C)
- The child should be referred for specialist management (e.g. an enuresis clinic) if there is no response to basic measures after the age of 7 years. (C)

e) Psychological issues

- All children and their families should have access to a clinical psychology service. (C)
- Cognitive behavioural therapy (CBT) should be offered in addition to standard management in children experiencing frequent pain episodes and emotional difficulties. (A)

Chronic complications

a) Cerebrovascular disease

- Annual TCD scans should be performed on all children with HbSS and HbS/β^0 thalassaemia from age 2. For children with abnormal TCD velocities, the risks and benefits of starting regular blood transfusions and/or other treatments should be fully discussed by an appropriate multidisciplinary team with parents/carers. (A) **See Standard 5**.
- The option of switching from transfusions to hydroxycarbamide should be discussed with eligible children and families. If it is agreed to switch to hydroxycarbamide, transfusions should be continued until the child is stabilised on the maximum tolerated dose of hydroxycarbamide (A).

- The symptoms and signs of stroke should be discussed with parents/carers in the first 2 years of life, with information given on what action to take should the child develop neurological symptoms. (C)
- Appropriate imaging studies to assess the extent of cerebrovascular disease should also be arranged if TCD scanning is abnormal, or there are learning difficulties, atypical symptoms such as unusual behaviour during acute pain, frequent headaches, fits or other unexplained neurological, psychiatric or psychological symptoms. (C)
- The advantages and disadvantages of starting regular blood transfusions should be discussed with all children and families if the child has one or more silent cerebral infarcts on magnetic resonance imaging (MRI). (A).
- Blood pressure should be measured and recorded annually. (C)
- Overnight oxygen saturation monitoring should be performed if a child has low steady-state oxygen saturations on air (<95%). (C)
- Children should have access to a clinical, educational or neuro-psychologist to assess cognitive function, learning and behavioural difficulties. (C)
- A comprehensive neuropsychological assessment should be carried out and repeated annually in all children who have had a stroke. (C)
- Cognitive (or where available, neuropsychological) assessment should be conducted in children with abnormal TCD or abnormal brain MRI. (C)
- Information about developmental progress and school performance should be ascertained for all children annually; if there are significant concerns, further assessments should be considered including cognitive or neuropsychological assessment and brain MRI scan. (C)
- Transfusion therapy should be offered throughout childhood for the secondary prevention of stroke. (B)

b) Priapism

- All boys and their parents/carers should be warned early in childhood about priapism being a complication of SCD. (C)
- Adolescent boys and their parents/carers should receive further information about priapism and know to seek treatment early. (C)
- An enquiry about priapism should be included as part of the outpatient consultation for pubertal boys. (C)
- For minor events, complete bladder emptying before sleep, pain relief and warm baths should be recommended. (C)
- Oral etilefrine should be considered in cases of stuttering priapism. (C)

c) Avascular necrosis of the femoral and humeral head

- An MRI scan should be carried out where there is persistent pain in the hip or shoulder. (C)
- The radiological stage of avascular necrosis should be documented. (C)

- Referral to an orthopaedic surgeon with an interest in SCD should be made if pain persists or if avascular necrosis is at stage III or more. (C)

d) Liver disease

- Annual steady-state liver function tests should be carried out; children with evidence of progressive hepatopathy (increasing bilirubin, persistently high ALT) should be referred to a paediatric hepatology service with experience of SCD. (C)
- Recurrent episodes of abdominal pain should be investigated with an ultrasound of the liver and biliary tree. (C)
- Elective cholecystectomy should be carried out in symptomatic biliary disease. (C)

e) Kidney disease

- Any child with a urinary tract infection should be treated and then investigated according to the NICE guidance. (C)
- Macroscopic haematuria should be fully investigated according to local protocols. (C)
- Blood pressure, urea, creatinine, electrolytes and urine albumin: creatinine ratio should be measured on a yearly basis and renal investigations initiated if hypertension is present, if there are raised creatinine and urea levels, or persistent significant albuminuria. (C)

