**National Institute for Health and Clinical Excellence**

**Sickle Cell**
**Guideline Internal Consultation Comments Table**
25th February 2012- 28th February 2012

| Type | Stakeholder | Order No | Document | Page No | Line No | Comments<br>Please insert each new comment in a new row. | Developer's Response<br>Please respond to each comment |
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| SH | NHS SICKLE CELL & THALASSAEMIA SCREENING PROGRAMME | 3 | Full | 5 | 83 - 113 | The SC&T Screening Programme is delighted to see that "patient-centred care" is put right at the front of the document and includes the need for<br>- Taking account of individual patient's needs and preferences;<br>- Giving patients the opportunity to make informed decisions about their care and treatment;<br>- Good communication between healthcare professionals and patient;<br>- Culturally appropriate treatment, care and information;<br>- Families and carers to be involved (if patient agrees) and to be supported;<br>- Age appropriate care including for young people in transition between paediatric & adult. | Thank you for your comment. |
| SH | The Sickle Cell Society | 3 | Full | 5 | 83-113 | The Society is delighted that patient will be allowed to work in partnership with their health professionals.<br>Other points which are has been address | Thank you for your comment. |

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| | | | | | | which I quite relevant are<br>• Communication between patients and healthcare professional<br>• Evidenced based written patient information<br>• We agree that the carers and families should be involved in the in decisions about treatment and care.<br>• The Transition process for young people is essential | |
| SH | RCOG | 2 | Full | 7 | 123 | We welcome this recommendation as acknowledging the patient's own knowledge and experience in long term conditions as being important and not always recognised. | Thank you for your comment. |
| SH | NHS SICKLE CELL & THALASSAEMIA SCREENING PROGRAMME | 4 | Full | 7 | 123 | Also very pleased to see recommendation that (wherever appropriate) patients (and/or carers) should be regarded as experts in their condition; | Thank you for your comment. |
| SH | The Sickle Cell Society | 4 | Full | 7 | 123 | The Society is please to see that patients being referred to as experts | Thank you for your comment. |
| SH | Napp Pharmaceutical Holdings Limited | 5 | Full | 7 | 130 – 132 | 1.1.3<br>We suggest that *record the pain score* should be added to the last sentence. | Thank you for your comment. Although it is acknowledged that recording the results of observations and assessments are important, it is assumed that this will be carried out as part of routine clinical practice. |
| SH | UK Forum on Haemoglobin Disorders | 6 | Full | 7 | 133 | The statement 'offer analgesia within 30 minutes of presentation' might be strengthened to 'administer appropriately effective analgesia within 30 minutes'. | Thank you for your comment. Recommendation 1.1.4 aims to ensure that patients are offered analgesia without delay. Details about the primary analgesia are |

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| | | | | | | | provided in recommendations 1.1.7 to 1.1.10. Further recommendations on reassessment and monitoring provide details about the effectiveness of the analgesia in providing individual patients with pain relief. As pain assessments are subjective and will vary between individuals, effective pain control may not always be achieved within the initial 30 minutes. |
| SH | NHS SICKLE CELL & THALASSAEMIA SCREENING PROGRAMME | 5 | Full | 7 | 133 | Analgesia to be offered within 30 minutes of presentation at hospital - Patient representative has suggested that analgesia/pain relief might also be given whilst patient is in transit to the hospital in an ambulance etc, particularly if the journey time is quite long. This would obviously involve apropriate training of ambulance staff. | Thank you for your comment. Although we understand the importance of patient care within pre-hospital settings, the scope of this guideline was restricted to in-hospital settings and specialised centres. |
| SH | The Sickle Cell Society | 5 | Full | 7 | 133 – 140 | Offering analgesia within 30mins hopefully all hospital will consider this. The Society supports the 30mins time limit however, the patients' pain need to be controlled also within 30mins. | Thank you for your comment. Recommendation 1.1.4 aims to ensure that patients are offered analgesia without delay. However, as pain assessments are subjective and will vary between individuals, effective pain control may not always be achieved within the initial 30 minutes. Recommendations 1.1.12 to 1.1.19 provide details on reassessment and on-going monitoring which aim to assess the on-going effectiveness of pain relief. |
| SH | Napp Pharmaceutical | 6 | Full | 7 | 133- | 1.1.4 | Thank you for your comment. |

