SPH
Solutions for Public Health

NHS
Arden and
Greater East Midlands
Commissioning Support Unit

A rapid evidence review on care models for people with sickle cell disease in uncomplicated crisis: An evidence review for NHS England

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Arden&GEM
Health and social care systems support

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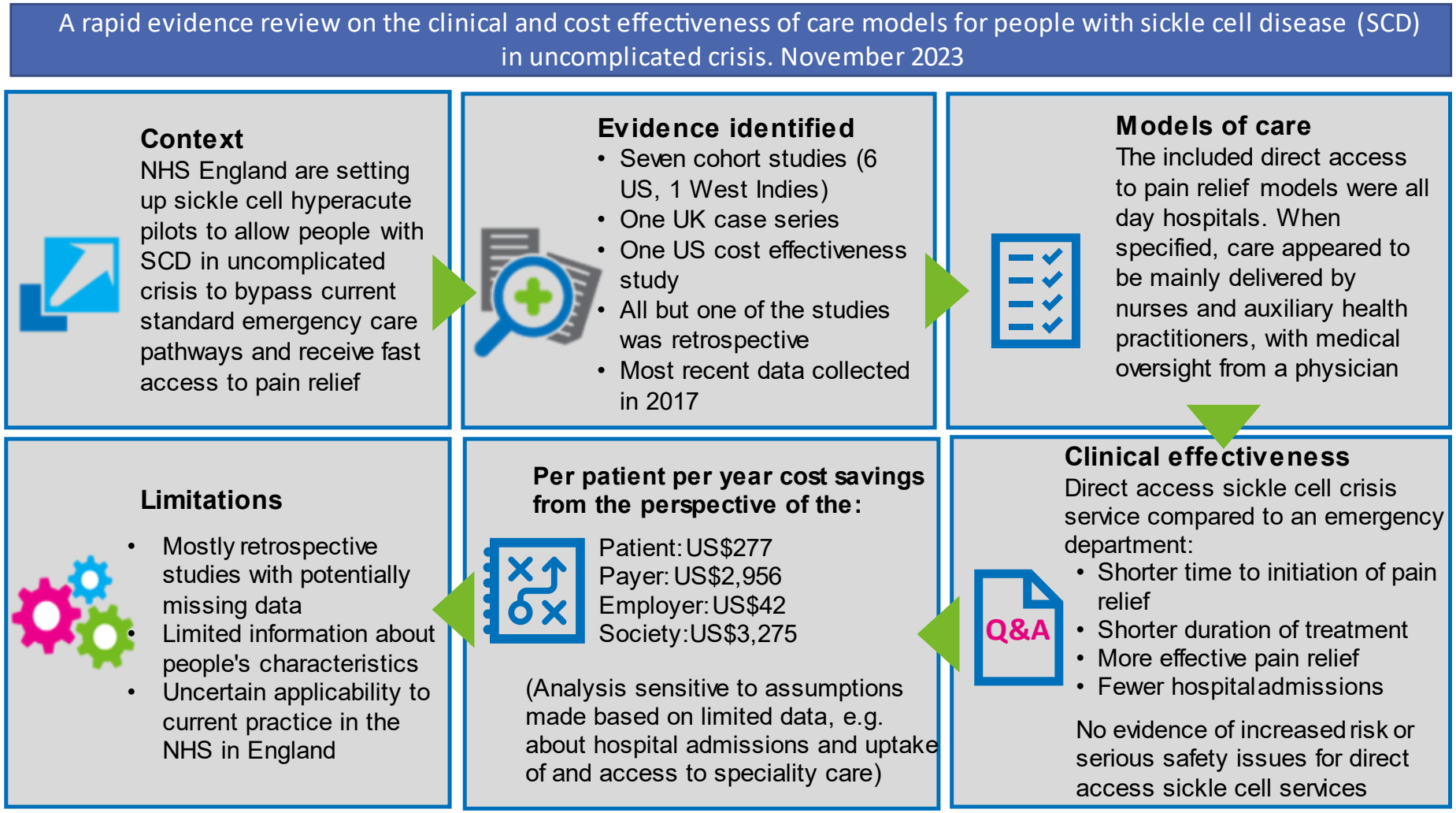
1 Key headlines



2 Executive summary

2.1 Introduction

People with sickle cell disease (SCD) can experience issues in receiving timely and appropriate care when experiencing vaso-occlusive crisis. NHS England are setting up several sickle cell hyperacute pilots that would allow people with SCD who are experiencing an uncomplicated vaso-occlusive crisis (uVOC) to bypass the current standard emergency care pathways and receive fast access to pain relief. The purpose of this rapid evidence review is to systematically identify, summarise and appraise the best available evidence on the clinical and cost effectiveness of care models for people with SCD in uVOC. Solutions for Public Health, part of NHS Arden and Greater East Midlands Commissioning Support Unit, were commissioned by NHS England to produce this rapid evidence review.

2.2 Methodology and studies identified

This review searched for peer-reviewed studies published between 1st January 2000 and 11th September 2023. Eight studies on clinical effectiveness were selected for inclusion. These consisted of one prospective cohort study from four centres in the United States (US) and six single centre retrospective cohort studies (five US; one West Indies) comparing the management of people with SCD in uVOC in a setting providing direct access to care compared to an emergency department. The eighth study was a retrospective case series from a single UK centre reporting outcomes before and after the opening of a sickle cell day centre. One study concerned a paediatric sickle cell service. The remaining studies related to the treatment of adults. The direct access sickle cell crisis care models in the included studies were all forms of day hospital with restricted opening hours. The included studies all had more than 100 participants and several included data from more than 1,000 visits. The data collection time periods varied from two months to five years. The most recent data were collected in 2017. One US study on cost effectiveness was also identified.

2.3 Key findings

The findings are summarised against the key questions explored in this review. These considered the clinical effectiveness, safety and cost effectiveness of managing people with SCD experiencing uVOC in a setting that provides direct access to care (bypassing A&E) compared to the current standard model of care. In addition, three further questions highlighted any information in the selected studies about subgroups of people who might benefit more from rapid access crisis pain management, the models of care and who it was delivered by and the geographical area covered by the centres and their population density.

Clinical effectiveness and safety

Direct access sickle cell crisis services had a shorter time to initiation of pain relief and shorter duration of treatment than emergency departments, with the difference being statistically significant when statistical analysis was conducted. For example, in three studies of adults, the average time to initiation of pain relief ranged from 38 to 62 minutes in a day hospital and 111 to 190 minutes in an emergency department. In the one study reporting this outcome in children, the median time from triage to first analgesic was 32.5 minutes in the day hospital and 70 minutes in the emergency department. In two studies, the average duration of treatment for adults was 2.9 and 4.5 hours respectively in a day hospital and 13 hours (in both studies) in an emergency department. In one study, length of stay for children was 255 minutes in the day hospital and 444 minutes in the emergency department.

Outcomes comparing the effectiveness of pain relief focused on different factors in the included studies, but all the results favoured direct access sickle cell crisis services compared to emergency departments. One study reported that discharge pain was lower in adults treated at a day hospital and that the proportion of adults receiving pain relief that was below standard (based on guidance) was lower in the day hospital. Two studies respectively reported that for adults, treatment in a day hospital was associated with a higher probability of pain reassessment within 30 minutes of the first dose of parenteral pain medication and a lower average time between medication doses. This outcome was not reported by the study of children with SCD in uVOC.

There were also statistically significantly fewer hospital admissions following treatment at a direct access sickle cell crisis service than an emergency department in most studies reporting this outcome. When this was reported as a proportion (in three studies), the percentage of adults who were admitted was between 8% and 37% from a day hospital and between 36% and 70% from an emergency department. For children, this was 29% in the day hospital and 57% in the emergency department. However, two studies differed, with one reporting a similar proportion of adults discharged home from a day hospital and emergency department and another study reporting that inpatient admissions per patient were higher during a time period when a day hospital was operational than a later period when the care model was changed to a fast-track from the emergency department to an observation unit. The data for this comparison were collected in different years and there was limited information to interpret this result.

For other outcomes such as length of hospital admission, readmission and uptake of the direct access sickle cell service, the reporting was more descriptive and varied and did not provide the type or level of detail to draw conclusions comparing the two models of care. No data were identified reporting outcomes relating to activities of daily living, quality of life or patient experience.

Few safety concerns were reported by the studies that reported safety outcomes. In one study, 20% of patients treated at a day hospital experienced side effects such as nausea, pruritus, vomiting or sedation. There were no cases of seizures, clonus or respiratory depression. Two further studies reported no requirement for naloxone reversal and no deaths in the community amongst people who had recently attended the day hospital respectively.

Most studies took some steps to reduce confounding factors in comparing outcomes for people treated at the different types of centre. For example, limiting the analysis to people with uVOC for both those treated in the direct access sickle cell crisis service and the emergency department. However, in some of the studies differences between the people attending the different types of centre could have impacted the outcomes reported.

Cost effectiveness

One study reported potential cost savings associated with increased use of direct access sickle cell crisis services rather than emergency department care for the US national population of adults with SCD in VOC using a 10-year time horizon. No year was given for the costs used. The model estimated annual per patient savings of 0.09 hospital admissions and 0.29 visits to an emergency department. Per patient per year cost savings were estimated from a patient perspective (US$277), payer perspective (US$2,956), employers perspective (US$42) and societal perspective (US$3,275). A limitation of the analysis was

the limited availability of published data to inform several of the model parameters. The results should be treated with caution as the model was also sensitive to variation in assumptions related to the proportion of people who seek treatment at the emergency department who are admitted to hospital and to the initial uptake of speciality care and the proportion of people with access to speciality care. These study limitations and the US healthcare setting limit the generalisability of the outcomes to the NHS in England.

Subgroups

Although some studies reported outcomes for subgroups of people by pain frequency or level, these were not reported in a way that supports conclusions about whether there are any subgroups of people that may benefit more from rapid access crisis pain management.

Models of care

The direct access sickle cell crisis services reported by the included studies were all forms of day hospital operating either as a dedicated facility for adults with SCD or combined with other haematology/oncology services. When this was reported, the day hospitals were located on the same sites as the emergency departments. Details about the models of care were reported to a varying but often limited degree across the different studies. The day hospitals were most commonly open Monday to Friday from 9am to 5pm, although one centre also started opening at the weekends after the first few years of operation. Two studies specified that people were asked to call ahead before presenting to the day hospital. Three studies reported the number of beds which were three, four and five respectively. When specified, the care in day hospitals appeared to be mainly delivered by nurses and auxiliary health practitioners (physician extenders, nurse associates or medical assistants), with medical oversight from a physician. Some studies also specifically mentioned access to social workers and psychiatry/psychology services.

Geographical areas covered by the centres and their population density

There were few details relating to the geographical areas covered by the direct access sickle cell crisis services. The location of the services, when provided, within the US (six studies), West Indies (one study) or UK (one study) suggests that these were mostly based in large urban areas. In the UK study the day hospital was located in Birmingham.

2.4 Conclusion and limitations

In conclusion, evidence was identified that managing people with SCD who are experiencing uVOC in a setting that provides direct access to care (bypassing A&E) is associated with a shorter time to initiation of pain relief, shorter duration of treatment, more effective pain relief and fewer hospital admissions than care in emergency departments. There was no evidence of increased risk or serious safety issues.

The retrospective nature of most of the studies introduces potential risks of bias. Details were taken from patient records with some concerns about missing or incomplete data and in some studies there was limited information about people's characteristics and uncertainty about the similarity of the people seeking treatment at the different centres compared. The included studies were based on data collected some years ago and primarily in the US. The applicability of the results to current practice in the NHS in England is therefore uncertain.

3 Introduction

Sickle cell disease (SCD) is a genetic disorder of the blood, affecting between 80,000 and 100,000 people in the United States (Lanzkron et al 2015). In England, SCD is estimated to affect one in every 2,000 live births and there are between 12,500 and 15,000 people living with SCD (NICE 2021). Sickle cell disease predominantly occurs in people from an African or African-Caribbean family background, but cases also occur in families where there is a history of migration from a malarial area and prevalence is increasing in mixed race families (NICE 2021).

A common complication of SCD is acute painful crisis, also called vaso-occlusive crisis (VOC) (Augier et al 2014). These crises can vary in severity and frequency based on both intrinsic (genotype/phenotype) and extrinsic (infection, exposure to cold, stress) factors (Augier et al 2014). People with sickle cell disease can experience issues in receiving timely and appropriate care when experiencing VOC (Benjamin et al 2000).

NHS England are setting up several sickle cell hyperacute pilots that would allow people with SCD who are experiencing an uncomplicated vaso-occlusive crisis (uVOC) to bypass standard emergency care pathways and receive fast access to pain relief. Solutions for Public Health, part of NHS Arden and Greater East Midlands Commissioning Support Unit, were commissioned by NHS England to produce this rapid evidence review. The key questions explored are:

1. For individuals with SCD who are experiencing uncomplicated VOC, what is the clinical effectiveness and safety of managing individuals in a setting that provides direct access to care (bypassing A&E) compared to the current standard model of care?
2. For individuals with SCD who are experiencing uncomplicated VOC, what is the cost effectiveness of managing individuals in a setting that provides direct access to care (bypassing A&E) compared to the current standard model of care?
3. From the evidence selected, are there any subgroups of people that may benefit from rapid access crisis pain management more than the wider population of interest?
4. From the evidence selected, what was the model of care and who was the care delivered by?
5. From the evidence selected, what were the geographical areas covered by the centres and their population density?

The review also identifies and discusses gaps and weaknesses in the evidence base.

To meet the aims of this evidence review, a broad systematic search strategy for peer-reviewed literature was applied. This report summarises the approach used for the identification and selection of relevant papers and discusses the key findings and limitations.