f) Lung disease

- Children with either two or more episodes of acute chest syndrome in the last 2 years, or one episode requiring ventilatory support, should be offered hydroxycarbamide. (A)
- A systematic and complete evaluation of asthma should be undertaken if the diagnosis is suspected or if there are repeated episodes of acute chest syndrome. (C)
- Oxygen saturations in air should be recorded on an annual basis using pulse oximetry when the patient is well and seen in outpatients. If saturations are <95%, overnight oxygen saturation monitoring should be performed. (C)
- If the mean overnight oxygen saturation is <95%, the child should be investigated for cerebrovascular disease and obstructive sleep apnoea; formal pulmonary function tests and echocardiography should also be arranged. (C)
- If pulmonary function tests suggest chronic sickle lung disease, the child should be monitored with regular pulmonary function tests, plus overnight pulse oximetry and a high-resolution computed tomography (CT) scan of the lungs should be considered; treatment with home oxygen, hydroxycarbamide or regular blood transfusions should be considered in children who show signs of deterioration. (C)

- Echocardiography to assess for pulmonary hypertension should be arranged if there is evidence of chronic sickle lung disease, chronic unexplained hypoxia (oxygen saturations <95%) or other symptoms/signs suggestive of pulmonary hypertension. (C)
- A child with significant pulmonary hypertension should be referred to a specialist pulmonary hypertension centre with an interest in SCD. (C)

g) Eye complications

- Children and their carers should be made aware of this potential complication. (C)
- Any significant visual symptom should be reported immediately and the child referred urgently for an ophthalmologic opinion. (C)

h) Hearing impairment

- Parents and carers should be aware of the possibility of acquired hearing problems which may be sudden. (C)
- All children with abnormal TCDs or following a cerebral infarct should have a baseline hearing test. (C)
- All children receiving iron chelating agents should have hearing tests annually. (C)

i) Leg ulcers

- Debridement of the ulcer and antibiotic therapy should be started if infection is present. (C)
- Adequate pain relief should be prescribed. (C)
- Compression bandaging and physiotherapy should be arranged to improve ankle mobility. (C)
- Oral zinc sulphate should be considered in children with persistent leg ulcers. (B)

Acute complications

a) Severe pain requiring management in hospital

- Pain assessment should include the use of a validated pain assessment tool that is developmentally age appropriate. (C)
- There should be a policy in the A&E department regarding triage, pain assessment and length of acceptable time (not exceeding 30 minutes) from arrival to administration of analgesia. (C)
- Children should be managed according to a standard local protocol. This should be developed by collaboration between the LHT and SHT and should include input from a pain control team, paediatric pharmacist and a paediatric anaesthetist. The protocol should provide clear guidance on drugs, route of administration, dosage, and monitoring for analgesic effect and side effects. (C)

- Medical and nursing staff involved in treating children for severe acute pain should have regular training in pain management and in the application of the local protocols. (C)
- Children should be monitored regularly for the effectiveness of their analgesia and for signs of adverse effects (e.g. opiate-induced narcosis and hypoventilation and acute sickle chest syndrome, among others). (C)
- The psychological needs of the child and family regarding coping with pain and avoiding painful sickle cell episodes should be addressed during the admission. (C)

b) Management of the febrile child

- A protocol for antibiotic treatment of suspected or proven acute infection should be prepared by the SHT in collaboration with the LHT and a designated paediatric microbiologist. (C)
- Cultures of blood, urine and other possible sites of infection should be routinely done on any child presenting with acute pain and fever. (C)
- Malaria films should be sent if there is any suspicion of malaria or if a patient has returned from a malarial region in the previous year. (C)

c) Acute anaemia

- There should be a protocol for recognition and investigation of children presenting with pallor with or without pain in hospital. (C)
- Parents should be taught how to palpate for splenic enlargement and should be aware of the need to bring the child to hospital if they detect pallor and/or an enlarging spleen; they should be aware of the local procedure for emergency assessment. (C)
- Medical staff assessing children with acute sickle cell complications should be made aware of these complications through regular training/education sessions. (C)
- A local protocol for management, including indications for transfusion, should be available. (C)
- Children with two or more episodes of acute splenic sequestration should be considered for splenectomy. (C)

d) Acute chest symptoms

- Parents, patients and carers should be made aware of this complication; they should know how to recognise the symptoms and should be familiar with the local procedure for emergency assessment. (C)
- Children with chest pain, cough, respiratory distress, new chest signs or worsening hypoxia, presenting either in A&E or during the course of a hospital admission, should be carefully assessed and monitored and a chest X-ray organised urgently. (C)
- Incentive spirometry should be used in children with acute chest and or back pain admitted to hospital and requiring opiate analgesia. (A)

