An update from the National Sickle Pain Group

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UNIVERSITY HOSPITAL OF BRISTOL FOUNDATION TRUST

PROF PAUL TELFER
BART'S HEALTH NHS TRUST

22TH NOVEMBER 2023

HAEMOGLOBINOPATHY UK FORUM

Overview

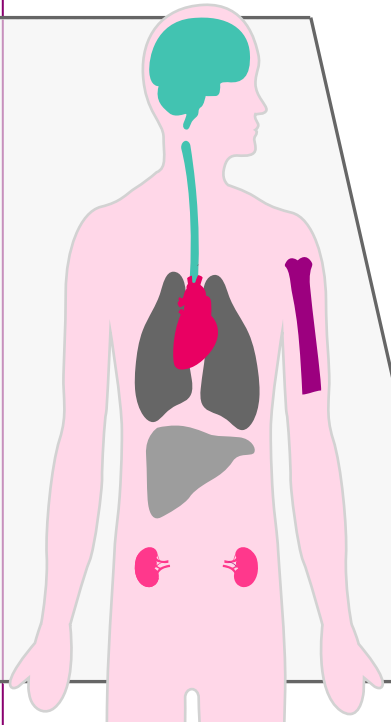
- Acute Pain in SCD

- National Sickle Pain Group
- National Audit
- Outcomes

- Acute pain
- Chronic pain
- Research

- Future Projects

Acute pain episodes are the hallmark of SCD



Average annual number of APEs per patient with SCD globally[2,a]

Among US adults with SCD, acute pain is the reason for:

78%

Of ED visits[b]

95%

Of hospital admissions[c]

In the UK, the most common reason for admission is acute pain crises

50%

Admissions of patients with SCD have risen more than 50% between 2001/2002 and 2009/2010[1]

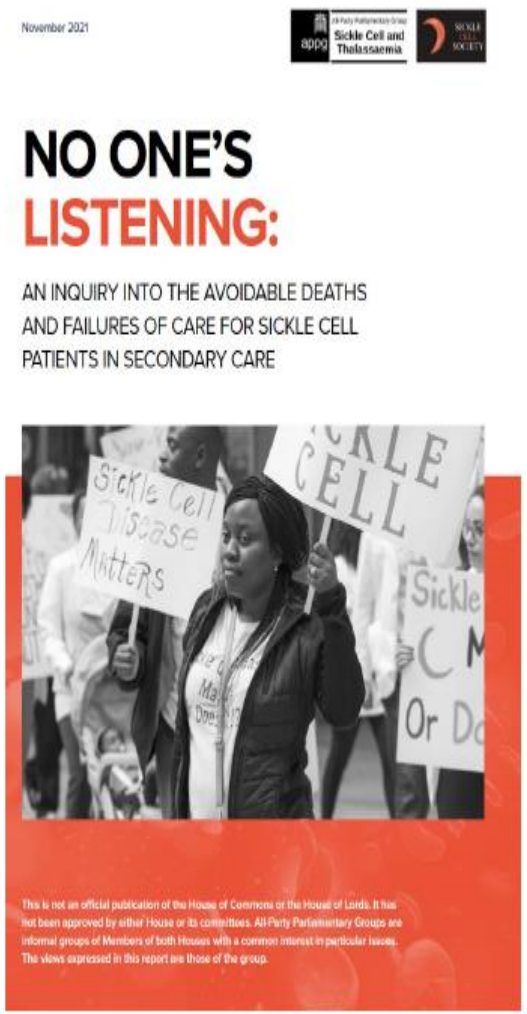
Recurrent APEs -> Cumulative severe end-organ damage -> impaired QoL, significant morbidity, and early mortality.

[a]In a global survey (Sickle Cell World Assessment Survey) of patients with SCD (N = 2,145). [b]Study included approximately 197,333 ED visits (1999-2007) among patients with a diagnosis of SCD [c]Study included 136 adults with SCD admitted to Thomas Jefferson University Hospital (1998-2002). ; 1. Telfer P, et al. *Br J Haematol* 2014;166(2):157–164; 2. Osunkwo I, et al. *Am J Hematol* 2021;96(4):404–417

Can we identify the current challenges in pain management in sickle cell disease ?

1. Failure to comply with national standards (NICE)
2. Poor patient experience

- APPG report 'No one's listening'
- Routine failure to comply to national care standards (NICE standards)
- Significant variations in care between units
- Lack of effective joined up care
- Inadequate community care
- Staffing education and attitudes require attention


November 2021

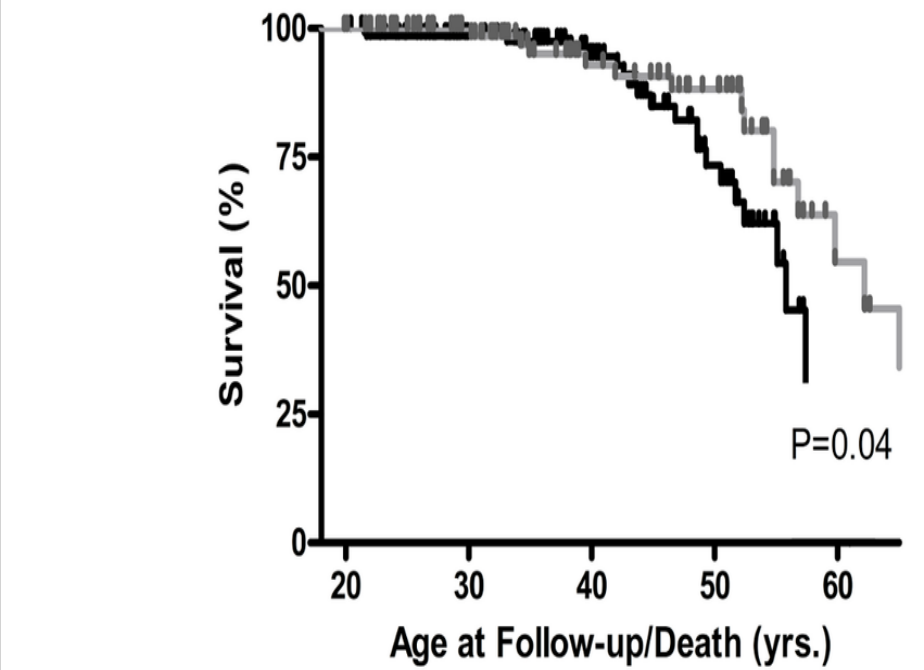
appg All-Party Parliamentary Group Sickle Cell and Thalassaemia

NO ONE'S LISTENING:

AN INQUIRY INTO THE AVOIDABLE DEATHS AND FAILURES OF CARE FOR SICKLE CELL PATIENTS IN SECONDARY CARE

This is not an official publication of the House of Commons or the House of Lords. It has not been approved by either House or its committees. All-Party Parliamentary Groups are informal groups of Members of both Houses with a common interest in particular issues. The views expressed in this report are those of the group.