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| | Holdings Limited | | | | 140 | We agree that patients should be assessed and that an account of existing analgesia and the patients care plans should be taken into account. This is particularly important for continuity of care when patients have been stabilised on a particular opioid following previous crises. | |
| SH | British Pain Society | 2 | Full | 7 | 136 | You recommend taking into account any analgesia taken for the current episode before presentation. It is very important also to take into account any analgesia used regularly by the patient between acute episodes as this leads to tolerance and higher, often much higher, bolus doses are needed during the acute episode. In our view this is a common cause for the under-treatment of pain. | Thank you for your comment. It is assumed that details of regular analgesia will be included as part of the patient's individual care plan (where available) which is included in recommendation 1.1.7 |
| SH | British Pain Society | 3 | Full | 7 | 138 | The subcutaneous route is useful for both boluses of opioids and PCA. You have mentioned that venous access may be difficult, the subcutaneous route should be recommended more strongly. | Thank you for your comment. The GDG discussed the route of administration during the development of the guideline. It was agreed that the use of a bolus dose would allow healthcare professionals to select the most appropriate route for each individual patient. There was no evidence comparing pain relief using IV routes compared to subcutaneous routes; therefore the GDG did not make a stronger recommendation. |
| SH | NHS SICKLE CELL & THALASSAEMIA SCREENING | 6 | Full | 7 | 140 | Patient representative has commented that Care Plans are key, especially if patient is not supported by a carer, as communication | Thank you for your comment. |

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| | PROGRAMME | | | | | exchanges between medical staff and patients can be difficult if the patient is in severe pain; if hypoxic, patients may not remember what pain killers they took or at what intervals. | |
| SH | UK Forum on Haemoglobin Disorders | 7 | Full | 7 | 141 | It is suggested that initial observations should also include a sedation score, in case the patient has been taking opiate analgesia before presentation. | Thank you for your comment. The GDG discussed this issue during the post-consultation GDG meeting and agreed that recommendation 1.1.5 provides a list of clinical assessments which is not exhaustive. It was also discussed that the risk of sedation following a bolus dose of strong opioids is accounted for in recommendation 1.1.16. This recommendation has been amended to ensure clinical assessments are carried out hourly for the first 6 hours. The group also agreed that respiration rate will also provide a measure of sedation at initial presentation. |
| SH | British Pain Society | 4 | Full | 7 | 141 | You do not recommend use of a sedation score, though this is mentioned in ongoing monitoring 1.1.15 on a 2-4hrly basis. We believe that this is an indicator for possible opioid induced respiratory depression, it has been shown to be more sensitive than respiratory rate, and should be measured routinely and at 30 minute intervals if repeated boluses of opioids are being used. Ref: Macintyre PE and Schug SA 2007 Acute Pain Management: a practical guide. London Saunders Elsevier | Thank you for your comment. The GDG discussed this issue during the post-consultation GDG meeting and agreed that recommendation 1.1.5 provides a list of clinical assessments which is not exhaustive. It was also discussed that the risk of sedation following a bolus dose of strong opioids is accounted for in recommendation 1.1.16. This recommendation has been amended to ensure clinical assessments are carried out hourly for the first 6 hours. |
| NICE | CCP Technical Team | 1.2 | Full | 7-8 | 130- | Unsure about the ordering of | Thank you for your comment. The GDG |