- Oxygen saturation monitoring should be used routinely, particularly in those children with respiratory signs and symptoms, acute pain affecting the trunk and girdle regions and those treated with opiates. (C)
- A local protocol should be available for the management of the acute chest syndrome, which should include clear guidance on analgesia, observations, oxygen delivery, antibiotics, intravenous fluids, bronchodilators, physiotherapy, incentive spirometry and nursing observations, as well as the indications for top-up transfusion, exchange transfusion and ventilator support. There should also be a local protocol covering the practical issues of carrying out an exchange transfusion. (C)
- Medical and nursing staff should be made aware of this complication; regular training and education sessions should advise on how to recognise it and provide updates on the local policy for management. (C)
- An agreement should be reached with the local paediatric intensive care unit about the indications for transfer, means of communication and the protocol for treatment in the intensive care unit. (C)

e) Acute neurological complications

- Each SHT should have access to a designated paediatric neurologist who can assess and advise on acute neurological complications. (C)
- Each SHT should have a clear plan for access to a neurosurgical unit for managing children and adolescents with cerebral haemorrhage and subarachnoid bleeds. (C)
- Royal College of Paediatrics and Child Health (RCPCH) guidelines on the management of acute stroke should be followed and specific guidelines for acute stroke in SCD should be prepared for the local unit (LHT) by the SHT. (C)
- Each SHT should have access to neuroimaging facilities including paediatric CT, MRI/MRA and electroencephalogram (EEG). (C)

f) Fulminant priapism

- A policy for the management of severe fulminant priapism should be agreed with the appropriate paediatric urology team. (C)
- Priapism should be discussed with all boys and their carers at annual review, and written information given, including the need to seek urgent medical attention for prolonged (>2 hours) episodes of priapism. (C)
- Aspiration and irrigation with etilefrine or epinephrine should be the initial treatment of choice. (C)

Elective surgery and perioperative care

- A clear management plan, agreed by all healthcare professionals involved, should be made and recorded before surgery. (C)

- SHTs should have guidelines on perioperative management in patients with SCD to share with local hospitals. (C)
- The transfusion laboratory should know the red cell phenotype/genotype and a recent antibody screen should be available in case blood transfusion becomes necessary before or after the operation. (C)
- Children with HbSS and HbS/β^0 thalassaemia undergoing low- and moderate-risk surgery should have a preoperative transfusion to increase the Hb level to 100 g/L. (A)
- Children with SCD undergoing high-risk surgery, including neurosurgery and cardiovascular operations, should have a preoperative transfusion to reduce HbS to <30%, which will usually involve an exchange transfusion. (C)

Specific treatments

a) Hydroxycarbamide (previously known as hydroxyurea)

- Hydroxycarbamide, including its potential benefits and side-effects, should be discussed with all children and parents in the first year of life, and at subsequent annual reviews. (C)
- Hydroxycarbamide should be offered to all children with HbSS and HbS/β^0 thalassaemia aged 9–42 months regardless of the clinical severity of their illness. (A) **See Standard 6**.
- Hydroxycarbamide should be offered to all children older than 42 months who have recurrent episodes of acute pain or who have had two or more episodes of acute sickle chest syndrome. (A)
- Hydroxycarbamide should be offered to all children older than 42 months whose lives are significantly affected by symptoms of SCD, including those with frequent episodes of pain that disrupt normal activities (A)
- Hydroxycarbamide should be offered to all children older than 42 months who are at high risk of progressive organ damage caused by SCD, including those with hypoxemia, significant albuminuria, conditional TCD velocities, or significant anaemia (steady state Hb<70 g/L). (B)
- The decision to start hydroxycarbamide should be made in conjunction with the SHT, and agreement should be reached as to which centre will monitor blood counts and maintain the optimal dose, and how these will be communicated between centres. (C)
- The protocol should include information about dose regimen, frequency of blood test monitoring, management of myelosuppression and contraindications for the use of hydroxycarbamide. (C)
- The patient and/or their parents/carer should be given a patient information sheet. Current knowledge about side effects, including subfertility, cytopenias and the possible risk of leukaemia or other malignancies,

should be discussed; this discussion should be documented in the patient's notes. (C)
- Boys of the appropriate age should be offered semen storage before starting hydroxycarbamide. (C)