4 Methodology

This rapid evidence review identified, summarised and appraised the available evidence in a focused area. The research questions and PICOS used as the framework to search for and select evidence were agreed with NHS England at the project outset and are presented in Appendix 1. Searches for peer-reviewed studies published since 2000 were conducted on 11th September 2023 on the electronic databases Medline, Embase, the Cochrane Database

of Systematic Reviews and Central Register of Controlled Trials and the TRIPdatabase. The detailed search strategies are provided in Appendix 2.

Titles and abstracts were reviewed by one reviewer and those clearly ineligible were excluded. The SPH quality assurance (QA) lead also reviewed the titles/abstracts and reviewer's decisions about eligibility against the PICOS. Full papers for studies that met the inclusion criteria, or where there was any uncertainty, were ordered and reviewed by one reviewer with decisions about whether studies met the inclusion criteria recorded. The QA lead assessed the reviewer's study selection decisions, and any studies where there was uncertainty about inclusion were discussed in detail.

Data extraction and critical appraisal of the selected studies was conducted by one reviewer. The results were presented in tabular form with critical appraisal using a checklist aligned to the study design. The checklists used are provided in Appendix 3.

5 Study findings

The searches returned 1,146 unique studies. Thirty-four studies were judged to be of potential relevance from the title and abstract and were reviewed at full text. Nine studies were selected for inclusion. The studies excluded at the full text stage are listed in Appendix 4 with the reasons for exclusion.

The nine included studies are briefly introduced below. Outcomes relating to clinical effectiveness, safety and cost effectiveness are discussed in sections 5.1 and 5.2 respectively. Information relating to subgroups is discussed in section 5.3. More details about the models of care and the geographical areas covered by the centres are presented in sections 5.4 and 5.5 respectively. The identified studies included:

One prospective cohort study

- Lanzkron et al (2021) included 269 adults (1,441 visits) with SCD in uVOC, treated at either an infusion centre (day hospital) (1,200 visits) or emergency department (241 visits) at four US sites between 2015 and 2016.

Six retrospective cohort studies

- Augier et al (2014) included 109 adults with SCD and uncomplicated acute painful crisis, treated at a sickle cell unit (day hospital) (n=81; 100 visits) or an emergency department (n=28; 64 visits) in the West Indies (one site) in 2010.
- Benjamin et al (2000) included adults with SCD and uncomplicated painful crisis, treated at a day hospital (n=144; 2,554 visits) or emergency department (number of people/visits not stated) in the US (one site) between 1989 and 1993.
- Karkoska et al (2019) included 140 children (aged ≤21 years old) with SCD in uVOC, treated at a paediatric day hospital (n=46; 84 visits) or emergency department (n=125; 286 visits)[1] in the US (one site) between 2014 and 2015.

[1] The number of patients attending each site includes 31 patients who visited both the day hospital and emergency department

- Lanzkron et al (2015) included adults with SCD in uVOC, treated at an infusion centre (day hospital) (n=361; 3,874 visits) or emergency department[2] (n=558; 3,408 visits) in the US (one site) between 2008 and 2011.
- Molokie et al (2018) included 148 adults (217 visits) with SCD in uVOC and pain, treated at an acute care unit (day hospital) (73 visits) or emergency department[3] (144 visits) in the US (one site) over a two year period (dates not specified).
- Rizk et al (2020) included 686 adults with SCD and uncomplicated VOC in the US (one site). People were either treated between 2013 and 2014 when a day unit was operational (n=242) or between 2016 and 2017 when people with SCD were fast-tracked through the emergency department to an observational unit (n=444).

One retrospective case series

- Wright et al (2004) included people with SCD and uncomplicated painful crisis treated at one UK hospital before and after the opening of a sickle cell day centre. The day centre treated 89 people (677 visits) between July 2000 and June 2003. People treated at the main hospital before the day centre opened included 141 people between July 1998 and June 1999 and 139 people between July 1999 and June 2000.

One cost-effectiveness study

- Skinner et al (2022) estimated potential cost savings associated with increased use of speciality infusion centres compared to emergency departments for adults with SCD and VOC. The model used a 10-year time horizon from a patient, family, payer, employer and societal perspective for the US national population.

Further information is provided in the data extraction tables in Appendix 5.

5.1 For individuals with sickle cell disease who are experiencing uncomplicated vaso-occlusive crisis, what is the clinical effectiveness and safety of managing individuals in a setting that provides direct access to care (bypassing A&E) compared to the current standard model of care?

Seven studies compared the management of people with SCD in uVOC in a setting providing direct access to care compared to an emergency department. An eighth study (Wright et al 2004) reported outcomes before and after the opening of sickle cell day centre.

Clinical effectiveness

The clinical effectiveness outcomes reported are summarised below. Within this summary, the term ‘day hospital’ is used to describe outcomes relating to direct access sickle cell crisis care models. No studies reported outcomes on activities of daily living, quality of life or patient experience[4].

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[2] In Lanzkron et al (2015), patients with more complex presentation were excluded from treatment at the infusion centre. It is not clear that outcomes relating to the emergency department were limited to patients with uVOC

[3] In Molokie et al (2018), only patients with uncomplicated pain were treated in the acute care unit whereas patients treated in the emergency department could have had complicated pain

[4] Lanzkron et al (2021) collected data on patient experience but have not to date published these results in a peer reviewed publication

Time to initiation of pain relief (five studies)

Lanzkron et al (2021) and Karkoska et al (2019) both reported a statistically significantly shorter time to initiation of pain relief for people with SCD in uVOC treated at a day hospital compared to an emergency department. In Lanzkron et al (2021) (n=296), mean time to first treatment dose for adults was 62 minutes (95%CI 60 to 65) in the day hospital and 132 minutes (95%CI 116 to 161) in the emergency department (mean difference 70 minutes (95%CI 54 to 98), p<0.001)[5]. In Karkoska et al (2019) (n=140), median (IQR) time from triage to first analgesic for children was 32.5 (15 to 60) minutes in the day hospital and 70 (45 to 105) minutes in the emergency department (p<0.0001).

Two further studies also reported a shorter time to initiation of pain relief for adults treated at a day hospital and an emergency department but did not statistically compare the care models. In Augier et al (2014) (n=109), the mean (IQR) time from triage to initiation of analgesics was 38 (25 to 50) minutes in the day hospital and 111 (50 to 150) minutes in the emergency department. In Lanzkron et al (2015) (n=655), the mean time to receipt of first opioid dose was 57.7 minutes (95%CI 56.5 to 58.8) in the day hospital and 190 minutes (SD 129.8) in the emergency department. A fifth study, Benjamin et al (2000) (n=144) reported that the assessment and initial treatment of adults with SCD in uVOC at the day hospital occurred within 20 minutes of arrival.

Time to achievement of pain relief (one study)

Benjamin et al (2000) (n=144) reported that 40% of adults with SCD in uVOC treated at a day hospital (2,554 visits) achieved pain relief within one hour. The mean time to relief was 2.5 hours. No results relating to treatment in an emergency department were identified for this outcome.

Effectiveness of pain relief (five studies)

Several outcomes relating to the effectiveness of pain relief for people with SCD in uVOC were reported in different studies.

Three studies reported outcomes relating to pain levels:

- Molokie et al (2018) (n=148) reported mean (SD) initial pain score and pain score on discharge for adults treated in the day hospital (8.0 ± 1.6 and 4.5 ± 2.5 respectively) and emergency department (8.7 ± 1.5 and 6.4 ± 3.0 respectively). After controlling for initial pain, Molokie et al (2018) reported that adults visiting the emergency department had an average discharge pain that was 1.34 (standard error 0.35) points higher than people visiting the day hospital (p<0.001). Molokie et al (2018) also reported first pain relief and hourly pain relief dose against guidance[6]. The proportion of people receiving

[5] Lanzkron et al (2021) also reported time to first treatment dose for the four individual study sites (see Appendix 5)

[6] Based on guidelines for higher mg/kg doses or morphine or hydromorphone for the management of acute pain episodes of SCD. Patients were grouped into the four categories (below standard, standard, augmented and enhanced) based on mg/kg treatment groups

pain relief that was below standard (based on guidance) was lower in the day hospital (73 visits) than the emergency department (144 visits) (7% vs 19% for first pain relief dose; 12% vs 32% for hourly pain relief dose). After controlling for initial pain, the differences in first dosage and hourly pain relief levels in the different care models were statistically significant (see Appendix 5 for further details).

- Lanzkron et al (2015) reported a mean pain level[7] of 8.4 (95%CI 8.3 to 8.4) at arrival at the day hospital for adults (n=361, 3,874 visits), with a mean decrease in pain score from arrival to discharge from the day hospital of 2.62 (95%CI 2.55 to 2.69). No details of pain levels in adults treated at the emergency department were reported.
- Benjamin et al (2000) (n=144) reported that 84% of adults treated at the day hospital (2,554 visits) were titrated with medication to pain relief. The mean pain relief score[8] (after treatment) was 2.5 (SD not reported).

Two studies reported outcomes relating to the management of pain relief:

- Lanzkron et al (2021) (n=296) reported that the probability of pain reassessment within 30 minutes of the first dose of parenteral pain medication was statistically significantly higher with adults treated in the day hospital (0.38 (95%CI 0.35 to 0.41)) compared to the emergency department (0.1 (95%CI 0.07 to 0.15) (risk ratio 3.8 (95%CI 2.63 to 5.64), p<0.0019.
- Augier et al (2014) (n=109) reported the mean time between medication doses for adults treated at the day hospital (84 minutes) and emergency hospital (227 minutes). Range was not reported and the care models were not statistically compared.

Duration of treatment (four studies)

Karkosa et al (2019) (n=140) reported a statistically significantly shorter median length of stay for children with SCD in uVOC at a paediatric day hospital (255 minutes) compared to the emergency department (444 minutes) (p<0.0001) (range not reported). Two further studies also reported a shorter length of stay for adults with SCD in uVOC treated at a day hospital compared to an emergency department but did not statistically compare the care models. In Augier et al (2014) (n=109), mean (IQR) length of stay was 2.9 (1.9 to 3.8) hours in the day hospital and 13.0 (8.3 to 16.9) hours in the emergency department. In Benjamin et al (2000) (n=144), average[10] (range) length of stay was 4.5 (2 to 7) hours in the day hospital and 13 hours (11 minutes to 90 hours) in the emergency department. In a fourth study (Lanzkron et al 2015), adults with SCD in uVOC spent a mean of 4 hours and 55 minutes (range not reported) in the day hospital (n=361) but length of stay for the emergency department was not reported.

[7] Pain was assessed on the numerical rating scale (no further information provided)
[8] Medication to pain relief was assessed on a scale of 0 to 4 where 0= none; 1 = a little; 2 = moderate; 3 = good; 4 = complete relief. Pain relief was defined as a score of 2 or more
[9] Lanzkron et al (2021) also reported probability of pain reassessment within 30 minutes for the four individual study sites (see Appendix 5)
[10] It is not stated if this is median or mean

Hospital inpatient admission and length of admission (eight studies)

Hospital inpatient admission

Six of the eight studies reported lower inpatient admissions for people with SCD in uVOC following treatment in a day hospital setting. Four of these studies reported statistically significantly lower hospital admissions following treatment at a day hospital compared to an emergency department. In Lanzkron et al (2021) (n=296), the probability that a visit would end in a hospital admission was lower from the day hospital (0.09 (95%CI 0.075 to 0.11)) than from the emergency department (0.37 (95%CI 0.29 to 0.48) (risk ratio 0.25; 95% 0.18 to 0.33, p<0.001)[11]. In Molokie et al (2018) (n=148) and Lanzkron et al (2015) (n=655) the proportion of adults who were admitted was lower from the day hospital than the emergency department. In Molokie et al (2018), this was 37% (73 visits) vs 70% (144 visits) which was statistically significant after controlling for initial pain (odds ratio 4.1, p<0.001) (CI not reported). In Lanzkron et al (2015), this was 15.2%[12] (3,874 visits) vs 35.9% (3,408 visits) (p<0.001). In Karkoska et al (2019) (n=209), the proportion of children who were admitted was also lower from the day hospital than the emergency department. This was 29% (84 visits) vs 57% (286 visits), p<0.0001, with people presenting to the emergency department more likely to be admitted (odds ratio 3.8, (95%CI 1.9 to 7.8), p<0.001).

In a fifth study (Benjamin et al 2000) (n=144), the mean proportion of visits for adults resulting in an admission was lower from the day hospital (8.3%) (2,033 visits) than the emergency department (42.7%) (1,818 visits). The care models were not statistically compared. A sixth study (Wright et al 2004) (n=89) reported a decrease in hospital admissions of 43% for adults after a day hospital opened. In the two years before the day hospital opened there were more than 200 admissions each year. In the three years after the day hospital opened this was between 104 and 126 each year. Wright et al (2004) also reported that fewer people required repeat admissions.

However, two studies reported no reduction in inpatient admissions following day hospital access to treatment for uVOC. Augier et al (2014) (n=109) reported that the proportion of adults discharged home was similar from the day hospital (94%) (100 visits) and from the emergency department (93%) (64 visits). No statistical comparison was reported. Rizk et al (2020) reported that inpatient admissions per patient at a hospital in the US was higher between November 2013 and June 2014 when a day hospital for adults was operational (0.63) (n=242) compared to the period July 2016 to July 2017 after the care model was changed to a fast-track from the emergency department to an observation unit (0.29) (n=444), p<0.0001.