3. Inferior outcome: ED attendance correlates with outcome

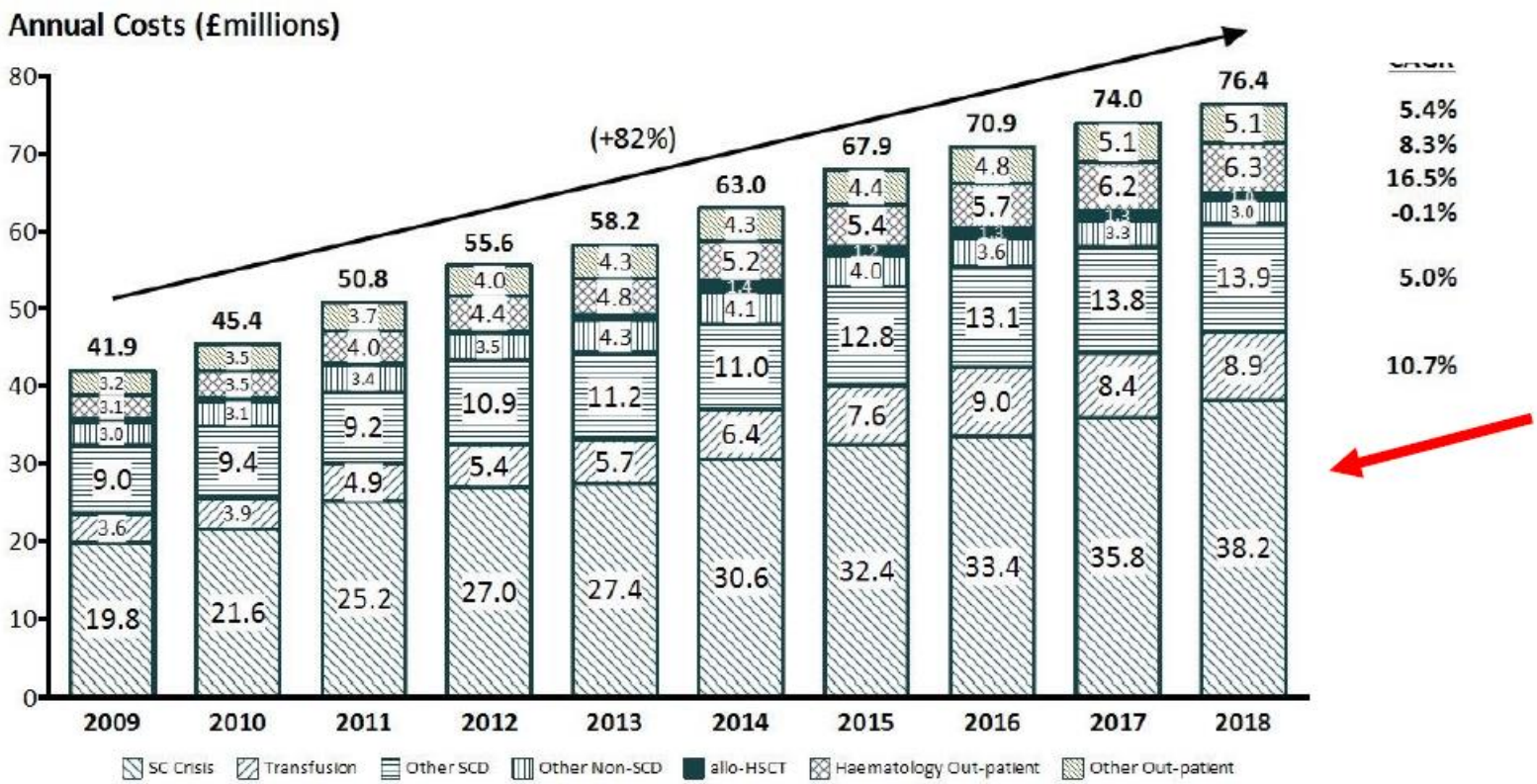


No. at Risk

No ED/Admits	95	69	44	30	7
≥1 ED/Admits	138	101	62	24	3

- Severe Painful Vaso-Occlusive Crises and Mortality in a Contemporary Adult Sickle Cell Anemia Cohort Study November 2013 PLoS ONE 8(11):e79923. DOI: 10.1371/journal.pone.0079923

4. Costs: NHS costs of treating SCD crisis have doubled over the last 10 years



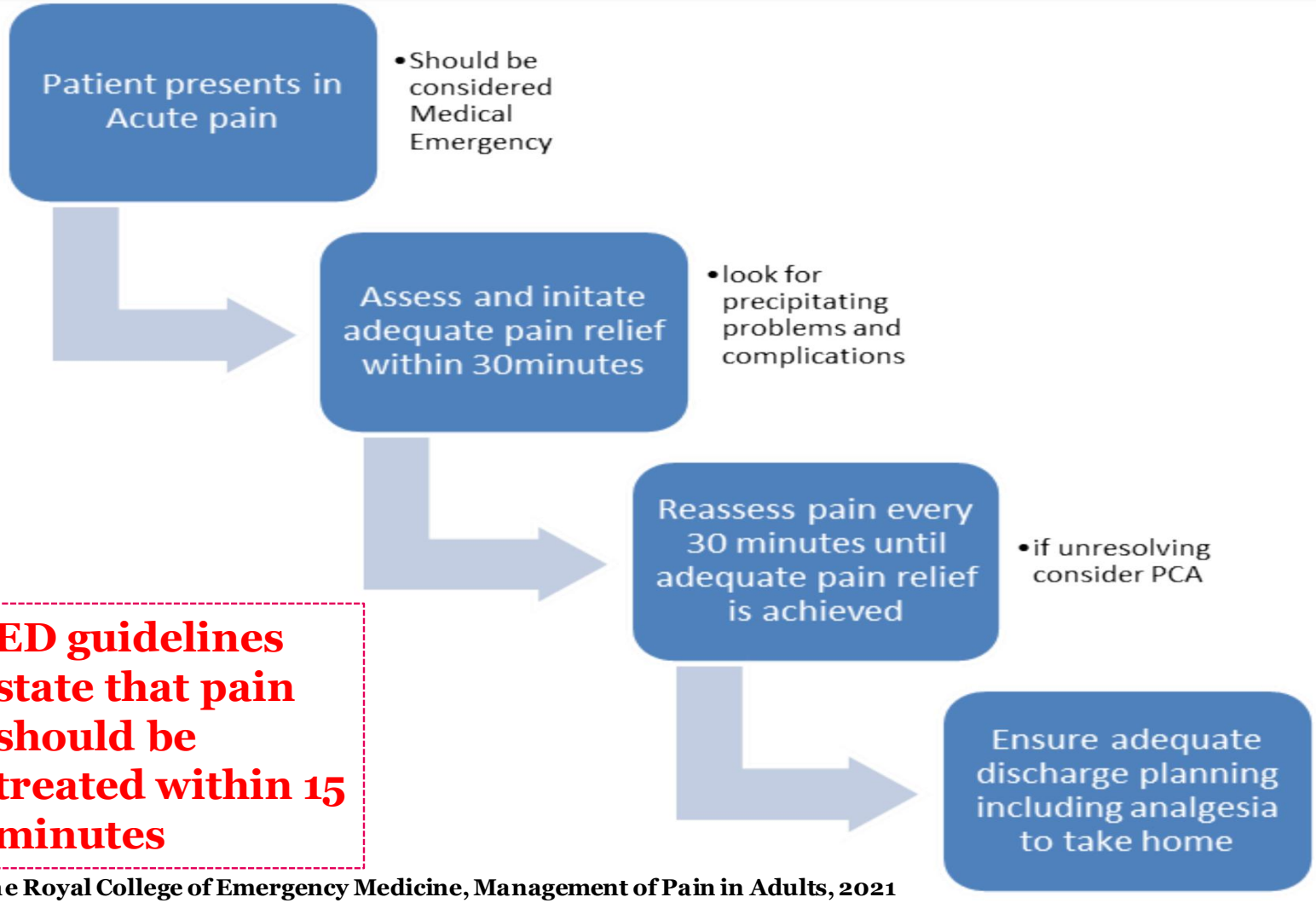
Piel et al, Bl cells mol dise 2021, e-pub
Al Jubari et al, J Pub Health 34, 570–576

What are the current pain management guidelines in SCD?