b) Use of transfusion therapy

- At diagnosis or first clinic attendance, all patients should have an extended red cell phenotype performed. As an alternative, a red cell genotype with variant antigen analysis may be obtained. (C)
- All blood transfused should be matched for Rhesus and Kell blood groups. If alloantibodies are identified, further transfusions should be negative for the corresponding antigen. (C)
- Blood group genotyping should be considered in children with SCD who develop alloantibodies or who start a long-term transfusion programme. (C).
- Red cells for transfusion to patients with SCD should be sickle test negative and if possible <7 days old for exchange or <10 days for top up transfusion. (C)
- Urgent red cell transfusion should be used in children with rapidly progressive acute chest syndrome or acute neurological symptoms or in those who are severely unwell, aiming to achieve an HbS level <30% and an Hb of 100–110 g/L. This will often require an exchange transfusion. (C).
- Long-term transfusion regimens should be used after a cerebrovascular event to prevent recurrence and should be considered if cerebral artery velocities are abnormal on TCD scans. (A)
- Iron chelation should be considered in all children on regular blood transfusions. (C)
- Immunisation against hepatitis A and B should be offered to all those on long-term transfusion programmes. (C)
- Children starting regular blood transfusions should be reviewed initially by a multidisciplinary team (including checks of HbS levels, iron stores and neurological status, as appropriate) and regularly thereafter. (C)

c) Haemopoietic stem cell transplantation

- All patients or families with a child with SCD should be offered the opportunity to discuss stem cell transplantation as a treatment option; this should not depend on the family having an available donor at the time. (C)
- Haemopoietic stem cell transplantation should be performed in centres experienced in transplants for haemoglobinopathies. Transplants from any donor other than an HLA-identical family member should be undertaken only in exceptional circumstances and as part of a clinical trial. Each SHT should have clear referral links to a suitable transplant centre. (C)

Standards

Standard 1 (SCT-S08): Sickle cell and thalassaemia screening – reporting newborn screen-positive results to parents

<table>
<tr><td>Description</td><td>Proportion of parents receiving newborn screen-positive results ≤28 days of age</td></tr>
<tr><td>Rationale</td><td>To provide timely results to parents of screen-positive infants in order to give support to parents and carers, emphasise the importance of early penicillin prophylaxis and to ensure prompt referral into treatment (see page 7)</td></tr>
<tr><td>Definition</td><td>
<table>
<tr><td>Number of newborn infants with screen-positive results for whom parents receive results ≤28 days of age</td><td rowspan="2">Expressed as a percentage</td></tr>
<tr><td>Number of newborn infants born within the reporting period with screen-positive results</td></tr>
</table>
Specified conditions to be detected in newborn screening are: HbSS, HbSC, HbS/β thalassaemia (S/β^+, S/β^0, HbS/δβ, HbS/γδβ, S/Lepore), HbS/D^{Punjab}, HbS/E, HbS/O^{Arab}, HbS/HPFH, HbS with any other variant and no HbA, and other clinically significant haemoglobinopathies likely to be detected as by-products of newborn screening, including β thalassaemia major, HbE/β thalassaemia and β thalassaemia intermedia
Carrier results need to be followed up but are excluded from this standard</td></tr>
<tr><td>Performance thresholds</td><td>Acceptable: ≥90%
Achievable: ≥95%</td></tr>
<tr><td>Caveats</td><td>Detection of thalassaemia is not part of the programme but we expect β thalassaemia major to be detected as a by-product and the same standards for communicating results to parents and enrolment into care apply</td></tr>
<tr><td>Data collection and reporting</td><td>Reporting focus: haemoglobinopathy centre
Publishing focus: haemoglobinopathy centre
Data source: haemoglobinopathy centre
Responsible for submission: newborn screening outcomes system
Responsible for data quality and completeness: haemoglobinopathy centre</td></tr>
</table>

Reporting period	Annually: 1 April–31 March Deadline: 30 June

Standard 2 (SCT-09): Sickle cell and thalassaemia screening – timely follow-up, diagnosis and treatment of newborn infants with a positive screening result