[11] Lanzkron et al (2021) also reported probability that a visit would end in hospital admission for the four individual study sites (see Appendix 5)

[12] This figure includes patients admitted from the day hospital or transferred from the day hospital to ED

Length of admission

Three studies reported length of admission. In Molokie et al (2018) (n=148), the mean (SD) length of admission for adults initially treated at the day hospital was 8.7 ± 7.1 days compared to 9.3 ± 5.9 days at the emergency department. After controlling for initial pain this difference was not statistically significant (p=0.36) (odds ratio and CI not reported).

In Benjamin et al (2000) (n=144) and Wright et al (2004) (n=89), length of admission from a day hospital was not compared to an emergency department. Benjamin et al reported that average length of admission for adults, regardless of whether they were admitted from the day hospital or emergency department, reduced from 9.3 days in the first year after the establishment of the day hospital to 7.3 days in the fifth year. Wright et al (2004) reported a similar median duration of admission for adults in the years before and after the day hospital opened (6.0 or 6.5 over a five-year period, range not reported). There was however a decrease in occupied bed days of 49% after the day hospital opened (see Appendix 5 for further details).

Readmission (four studies)

- Lanzkron et al (2015) (n=655) reported that the 30-day readmission rate for adults at their hospital was 42% prior to the opening of the day hospital in 2008 and 31% in 2011 (the final year of data collection in this study). The likelihood that a SCD-related discharge was categorised as a 30-day readmission decreased by 8% annually. This was not statistically significant (odds ratio 0.92, p=0.093) (confidence intervals not reported).
- Benjamin et al (2000) (n=144) reported that the proportion of adults who sought further medical care at the day hospital or emergency department within three days of discharge from the day hospital was 9.5%. Of these, 21% were admitted to hospital.
- Molokie et al (2018) (n=148) reported five occasions where adults who were discharged home returned to the emergency department on the same or next day. People had originally attended the day hospital on two occasions and emergency department on three occasions. On all five occasions, they were admitted to hospital.
- Wright et al (2004) (n=89) reported that 10% of people returned to the day hospital for further care.

Uptake of the service and by whom (seven studies)

The amount of data provided on people's characteristics varied between the studies.

Four studies provided characteristics separately for people who attended either a day hospital or emergency department:

- In Augier et al (2014) (n=109), the mean age was similar for the day hospital and emergency department attendees (33 and 35 years). For some characteristics, the proportion of people with these characteristics attending the day hospital appeared lower than the emergency department. For example, males (45% vs 67%), homozygous SCD (71% vs 84%) and median pain score at admission (7 vs 10).

However, only 39% of emergency department people had a documented pain score and the groups were not statistically compared. Augier et al noted that no-one had attended both centres. However, this could have been affected by the short duration of the data collection period (two months).

- In Karkoska et al (2019) (n=140), the mean age (12.1 and 10.5 years) was similar for the day hospital and emergency department and 50% of people were male in both centres. The proportion of people with homozygous SCD was lower for the day hospital (50% vs 61%), as was the proportion of people with fever at presentation (4% vs 10%). However, these differences were not statistically significant. People presenting at the day hospital did have a statistically significantly lower pain score at presentation (6 vs 7). There was no difference in the proportion of people visiting each centre who were classed as having frequent pain (61% vs 57%).
- In Lanzkron et al (2015) (n=655), the mean age (32 and 33 years) was similar for the day hospital and emergency department and 42% of people were male in both centres.
- In Molokie et al (2018) (n=148), characteristics were reported for people who only attended the day hospital, people who attended the day hospital and emergency department and people who only attended the emergency department. There were no differences between these groups when they were statistically compared. However, people who only attended the day hospital had a higher mean age (41 vs 35 vs 35), a lower proportion of males (25% vs 32% vs 39%) and a lower proportion of people with homozygous SCD (50% vs 71% vs 79%). The majority of all individuals (95%) were of Black ethnicity.

Three studies only provided characteristics for people who attended a day hospital and did not provide the equivalent information for patients who attended an emergency department:

- In Benjamin et al (2000) (n=144), the median age of day hospital attendees was 30 years, 53% were male and 83% had homozygous SCD. The majority of people (79%) were of African-American ethnicity with 20% of Hispanic-American ethnicity. In the first two years of the day hospital's operation, 76% of people presented directly to the day hospital, with the remainder transferred from the emergency department. In the third to fifth years of the day hospital's operation, the proportion of people who directly presented had risen to 94%.
- In Lanzkron et al (2021) (n=296), the mean age of day hospital attendees was 34 years, 39% were male and 71% had homozygous SCD.
- Wright et al (2004) (n=89), reported that 74% of the people treated at the day centre had homozygous SCD.

Two studies provided some additional information relating to the uptake of the service. Lanzkron et al (2015) reported details of hospital discharges for people with SCD across the 13 community hospitals and two academic centres within the John Hopkins Hospital 'market zone'. They reported that nine of these 15 hospitals saw a reduction in hospital discharges for SCD after the day hospital opened at the John Hopkins Hospital (located in Baltimore), whereas there was an increase in SCD discharges at the John Hopkins Hospital. Lanzkron et al (2015) stated that the odds that a person with SCD admitted to John Hopkins Hospital did not live in Baltimore increased by 15% each year in the three years after the day hospital opened (see Appendix 5 for further details). Wright et al (2004), reported that 96 new people

with SCD were referred to the day hospital in the three years after it opened, an increase of 40%. No further information was provided about these people.

Safety (four studies)

Few safety concerns for people with SCD in uVOC were reported by the studies that reported safety outcomes:

- In Augier et al (2014), one adult treated at the day hospital (n=81) had nausea and vomiting and two adults treated at the emergency department (n=28) had nausea and vomiting or pruritis requiring intervention respectively.
- In Benjamin et al (2000), 20% of the 144 adults treated at the day hospital experienced side effects such as nausea, pruritus, vomiting or sedation (no further details reported). There were no cases of seizures, clonus or respiratory depression.
- In Molokie et al (2018) (n=148), no adults were reported as requiring naloxone reversal.
- In Wright et al (2004) (n=89), the authors stated that there had been no deaths in the community amongst people who had recently attended the day hospital.

5.2 For individuals with sickle cell disease who are experiencing uncomplicated vaso-occlusive crisis, what is the cost effectiveness of managing individuals in a setting that provides direct access to care (bypassing A&E) compared to the current standard model of care?

One US study (Skinner et al 2022) estimated the economic impacts of increased use of speciality infusion centres compared to emergency department care for treating adults with SCD experiencing VOC. The model used a 10-year time horizon for the US national population. No year was given for the costs used. The model estimated annual per patient savings of 0.09 hospital admissions and 0.29 visits to an emergency department. Per patient per year cost savings were estimated from several perspectives:

- Patient perspective: US$277
- Payers perspective: US$2,956
- Employers perspective: US$42
- Societal perspective: US$3,275

As many infusion centres are on the same site as an emergency department, the model estimated no difference in family time or costs.

5.3 From the evidence selected, are there any subgroups of people that may benefit from rapid access crisis pain management more than the wider population of interest?

None of the included studies reported results for both adults and children and young people. Instead the papers reported outcomes for centres that provided services for either adults or children and young people. Results for these populations are therefore discussed above in reference to the question on clinical effectiveness and safety.

Two studies reported outcomes for subgroups of people according to pain frequency:

- Benjamin et al (2000) (n=144) reported results separately for adults with SCD and frequent pain, defined as people who experienced more than five visits and more than two hospitalisations per year. Frequent pain adults had a statistically significantly longer mean time to the achievement of pain relief than infrequent pain adults (3.5 hours (SD 1.2) vs 1.7 hours (SD 0.7), p<0.0001). They also had less pain relief, indicated by lower pain relief scores[13] at discharge (2.20 (SD 0.4) vs 3.1 (SD 0.7), p<0.0001). Benjamin et al (2000) reported that all people who sought further care at the day hospital or emergency department within three days of discharge from the day hospital were frequent pain adults.
- Karkoska et al (2019) (n=140) reported that children with SCD and frequent pain, who were at least 12 years old and had at least four admissions for uVOC during the study period, had statistically significantly more hospital admissions (odds ratio 4.35 (95%CI 2.11 to 8.99) p=0.002).

One study (Lanzkron et al 2015) (n=655) reported outcomes separately for subgroups of adults with SCD in uVOC who were either discharged home from the day hospital or who required ongoing hospital care. The mean pain level on arrival at the day hospital was statistically significantly lower for people who were sent home (8.3) compared to people who required ongoing hospital care (8.7) (p<0.001). There was no statistically significant difference in mean time to receipt of opioid dose between these groups (57.2 vs 60.3 minutes, p<0.06).

Lanzkron et al (2015) also reported some outcomes for adults with SCD treated in the emergency department by Emergency Severity Index (ESI)[14]. Mean time to receipt of first opioid dose was lower for people with an ESI of two (more urgent) (n=123) rather than three (n=1,426) (134.7 minutes vs 195.2 minutes, p<0.001). The mean time spent in the emergency department was also lower for people with an ESI of two (838.8 vs 1,018 minutes, p<0.001). The proportion of people with an ESI of two admitted from the emergency department was higher (59% vs 29%, p<0.001).

5.4 From the evidence selected, what was the model of care and who was the care delivered by?

The direct access sickle cell crisis services reported by the studies were all forms of day hospital. The level of detail provided on the model of care was often limited. The details that were reported to a varying degree across the different studies related to hours of operation, facilities and staffing:

- In Augier et al (2014), the sickle cell unit was described as a speciality day hospital model. No details on the hours of operation or staffing were reported.

[13] Medication to pain relief was assessed on a scale of 0 to 4 where 0= none; 1 = a little; 2 = moderate; 3 = good; 4 = complete relief. Pain relief was defined as a score of 2 or more

[14] The Emergency Severity Index is a five-level triage algorithm that is used to clinically stratify patients into five groups from 1 (most urgent) to 5 (least urgent) on the basis of acuity and resource needs

- In Benjamin et al (2000), the day hospital, which included a triage room, three beds and a clinical laboratory, was open Monday to Friday, 9am to 5pm. People were assessed by a nurse and physician prior to the initiation of therapy.
- In Karkoska et al (2019), the day hospital (Pediatric Ambulatory Chemotherapy and Transfusion Unit) was open Monday to Friday 8am to 6pm and was staffed by nurse practitioners familiar with SCD.
- In Lanzkron et al (2021), the infusion centres at the four study sites were open Monday to Friday and were described as not open 24 hours (not further specified). In two of the four sites the infusion centres were solely for the use of people with SCD. The remaining two centres were shared with people with other haematology-oncology conditions.
- In Lanzkron et al (2015), the infusion centre had five treatment slots for acute care visits. It was initially open Monday to Friday, 9am to 5pm, but after a few years also stated opening at weekends between 10am and 8pm. The centre was staffed by a clinic coordinator, nurse, clinical nurse associate, social worker and physician extender, with supervision from a medical director. Part-time psychiatry services were also available. People are assessed by a nurse and physician extender. People are asked to call prior to presenting to the centre, with these calls triaged by a nurse.
- In Molokie et al (2018), the acute care unit was open Monday to Friday 8am to 5pm. The unit was located within the hospital's sickle cell clinic and staffed with healthcare providers with expertise managing SCD pain crisis.
- Rizk et al (2020) reported details of the changes to their sickle cell programme since 2003. From 2003 to 2016 people with SCD and uncomplicated VOC were treated in a dedicated day unit, open 9am to 5pm, Monday to Friday. This unit had four fixed beds and was staffed by a nurse practitioner, a medical assistant and two registered nurses. People were required to call in before presenting to the unit and the nurse practitioner would conduct the triage. In June 2016, the day unit was closed and care was transferred to an observation unit located on a hospital floor. This unit was open 24 hours a day, seven days a week. The sickle cell team included hospitalists, haematologists, internal medicine physicians, a social worker, nurse practitioner and other nurses.
- In Wright et al (2004), the sickle cell day centre operated from 9am to 5pm Monday to Friday. The centre was staffed by three specialist nurses, a half-time psychologist, a nursing auxiliary and a receptionist. There was access to a social worker on a sessional basis. Haematology staff from the main hospital provided medical cover. An additional 0.5 whole time equivalent consultant haematologist was funded as part of the development of the centre. People were assessed by specialist nursing staff using a standardised pathway.

5.5 From the evidence selected, what were the geographical area covered by the centres and their population density?

Few details were reported about the geographical areas covered by the centres or the population density. Lanzkron et al (2021) did specify that only adults with SCD living within 60 miles of a study site were eligible for inclusion in their study. However, this criterion appeared to be related to the likely location of emergency department care so it is not clear that this same criterion was used to determine eligibility for treatment at the sickle cell infusion centres.

The details provided about the location of the studies, with any additional contextual information, is presented below:

- In Augier et al (2014), the sickle cell unit was located at the Tropical Medicine Research Institute in the University Hospital of the West Indies (Jamaica) on the same site as the emergency department. The authors stated that people with SCD can present to the emergency department on their own or be referred from healthcare facilities island-wide. Criteria specifically relating to the geographical area covered by the sickle cell unit were not reported. However, the authors stated that (at the time of the paper) Jamaica had a population of approximately 2.7 million, with approximately 300 new cases of SCD per year.
- In Benjamin et al (2000), the day hospital was located in the Montefiore Medical Center in the Bronx area of New York.
- Karkoska et al (2019) did not provide any information about the location of the study centre within the US.
- In Lanzkron et al (2021), the four US study sites were located in Baltimore, Cleveland, Baton Rouge and Milwaukee.
- In Lanzkron et al (2015), the sickle cell infusion centre was located at the John Hopkins Hospital in Baltimore, Maryland.
- In Molokie et al (2018), the sickle cell acute care unit and emergency department were part of the University of Illinois Hospital, which is located in Chicago.
- In Rizk el al (2020), the US sickle cell care centres discussed were located at a large urban academic medical centre that formed part of Thomas Jefferson University, which is located in Philadelphia, Pennsylvania.
- In Wright et al (2004), the day centre was located on the City Hospital campus in Birmingham in the UK.