UK NICE Guideline 2016

- Provide timely pain relief within 30 min of presentation with a APE
- Re-assessment of pain every 30 min until pain relieved or discharged
- Thereafter assess pain every 4 hours
- Assess clinically every hour for the first 6 hours (BP, RR, Sats, HR)
- Consider patient-controlled-analgesia (PCA) pump
- Do not use pethidine
- *To date no scope for an update as 'definitive' literature has not significantly changed, nor have there been groundbreaking novel specific pain treatments in sickle cell disease*
- **Challenge**: unclear definitions

Acute pain should be treated within 30 minutes of arrival



ED guidelines state that pain should be treated within 15 minutes

The Royal College of Emergency Medicine, Management of Pain in Adults, 2021

(PCA: Patient controlled analgesia)

American Society of Hematology Guideline 2020

- Panel experts plus extensive literature search (2017)
- Rapid assessment (1h of ED arrival) and administration of analgesia
- Frequent reassessments (every 30-60 min)
- Non-iv routes of administration (sc, in) can facilitate rapid analgesic treatment
- Tailored opioid dosing with individualized care plan
- Subanaesthetic ketamine (0.1-0.3 mg/kg/h) if pain is not adequately controlled and opioid refractory
- Addition of non-pharmacological management using transcutaneous electrical nerve stimulation, virtual reality

CLINICAL GUIDELINES

blood advances

American Society of Hematology 2020 guidelines for sickle cell disease: management of acute and chronic pain

Amanda M. Brandow,[1] C. Patrick Carroll,[2] Susan Creary,[3] Roniela Edwards-Elliott,[4] Jeffrey Glassberg,[5] Robert W. Hurley,[6,7] Abdullah Kutlar,[8] Mohamed Seisa,[9] Jennifer Stinson,[10] John J. Strouse,[11,12] Fouzia Yusuf,[13] William Zempsky,[14] and Eddy Lang[15]

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Background: The management of acute and chronic pain for individuals living with sickle cell disease (SCD) is a clinical challenge. This reflects the paucity of clinical SCD pain research and limited understanding of the complex biological differences between acute and chronic pain. These issues collectively create barriers to effective, targeted interventions. Optimal pain management requires interdisciplinary care.

Objective: These evidence-based guidelines developed by the American Society of Hematology (ASH) are intended to support patients, clinicians, and other health care professionals in pain management decisions for children and adults with SCD.

Methods: ASH formed a multidisciplinary panel, including 2 patient representatives, that was thoroughly vetted to minimize bias from conflicts of interest. The Mayo Evidence-Based Practice Research Program supported the guideline development process, including updating or performing systematic reviews. Clinical questions and outcomes were prioritized according to importance for clinicians and patients. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used, including GRADE evidence-to-decision frameworks, to assess evidence and make recommendations, which were subject to public comment.

Results: The panel reached consensus on 18 recommendations specific to acute and chronic pain. The recommendations reflect a broad pain management approach, encompassing pharmacological and nonpharmacological interventions and analgesic delivery.

Conclusions: Because of low-certainty evidence and closely balanced benefits and harms, most recommendations are conditional. Patient preferences should drive clinical decisions. Policymaking, including that by payers, will require substantial debate and input from stakeholders. Randomized controlled trials and comparative effectiveness studies are needed for chronic opioid therapy, nonopioid therapies, and nonpharmacological interventions.

Summary of Recommendations

Background

Pain causes significant morbidity for those living with sickle cell disease (SCD) and has a profoundly negative impact on patients' health-related quality of life (HRQOL). Pain manifests as both acute intermittent pain, chronic daily pain, and acute on chronic pain. Pain severe the life course and hardness

Uniform management to tackle current challenges

The National Sickle Pain Group

– who are we and what do we do ?

The National Sickle Pain Group (NSPG) was formed on recommendation of NHS Haemoglobinopathy CRG

- The NSPG was initiated by Jo Howard and Prof Paul Telfer in **April 2021**
- Virtual meetings every 3-4 months
- Consists of a variety of experts:
  - Haematologists (adult)
  - Haematologist (paed)
  - CNSs
  - Pharmacist
  - Physiotherapy
  - Chronic pain specialist
  - Palliative care/ pain specialist
  - Acute pain specialist
  - Patient representative
  - ED consultants
  - (Ambulance services)
- *Interested to join ? Please contact sanne.lugthart@uhbw.nhs.uk*

NSPG's aim is to improve pain management in sickle cell disease

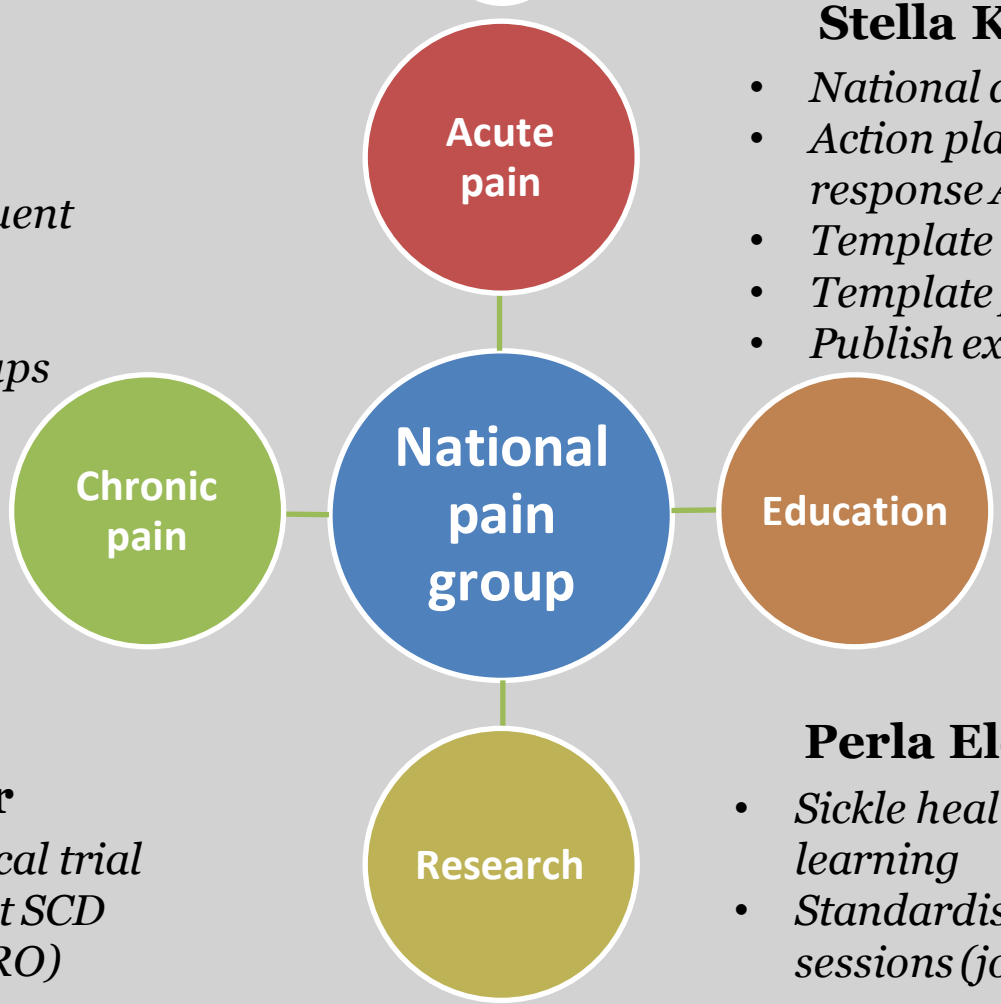
- What is the current management in sickle cell disease ?
- - acute pain
- - chronic pain

- Identify differences in practise nationally
  - Pathways that work well – what can we learn and improve ?