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| | | | | | 152 | recommendation 1.1.3 to 1.1.6. The recommendations seem jumping around, started from assessing pain, then talked about offering analgesia, then back to clinical assessment again but with element of monitoring, and back to assess pain. Should there be a logical order of the sequence of events? As all these recommendations have a phrase of 'all patients presenting at hospital'. If recommendation 1.1.3 to 1.1.6 should happen simultaneously perhaps need to think about the ordering of the recommendations again? | discussed the ordering of the recommendations during the development of the guideline. It was agreed that although the numbering of the recommendations did not always follow the specific review questions, it was important to follow the order in which assessments and treatments would be carried out in clinical practice. Specifically, recommendations 1.1.3 to 1.1.6 should be carried out on presentation to hospital and provide details of assessment of pain, pain relief and clinical assessment (including possibility of acute complications). |
| SH | Royal College of Paediatrics and Child Health | 4 | Full | 7-11 | | This guideline is for adults, young people and children. Do all recommendations apply for all age groups? | Thank you for your comment. The guideline refers to subgroups (as set out in the scope, see appendix C) as appropriate. The GDG discussed the evidence relating to children and young people and felt that the recommendations would apply to all patients presenting with an acute painful sickle cell episode regardless of their age. Specifically, the GDG discussed the use of age appropriate pain rating scales and settings, and these are referred to in the final recommendations. Drug dosing for children and young people should be in line with the BNF for both adults and children. |
| SH | UK Forum on Haemoglobin Disorders | 8 | Full | 8 | 144 | The suggested 'cut-off' of O2 saturation 94% should mention referring to the individual patient's normal baseline level, recorded in | Thank you for your comment. This issue was discussed at the post consultation GDG and has been amended to 95%. This cut-off level |

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| | | | | | | outpatient clinics when they are well. For some patients, 94% [or even 91 – 92%] is approximately baseline, for others – whose baseline is 99 – 100% - even 95% might represent a potentially important deterioration. | was agreed based on GDG consensus and expertise and was felt to be a widely agreed clinical threshold for treatment of hypoxia in patients with an acute sickle cell episode. The GDG also agreed that baseline levels of oxygen saturation may not be available on presentation to hospital and agreed that this should not delay treatment. As a result, baseline levels are not specifically referred to in the final recommendations. |
| SH | RCOG | 3 | Full | 8 | 144 | NICE state that facial oxygen should be prescribed if oxygen saturations fall below 94%. This is present in several sections. The RCOG Green-Top Guideline 61 states that facial oxygen should be prescribed if oxygen saturations fall below the woman's baseline or 95% in pregnancy. We would suggest that NICE either state that facial oxygen be prescribed below 95% in pregnancy or refer to the RCOG Green-Top Guideline for recommendations regarding oxygen therapy in pregnancy. | Thank you for your comment. This issue was discussed at the post consultation GDG and has been amended to 95%. This threshold was agreed to apply to all patients presenting to hospital with an acute painful sickle cell episode, including pregnant women. |
| SH | UK Forum on Haemoglobin Disorders | 15 | Full | 8 | 151, and various other places referring to same | In a number of places, there is a suggestion of diagnoses 'alternative' to sickle pain crisis, which should better say 'in addition to' sickle pain crisis, as pain is often present as a feature of the other acute complications. | Thank you for your comment. The GDG agreed this wording to include other potential non-sickle related causes of pain. Although pain may be present as a feature of an acute complication, the aim of recommendation 1.1.6 is to assess the underlying cause of the pain. |

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| | | | | | issue | | |
| SH | UK Forum on Haemoglobin Disorders | 9 | Full | 8 | 154 | The suggestion of giving 'a bolus of strong opioid by a suitable route' is a specific instance of the issue raised in comment 1 above. | Thank you for your comment. |
| SH | UK Forum on Haemoglobin Disorders | 10 | Full | 8 | 156 | Suggest guidance might include guidance re 'severe pain' in terms of pain score [7/10? 8/10?] | Thank you for your comment. The GDG discussed the severity of pain during the development of the guideline and at the post consultation GDG meeting. Specifically, the GDG discussed that pain is a subjective judgement and as it differs between individuals, it would be difficult to provide general numerical definitions which would apply to all patients. The GDG also discussed that there is lack of definitions for moderate and severe pain which are widely agreed. General definitions of moderate and severe pain have been added to the glossary section of the guideline, however it is noted that these will not apply to all patients as pain is subjective but will provide a typical range of VAS (or equivalent) scores for use with clinical judgement. |
| SH | NW London Hospitals NHS Trust | 3 | Full | 8 | 157 | This is dependent on type, dose and time that analgesia was taken (given) at home before arrival at hospital especially in view of some units offering opiates in the community. | Thank you for your comment. The ordering of the recommendations has been amended following the post-consultation GDG. Healthcare professionals should also refer to recommendation 1.1.7 which takes into account analgesia that has been used for the current episode. This will include information |