6 Discussion and conclusions

The eight included studies on clinical effectiveness consisted of one prospective cohort study, six retrospective cohort studies and one retrospective case series. The retrospective nature of most of the studies introduces some potential risks of bias. For example, details were taken from patient records with some concerns about missing or incomplete data and in some studies there was limited information about people's characteristics and uncertainty about the similarity of the people seeking treatment at the direct access sickle cell crisis services, all of which had restricted opening hours, or an emergency department.

Most studies took some steps to try and ensure more similarity or reduce confounding factors in comparing outcomes for people treated at the different types of centre. For example five studies limited their analyses to people with SCD and uncomplicated pain for both people treated in the direct access sickle cell crisis service and the emergency department. The prospective cohort study (Lanzkron et al 2021) also limited their analysis to people who were treated at the emergency department during a time when the direct access sickle cell crisis service was open and took additional steps within the analysis to minimise the impact of confounding factors. However, in some of the studies it is possible that there may have been important differences between the people attending the different types of centre which could have impacted the outcomes reported. For example, in the three studies that reported pain score at initial presentation for people where these data were available, this was higher for people presenting to the emergency department. Some studies took account of this within

the analysis comparing groups, however, most studies did not report taking this into consideration.

One study concerned a paediatric sickle cell service. The remaining studies only related to the treatment of adults with sickle cell disease. The number of people included in the studies varied, although all of the included studies had more than 100 individuals and several included data relating to more than 1,000 visits. One study (Augier et al 2014) stated that there was no overlap in people seen in the day hospital and emergency department. However, in the other studies it is likely, or occasionally explicitly stated, that the same people sought and received care at both the direct access sickle cell crisis service and the emergency department. It is not clear if this reflected personal choice or practical considerations such as the opening hours or capacity of the direct access services.

A few studies reported details relating to the operation of the direct access sickle cell crisis services, such as details of staffing. However, the provision of such information was limited and insufficient to draw any conclusions about similarities or differences between the models of care. There were even fewer details relating to the geographical areas covered by the direct access sickle cell crisis services. Although the location of the services, when provided, suggests that these were mostly based in large urban areas.

Although the groups were not always statistically compared, studies reporting these outcomes consistently found that direct access sickle cell crisis services had shorter time to initiation of pain relief, shorter duration of treatment than emergency departments and more effective pain relief. In six of the eight studies there were also fewer hospital admissions following treatment at a direct access sickle cell crisis service than an emergency department. In contrast, two studies appeared to report either no difference in admissions or, in one study that inpatient admissions per patient were higher during a period of time when a day hospital was operational than a later period when the care model was changed to a fast-track from the emergency department to an observation unit. However, the data for this comparison were collected in different years and there was limited information to interpret this result. For other outcomes such as length of hospital admission, readmission, and uptake of the direct access sickle cell service the reporting was more descriptive and varied in the type of detail reported and did not provide the type or level of detail to draw conclusions comparing the two models of care. No data were identified reporting outcomes relating to activities of daily living quality of life or patient experience.

Few safety concerns were reported by the studies that reported safety outcomes with no evidence of increased risk. Although some studies reported outcomes for subgroups of people according to pain frequency or level, these were not reported in a way that supports conclusions about whether there are any subgroups of patients that may benefit more from rapid access crisis pain management.

One US study reported potential cost savings associated with increased use of speciality infusion centres rather than emergency department care for adults with SCD and VOC from a range of perspectives. A limitation of the analysis was the limited availability of published data to inform several of the model parameters. The results should therefore be treated with caution as the model was also sensitive to variation in assumptions related to the proportion of people who seek treatment at the emergency department who are admitted to hospital and

to the initial uptake of speciality care and the proportion of people with access to speciality care.

The time periods covered by the studies varied from two months to five years. All but one of the studies included data from one centre. The most recent data were collected in 2017 and six of the eight studies and the cost effectiveness study were from the United States. The remaining studies were set in the West Indies and the UK although the UK study was based on data collected between 1998 and 2003.

The generalisability of the results from studies from the USA and Jamaica and a UK study which reported outcomes from two decades ago to current clinical practice in the NHS in England is uncertain.

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Appendix 1: Research question and search frameworks

The evidence review explores five questions:

1. For individuals with sickle cell disease who are experiencing uncomplicated vaso-occlusive crisis, what is the clinical effectiveness and safety of managing individuals in a setting that provides direct access to care (bypassing A&E) compared to the current standard model of care?
2. For individuals with sickle cell disease who are experiencing uncomplicated vaso-occlusive crisis, what is the cost effectiveness of managing individuals in a setting that provides direct access to care (bypassing A&E) compared to the current standard model of care?
3. From the evidence selected, are there any subgroups of people that may benefit from rapid access crisis pain management more than the wider population of interest?
4. From the evidence selected, what was the model of care and who was the care delivered by?
5. From the evidence selected, what were the geographical area covered by the centres and their population density?

The framework used to guide the searches and study selection is set out below:

Search framework PICOS

	Inclusion/exclusion criteria
Population	Individuals (of all ages) with sickle cell disease who are experiencing uncomplicated vaso-occlusive crisis requiring pain relief [Sickle cell crisis are episodes of pain that can be severe and can last for several days or weeks. The frequency of crisis varies with some people experiencing frequent (e.g. weekly) crisis and others having less than one crisis a year. Some crisis can be managed by the person at home, however if the pain is more severe then a more extensive pain management intervention may be required] Sickle cell disease - Treatment - NHS (www.nhs.uk) [Uncomplicated crisis excludes people with priapism or acute chest syndrome etc] Subgroups of interest are adults and children and young people
Intervention	Rapid access pain relief delivered by a direct access sickle cell crisis service [Other terms of interest include direct ward access, sickle cell day hospitals, sickle cell disease day care units, sickle cell wards or enhanced emergency department (e.g. that employ nurses responsible for people with sickle cell disease)]
Comparator	Current standard model of care including: • Emergency department • Urgent and Emergency Care • A&E • Urgent treatment centres No comparator

Outcomes	Any outcome assessing the impact of management of people. For example: • Time to initiation of pain relief treatment • Time to achievement of pain relief • Effectiveness of pain relief • Duration of treatment • Hospital inpatient admissions and length of admission • Readmission • Activities of daily living • Quality of life • Patient experience • Uptake of the service and by whom Safety • Mortality • Death due to inappropriate location of care [for example a person who should have been seen in an emergency department for a heart attack being taken to a direct access sickle cell crisis unit] • Number that needed to be redirected to an emergency department because they had a complicated crisis • Long term sequalae of chronic pain • Resistance/addiction to analgesia Cost effectiveness [Outcomes can be assessed using standardised, validated measures or bespoke measures designed for a study] [Short and longer term outcomes are of interest]
Study designs	Studies published in peer-reviewed publications. The best available study designs will be prioritised according to hierarchy of evidence principles. Study designs of interest in order of priority include systematic reviews, randomised controlled trials, controlled clinical trials and cohort studies. If no higher-level quality evidence is found, case series can be considered Exclusions: narrative reviews, case reports, commentaries and letters. Conference abstracts, publications only available as an abstract or summary and posters are also excluded as they do not provide sufficient information for critical appraisal. Grey literature will be excluded.
Date and language	Studies and reports published in English since 2000

Appendix 2: Search strategy

Medline, Embase, the Cochrane Database of Systematic Reviews and Central Register of Controlled Trials and the TRIPdatabase were searched limiting the search to papers published in the English language since 2000. Conference abstracts, narrative reviews, commentaries, letters, editorials, case reports and trial registrations were excluded.

Search dates: 1st January 2000 to 11th September 2023 (search one) and 13th September (search two).

Medline search strategy one:

1	exp Anemia, Sickle Cell/
2	(sickle cell adj2 (an?emia? or trait? or disease?)).ti,ab,kf.
3	scd.ti,ab,kf.
4	1 or 2 or 3
5	((direct* or enhanc* or fasttrack* or fast track*) adj3 access*).ti,ab,kf.
6	(access* adj3 (care or healthcare or service?)).ti,ab,kf.
7	((care or healthcare or service?) adj5 model?).ti,ab,kf.
8	Crisis Intervention/
9	(cris?s adj5 (model* or care or healthcare or service?)).ti,ab,kf.
10	(cris?s adj5 (intervention? or program* or initiative?)).ti,ab,kf.
11	(cris?s adj3 (unit? or ward? or department? or dept? or clinic? or service? or setting? or center? or centre?)).ti,ab,kf.
12	Day Care, Medical/
13	Ambulatory Care/
14	ambulatory care facilities/ or community health centers/ or exp outpatient clinics, hospital/
15	((day* or ambulatory or shortstay or short stay or outpatient) adj3 (unit? or ward? or department? or dept? or clinic? or service? or center? or centre? or setting? or hospital?)).ti,ab,kf.
16	((specialty or speciali?ed or specialist) adj3 (unit? or ward? or department? or dept? or clinic? or service? or center? or centre? or setting?)).ti,ab,kf.
17	((day* or ambulatory or shortstay or short stay or outpatient) adj3 (care or healthcare)).ti,ab,kf.
18	((day* or ambulatory) adj3 (visit* or admission?)).ti,ab,kf.
19	(infusion? adj (unit? or ward? or department? or dept? or clinic? or service? or center? or centre? or setting?)).ti,ab,kf.
20	(pain adj (unit? or ward? or department? or dept? or clinic? or service? or center? or centre? or setting?)).ti,ab,kf.
21	or/5-20
22	4 and 21
23	((sickle cell or scd) adj5 (unit? or ward? or department? or dept? or clinic? or service? or center? or centre?)).ti,ab,kf.
24	22 or 23
25	pain/ or acute pain/
26	Pain Management/
27	exp Analgesics, Opioid/ad, tu [Administration & Dosage, Therapeutic Use]
28	exp Morphine Derivatives/ad, tu [Administration & Dosage, Therapeutic Use]
29	exp Fentanyl/ad, tu [Administration & Dosage, Therapeutic Use]
30	infusions, parenteral/ or infusions, intravenous/
31	Anemia, Sickle Cell/th [Therapy]
32	(((vasoocclusive or vaso-occlusive or sickle cell) adj (cris?s or episode?)) or (voc? or voe?)).ti,ab,kf.

33 pain.ti,kf. or (pain adj5 (relief or manage* or treat* or therap*)).ab. or (pain adj3 (cris?s or flare or acute)).ab.
34 (analgesi* or opioid? or opiate? or codeine or dihydrocodeine or morphine or diamorphine or oxycodone or fentanyl).ti,ab,kf.
35 or/25-34
36 24 and 35
37 limit 36 to (english language and yr="2000 -Current")

Medline search strategy two:

1 exp Anemia, Sickle Cell/
2 (sickle cell adj2 (an?emia? or trait? or disease?)).ti,ab,kf.
3 scd.ti,ab,kf.
4 1 or 2 or 3
5 (direct* adj3 access*).ti,ab,kf.
6 (access* adj3 (care or healthcare or service?)).ti,ab,kf.
7 ((care or healthcare or service?) adj5 model?).ti,ab,kf.
8 ((enhanc* or fasttrack* or fast track* or improv*) adj3 (care or healthcare or service? or access*)).ti,ab,kf.
9 (quality improvement or qi).ti,kf.
10 ((quality improvement or qi) adj5 (program* or intervention? or initiative? or model* or implement*)).ab.
11 Crisis Intervention/
12 (cris?s adj5 (model* or care or healthcare or service?)).ti,ab,kf.
13 or/5-12
14 Emergency Service, Hospital/
15 (emergency adj3 (department? or dept? or unit? or ward? or hospital?)).ti,ab,kf.
16 14 or 15
17 pain/ or acute pain/
18 Pain Management/
19 exp Analgesics, Opioid/ad, tu [Administration & Dosage, Therapeutic Use]
20 exp Morphine Derivatives/ad, tu [Administration & Dosage, Therapeutic Use]
21 exp Fentanyl/ad, tu [Administration & Dosage, Therapeutic Use]
22 infusions, parenteral/ or infusions, intravenous/
23 Anemia, Sickle Cell/th [Therapy]
24 (((vasoocclusive or vaso-occlusive or sickle cell) adj (cris?s or episode?)) or (voc? or voe?)).ti,ab,kf.
25 pain.ti,kf. or (pain adj5 (relief or manage* or treat* or therap*)).ab. or (pain adj3 (cris?s or flare or acute)).ab.
26 (analgesi* or opioid? or opiate? or codeine or dihydrocodeine or morphine or diamorphine or oxycodone or fentanyl).ti,ab,kf.
27 or/17-26
28 4 and 13 and 16 and 27
29 limit 28 to (english language and yr="2000 -Current")

Appendix 3: Critical appraisal checklists

JBI Critical Appraisal Checklist for Cohort Studies

1. Were the two groups similar and recruited from the same population?
2. Were the exposures measured similarly to assign people to both exposed and unexposed groups?
3. Was the exposure measured in a valid and reliable way?
4. Were confounding factors identified?
5. Were strategies to deal with confounding factors stated?
6. Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?
7. Were the outcomes measured in a valid and reliable way?
8. Was the follow-up time reported and sufficient to be long enough for outcomes to occur?
9. Was follow-up complete, and if not, were the reasons to loss to follow-up described and explored?
10. Were strategies to address incomplete follow-up utilized?
11. Was appropriate statistical analysis used?