- Identify unmet needs of education, training and research
  - Share protocols, experience and practise

- Patient input is paramount, 3 PPVs in our group for continious input

The NSPG consist of 4 subgroups working on different goals within pain management



Asad Luqmani

- *National audit chronic pain*
- *Guidance on frequent attenders and complex pain*
- *Patient voice groups*

Stella Kotsiopoulou

- *National audit acute pain*
- *Action plan for Trusts (joint response APPG report)*
- *Template individual pain plan*
- *Template pain audit*
- *Publish examples of good care*

Paul Telfer

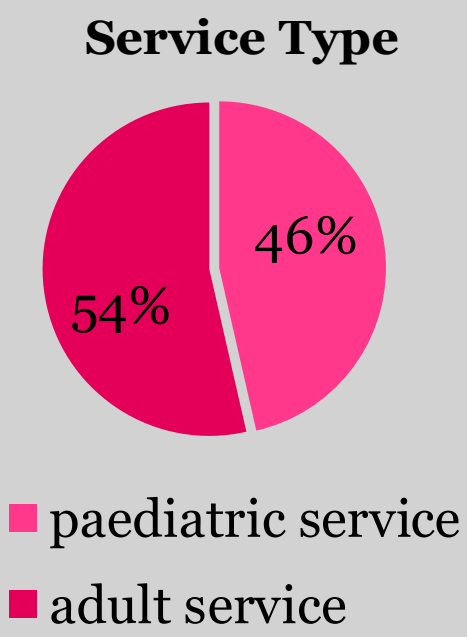
- *Multi-centre clinical trial pain management SCD (protocol NHS HRO)*

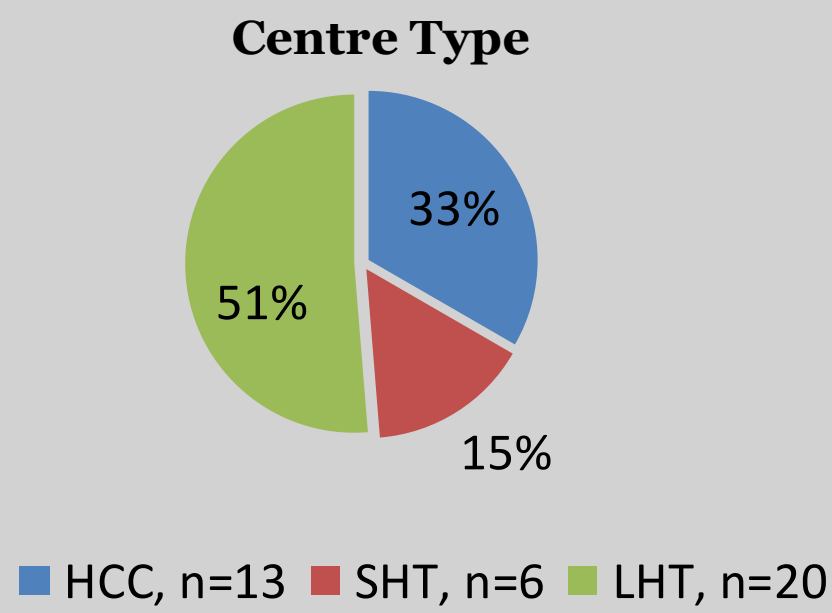
Perla Eleftheriou

- *Sickle health inequalities e-learning*
- *Standardise education sessions (joint NHP initiative)*

National audit : acute pain in SCD
Half participated centres are LHTs

- Nationally 39 centres completed the audit for their paediatric and/or adult services (56 responders)
- There is a large range between SCD patient numbers (0-800 patients per service)
- An equal distribution in audit responses of Adult and Paediatric services





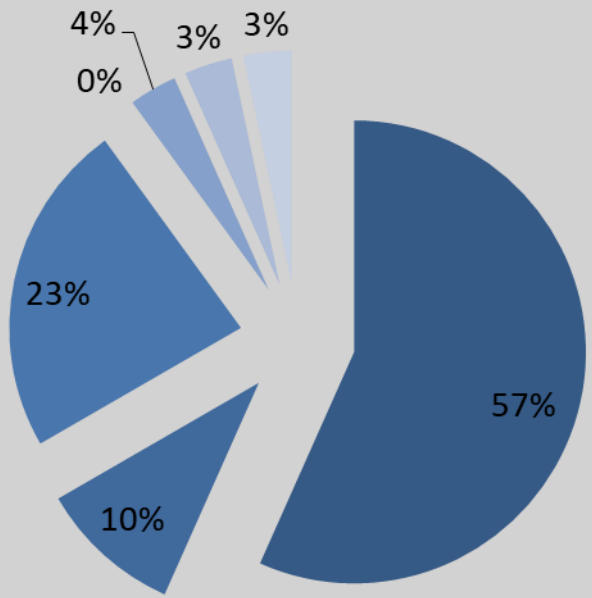
Lugthart et al., Hemaspere S110, 2022

Acute pain

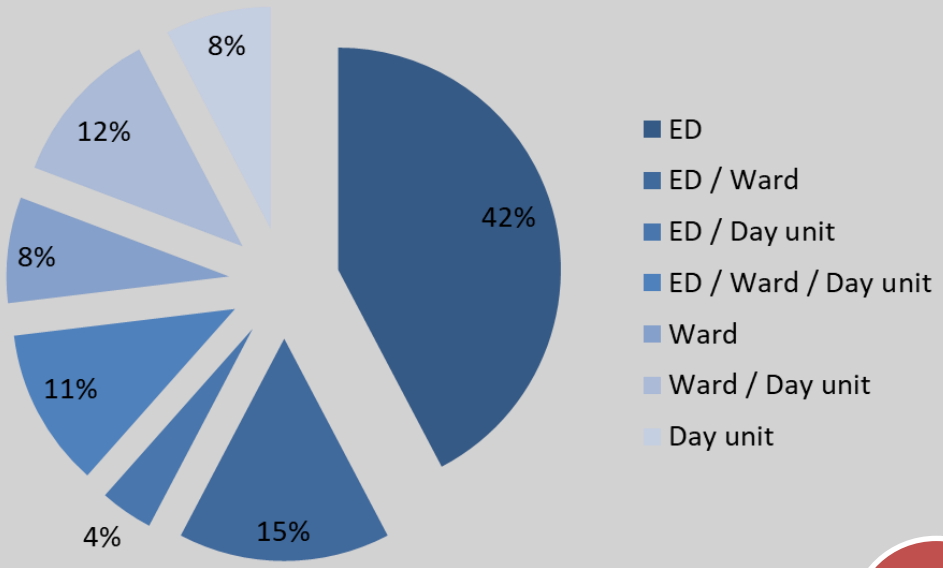
In half the centres SCD patients who present with acute pain are initially managed in the ED