<table>
<tr><td>Description</td><td>Proportion of newborn infants with a positive screening result who are (a) seen at a paediatric clinic or (b) discharged for insignificant results by ≤90 days of age</td></tr>
<tr><td>Rationale</td><td>To optimise individual health outcomes, penicillin prophylaxis should start by 90 days of age in children with SCD. Parents of infants with insignificant results must be informed and reassured as early as possible (see page 7)</td></tr>
<tr><td>Definition</td><td>
<table>
<tr><td>Number of newborn infants:
a) with clinically significant results who are seen by a paediatrician by ≤90 days of age; and
b) with insignificant results who are discharged by ≤90 days of age</td><td rowspan="2">Expressed as a percentage</td></tr>
<tr><td>Number of newborn infants with screen-positive result born within the reporting period</td></tr>
</table>

Specified conditions to be detected in newborn screening are: HbSS, HbSC, HbS/β thalassaemia (S/β^{+}, S/β^{0}, HbS/δβ, HbS/γδβ, S/Lepore), HbS/D^{Punjab}, HbS/E, HbS/O^{Arab}, HbS/HPFH, HbS with any other variant and no HbA, and other clinically significant haemoglobinopathies likely to be detected as by-products of newborn screening, including β thalassaemia major, HbE/β thalassaemia and β thalassaemia intermedia.
Exclusions include:
– infants born outside of England
– infants who die or move abroad before 90 days of age</td></tr>
<tr><td>Performance thresholds</td><td>Acceptable: ≥90%
Achievable: ≥95%</td></tr>
<tr><td>Caveats</td><td>None</td></tr>
</table>

Reporting	Reporting focus: haemoglobinopathy centre Publishing focus: haemoglobinopathy centre Data source: haemoglobinopathy centre Responsible for submission: newborn screening outcomes system Responsible for data quality and completeness: haemoglobinopathy centre See dashboard HAEM04A Screening to access to specialist care
Reporting period	Annually: 1 April–31March Deadline: 31 July

Standard 3: Timeliness of penicillin prophylaxis

Description	The proportion of infants with HbSS and HbS/β^0 thalassaemia who are offered penicillin (or alternative) prophylaxis by ≤90 days of age
Rationale	To ensure optimum protection against invasive pneumococcal infection before the onset of hyposplenism (see page 9)
Definition	Number of infants with SCD offered penicillin (or equivalent) prophylaxis ≤90 days / Number of infants born with SCD and eligible* for antibiotic prophylaxis — Expressed as a percentage * Infants with HbSC disease are excluded because the evidence is only available for giving penicillin prophylaxis to children with HbSS and HbS/β^0 thalassaemia. However, most centres will offer penicillin prophylaxis to children with HbSC disease as hyposplenism can develop but at a later age
Performance thresholds	Acceptable: ≥95% Achievable: ≥99%
Caveats	Record parental refusal and reason
Reporting arrangements	Reporting focus: paediatric service Data source: paediatric service responsible for submission to newborn outcomes system
Reporting period	Annually: 1 April–31 March Deadline: 30 September See dashboard HAEM04B Screening to access to specialist care

Standard 4: Coverage of pneumococcal immunisation at 2 years

Description	The proportion of infants with SCD who have been given polysaccharide pneumococcal antigen (PPV) between 24 and 27 months of age
Rationale	To ensure optimum protection against invasive pneumococcal infection as PPV contains more serotypes than Prevenar 13. PPV is less effective before 2 years of age (see page 9)
Definition	Number of children with SCD given PPV at 24–27 months / Number of children born with SCD aged 24–27 months — Expressed as a percentage
Performance thresholds	Acceptable: ≥95% Achievable: ≥99%
Caveats	Record parental decline. The paediatric service is responsible for monitoring coverage wherever the vaccine is given
Reporting arrangements	Reporting focus: paediatric service Data source: to be determined
Reporting period	Annually: 1 April–31 March Deadline: 30 September

Standard 5 Coverage of transcranial Doppler (TCD) scanning

Description	(1) The proportion of children with HbSS and HbS/β^0 thalassaemia who have their first TCD at 24–36 months (2) The proportion of children with HbSS and HbS/β^0 thalassaemia aged 3–16 years who have annual TCD
Rationale	To ensure timely screening of cerebral blood vessels to determine a child's potential risk of stroke and to continue to monitor throughout childhood. The incidence of stroke is highest in younger children (see page 11)
Definition 1	Number of children with HbSS and HbS/β^0 thalassaemia who have their first TCD aged ≥24 and ≤36 months / Number of children with HbSS and HbS/β^0 thalassaemia aged ≥24 and ≤36 months — Expressed as a percentage