JBI Critical Appraisal Checklist for Case Series

1. Were there clear criteria for inclusion in the case series?
2. Was the condition measured in a standard, reliable way for all participants included in the case series
3. Were valid methods used for the identification of the condition for all participants included in the case series?
4. Did the case series have consecutive inclusion of participants?
5. Did the case series have complete inclusion of participants?
6. Was there clear reporting of the demographics of the participants in the study?
7. Was there clear reporting of clinical information of the participants?
8. Were the outcomes or follow up results of cases clearly reported?
9. Was there clear reporting of the presenting site(s)/clinic(s) demographic information?
10. Was statistical analysis appropriate?

Appendix 4: Excluded studies table

Study reference	Reason for exclusion
Allen Liles E, Kirsch J, Gilchrist M, Adem M. Hospitalist management of vaso-occlusive pain crisis in patients with sickle cell disease using a pathway of care. Hospital Practice (1995). 2014;42(2):70-6.	This is about pathways and guidance for people who are either admitted or attend an emergency department. It is not about a direct access SCD crisis service
Andemariam B, Jones S. Development of a new adult sickle cell disease center within an academic cancer center: Impact on hospital utilization patterns and care quality. Journal of Racial & Ethnic Health Disparities. 2016;3(1):176-82.	This describes outcomes for an SCD clinic. It is not about the effectiveness of a direct access SCD crisis service
Arnold T, Coffee RL, Jr., Rosenberg L, Jacob SA, Thompson S, Saavedra H, et al. A quality improvement initiative to decrease time to analgesia in patients with sickle cell and vaso-occlusive crisis: A population with disparities in treatment. Cureus. 2022;14(9):e29569.	This paper is about a protocol and education for staff in a paediatric emergency department. It is not about a direct access SCD crisis service
Artz N, Whelan C, Feehan S. Caring for the adult with sickle cell disease: results of a multidisciplinary pilot program. Journal of the National Medical Association. 2010;102(11):1009-16.	This paper is about using a chronic care model for people with SCD. It is not about a direct access SCD crisis service
Ballas SK, Dampier C. Risk factors associated with increased emergency department utilization in patients with sickle cell disease: a systematic literature review. Annals of Hematology. 2020;99(11):2483-95.	This review does not consider models of care delivery or settings for managing people with SCD with a VOC
Balsamo L, Shabanova V, Carbonella J, Szondy MV, Kalbfeld K, Thomas DA, et al. Improving care for sickle cell pain crisis using a multidisciplinary approach. Pediatrics. 2019;143(5):05.	This paper is about interventions to improve the care of SCD inpatients. It is not about a direct access SCD crisis service
Binding A, Ward R, Phua C, Naessens V, O'Brien T, Bhatia S, et al. An innovative short-stay health care model for treatment of uncomplicated vaso-occlusive crisis in adult sickle cell disease patients in Canada to reduce emergency department utilization. CJEM Canadian Journal of Emergency Medical Care. 2019;21(1):55-62.	This small (n=21) study compared acute care in a day hospital and an emergency department. Studies with <100 people are not included as larger studies are available
Brandow AM, Weisman SJ, Panepinto JA. The impact of a multidisciplinary pain management model on sickle cell disease pain hospitalizations. Pediatric Blood & Cancer. 2011;56(5):789-93.	This is about a pain clinic for children with SCD and recurrent or chronic pain. It is not about treating a population with uncomplicated VOC in a direct access SCD crisis service
Brennan-Cook J, Bonnabeau E, Aponte R, Augustin C, Tanabe P. Barriers to care for persons with sickle cell disease: The case manager's opportunity to improve patient outcomes. Professional Case Management. 2018;23(4):213-9.	This paper outlines the sorts of issues that people with SCD face. It is not about a direct access SCD crisis service
Cline DM, Silva S, Freiermuth CE, Thornton V, Tanabe P. Emergency department (ED), ED observation, day hospital, and hospital admissions for adults with sickle cell disease. The Western Journal of Emergency Medicine. 2018;19(2):311-8.	This study compared geographic sites using different emergency department models. Both sites also had a day hospital. The focus of the study is on comparing outcomes at each site, not about the effectiveness of a direct access SCD crisis service
Givens M, Rutherford C, Joshi G, Delaney K. Impact of an emergency department pain management protocol on the pattern of visits by	This is about the development of an emergency department pain management

patients with sickle cell disease. Journal of Emergency Medicine. 2007;32(3):239-43.	guideline. It is not about a direct access SCD crisis service
Haywood C, Jr., Beach MC, Lanzkron S, Strouse JJ, Wilson R, Park H, et al. A systematic review of barriers and interventions to improve appropriate use of therapies for sickle cell disease. Journal of the National Medical Association. 2009;101(10):1022-33.	This review does not consider models of care delivery or settings for managing people with SCD
Kim S, Brathwaite R, Kim O. Evidence-based practice standard care for acute pain management in adults with sickle cell disease in an urgent care center. Quality Management in Health Care. 2017;26(2):108-15.	This is about the development of a protocol to improve care in an urgent care centre. It is not about a direct access SCD crisis service
Lanzkron S, Little J, Field J, Shows JR, Wang H, Seufert R, et al. Increased acute care utilization in a prospective cohort of adults with sickle cell disease. Blood Advances. 2018;2(18):2412-7.	This paper describes the people included in the Lanzkron et al 2021 paper which has been included. However, this paper does not distinguish between people who received care at the infusion clinic or emergency department. It therefore does not provide any additional information to inform the interpretation of outcomes
Lee S, Vania DK, Bhor M, Revicki D, Abogunrin S, Sarri G. Patient-reported outcomes and economic burden of adults with sickle cell disease in the United States: A systematic review. International Journal of General Medicine. 2020;13:361-77.	This review is not about models of care delivery or settings for managing people with SCD. The management of people in different settings was discussed in one of the seven included studies. This study (Molokie et al 2018) has been separately considered and included
Lyon M, Sturgis L, Lottenberg R, Gibson ME, Eck J, Kutlar A, et al. Outcomes of an emergency department observation unit-based pathway for the treatment of uncomplicated vaso-occlusive events in sickle cell disease. Annals of Emergency Medicine. 2020;76(3S):S12-S20.	This study is about outcomes before and after the implementation of an observation unit as part of an emergency department. It is not about a direct access SCD crisis service, bypassing A&E
Myrick R, Blakemore S, Waite E, Pernell B, Madan-Swain A, Hilliard L, et al. Outpatient pain clinic and intranasal fentanyl to improve sickle cell disease outcomes. Pediatric Blood & Cancer. 2020;67(10):e28648.	This small (n=30) study compared acute care management in an outpatient clinic and an emergency department. Studies with <100 people are not included as larger studies are available
Paquin H, E DT, Robitaille N, Pastore Y, Dore Bergeron MJ, Bailey B. Oral morphine protocol evaluation for the treatment of vaso-occlusive crisis in paediatric sickle cell patients. Paediatrics & Child Health. 2019;24(1):e45-e50.	This is about a new pain management protocol. It is not about a direct access SCD crisis service
Pohl E. Sickle Cell Disease: Considerations for acute pain management in the hematology-oncology ambulatory setting. Clinical Journal of Oncology Nursing. 2021;25(5):605-7.	This is a discussion paper
Raphael JL, Kamdar A, Wang T, Liu H, Mahoney DH, Mueller BU. Day hospital versus inpatient management of uncomplicated vaso-occlusive crises in children with sickle cell disease. Pediatric Blood & Cancer. 2008;51(3):398-401.	This study compares inpatient vs outpatient (day hospital) care. This comparison is not in scope
Rousseau R, Weisberg DF, Gorero J, Parwani V, Bozzo J, Kenyon K, et al. Utilization, financial outcomes and stakeholder perspectives of a re-organized adult sickle cell program. PLoS ONE. 2020;15(7):e0236360.	This paper is about the management of SCD with a focus on inpatients. It is not about the treatment of VOC or a direct access SCD crisis service
Tsitsikas DA, Lewis N, McCloskey K, Meenan J, Hall R, Osakonor DK, et al. Remodelling of	This paper describes actions put in place during COVID such as keeping the outpatient

specialist services enables safe reduction in hospital admissions of patients with sickle cell disease: Lessons from the COVID-19 pandemic. Clinical Medicine. 2020;20(6):e241-e3.	clinic open and telephone contact with people and impact on hospitalisations. It is not about the effectiveness of a direct access SCD crisis service
Welch-Coltrane JL, Wachnik AA, Adams MCB, Avants CR, Blumstein HA, Brooks AK, et al. Implementation of individualized pain care plans decreases length of stay and hospital admission rates for high utilizing adults with sickle cell disease. Pain Medicine. 2021;22(8):1743-52.	This is about individual care plans for hospitalised people with SCD. It is not about a direct access SCD crisis service

Appendix 5: Evidence summary tables

Reference	Population	Intervention & comparator	Key results	Quality appraisal
Augier et al 2014 **Study design** Retrospective cohort study **Country** One site in the West Indies **Study aim** To establish the pain management approaches to acute painful crisis in people with SCD at a sickle cell unit and ED **Study dates** April to May 2010	Adults (≥18 years old) with SCD and uncomplicated acute painful crisis (n=109) with 164 visits 81 people made 100 visits to the sickle cell unit 28 people made 64 visits to the ED The authors stated that the data suggested no overlap between the people seen at each centre **Inclusion criteria** People with SCD and uncomplicated acute painful crisis whose pain was severe enough to require admission to an observation ward for extended analgesia care and monitoring **Exclusion criteria** People presenting with acute painful crisis complicated by infection or sequestration **Baseline characteristics** Mean (IQR) age (years): • Sickle cell unit: 33 (24 to 39) • ED: 35 (24 to 39) Male:	**Intervention** Sickle cell unit, described as a speciality day hospital model. The hours of operation and staffing were not reported **Comparator** ED	Data were extracted from patient records for the 2 month study period. The models were not statistically compared **Time to initiation of pain relief treatment** Mean (IQR) time from triage to initiation of analgesics (minutes): • Sickle cell unit: 38 (25 to 50) • ED: 111 (50 to 150) **Effectiveness of pain relief** Mean time between medication doses (minutes): • Sickle cell unit: 84 • ED: 227 **Duration of treatment** Mean (IQR) duration of stay (hours): • Sickle cell unit: 2.9 (1.9 to 3.8) • ED: 13.0 (8.3 to 16.9) **Hospital inpatient admission** Proportion of people discharged home: • Sickle cell clinic: 94% The 6 remaining people were referred to the ED, with 2 known to have been admitted (the outcome for the other people is not known) • ED: 93% It is not explicitly stated that the remaining people were admitted to hospital **Safety** Sickle cell clinic: • 1 person had nausea and vomiting ED:	The study was appraised using the JBI checklist for cohort studies. As this was a retrospective comparison, people were not assigned to groups. Characteristics were separately reported for people treated at the sickle cell unit and ED. People treated at the ED had a higher initial pain score, a potential confounding factor. However, these data were not available for all people. The proportion of people who were male and had homozygous SCD was also higher for the ED. The authors did not adjust for any confounding factors. Outcome data were taken from patient records. It is not clear if all outcomes were

	• Sickle cell unit: 45% • ED: 67% Homozygous SCD: • Sickle cell unit: 71% • ED: 84% People with a documented pain score at presentation: • Sickle cell unit: 67/100 (67%) • ED: 25/64 (39%) Median (range) pain score[15] at admission: • Sickle cell unit: 7 (5 to 10) • ED: 10 (7 to 10) The sickle cell unit is located at the Tropical Medicine Research Institute, University Hospital of the West Indies on the same site of as the ED. People with SCD can present to the ED on their own or be referred from healthcare facilities island-wide. No specific details about the geographical area covered by the sickle cell unit were reported. No subgroups were reported		• 1 person had nausea and vomiting • 1 person had pruritis requiring intervention	measured in a valid and reliable way. There were some issues with missing data, for example pain scores. No statistical analysis was conducted comparing people treated at the sickle cell unit or ED **Other comments** The authors stated that access to pain medications differed between the centres. The sickle cell unit had access to oral morphine and codeine but not parenteral opioids. The ED had access to parenteral and oral opioids but codeine was not routinely available. The authors noted that no-one had attended both centres. However, this could have been affected by the short duration of the data

[15] Assessed using a numerical rating scale with higher scores indicating more severe pain

				collection period (2 months). The authors concluded that the management of people with SCD in acute painful crisis differed between the two centres. This study was conducted at one centre in the West Indies with data collected in 2010. The applicability to the NHS in England is uncertain.
Benjamin et al 2000 **Study design** Retrospective cohort study **Country** One US site **Study aim** To establish a day hospital to determine if an alternative to emergency department (ED) care could improve pain relief and reduce unnecessary	Adults with SCD and uncomplicated painful crisis treated at a day hospital (n=144) Number of people treated in ED not stated Total number of day hospital visits: 2,554 Mean number of day hospital visits per year: 511 **Inclusion criteria** People with SCD and uncomplicated painful crisis. These were people who were admitted with only unrelieved	**Intervention** Day hospital, operating 9am-5pm Monday to Friday and including a triage room, 3 beds and a clinical laboratory. People were assessed by a nurse and physician prior to initiation of therapy **Comparator** ED	Outcomes were reported for the first five years of the day hospital's operation. Unless otherwise stated, outcomes relate to people treated at the day hospital **Time to initiation of pain relief treatment** Assessment and initial treatment at the day hospital occurred within 20 minutes of arrival **Time to achievement of pain relief** People with pain relief within 1 hour: 40% Mean time to relief (hours): 2.5 (SD not reported) *For subgroups of people by frequency of pain* Mean (SD) time to relief (hours): • Frequent pain[16]: 3.4 (SD 1.2) • Infrequent pain: 1.7 (SD 0.7) p<0.0001	The study was appraised using the JBI checklist for cohort studies. As this was a retrospective comparison, people were not assigned to groups. The potential difference in people treated in an ED and day hospital was identified as a potential confounder and measures were taken to address this by excluding people with