- ED is the first point of call for sickle cell patients : 46 (82%) responders - (19 paediatric centres, 27 adult centres)

Adult Services



Paediatric Services

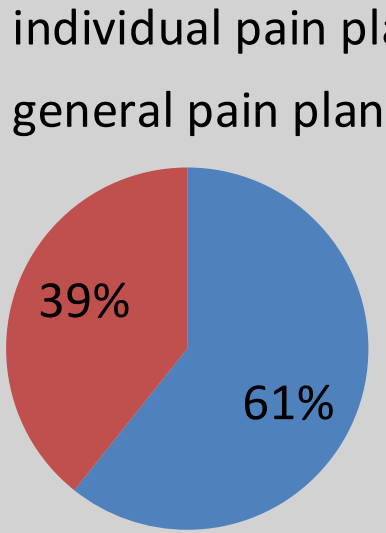


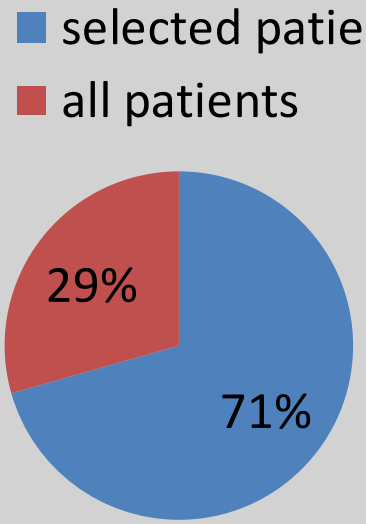
Lugthart et al., Hemaspere S110, 2022

Acute pain

Individualised pain protocol is used in 61% of the centres for a selected group of patients

- Nearly 90% (n=50) of the services have a generic pain protocol available
- Most common analgesia used:
- Adults: **Morphine/Oxycodone** -> Route: PO/SC bolus/PCA
- Paeds: **Morphine/Diamorphine** -> Route: PO/PCA/intranasal





Lugthart et al., Hemaspere S110, 2022

Acute pain

Availability ambulatory care service for management of sickle pain was limited to 14 centres

- 14 services (25%) have an ambulatory care service for pain management of SCD patients
- Opening days and times varied between 5-7 days and 8 am - 5 pm.
- Access to ambulatory care varied between:
  - all patients - no red flags - pre-book - known patients
- A trend towards more timely delivered pain relief was seen in these centres, 7 services (50%) met the '30 minute to first analgesia criteria' (NICE guideline)

Lugthart et al., Hemaspere S110, 2022

Acute pain

Time to first analgesia (30 minutes) was met in 21% of the responding paediatric and adult services

- **Time to first analgesia in centres (without ambulatory service)**
- Adult averages: 30-60 min
  - outliers around 80 min (via ED)
- Paediatric averages: 20-60 min
  - outliers around 128 min

- Average length of stay per admission is 3-5 days
- A small proportion of patients (0-5%) were reported to have a long admission (> 21 days)
- Between 2-10% of patients have frequent re-admissions (3 or more admissions/year)

Acute pain

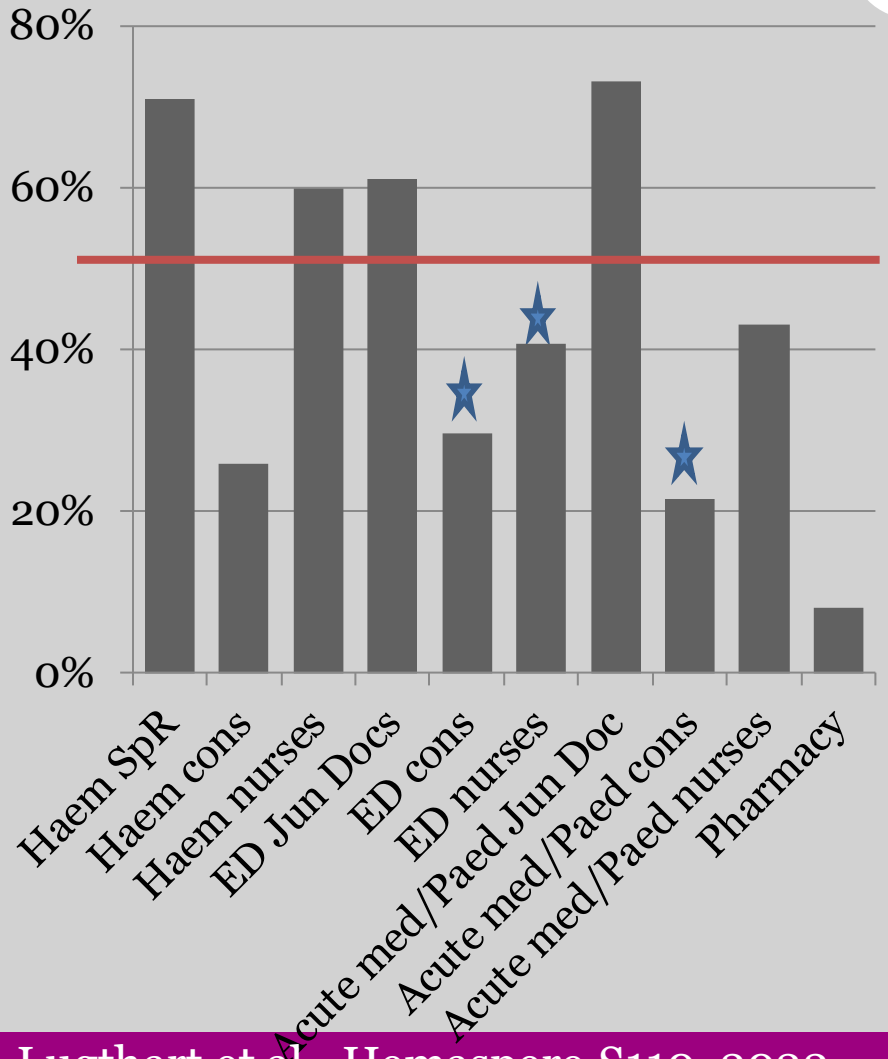
Lugthart et al., Hemaspere S110, 2022

Re-survey completed in Summer 2023 focussing on ED and day-unit facilities

- 47 centres completed survey (65% adults/ 35% paeds; 40% LHT)
- Majority of centres have access to the ED (n=42), 5 paediatric units direct ward access
- No dedicated haemoglobinopathy staff available for 48% of the centres (n=20)
- Increase in SDEC/Day-unit/HAU from 25% to 51% (n=24), only 29% open 24h (n=7)
- Idea of dedicate nurse of SCD patients in ED – 96% agreed that this could be a great idea -> cost implications

Acute pain

Training in sickle cell pain management is not consistently delivered across staff and departments



- Training for consultants in Haematology, ED and Acute medicine/paediatric is delivered infrequently (yearly/6-monthly).
- 49% of the responders provided examples of training, 46% is willing to share them.