<table>
<tr><td>Definition 2</td><td>
<table>
<tr><td>Number of children with HbSS and HbS/β^0 thalassaemia ≥3 to ≤16 years tested by TCD in the last 12 months</td><td rowspan="2">Expressed as a percentage</td></tr>
<tr><td>Number of children with HbSS and HbS/β^0 thalassaemia aged ≥3 and ≤16 years</td></tr>
</table>
</td></tr>
<tr><td>Performance thresholds</td><td>Acceptable: 99%</td></tr>
<tr><td>Caveats</td><td>Record parental decline
Record other means of surveillance e.g. if technically difficult and child having regular MRI scan</td></tr>
<tr><td>Reporting arrangements</td><td>Reporting focus: paediatric service
Data source: paediatric service</td></tr>
<tr><td>Reporting period</td><td>Annually: 1 April–31 March
Deadline: 30 September
See dashboard HAEM02 Transcranial Doppler (TCD) monitoring</td></tr>
</table>

Standard 6: Coverage of hydroxycarbamide (hydroxyurea) therapy

<table>
<tr><td>Description</td><td>Documented evidence that a discussion has been held with a child's parents regarding the beneficial effects of hydroxycarbamide
The proportion of children with HbSS and HbS/β^0 thalassaemia who are offered hydroxycarbamide</td></tr>
<tr><td>Rationale</td><td>To optimise long-term clinical outcome in children with HbSS and HbS/β^0 thalassaemia (see page 16)</td></tr>
<tr><td>Definition</td><td>
<table>
<tr><td>Number of children with HbSS and HbS/β^0 thalassaemia aged ≥9 to ≤42 months where there is documented evidence of a discussion about hydroxycarbamide</td><td rowspan="2">Expressed as a percentage</td></tr>
<tr><td>Number of children with HbSS and HbS/β^0 thalassaemia aged ≥9 to ≤42 months</td></tr>
<tr><td>Number of children with HbSS and HbS/β^0 thalassaemia aged ≥2 to ≤16 years prescribed hydroxycarbamide</td><td rowspan="2">Expressed as a percentage</td></tr>
<tr><td>Number of children with HbSS and HbS/β^0 thalassaemia aged ≥2 to ≤16 years</td></tr>
</table>
</td></tr>
</table>

Performance thresholds	Acceptable (for children aged ≥9 to ≤42 months): ≥99% (see also BSH guideline) Acceptable (aged ≥2 to ≤16 years): to be determined
Caveats	Hydroxycarbamide is only licensed for use in children over the age of 2 years
Reporting arrangements	Reporting focus: paediatric service Data source: to be determined
Reporting period	Annually: 1 April–31 March Deadline: 30 September

Standard 7: Coverage of children identified through the screening programme subsequently registered on the national haemoglobinopathy registry (NHR)

Description	Proportion of children with SCD identified by the newborn screening programme registered on the NHR
Rationale	Completeness of coverage on the NHR is important to fulfil its central aim of improving patient care. The newborn outcomes system when fully implemented will hold denominator data and record data transfer to the NHR. This will identify variance across networks which can be further explored (see page 7)
Definition	Number of infants with SCD registered on the newborn outcomes system where data has been pulled through to the NHR / Number of infants with SCD registered on the newborn outcomes system — Expressed as a percentage
Performance thresholds	Acceptable: to be determined Achievable: to be determined
Caveats	From 2019, all infants identified as having SCD will be referred from the newborn screening laboratory to paediatric care using the newborn outcomes system. Data can be pulled through to the NHR when key data and parental consent are recorded on the newborn outcomes system
Reporting arrangements	Reporting focus: paediatric service Data source: paediatric service responsible for submission to newborn outcomes service

Reporting period	Annually: 1 April–31 March Deadline: 30 September

Standard 8: Coverage of children who have had an annual review

Description	Proportion of children with SCD that have an annual review
Rationale	To ensure all children with SCD have the benefit of annual assessment and do not miss out on screening tests and treatment interventions (see page 8)
Definition	Number of children with SCD aged ≥1 to ≤16 years who have started annual review / Number of children with SCD aged ≥1 to ≤16 years — Expressed as a percentage
Performance thresholds	Acceptable: ≥85%
Caveats	None
Reporting arrangements	Reporting focus: paediatric service Data source: paediatric service
Reporting period	Annually: 1 April–31 March Deadline: 30 September See dashboard HAEM05 Annual review via NHR

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