[16] Frequent pain patients experienced more than five visits and more than two hospitalisations per year

hospital admissions for people with sickle cell disease (SCD) and uncomplicated crises **Study dates** 1989 to 1993	pain, or people who were discharged home from the ED or day hospital **Exclusion criteria** People with complicated crisis. For example, with comorbidities **Baseline characteristics** Median age: 30 years (range not reported) Male: 53.4% Homozygous SCD: 82.8% Ethnicity: • African-American: 79.3% • Hispanic-American: 19.8% • Other: 0.8% Source of day hospital attendees in years 1 and 2: • Walk-in patients: 76% • Transfer from ED: 24% Source of day hospital attendees in years 3 to 5: • Walk-ins: 94% • Transfer from ED: 6% The day hospital was located in the Montefiore Medical Center in the Bronx area of New York. The day hospital was open to walk-ins and people transferred from the ED. No further information was provided about	People were treated in the ED outside of the day hospital's operating hours	**Effectiveness of pain relief** People titrated with medication to pain relief: 84% Mean pain relief scores at discharge[17]: 2.5 (SD not reported) *For subgroups of people by frequency of pain* Mean (SD) pain relief scores at discharge • Frequent pain: 2.20 (SD 0.4) • Infrequent pain: 3.1 (SD 0.7) p<0.0001 **Duration of treatment** Average[18] length of stay (hours): • Day hospital: 4.5 (range 2 to 7) • ED: 13 (range 11 minutes to 90 hours) **Hospital inpatient admission and length of admission** Mean proportion of visits that resulted in an admission (for people with uncomplicated pain) during 5 year study period: • Day hospital: 168/2,033 (8.3%) • ED: 776/1,818 (42.7%) The authors noted that in the year prior to the establishment of the day hospital, 92% of people presenting at the ED were admitted The average length of admission for people followed by day hospital physicians with house staff assistance (regardless of whether they were admitted through the	comorbidities or complicated pain from comparisons between the day hospital and ED. Outcome data were taken from patient records. Pain relief was assessed on a scale of 0 to 4. It is not clear if all outcomes were measured in a valid and reliable way. It is not clear if all individuals were followed-up for longer term outcomes, for example, whether they could have sought further care at another hospital. No statistical analysis was conducted comparing people treated at the day hospital or ED **Other comments** The data reported primarily relates to people treated at the day hospital. Comparison to ED data was only reported for duration of treatment in the day hospital or ED

[17] Medication to pain relief was assessed on a scale of 0 to 4 where 0= none; 1 = a little; 2 = moderate; 3 = good; 4 = complete relief. Pain relief was defined as a score of 2 or more

[18] It is not stated if this is median or mean

	the geographical area covered by the day hospital Some outcomes were separately reported for subgroups of frequent and infrequent pain individuals		day hospital or ED) reduced from 9.3 days in the first year after the establishment of the day hospital to 7.3 days in the firth year The authors stated that the average length of admission was unchanged for people followed by private physicians who were not connected with the day hospital **Readmission** Proportion of people who sought further medical care at the day hospital or ED within 3 days of discharge from the day hospital: 9.5% 21% of people re-visiting were admitted to hospital *For subgroups of people by frequency of pain* The authors reported that all people who sought further medical care at the day hospital or ED within 3 days of discharge from the day hospital had frequent pain **Safety** The authors stated that 20% of people treated in the day hospital experienced side effects such as nausea, pruritus, vomiting or sedation (no further details reported) The authors stated that no seizures, clonus or respiratory depression events were observed	or in relation to inpatient admissions. It is not clear how many people were included in the ED data. As the ED treats both complicated and uncomplicated crisis, the day hospital visits were compared to people visiting the ED with uncomplicated crisis. The paper also reported estimated cost savings associated with reductions in hospital admissions and length of admission (data not extracted) The authors concluded that the dedicated facility supported effective and rapid painful crisis management, reduced hospitalisations and facilitated the integration of the approach into other areas of care. This study was conducted at one centre in the US with data collected between

				1989 and 1993. The applicability to the NHS in England is uncertain.
Karkoska et al 2019 **Study design** Retrospective cohort study **Country** One US site **Study aim** To compare the rate of hospital admission from the ED versus day hospital for uncomplicated vaso-occlusive episodes based on the use of institutional guidelines for analgesic administration **Study dates** February 2014 -May 2015	People aged ≤21 years old with SCD and uncomplicated VOC (n=140) with 370 visits 46 people made 84 visits to the day hospital 125 people made 286 visits to the ED NB: These numbers include 31 people who visited both the day hospital and ED **Inclusion criteria** People aged ≤21 years old with SCD who visited the day hospital or ED for uncomplicated VOC during the study period **Exclusion criteria** People were excluded if they had criteria that necessitated automatic admission. These included acute chest syndrome, hypoxaemia, concomitant fever with white blood cell count >30 x 10^9/l, greater than 20 g/l drop in haemoglobin from baseline, absolute reticulocyte count <50 x 10^9/l or reticulocyte percentage <2%, or splenic sequestration **Baseline characteristics** Mean (SD) age (years): 10.9 ± 5.5	**Intervention** Day hospital (Pediatric Ambulatory Chemotherapy and Transfusion Unit), operating 8am-6pm Monday to Friday. The day hospital was staffed by nurse practitioners familiar with SCD **Comparator** ED People were treated in the ED outside of the day hospital's operating hours or if there was no bed availability in the day hospital	Data were extracted from patient records for the 15 month study period **Time to initiation of pain relief treatment** Median (IQR) time from triage to first analgesic (minutes): • Day hospital: 32.5 (15 to 60) • ED: 70 (45 to 105) p<0.0001 **Duration of treatment** Median length of stay (minutes) (range not reported): • Day hospital: 255 • ED: 444 p<0.0001 **Hospital inpatient admission** • Day hospital: 29% • ED: 57% p<0.0001 In regression analysis, people presenting to ED were significantly more likely to be admitted (OR 3.8; 95%CI 1.9 to 7.8, p<0.001) The authors noted that the admission rate from ED was not statistically different during hours when the day hospital was or was not open *For subgroups of people by frequency of pain* People with frequent pain had significantly greater admissions (OR 4.35; 95%CI 2.11 to 8.99, p=0.002)	The study was appraised using the JBI checklist for cohort studies. As this was a retrospective comparison, people were not assigned to groups. However, the characteristics of people treated at the day hospital and ED were compared. People treated at the ED had a higher initial pain score, a potential confounding factor. This was taken into account in the statistical analysis. The groups were otherwise similar. Outcome data were taken from patient records. No information was provided about the scale/ method used to determine the pain score. It is not clear if all outcomes were measured in a valid and reliable way. **Other comments**

	• Day hospital: 12.1 ± 4.9 • ED: 10.5 ± 5.6 p=0.40 Male: 50.3% • Day hospital: 50.0% • ED: 50.4% p=0.51 Homozygous SCD: • Day hospital: 50% • ED: 61% p=0.48 Median (IQR) initial pain score[19]: • Day hospital: 6 (4-8) • ED: 7 (5-9) p=0.04 Fever at presentation: • Day hospital: 3.6% • ED: 10.3% p=0.21 60 people met the criteria for frequent pain[20] accounting for 174 visits. There was no difference in the proportion of visits from people with frequent pain to the day hospital or ED (61% vs 57%, p=0.84) The authors reported that a higher proportion of people presenting to the day hospital were on simple transfusion therapy (p=0.04). The authors			The centre introduced a guideline to standardise VOC management in both the day hospital and ED in December 2013. The regression analysis was adjusted for baseline factors such as initial pain score, fever and frequent pain. The authors concluded that people were more likely to be admitted if they presented to the ED. The authors also concluded that a sickle cell day hospital is a viable alternative to the ED for acute pain management. This study was conducted at one centre in the US with data collected between 2014 and 2015. The applicability to the NHS in England is uncertain.

[19] Assessment scale not stated
[20] Frequent pain patients were at least 12 years old and had at least four admissions for VOC during the study period

	reported that there was no difference between the groups for those on hydroxycarbamide, exchange transfusion, a combination of therapy or no therapy. There was no difference in whether people had adequate[21] received previous treatment at home (66% vs 41%, p=0.07) No information was provided about the location or geographical area covered by the day hospital One outcome was separately reported for a subgroup with frequent pain			
Lanzkron et al 2021 **Study design** Prospective cohort study (ESCAPED; Examining Sickle Cell Acute Pain in the Emergency Versus Day Hospital) **Country** Four US sites	Adults (aged ≥18 years) with SCD and uncomplicated VOC (n=269) with 1,441 visits 1,200 visits were to an infusion centre 241 visits were to an ED The median visits per person was 3 (IQR 1 to 8) Visits per study site: • Baltimore: 454	**Intervention** Infusion centres. The infusion centres were open Monday to Friday and were not open 24 hours (hours of operation not stated) The sites in Baltimore and	People were followed-up for 18 months **Time to initiation of pain relief treatment** Mean time to first treatment dose (minutes): • Infusion centre: 62 (95%CI 60 to 65) • ED: 132 (95%CI 116 to 161) (Mean difference (MD) 70 minutes; 95%CI 54 to 98, p<0.001. E value 2.8[22]) Mean (95%CI) time to first treatment dose (minutes) was also presented for each of the individual study sites. For each site p<0.001:	The study was appraised using the JBI checklist for cohort studies. The included population was limited to people who were treated during a time when the infusion centre was open and characteristics, such as education, employment

[21] Defined as use of both an opioid and NSAID
[22] The E value represents the robustness of the findings to the threat of unmeasured confounding. Larger values represent greater robustness. The authors stated that an E value of 2.8 indicates that "an unmeasured confounder must be 2.8 for it to nullify the estimated treatment effect, but weaker associations cannot nullify the treatment effect"

Study aim
To assess whether care in infusion centres or EDs leads to better outcomes for the treatment of uncomplicated VOC

Study dates
April 2015 – December 2016

- Cleveland: 283
- Baton Rouge: 385
- Milwaukee: 319

Inclusion criteria
Adults with SCD living within 60 miles of a study site who had at least one acute care visit for uncomplicated VOC. Only visits made to the infusion centre or ED on a weekday at a time when the infusion centre on that site was open were included

Exclusion criteria
People were excluded if their SCD was well controlled with long-term transfusion therapy and who had also had no acute care visits in the last two years. Pregnant women were also excluded. Data were not collected for visits that met the criteria for complicated VOC, such as acute chest syndrome, priapism or stroke

Baseline characteristics
Mean (SD) age (years): 33.6 (10.8)
Male: 39.0%
Homozygous SCD: 71.0%

The study sites were in four US cities: Baltimore, Cleveland, Baton Rouge and Milwaukee. No further details were provided about the locations

Milwaukee had infusion centres solely for the use of people with SCD. The centres in Cleveland and Baton Rouge were shared with people with other haematology-oncology conditions

Comparator
ED

For visits made to the ED at a time when the infusion centre on that site was open

The Baltimore ED had a fast-tracked system where people with SCD were given priority over all other people and placed in a bed in an ED-run 15-bed observation unit

Site	Infusion Centre	ED	MD (95%CI)
Baltimore	73 (70 to 76)	128 (100 to 176)	55 (27 to 103)
Cleveland	49 (44 to 55)	140 (99 to 198)	91 (51 to 151)
Baton Rouge	71 (68 to 76)	115 (84 to 159)	44 (13 to 90)
Milwaukee	46 (42 to 50)	160 (91 to 284)	114 (44 to 238)

Effectiveness of pain relief
Probability of pain reassessment within 30 minutes of the first dose of parenteral pain medication:
- Infusion centre: 0.38 (95%CI 0.35 to 0.41)
- ED: 0.1 (95%CI 0.07 to 0.15)

(Risk ratio (RR) 3.8; 95%CI 2.63 to 5.64, p<0.001. E value 4.7)

Probability (95%CI) of pain reassessment within 30 minutes of the first dose of parenteral pain medication was also presented for each of the individual study sites. For each site p<0.001:

Site	Infusion Centre	ED	RR (95%CI)
Baltimore	0.28 (0.24 to 0.32)	0.054 (0.01 to 0.09)	5.1 (3 to 22)
Cleveland	0.46 (0.42 to 0.51)	0.013 (0 to 0.04)	34.7 (11.5 to 240.1)
Baton Rouge	0.42 (0.37 to 0.46)	0.19 (0.1 to 0.3)	2.2 (1.3 to 4.3)
Milwaukee	0.37 (0.3 to 0.43)	0.15 (0.05 to 0.26)	2.4 (1.4 to 6.7)

Hospital inpatient admission
Probability that a visit would end in hospital admission rather than discharge home:
- Infusion centre: 0.09 (95%CI 0.075 to 0.11)
- ED: 0.37 (95%CI 0.29 to 0.48)

(RR 0.25; 95% 0.18 to 0.33, p<0.001. E value 5.4)

and medical conditions were reported. However, these data were not separately reported for people who attended an infusion centre or ED. The extent to which the populations were similar is therefore unclear.

Each sites principal investigator reviewed visits and confirmed that they were for uncomplicated VOC.

The authors conducted analysis using a propensity score methodology to adjust for confounding factors by balancing people's characteristics in the two groups. The authors calculated E values to assess the potential vulnerability of their treatment effect to residual confounding. The authors stated that the E values observed for the study outcomes were sufficiently large to alleviate major concerns about confounding.