Lugthart et al., Hemaspere S110, 2022

Educa tion

Conclusions National Pain Audit

- The majority of acute sickle cell pain presentations are managed via the emergency department and time to analgesia is often delayed (>30 minutes)
- Protocols of pain management in sickle cell disease show a large variation across centres
- Centres with an ambulatory care service show a trend of reduced times to analgesia and more unites have these services available in time (re-survey).
- Education and training for different specialities (ED, acute med/paediatric, pharmacy) is lacking or given infrequently.
- Not discussed: Few centres (n=14) have a patient satisfaction questionnaire

Acute sickle pain subgroup

DEFINING GOOD PRACTICE IN THE ACUTE SICKLE PAINFUL EPISODE CARE

STELLA KOTSIOPOULOU

Acute pain

Action plan for Trust to facilitate

June 2022

NHP Publishes a National Acute Sickle Pain Action Plan

Read More

Acute pain

Key Recommendations of the Action Plan

- **Develop multidisciplinary teams for acute sickle pain** involving Emergency Department Specialists, Acute /General medicine specialists, haematologists, ITU specialists and pain /palliative care team representatives.
- **Develop education plans for staff** providing care to sickle cell patients receive education around sickle cell acute pain care and positive, caring attitudes.
- **Develop patient sickle cell pain management protocols**, with the involvement of patient representatives.
- **Explore alternative routes for analgesia administration** in case intravenous (iv) access is difficult (such as subcutaneous, transmucosal or intranasal) and incorporate these into patient pain management protocols.
- For **complex pain or suboptimal pain** response to analgesia according to patient protocol, Trusts need to develop pathways with **expert pain team** involvement to guide pain relief.
- Explore **Day Unit setting development for treating patients presenting with acute sickle pain**, where possible, to improve and optimise management

Acute pain

HAEMATOLOGY DEPARTMENT **Trust address and contact numbers**

INDIVIDUAL SICKLE CELL PAIN PLAN

Acute painful crisis is a medical emergency and requires analgesia within 30 minutes of presentation to hospital. Sickle cell disease is a life-long painful condition. Please listen to the patients and gauge their pain from what they tell you they are experiencing.

Personal Details:			
Surname:		*Hospital No.:*	
Forenames:		*Sex:*	
D.O.B:		*NHS No.:*	
Clinical Details:			
Sickle Genotype:		*Other important PMH:*	
Allergies:		*Weight (kg):*	
Steady State Values:	*Hb (g/l):*	*Retics ($x10^{12}$/l):*	*O_2 sats on air (%):*

Analgesia Care Plan:

A&E /Haematology Supportive Day Unit:

1. Paracetamol 1g PO QDS → if not taken by patient in the last 6 hours
2. Non-steroidal anti- inflammatory drug, for example Ibuprofen 400mg PO TDS → if not taken by patient recently
3. Opiate analgesia – complete as appropriate- dose- route oral/subcutaneous

Do not delay giving analgesia as the patient does not need to be cannulated

Inpatient:

1. Paracetamol 1g PO QDS prescribed and given regularly
2. Ibuprofen 400mg PO TDS (or other NSAID) prescribed and given regularly
3. Opiate analgesia – complete as appropriate – dose- route

Reassess pain score every 30 minutes for the first 4 hours and document this in patient's notes.

Additional supportive treatment with:

- Antipruritic e.g. hydroxyzine PO 25mg BD.
- Antiemetics e.g. metoclopramide PO 10mg TDS. Cyclizine IV is not recommended.
- Laxatives whilst on opiates, i.e. lactulose, Movicol or docusate

Outpatient:

1. Paracetamol 1g PO QDS
2. Ibuprofen 400mg PO TDS
3. Oral long acting or immediate acting opiate as appropriate

Other Medication:

Acute pain

Other Medication:

Comments /Additional Information:
The management of an acute painful crises include several investigations and observations. **Link to local guideline.** Please do not hyperhydrate- this can cause circulatory overload and respiratory failure and worsen or precipitate acute chest syndrome. Encourage oral intake if possible. Please contact the haematology team on arrival of the patient. Do not transfuse the patient without consulting haematology. **Include contact details.**

Date completed: Day th Month, **2023**

Completed by: **(Specialist Nurse)**

Valid for:

Signature:

Authorized by: **(Consultant)**

Guidance Individualised Sickle Pain Plan

- This guidance contains the minimal information that is advised to include in an individualised sickle pain plan for patients known with sickle cell disease.
- Each centre can adapt and add additional important information to this plan, if felt needed.
- If a general pain protocol is used, please make sure the patient is aware of this.
- The Individualised Sickle Pain Plan can be uploaded onto the National Haemoglobinopathy Registry.

Guidance on Morphine doses in adult patients

(please make sure this is tailored to the patient pain plan above)
Opioid naïve: morphine 0.15mg/kg SC every 4 hours until pain is well controlled (VAS < 7)
Non-opioid naïve: morphine 0.3mg/kg SC every 4 hours until pain is well controlled (VAS < 7)
For Oxycodone PO, the morphine dose SC can be halved.

Acute pain

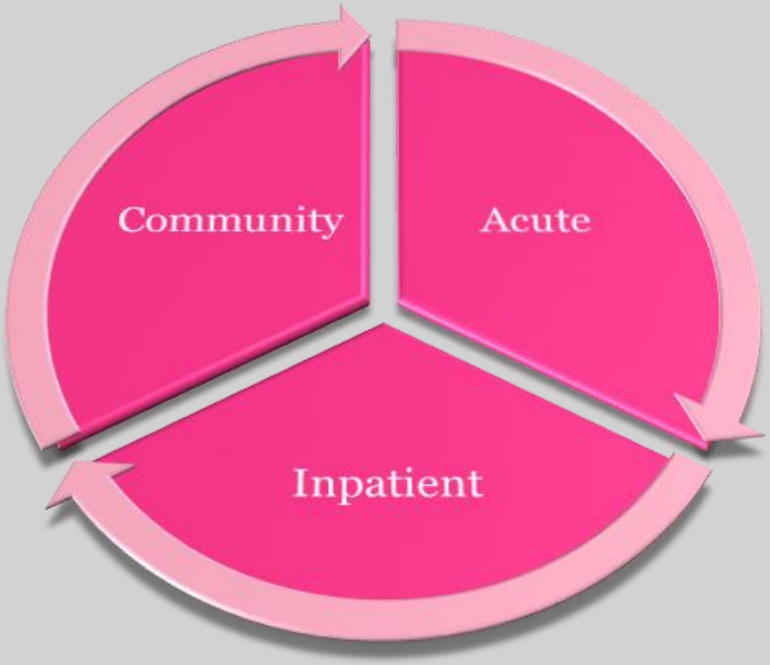
Current status

- Recommendations proposed (National Sickle Pain Group, Acute Sickle Pain Subgroup: Proposed Action Plans to Providers to improve care for sickle cell patients presenting with acute sickle pain. June 2022).
- NICE guidelines: No scope to update currently (NHSE).
- Acute pain protocol template.