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| | | | | | | | on type, dose and time. The GDG agreed that it is important to ensure that the use of strong opioids is not delayed in the treatment of an acute painful sickle cell episode. |
| SH | Royal College of Paediatrics and Child Health | 5 | Full | 8 | 157 | Patients with moderate pain may have had analgesia at home but may not have been optimal or reasonable dose: wording needs to state '…already had reasonable analgesia before presentation'. | Thank you for your comment. This recommendation has been re-worded following GDG discussions to refer to patients who have not responded to analgesia. The GDG discussed that patients who have responded to analgesia are unlikely to present to hospital. |
| SH | RCOG | 4 | Full | 8 | 159 | The draft NICE guideline states that non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided in pregnancy and are contraindicated in the third trimester with reference to the British National Formulary. The RCOG Green-Top Guideline states that NSAIDs may be administered between 12 and 28 weeks of pregnancy. We would suggest a reference to the RCOG Guideline at this point when discussing analgesic requirements in pregnancy | Thank you for your comment. The GDG discussed the use of NSAIDS during pregnancy and agreed that prescribing should be limited using up-to-date information from the BNF. |
| SH | Napp Pharmaceutical Holdings Limited | 7 | Full | 8 | 159 | 1.1.8<br>Low doses of strong opioids have similar efficacy to high doses of weak opioids. In the case of morphine and oxycodone this allows patients to be titrated from low dose to higher doses and moved to PCA with the same molecule. This option is not available | Thank you for your comment. The evidence reviewed did not include comparisons of low doses of strong opioids with high doses of weak opioids. We understand the importance of using appropriate doses and drug types for each individual patient and recommendations 1.1.7 to 1.1.10 allow |

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| | | | | | | with all weak opioids. For continuity of care we recommend that patients on low doses of strong opioids should be allowed to continue where appropriate. | healthcare professionals to make this choice based on the patient's level of pain. The management of pain requires a continuous re-assessment of the patient's pain relief and health care professionals should make decisions to escalate or lower doses based on the recommendations set out in the guideline and up-to-date information from the BNF. |
| SH | NW London Hospitals NHS Trust | 4 | Full | 8 | 163 | Some patients may be intolerant of other opiates so Pethidine may still be needed but we agree that its use should be discouraged. | Thank you for your comment. The recommendations set out in NICE clinical guidelines do not cover all possible situations and does not replace clinical judgement. Recommendation 1.1.9 suggests that pethidine should not be routinely used for the treatment of acute painful sickle cell episodes as it is associated with high risk of fits and is not appropriate for the treatment of continuous or on-going pain (for details see section 2.1.5). The GDG acknowledged that in some circumstances pethidine may be appropriate (e.g. allergy or if it is in the patient's individualised patient care plan) but should not be routinely offered to patients. |
| SH | Napp Pharmaceutical Holdings Limited | 8 | Full | 8 | 166 | 1.1.10<br>Assess the effectiveness of pain relief……..We suggest that NICE add the following: *and record the pain scores* | Thank you for your comment. Although it is acknowledged that recording the results of observations and assessments are important, it is assumed that this will be carried out as part of routine clinical practice. |
| SH | UK Forum on | 14 | Full | 9 | 176 | PCA: suggest include recommendation that | Thank you for your comment. Although it is |