<table>
<tr>
<td></td>
<td>No outcomes were reported by subgroups</td>
<td></td>
<td>Probability (95%CI) that a visit would end in hospital admission rather than discharge home was also presented for each of the individual study sites. For each site p<0.005:
<table>
<tr><th>Site</th><th>Infusion Centre</th><th>ED</th><th>RR (95%CI)</th></tr>
<tr><td>Baltimore</td><td>0.02 (0.004 to 0.03)</td><td>0.27 (0.14 to 0.41)</td><td>0.076 (0.02 to 0.16)</td></tr>
<tr><td>Cleveland</td><td>0.2 (0.16 to 0.26)</td><td>0.52 (0.32 to 0.76)</td><td>0.39 (0.25 to 0.69)</td></tr>
<tr><td>Baton Rouge</td><td>0.089 (0.07 to 0.12)</td><td>0.36 (0.17 to 0.63)</td><td>0.25 (0.14 to 0.53)</td></tr>
<tr><td>Milwaukee</td><td>0.064 (0.03 to 0.11)</td><td>0.35 (0.19 to 0.06)</td><td>0.18 (0.08 to 0.40)</td></tr>
</table>
</td>
<td>Missing data were imputed for people’s medical characteristics but not for outcome data. The outcomes reported were objective.

Other comments
Data were collected at the time of a visit. Some data (e.g. baseline and demographic data) were collected through a survey. However, if a person visited the same infusion centre or ED more than once in a calendar month, data were only collected at the first visit.

Some of the confidence intervals reported for individual sites are wide reflecting the small number of visits.

Limited information was provided about the study centres. For example, there was no information on size or staffing.

The authors noted that the Baltimore ED site had a fast-tracked</td>
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				system for people with SCD who were placed in an observation unit. However, people treated in the infusion centre in Baltimore received their first dose of parenteral pain medication a mean of 55 minutes faster than people treated in the Baltimore ED. The authors stated that patient satisfaction data were also collected and would be separately published. No separate publication relating to these data was identified at the time of this review. The authors concluded that treatment in an infusion centre for adults with SCD leads to substantially better outcomes than treatment in an ED. This study was conducted at 4 centres in the US with data collected between 2015 and 2016. The applicability to the NHS in England is uncertain.

Lanzkron et al 2015 **Study design** Retrospective cohort study **Country** One US site **Study aim** To describe the impact of opening a Sickle Cell Infusion Clinic **Study dates** February 2008 – December 2011	Adults (≥ 18 years) with SCD (n=655) with 7,282 visits 361 people made 3,874 visits to the infusion centre. Of these, 3,221 visits were for an acute VOC. The remainder were acute follow-up visits 558 people made 3,408 visits to the ED. Some outcomes, reported between April 2010 and July 2012 (see results), were available for 254 people who made 1,554 ED visits Some people visited both the infusion centre and ED. 98 people only visited the infusion centre Median (IQR) visits per patient: • Infusion centre: 3 (10) • ED: 2 (5) 106 people had a single visit to the infusion centre **Inclusion criteria** Adults with SCD **Exclusion criteria** People complaining of severe chest pain, shortness of breath or who were judged by the triage nurse as too sick were not eligible for treatment in the infusion centre. Unstable patients who present to the	**Intervention** Infusion centre, opened as a dedicated acute care facility for adults with VOC in 2008. The infusion centre was open Monday to Friday 9am – 5pm. From May 2011, the centre was also open 10am – 8pm at weekends. The centre has 5 treatment slots for acute care visits and was staffed by a clinic coordinator, nurse, clinical nurse associate, social worker and physician extender, with supervision from a medical director. Part-time psychiatry services were also available. People were assessed by a nurse and physician extender	Data were extracted from patient records for the study period (2008-2011). ED data for outcomes relating to pain relief were available for the period April 2010 to July 2012 due to the implementation of electronic medical records **Time to initiation of pain relief treatment** Mean time to receipt of first opioid dose from arrival (minutes): • Infusion centre: 57.7 (95%CI 56.5 to 58.8) • ED: 190 (SD 129.8) No statistical comparison reported *For subgroups of infusion centre attendees* Mean time to receipt of first opioid dose from arrival at the infusion centre (minutes) (CI not reported): • People sent home: 57.2 • People requiring ongoing hospital care: 60.3 p=0.06 *For subgroups of ED attendees* Mean time to receipt of first opioid dose from arrival at ED (minutes) (CI not reported): • Emergency Severity Index level 2 (n=123): 134.7 • Emergency Severity Index level 3 (n=1,426): 195.2 p<0.001 The authors stated that in a model controlling for severity, the relative risk of admission from the ED increased by 0.7% for every 10 minute increase in time to first dose of pain medication (p=0.024) **Effectiveness of pain relief**	The study was appraised using the JBI checklist for cohort studies. As this was a retrospective comparison, people were not assigned to groups. There were no differences between the groups for the characteristics reported, however limited information was provided on people's characteristics. It is not clear that the populations were similar. The authors did not identify or adjust for any confounding factors. Outcome data were taken from patient records. Limited information was provided about the scale/method used to determine the pain score. It is not clear if all outcomes were measured in a valid and reliable way. For outcomes relating to pain relief, data were collected for different

	centre were transferred to the ED **Baseline characteristics** Mean (SD) age (years): 32.4 (9.2) • Infusion centre: 31.9 (8.8) • ED: 33 (9.5) Male: 41.1% • Infusion centre: 41.9% • ED: 41.6% The centre was located at the John Hopkins Hospital in Baltimore. No further information was provided about the geographical area covered by the infusion centre Some outcomes were reported separately for subgroups who were either discharged home from the infusion centre or who required ongoing hospital care. Some outcomes for ED attendees were separately reported for subgroups by Emergency Severity Index[23]	People were asked to call prior to presenting to the centre, with these calls triaged by a nurse. People needed to present prior to 2:30pm on a weekday or 5:30 at a weekend to initiate care in the centre **Comparator** ED People without adequate pain control by the time the centre closed were either admitted or transferred to the ED If people presented to the ED during the centres opening hours they were	Mean pain level[24] on arrival at infusion centre: 8.4 (95%CI 8.3 to 8.4) Mean decrease in pain score from arrival to discharge from infusion centre: 2.62 (95%CI 2.55 to 2.69) *For subgroups of infusion centre attendees* Mean pain level on arrival at infusion centre (CI not reported; n not reported): • People sent home: 8.3 • People requiring ongoing hospital care: 8.7 p<0.001 Mean decrease in pain score from arrival to discharge from infusion centre: • People sent home: 2.9 • People requiring ongoing hospital care: 1.2 p<0.001 **Duration of treatment** Mean time spent in the infusion centre: 4 hours 55 minutes *For subgroups of ED attendees* Mean time spent in ED (minutes) (CI not reported): • Emergency Severity Index level 2 (n=123): 838.8 • Emergency Severity Index level 3 (n=1,426): 1,018 p<0.001 **Hospital inpatient admissions** Percentage of people admitted to hospital. The infusion centre figure includes people admitted from	time periods for people treated at the infusion centre and ED. This could have impacted the results. It is not clear if all people were followed-up for longer term outcomes, for example, whether they could have sought further care at another hospital. No statistical analysis was conducted for some outcomes. **Other comments** This paper is about the activity of the infusion centre rather than being specifically limited to the treatment of uncomplicated VOC. The majority of visits to the infusion centre (83%) were for an acute VOC. The authors discuss the exclusion of people with more complex

[23] The Emergency Severity Index is a five-level triage algorithm that is used to clinically stratify patients into five groups from 1 (most urgent) to 5 (least urgent) on the basis of acuity and resource needs

[24] Pain was assessed on the numerical rating scale (no further information provided)

		triaged and then transferred to the centre. If people presented to the ED overnight they were transferred to the centre in the morning	the infusion centre or transferred from the infusion centre to ED: • Infusion centre: 15.2% • ED: 35.9% p<0.001 The authors stated that there was a statistically significant decrease in the rate of hospital admissions from the ED each month after the opening of the infusion centre (data presented graphically). The admission rate was 20% by December 2011 *For subgroups of ED attendees* Proportion of people admitted from ED (CI not reported): • Emergency Severity Index level 2 (n=123): 59% • Emergency Severity Index level 3 (n=1,426): 29% p<0.001 **Readmission** 30-day readmission rate at the John Hopkins Hospital: • Prior to the opening of the infusion centre: 42% • In 2011: 31% No statistical comparison reported The authors stated that the likelihood that a SCD-related discharge was categorised as a 30-day readmission decreased by 8% annually. This was not statistically significant (OR 0.92, p=0.093) (CI not reported) **Uptake of the service and by whom** The authors stated that there are 13 community hospitals and 2 academic medical centres in the John Hopkins Hospital 'market zone'.	presentation from treatment at the infusion centre. Therefore, it seems likely that the majority of the infusion centre outcomes relate to people with uncomplicated VOC. It is not clear that the outcomes relating to the ED were limited to people with uncomplicated VOC. The authors concluded that the infusion centre model provides adults with SCD with access to high quality care that decreases the need for hospital admission. The authors also concluded that the impact of such a centre goes beyond the institution where it is based. This study was conducted at one centre in the US with data collected between 2008 and 2011. The applicability to the NHS in England is uncertain.

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9 of these 15 hospitals saw a reduction in hospital discharges for SCD between 2008 and 2011
John Hopkins Hospital saw an increase of 140 SCD discharges, with an increase in Baltimore City SCD discharges occurring at John Hopkins Hospital from 23% to 33% between 2008 and 2011
The odds that a person with SCD admitted to John Hopkins Hospital did not live in Baltimore increased by 15% each year

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<td>Molokie et al 2018

Study design
Retrospective cohort study

Country
One US site

Study aim
To compare outcomes for adults with SCD pain treated in acute care units or the ED

Study dates
Data were collected for a 2 year period (dates not specified)</td>
<td>Adults (aged ≥18 years) with SCD and pain (n=148) with 217 visits (73 to the ACU and 144 to the ED)

People could have visited both the ACU and ED (on different occasions)

4 people only visited the ACU
69 people visited the ACU and ED
75 people only visited the ED

Inclusion criteria
People admitted to the ACU had uncomplicated pain crisis that they were unable to manage at home. Data were</td>
<td>Intervention
Acute care unit (ACU), operating 8am-5pm Monday to Friday. The ACU was located within the hospital's sickle cell clinic and staffed with healthcare providers with expertise managing SCD pain crisis

Comparator
ED</td>
<td>Data were extracted from patient records for the 2 year study period

Effectiveness of pain relief
Mean (SD) initial pain score[25]:

ACU: 8.0 ± 1.6
ED: 8.7 ± 1.5

Mean (SD) pain score on discharge:

ACU: 4.5 ± 2.5
ED: 6.4 ± 3.0

After controlling for initial pain, people visiting the ED had an average discharge pain that was 1.34 (SE 0.35) points higher than people visiting the ACU (p<0.001)

First pain relief dose against guidance[26]:
<table>
<tr><th></th><th>ACU (n=73)</th><th>ED (n=144)</th></tr>
<tr><td>Below standard</td><td>7%</td><td>19%</td></tr>
<tr><td>Standard</td><td>30%</td><td>35%</td></tr>
<tr><td>Augmented</td><td>30%</td><td>21%</td></tr>
<tr><td>Enhanced</td><td>33%</td><td>25%</td></tr>
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<td>The study was appraised using the JBI checklist for cohort studies.

As this was a retrospective comparison, people were not assigned to groups. The authors stated that people were paired where possible but no further information on this was provided. Individuals could contribute results to both groups in separate visits to either the ACU or ED. The number of people who</td>
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[25] Assessed using a 0 to 10 verbal scale where 0 = no pain and 10 = worst pain

[26] Based on guidelines for higher mg/kg doses or morphine or hydromorphone for the management of acute pain episodes of SCD. Patients were grouped into the 4 categories (below standard, standard, augmented and enhanced) based on mg/kg treatment groups

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<td>analysed for the first visit to the ACU and first visit to the ED

Exclusion criteria
None stated

Baseline characteristics
Mean (SD) age (years): 35.1 (11.9)
• ACU: 40.5 (11.0)
• ACU & ED: 34.8 (11.7)
• ED: 35.0 (12.2)
p=0.65
Male: 35%
• ACU: 25%
• ACU & ED: 32%
• ED: 39%
p=0.67
Homozygous SCD: 74%
• ACU: 50%
• ACU & ED: 71%
• ED: 79%
p=0.34
Race/ethnicity:
• Black: 95%
• Hispanic: 3%
• White: 1%
• Mixed: 1%

The ACU and ED were part of the University of Illinois Hospital. No information was provided on the geographical area covered by the ACU

No outcomes were reported by subgroups</td>
<td>People were treated in the ED outside of the day hospital's operating hours or if they were experiencing a complicated pain crisis (eg. severe chest pain or headache, fever, crisis due to pregnancy)</td>
<td>After controlling for initial pain, the differences in the first dosage level between the ACU and ED were statistically significant (p=0.004)

Hourly pain relief dose against guidance:
<table>
<tr><th></th><th>ACU (n=73)</th><th>ED (n=144)</th></tr>
<tr><td>Below standard</td><td>12%</td><td>32%</td></tr>
<tr><td>Standard</td><td>22%</td><td>29%</td></tr>
<tr><td>Augmented</td><td>32%</td><td>15%</td></tr>
<tr><td>Enhanced</td><td>34%</td><td>24%</td></tr>
</table>
After controlling for initial pain, the differences in the hourly pain relief level between the ACU and ED were statistically significant (p<0.001)

Hospital inpatient admission and length of admission
Admitted from a visit:
• ACU: 27/73 (37%)
• ED: 101/144 (70%)
After controlling for initial pain, people had a statistically significantly higher chance of being admitted from the ED than from the ACU (OR 4.1, p<0.001) (CI not reported)

Mean (SD) length of admission (days):
• ACU: 8.7 ± 7.1
• ED: 9.3 ± 5.9
After controlling for initial pain there was no statistically significant difference in length of admission for people admitted from ED or from the ACU (p=0.36) (OR and CI not reported)

Readmission
On 5 occasions people discharged home returned to the ED on the same or next day. Of these, 2 people had originally visited the ACU and 3 the ED. All 5 were admitted to hospital</td>
<td>only attended the ACU was very small (n=4).