- NHSE initiatives:
  - Sickle cell pathways review (NHSE work streams, August 2022)
  - NHSE pilots (for community care models and Hyper-acute Units).
  - Digital sickle pain care plan in development

Future considerations for sickle acute pain care: Defining Good Practice

- Draw patient pathway: Continuum



Acute pain

Future considerations for sickle acute pain care: Defining Good Practice

Consider best practice metrics in each part of the pathway:

- Community (initial stages of pain):
  - Personal pain management, ?Opioid use outside of hospital, frequency of pain crises, frequency of strong opioid use, frequency of hospital attendances for acute pain.
  - Role for ambulance services - intervention
- Acute (established acute pain):
  - ED-related metrics- NICE guidance (% achievement of 30-min pain relief, pain score improvement, frequency of monitoring, number of repeated bolus opioid doses needed, PCA Vs bolus iv/sc vs oral/intranasal routes, supportive medication prescribed, opioid toxicity?
  - Inpatient: Time to Haematology team referral, ward destination, mode of analgesia (PCA vs iv/sc bolus vs oral route), total opioid dose, O2/iv Fluids prescription, Prescription of paracetamol/ibuprofen/laxatives/antiemetics/thromboprophylaxis etc), adverse events, duration of admission?

Acute pain

Future considerations for sickle acute pain care: Defining Good Practice

- **Suggested actions:**

- Adapt/formalise survey questionnaires: SL/All
- ED acute sickle pain guideline
- Services to propose their good practice (PDF flow charts): RSM Workshop presentations.
- Specific Analgesia protocols (opioid naïve / non-opioid naïve) – different medication options
- House resources at NHP or any other general agreed location
- Formal Discussion - UKFHD

Acute pain

Chronic Pain Subgroup

ASAD LAQMANI

- Chronic pain: persistent or intermittent pain that last more than 3 months
- Aim: Understand current practice of chronic pain management for patients with sickle cell disease.
- Comparing practice in different centres will give insights for developing national guidance on chronic pain management.

Chronic pain

Look out for a new audit send to your inbox

- Timeline 2 months
- Questions around prescribing behaviour
- Management chronic pain
- Availability of holistic and complementary therapies
- MS teams form -> see QR code
- Grateful for your help !!

National Survey of Chronic Pain Management for Sickle Cell Disease

Chronic pain

Education Subgroup

PERLA ELEFTHERIOU

- Collaboration with Education NHP group developing standard education sessions
- Connect with Colleges (Medicine, Emergency Care, Nursing, Pharmacist)

Educa
tion

Health Education England has made elearning available for all NHS staff

Educa
tion

Research Subgroup

Institutions

- *NHS England Specialised Commissioning for Haemoglobin Disorders Pain subgroup (CRG-Pain)*
- *Pragmatic clinical trials Unit (PCTU)*
- *Sickle Cell Society (SCS)*

Personnel

- ***Prof Paul Telfer*** *(QMUL and Bart's Health NHS Trust)*
- ***Dr Sanne Lugthart*** *(Bristol University Hospitals NHS Trust)*
- ***Dr Kofi Anie*** *(London NW University Healthcare NHS Trust)*
- ***Dr Stella Kotsiopoulou*** *(Croydon NHS Trust)*
- ***Dr Sara Stuart Smith*** *(Kings College Hospital NHS Trust)*
- ***Dr Richard Hooper*** *(PCTU)*
- ***Ms Carol Burt*** *(SCS)*

19-5-23 National Workshop

NHS RACE & HEALTH OBSERVATORY
Breaking barriers for better health

NHS England

Queen Mary University of London

SICKLE CELL SOCIETY

It is not too late to register for:

National Sickle Cell Disease Workshop

'How can we improve care pathways for acute sickle pain?'

Friday May 19th 2023
The Royal Society of Medicine, 1 Wimpole St, London W1G 0AE
Or Virtual attendance

Overview of agenda:

- Review of current practice
- Improving Emergency Department (ED) pathways
- Optimal design of for ambulatory care pathway as an alternative to ED
- Evaluating alternative care in a clinical trial setting
- Overview of future pilot projects in London for digital care plans and care units

Research

National Sickle Pathway Conference (May 23)

- Sophie Lanzkrom presented US data around improvement of timely analgesia using 'infusion centres' (day-unit)
- Paula Tunabe presented US data to improve pain management in SCD in the Emergency Department (ED toolbox) – successful in several centres
- NHSE presented the SCD pathways including Hyper-acute units and digital care plan pilots
- Several Trusts presented their audit data – shared good practise
- Improvement Sickle Cell Care Pathway- Shared screen with speaker view (vimeo.com)

Research

National Conference at Royal Society of Medicine (May 23)

- Paul Telfer: literature review analgesia
  - IN fentanyl more likely to get discharged from ED (Rees 2023) and reduce time to first analgesia (Myrick 2020)
  - SL fentanyl is effective and safe (Telfer 2022)
  - Sub-anaesthetic ketamine reduced morphine use, no difference in admission rate (Alshahrani 2022)
  - Oral arginine; Rapid pain control, time to crisis resolution and LoS reduced (Onalo Am J Haem 2021)
- Kofi Anie: literature review psychological interventions (psychoeducation / cognitive behavioural therapy)
- Carol Burt (PPV): Patient feedback on their experience during a VOC remains poor, but slight improvements are made – importance of patient voice

Research

Future Plans Research Subgroup

Funded* research project to deliver a trial protocol for optimization of management of acute pain in SCD (QMUL)

Scientific review paper evaluation evidence of different care pathways (1) / supportive therapies and opioid analgesia (2) / impact of social determinants of health (3)

*NHS Race and Health Observatory

Future plan to apply for funding a trial comparing outcomes of management of acute VOCs in ED versus day-unit

Take home messages

Acute pain

- Although there is **no one analgesia plan that fits all** – we would like to agree on an opioid naïve and non-opioid naïve protocol – support small centres and promote uniform management acute sickle pain across England

- **Protocols and guidelines are not the only answer** – we need input from pain experts, ED expert – importance of listening to their experience.

Education

- Continuous **education is key** for both patients and staff – consider implementing Health inequalities training in your local Trust.

- Re-discuss individual pain plans to prevent patient's disappointments.

Chronic pain

- Improvements take time but they are underway (**Acute pain re-audit coming soon**).

- Chronic pain management is not always addressed (**please complete survey using QR code**)

Research

- Location of management of acute pain – does this make a difference ? (ED versus hyper-acute unit) possibilities for a clinical trial

Acknowledgements

- **NSPG**
- Paul Telfer, Kofie Ani, Sara Stuart Smith, Stella Kotsiopoulou, Assad Laqmani, Perla Elefteriou, Carol Burt (PPV), Ben Bloom, and all other members

- **Bart's**
- Cythia Angarappillai

- **Bristol**
- Sandra Schneider, Rhynna Britton

- **HEE**

- **All of you for completing the online audits !**

If you are interested in getting involved – please contact me on sanne.lugthart@uhbw.nhs.uk

Questions ?