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| | Haemoglobin Disorders | | | | | the anaesthetic or other team who can set up / replace / troubleshoot pumps in progress need to be available to do so 24 / 7 if these are to be used successfully. | acknowledged that the set up and availability of staff may be important issues in the use of PCA, these are implementation issues and will not be covered in the guideline. These points will be passed onto the implementation team for their information. |
| SH | NW London Hospitals NHS Trust | 5 | Full | 9 | 176 | Consider and suggest alternatives if child/adolescent/adult is not suitable for PCA for example child <4years of age or a child/young person/adult who has cognitive impairment | Thank you for your comment. The review question for the pharmacological management of an acute painful sickle cell episode was restricted to whether PCA should be used where appropriate. It is assumed that information on suitable alternatives will be included as part of local protocols. A definition of PCA has now been added to the glossary for clarity. This also refers to examples of alternatives to PCA which may be considered for use in children and young people and adults with cognitive impairment. |
| SH | Royal College of Paediatrics and Child Health | 6 | Full | 9 | 176 | Does not mention nurse-controlled analgesia for younger children. | Thank you for your comment. The GDG discussed the use of PCA and decided that the decision to use PCA would not differ between adults and children. It was also agreed that details of its use, including when and how to use nurse controlled analgesia would be specified in local protocols. A definition of PCA has now been added to the glossary for clarity. This also refers to examples of alternatives to PCA which may |

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| | | | | | | | be considered for use in children and young people. |
| SH | NHS SICKLE CELL & THALASSAEMIA SCREENING PROGRAMME | 7 | Full | 9 | 183 | No mention is made of catheters – Patient representative has commented that high doses of opiates can "shut down" urinary system; at times infections can occur with use of catheters which should be monitored | Thank you for your comment. The GDG discussed that the side-effects of taking strong opioids are well known and that good clinical practice should include appropriate management of these symptoms. However, as the management of side effects was excluded from the scope (see appendix C), there was no specific review question assessing how they should be managed. As a result, the GDG made a consensus recommendation as it was felt that the well-known side effects should be managed as appropriate. The GDG did not consider urinary infection as a well known side effect and therefore this is not included in recommendation 1.1.14. |
| SH | Napp Pharmaceutical Holdings Limited | 9 | Full | 9 | 183 | 1.1.14<br>The recommendation given is to offer laxatives to all patients receiving strong opioids. We suggest this recommendation is expanded to all patients receiving opioids, whether strong or weak. Evidence suggests that weak opioids can constipate to a similar degree as strong opioids, e.g. The British National Formulary states that codeine is too constipating for long-term use.<br>It should also be noted that a number of patients who suffer from constipation | Thank you for your comment. The GDG discussed the side effects of opioids and this recommendation has been re-worded to refer to all opioids. The role of opioid antagonists in the management of pain was not included as part of the evidence review. However, the GDG agreed that opioid antagonists reverse the analgesic effects of opioids so are not used for pain relief. |

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| | | | | | | associated with opioid use will not adequately respond to laxatives, or will suffer from additional intolerable adverse effects as a consequence of laxative regimens.[1]. Peripherally selective opioid antagonists have become available in recent years that allow management of these patients[2] – we therefore suggest that the recommendation is amended to:<br><br>• Regular laxatives or peripheral opioid antagonists or agonist / antagonist combinations<br><br>1. Panchal SJ, Müller-Schwefe P, Wurzelmann JI. Opioid-induced bowel dysfunction: prevalence, pathophysiology and burden. Int J Clin Pract. 2007 Jul;61(7):1181-7.<br><br>2. Simpson K , Leyendecker P, Hopp M, et al. Fixed-ratio combination oxycodone/naloxone compared with oxycodone alone for the relief of opioid-induced constipation in moderate-to-severe non-cancer pain. Curr Med Res Opin 2008;24(12):3503-12. | |
| SH | NW London Hospitals | 6 | Full | 9 | 184 | Perhaps include antagonist when using strong | Thank you for your comment. The role of |