Initial pain score was identified as a confounding factor and adjusted for in the analysis. Another potential confounder was that only people with uncomplicated pain were treated in the ACU whereas people treated in the ED could have had complicated pain. This could affect the outcomes reported.

Outcome data were taken from patient records. The authors stated that there was minimal missing data (<1%). Imputation was performed for missing data.

It is not clear if all outcomes were measured in a valid and reliable way.

Other comments
Only data for the people's first visit to either the ACU or ED were included.</td>
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			Safety The authors reported that no-one required naloxone reversal	Additional outcomes relating to opioid dose received were not extracted. The authors concluded that applying guidance for higher dosing of opioids for acute painful episodes in adults with SCD in acute care units was associated with improved pain outcomes and fewer hospitalisations compared to treatment in the ED. This study was conducted at one centre in the US. It is not clear when the data were collected. The applicability to the NHS in England is uncertain.
Rizk et al 2020 **Study design** Retrospective cohort study **Country** One US site **Study aim** To examine the impact of changing the locus of care from a dedicated	Adults with SCD and uncomplicated VOC (n=686) Number of people (ED visits per patient) by time period • November 2013 to June 2014, before the day unit closed: 242 (2.14) • July 2016 to June 2017, after the observation unit was opened: 444 (0.47) The difference in ED visits per person was statistically significant (p<0.001)	**Intervention and comparator** Thomas Jefferson University has had a comprehensive sickle cell programme since 2003 which has undergone several transformations:	Data were extracted from patient records for the time periods reflecting the different operational models of care: • November 2013 to June 2014, before the day unit closed • July 2016 to June 2017, after the observation unit was opened **Hospital inpatient admission** Inpatient admissions per patient • November 2013 to June 2014: 0.63 • July 2016 to June 2017: 0.29 p<0.0001	The study was appraised using the JBI checklist for cohort studies. This was a retrospective comparison and people were not assigned to groups. Instead outcomes during periods when different models of care were in operation were

sickle cell day unit to an approach that fast-tracks people through the ED into an observation unit with 24/7 access **Study dates** Data were collected between November 2013 and June 2017	**Inclusion criteria** Adults with SCD and uncomplicated VOC **Exclusion criteria** None stated **Baseline characteristics** No characteristics reported The day unit and ED were part of Thomas Jefferson University, a large urban academic medical centre. No information was provided on the geographical area covered by the centre No outcomes were reported by subgroups	From 2003 to 2016 people with SCD and uncomplicated VOC were treated in a dedicated day unit, open 9am to 5pm, Monday to Friday. This unit had 4 fixed bed and was staffed by a nurse practitioner, a medical assistant and 2 registered nurses. The unit accepted adults who were part of the comprehensive programme. People were required to call in before presenting to the unit and the nurse practitioner would conduct the triage In June 2016, the day unit was closed and care was transferred to an observation unit located on a hospital floor. This unit was		compared. No details of people's characteristics were reported. It is not clear that the populations were similar. The authors identified confounding factors such as the gap between the time periods and other initiatives that occurred during these time periods. No strategies to deal with confounding factors were reported. Outcome data were taken from patient records. The outcome reported related to different time periods when different models of care were in place rather than care received at a specific location. This approach could have introduced confounding factors impacting the results. The authors noted that it was not known if people had sought treatment at another centre. **Other comments** The authors stated that Thomas Jefferson

		open 24 hours a day, 7 days a week and treated adults with uncomplicated VOC who were active participants on the programme. The sickle cell team included hospitalists, haematologists, internal medicine physicians, a social worker, nurse practitioner and other nurses		University has had a comprehensive sickle cell programme since 2003. Various transformations had occurred over time, including changes to protocols and training. The data relating to a change in the operational model of care has been extracted for this review. The authors concluded that the transformation from a dedicated day unit to an approach that fast-tracked people through the ED to an observation unit showed significant decreases in hospital admissions. This study was conducted at one centre in the US with data collected between 2013 and 2017. The applicability to the NHS in England is uncertain.
Skinner et al 2022 **Study design** Cost effectiveness study	Adults with SCD experiencing VOC The baseline cohort included 60,000 US adults with SCD who would seek care for SCD-	**Intervention** In the 'treated state' people received acute care in either an infusion centre or	The model used a 10-year time horizon **Utilisation** The model estimated total savings (total) and annual per patient (APP) savings	Data for this analysis was taken from the literature and publicly available data sources.

Country US population perspective **Study aim** To estimate the economic impacts of increased use of speciality infusion centres compared to emergency department care for treating adults with SCD experiencing VOC **Study dates** Not stated No year was given for the costs used	related pain crisis. A new cohort of 1,500 people was added to the model each year **Inclusion criteria** Adults with SCD experiencing VOC **Exclusion criteria** None stated **Infusion centre characteristics:** The model assumed that an infusion clinic with 4 beds would be able to care for 2 people per bed per day and would operate at 75% of maximum capacity. The model assumed staffing of a part-time haematologist, a registered nurse, a physician assistant, a nurse technician and a front office administrator	an ED. The number of acute events treated in the infusion centre was based on assumptions about the proportion of people with access to an infusion centre and the percentage of people seeking care when care in an infusion centre is available **Comparator** In the 'baseline state', all people requiring acute care for a VOC were treated in an ED	Number of hospital admissions: • Total: 55,086 • APP: 0.09 Number of ED visits: • Total: 175,460 • APP: 0.29 The model also estimated an increase of 204,897 visits to infusion centres at -0.33 annual per-patient savings **Patient perspective cost savings** • Over 10 years: US$170,014,834 • Per patient per year: US$277 **Family perspective cost savings** As many infusion centres are on the same site as an ED, the model estimated no difference in family time or costs **Payers perspective cost savings** • Over 10 years: US$1,811,386,274 • Per patient per year: US$2,956 **Employers perspective cost savings** • Over 10 years: US$25,752,439 • Per patient per year: US$42 **Societal perspective cost savings** • Over 10 years: US$2,007,153,548 • Per patient per year: US$3,275 **Sensitivity analysis** The model was most sensitive to variation in assumptions related to the proportion of people who seek treatment at the ED who are admitted to hospital. The model was also sensitive to the initial uptake of	The population was based on US prevalence and incidence data. The model assumed that adults with SCD experience an average of 2.7 pain crises requiring medical care each year. The model also assumed that the proportion of people with SCD with access to an infusion centre increased each year, reaching 35% by year 10. It was assumed that 70% of adults with SCD with access to an infusion centre would seek care at that centre. The analysis used a Markov model with a 10 year time horizon. The model used a patient, families, payers, employers and society perspective for the US population. Healthcare costs included inpatient hospital stay, ED costs and the costs of speciality care at an infusion centre. The

			speciality care and the proportion of people with access to speciality care	model also included productivity, caregiver, transportation and patient time costs. Societal costs were estimated by summing the costs from all payers, patient time and out-of-pocket healthcare costs and employer productivity costs. Sensitivity analysis explored the impact of allowing the value of one input parameter to vary by 20% above and below the mean. People's quality of life was not considered as part of the modelling exercise. The authors noted that limited published information was available to inform several of the model parameters. The authors concluded that the expansion of adult SCD centres across the US could lead to considerably better economic outcomes from reduced

				costs and hospital length of stay in addition to improved clinical outcomes. This analysis used a US population perspective. The applicability to the NHS in England is uncertain.
Wright et al 2004 **Study design** Retrospective case series **Country** One UK site **Study aim** To determine whether an alternative approach to the management of uncomplicated sickle pain through a day centre would improve the quality of care and reduce hospital admissions in people with SCD **Study dates**	People with SCD and uncomplicated painful crisis 89 people were treated in the day centre (677 visits for 440 episodes of pain) Number of people (n) treated each year In the years before the day centre opened: • 07/1998 – 06/1999: 141 • 07/1999 – 06/2000: 139 After the day centre opened: • 07/2000 – 06/2001: (n not available for this period) • 07/2001-06/2002: 209 • 07/2002- 06/2003: 235 Episodes of severe pain managed in day centre by year: • 07/2000 – 06/2001: 81 • 07/2001-06/2002: 148 • 07/2002- 06/2003: 211	**Intervention** Sickle cell day centre, operating 9am-5pm Monday to Friday. The centre was staffed by 3 specialist nurses, a half-time psychologist, a nursing auxiliary and a receptionist. There was access to a social worker on a sessional basis. Haematology staff from the main hospital provided medical cover. An additional 0.5	Data were reported for the 2 years prior to the opening of the day centre (07/1998 to 06/2000) and the 3 years after the day centre opened (07/2000 to 06/2003) **Hospital inpatient admission and length of admission** Hospital admissions for sickle cell pain (number of people, % of SCD population) In the years before the day centre opened: • 07/1998 – 06/1999: 207 (29, 21%) • 07/1999 – 06/2000: 205 (38, 27%) After the day centre opened: • 07/2000 – 06/2001: 126 (41, % not known) • 07/2001-06/2002: 123[27] (46, 22%) • 07/2002- 06/2003: 104 (54, 23%) Decrease in hospital admissions after the day centre opened: 43% The authors stated that fewer people required repeat admissions. The authors also stated that 69% of hospital admissions occurred as medical emergencies outside the centre's opening hours	The study was appraised using the JBI checklist for case series. There were no concerns about the identification of people. As data were collected retrospectively it was not clear if all relevant people were included. Very limited data were provided on the baseline characteristics of people. Data were reported for the years before and after the day centre opened. Some outcomes were reported for people treated at the hospital as a whole rather than

[27] The figure of 123 is taken from a table in the paper. In the text, the figure for this year is 119

1998 – 2002 (before and after the day centre opened)	Median (range) number of attendances per episode of pain: 1 (1 to 14) **Inclusion criteria** People with SCD and uncomplicated painful crisis presenting to the sickle cell day centre or main hospital **Exclusion criteria** None stated **Baseline characteristics** Homozygous SCD: In the years before the day centre opened: • 07/1998 – 06/1999: 63% • 07/1999 – 06/2000: 64% After the day centre opened: • 07/2000 – 06/2001: (not available for this period) • 07/2001-06/2002: 59% • 07/2002- 06/2003: 57% Treated at the day centre: 74% The day centre was located on the City Hospital campus in Birmingham. The centre accepted self-referrals and referrals from primary care and A&E. Medical notes of all registered people with SCD were stored in the centre to ensure continuity of care. No	whole time equivalent consultant haematologist was funded as part of the development of the centre. People were assessed by specialist nursing staff using a standardised pathway **Comparator** Outcomes were compared before and after the day centre opened. Prior to the day centre opening people were treated at the main hospital (not further specified)	Hospital admissions from the day centre (% of total admissions • 07/2000 – 06/2001: 46 (36%) • 07/2001-06/2002: 31 (25%) • 07/2002- 06/2003: 34 (33%) These admissions were for a total of 44 people Percentage of people with severe pain allowed home in the years after the day centre opened: • 07/2000 – 06/2001: 57%[28] • 07/2001-06/2002: 79% • 07/2002- 06/2003: 84% Median duration of admission (days) (total bed days) In the years before the day centre opened: • 07/1998 – 06/1999: 6.0 (1,662) • 07/1999 – 06/2000: 6.0 (1,651) After the day centre opened: • 07/2000 – 06/2001: 6.5 (851) • 07/2001-06/2002: 6.0 (1,069) • 07/2002- 06/2003: 6.5 (636) Decrease in occupied bed days after the day centre opened: 49% **Readmission** People returning to the day centre for further care: 10% **Uptake of the service** The authors stated that in the 3 years after the centre opened there were 96 new people referred to the centre (a 40% increase). No further information reported	specifically for people treated at the day centre. It is not clear precisely where these other people presented or were treated. No statistical analysis was reported. **Other comments** The paper also reported estimated cost savings associated with reductions in hospital admissions and length of admission (data not extracted) The authors concluded that a day centre for the management of painful crisis reduced unnecessary hospital admissions for uncomplicated pain. This study was conducted at one centre in the UK more than 20 years ago. The applicability to the current NHS in England is uncertain.

[28] The figure of 57% is taken from a table in the paper. In the text, the figure for this year is 43%

	information was provided on the geographical area covered by the day centre No outcomes were reported by subgroups		The authors stated that 9 people had attended the day centre on >10 occasions over a 12-month period, with 3 people attending >10 times for 3 consecutive years. The authors stated that all were referred to the psychologist **Safety** The authors stated that there were no deaths in the community amongst people who had recently attended the day centre	

Abbreviations:
ACU – acute care unit; APP - annual per patient; CI – confidence interval; ED – emergency department; IQR - interquartile range; JBI – Joanna Briggs Institute; kg – kilogram; l – litre; MD- mean difference; mg – milligram; n – number; OR- odds ratio; p – p-value; RR – risk ratio; SCD – sickle cell disease; SD – standard deviation; SE - standard error; UK – United Kingdom; US – United States; VOC – vaso-occlusive crisis