Future Plans NSPG Subgroups

Acute pain

- Publish local examples of successful care
- Re-audit national pain audit (2024)

Chronic pain

- National audit to review current practise
- Identify centres with pain programs and their outcome

Education

- Collaboration with Education NHP group developing standard education sessions
- Connect with Colleges (Medicine, Emergency Care, Nursing, Pharmacist)

If you are interested in getting involved – please contact me on sanne.lugthart@uhbw.nhs.uk

The search for acute therapies to the modify course of pain episode

	Action	Stage of development	Outcome	Reference
Rivipansel	Pan selectin inhibitor	Phase 3 RCT	NEGATIVE	Dampier et al, *Blood* (2023) 141 (2): 168–179.
Sevuparin	Heparinoid	Phase 2 RCT	NEGATIVE	Biemond et al, Lancet Haematol, 2021 May;8(5):e334-e343.
Inhaled nitric oxide	Vasodilation, reduced adhesion	Multicentre RCT	NEGATIVE	Gladwin et al, JAMA 2011
i.v. Magnesium	Vasodilation, anti-inflammatory, analgesic	Multicentre RCT	NEGATIVE	Brousseau et al, Blood 2015
Poloxamer 188	Non-ionic block surfactant	2X Multicentre RCT	NEGATIVE	Orringer et al, JAMA 2001, Casella et al, 2021

Prof P Telfer

Opioids

Drug	Study design	Comparator	Outcome	Reference
IN Fentanyl	Multi-centre retrospective, observational, non-randomized, paeds	Standard care without INF	Discharge from ED 9x more likely	Rees et al, Am J Hematol 2023 Apr;98(4):620-627
IN Fentanyl	retrospective non-inferiority cohort study, adults	Iv morphine	No –inferiority	Assad et al, Am J Emerg Med 2023 Feb;64:86-89
IN Fentanyl	Observational, quality improvement	No comparator	Reduced time to first analagesia in ED	Myrick et al, Paed Blood Cancer 2020 67(10):e28648
Sublingual fentanyl	Phase 1 dose finding and feasibility	No comparator	Effective and safe	Telfer et al, BJ Pain 2022
SL Sufentanyl	Observational case and historical control, single centre	Historical controls	Testing time to analgesia and time in hospital	PI Wilson, Tampa GH. Clinical trials.gov NCT05388188

Prof P Telfer

Sub-anaesthetic dose ketamine

Single low-dose of ketamine (0.3 mg/kg) VS i.v morphine (0.1 mg/kg)

- **Similar reduction in pain score to i.v. morphine**
- **Reduced i.v. morphine in ED**
- **No difference in admission rate**

ORIGINAL CONTRIBUTION

Ketamine administration for acute painful sickle cell crisis: A randomized controlled trial

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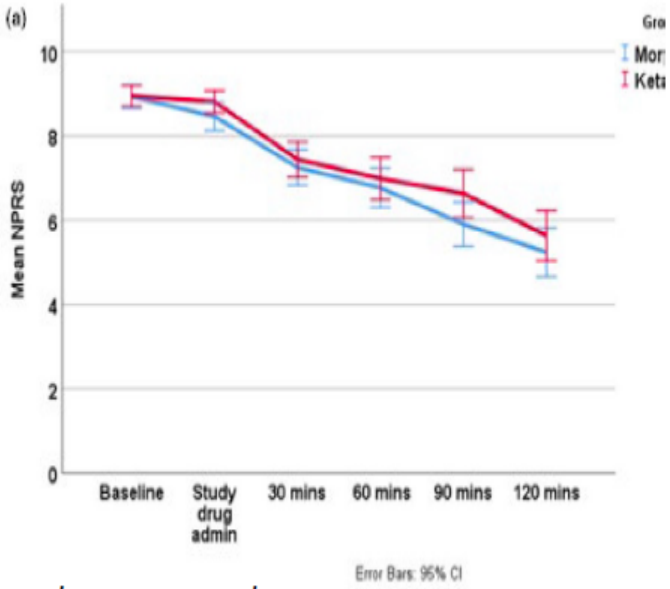
Abstract

Objective: The objective was to evaluate the efficacy and safety of single-dose ketamine infusion in adults with sickle cell disease (SCD) who presented with acute sickle vasoocclusive crisis (VOC).

Methods: This study was a parallel group, prospective, randomized, double-blind, pragmatic trial. Participants were randomized to receive a single dose of either ketamine or morphine, infused over 30 min. Primary outcome was mean difference in the numerical pain rating scale (NPRS) score over 2 h. NPRS was recorded every 30 min for a maximum of 180 min and secondary outcomes were cumulative dose of opioids, emergency department (ED) length of stay, hospital admission, change in vital signs, and drug-related side effects. Authors performed the analysis using intention-to-treat principle.

Results: A total of 270 adults with SCD and who presented with acute sickle VOC participated in this trial. A total of 138 were allocated to the ketamine group. Mean (standard deviation [SD]) NPRS scores over 2 h were 5.7 (±2.1) and 5.6 (±1.9) in



Acad Emerg Med. 2022;29:150–158.

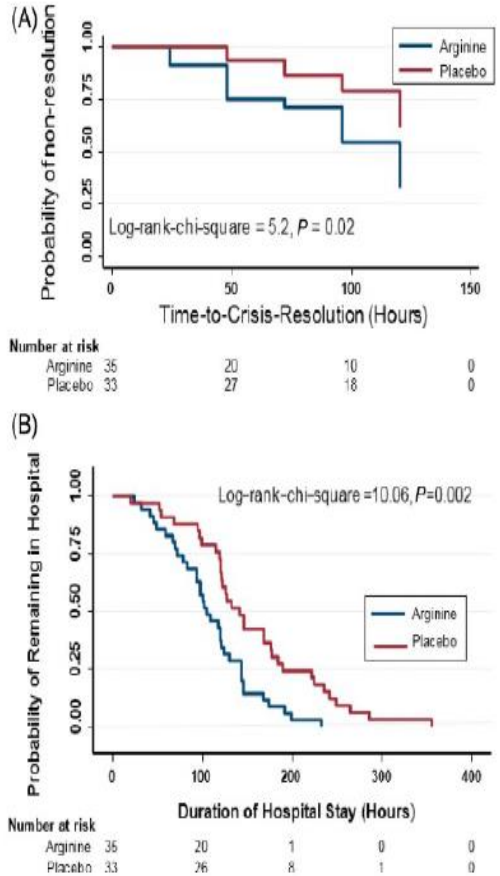
Prof P Telfer

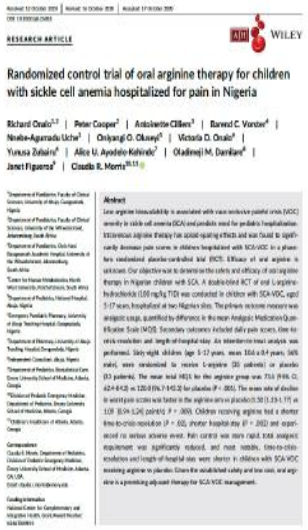
Oral arginine vs placebo-

RCT in children in Nigeria

- **Pain control more rapid**
- **Total analgesic requirement reduced**
- **Time-to-crisis-resolution and length-of-hospital-stay reduced**

Oral arginine is a promising adjuvant therapy for SCA-VOC management.




RESEARCH ARTICLE

WILEY

Randomized control trial of oral arginine therapy for children with sickle cell anemia hospitalized for pain in Nigeria

Richard Onalo | Peter Cooper | Antoinette Gibbs | Barend C. Vorster | Ntabe-Agumadu Uche | Oniyangi O. Olusegun | Victoria O. Onalo | Yunusa Zubairu | Alice U. Ayodele-Kehinde | Oladimeji M. Damilare | Janet Figueroa | Claudia R. Morris

Abstract

Onalo et al, *Am J Hematol. 2021;96:89–97.*