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| | NHS Trust | | | | | opioids | opioid antagonists in the management of pain was not included as part of the evidence review. However, the GDG agreed that opioid antagonists reverse the analgesic effects of opioids so are not used for pain relief |
| SH | NW London Hospitals NHS Trust | 7 | Full | 9 | 188 | Suggest clinical observations to include sedation scoring should be more regular in children who are receiving strong opioids intravenously | Thank you for your comment. Recommendation 1.1.16 which relates to the frequency of clinical assessments has been amended following GDG discussions. This recommendation now states that clinical assessments should be performed hourly for the first 6 hours (as the risk of adverse events and fluctuations may be higher in this initial period), and at least every 4 hours after this period. The GDG discussed the management of an acute painful sickle cell episode in all patients and decided that the frequency of on-going monitoring would not differ between adults and children. |
| SH | UK Forum on Haemoglobin Disorders | 11 | Full | 9 | 188 - 190 | It is suggested that observations are repeated hourly for at least the first 6 hours, including pain and sedation score. | Thank you for your comment. Recommendation 1.1.16which relates to the frequency of clinical assessments has been amended following GDG discussions. This recommendation now states that clinical assessments should be performed hourly for the first 6 hours (as the risk of adverse events may be higher in this initial period), and at least every 4 hours after this period. |
| SH | Royal College of | 7 | Full | 9 | 189 | Suggest add oxygen saturation monitoring in | Thank you for your comment. It is assumed |

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| | Paediatrics and Child Health | | | | | patients offered strong opoids. | that clinical observations will include oxygen saturations (see recommendation 1.1.5). |
| SH | UK Forum on Haemoglobin Disorders | 12 | Full | 10 | 197 | Suggest include specifically increased respiratory rate, and possible also chest wall or rib tenderness on examination | Thank you for your comment. It is assumed that increased respiratory rate is included as part of 'abnormal respiratory signs' and tenderness will be included as part of 'chest pain.' These signs and symptoms were agreed based on the evidence and the expertise of the GDG. |
| SH | UK Forum on Haemoglobin Disorders | 13 | Full | 10 | 201 | Suggest again indicates need to refer to recorded normal levels for this individual patient | Thank you for your comment. This issue was discussed at the post consultation GDG meeting and has been amended to 95%. This cut-off level was agreed based on GDG consensus and expertise and was felt to be an widely agreed clinical threshold for treatment of hypoxia in patients with an acute sickle cell episode. The GDG also agreed that baseline levels of oxygen saturation may not be available on presentation to hospital and agreed that this should not delay treatment. As a result, baseline levels are not specifically referred to in the final recommendations. |
| SH | NW London Hospitals NHS Trust | 8 | Full | 10 | 201 | <94% oxygen saturation should be interpreted in the context of previous results from the same patient. He or she may have chronically low oxygen saturations. | Thank you for your comment. This issue was discussed at the post consultation GDG and has been amended to 95%. This cut-off level was agreed based on GDG consensus and expertise and was felt to be a widely agreed clinical threshold for treatment of hypoxia in patients with an acute sickle cell episode. |

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| | | | | | | | The GDG also agreed that baseline levels of oxygen saturation may not be available on presentation to hospital and agreed that this should not delay treatment. As a result, baseline levels are not specifically referred to in the final recommendations. |
| SH | The Sickle Cell Society | 6 | Full | 10 | 203-210 | Other complication such as Dehydration should be taken in to consideration | Thank you for your comment. The clinical issues that will be covered by the guideline are set out in the scope and include signs and symptoms of acute complications (see appendix C). Although dehydration is an important issue, the evidence reviewed did not show that it was a complication specific to an acute painful sickle cell<br>The GDG agreed it was a general issue that should be considered as part of general medical practice and care |
| SH | NHS SICKLE CELL & THALASSAEMIA SCREENING PROGRAMME | 8 | Full | 10 | 214 | Patient representative has commented that the non-pharmacological interventions need much more conclusive research, both in hospital and community settings; these interventions may well tie in with the patient's own self-coping mechanisms. These interventions may also influence admission frequency, length of stay and thus cost implications. | Thank you for your comment. The GDG discussed the use of non-pharmacological interventions and agreed that there is a lack of evidence (see section 2.2.4). Research recommendations on the use of psychological and non-pharmacological interventions have also been made (see appendix B). |
| SH | NHS SICKLE CELL & THALASSAEMIA SCREENING PROGRAMME | 9 | Full | 10 | 214 | No mention of need for hydration – it may be difficult for patient to access water/drinks, particularly if not accompanied by a carer. | Thank you for your comment. The clinical issues that will be covered by the guideline are set out in the scope and include signs and symptoms of acute complications (see |

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| | | | | | | | appendix C). Although dehydration is an important issue, the evidence reviewed did not show that it was a complication specific to an acute painful sickle cell<br>The GDG agreed it was a general issue that should be considered as part of general medical practice and care |
| SH | NHS SICKLE CELL & THALASSAEMIA SCREENING PROGRAMME | 10 | Full | 10 | 214 | No mention of food – Patient representative commented that if the medication is not digested properly it can be less effective. Again it may be difficult for patient to access food, particularly if not accompanied by a carer. | Thank you for your comment. The clinical issues that will be covered by the guideline are set out in the scope and do not include food (see appendix C). Although access to food is an important issue, it was not included as part of the evidence base of any of the review questions, therefore specific recommendations have not been made. However, the GDG recognised that those involved in medication administration/advice would be aware of when food would be of benefit. |
| SH | UK Forum on Haemoglobin Disorders | 16 | Full | 10 | 220 - 222 | Re regular training for healthcare professionals – suggest specify 'yearly training with minimum CPD requirement for doctors and at least a half-day training for nurses'. | Thank you for your comment. Review question 4 aimed to address the optimal settings and skills required by healthcare professionals. The GDG discussed the issue of training and felt that this would differ according to settings and need. As a result a general recommendation setting out important topics that should be covered by all training programmes was made. |
| SH | British Psychological Society | 2 | Full | 10 & 76 | 217 & 1093 | Recommendations for non-pharmacological interventions 1.1.21 states '*Encourage the* | Thank you for your comment. This recommendation was discussed at the post- |

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| | | | | | | *patient to use their own coping mechanisms for dealing with acute pain'*. The BPS recommends amending this to read '*Encourage patients to use coping strategies that they have previously found effective to manage their own pain'.* In addition, we recommend adding *'providing these are not harmful*' to the end of the sentence, in order to highlight the fact that not all patients' attempts at coping are ultimately helpful.<br><br>While we agree it is important to recognise that many patients have learnt helpful strategies to cope with acute pain and that encouraging the use of these is empowering for the patient, we believe it is also important to note that some attempts to cope are not always helpful.<br><br>For example, clinical experience with patients with SCD in hospital shows that, in order to attempt to cope, some patients shout, sing loudly, scream or move around a lot for prolonged periods whilst in acute pain. Although this may provide them with short-term relief due to the release of tension and the diverting of their attention away from their pain, such behaviours can prove disturbing for other patients (leading, on occasion, to arguments), interfere with | consultation GDG meeting and has been re-worded to include an example of a coping technique that is not harmful. It is assumed that harmful behaviours will be accounted for as part of general hospital policies and are not referred to in the final recommendations. |

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| | | | | | | communication with hospital staff, put the patient at risk of injury, and may lead to inappropriate referrals to hospital psychiatric services. Such consequences may be stressful and can exacerbate the pain experience.<br><br>In other cases, patients may attempt to cope by fully adopting the sick role and asking for medical interventions which are not in their best interests long-term (such as requesting intravenous fluids, which requires cannulation and may therefore result in difficult access to veins in the future.<br><br>In the above examples, the patient would benefit from a discussion with health care professionals (including a psychologist if available) in order to consider more helpful coping mechanisms.<br><br>The potential for some coping mechanisms to be harmful is alluded to on page 74, line 1089, in the 'Evidence to recommendations' table, where it states that '*non-pharmacological treatments…. that are not likely to cause harm should be encouraged….*'. However, the BPS considers it important that such references should also be included in the summary statement recommendation (page 10 line 217, and page 76, line 1093), which is | |

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| | | | | | | what most health care professionals are likely to read when looking at the NICE guidance. | |
| SH | Napp Pharmaceutical Holdings Limited | 10 | Full | 11 | 223 | 1.1.22<br>Pain monitoring and relief<br>This could be expanded to say: Pain monitoring, use of assessment tools, recording of scores and use of pain relief. | Thank you for your comment. This recommendation was kept general in order to avoid making prescriptive lists which may miss important issues. |
| SH | NHS SICKLE CELL & THALASSAEMIA SCREENING PROGRAMME | 11 | Full | 11 | 225 | Also very pleased to see that staff training should include attitudes towards and preconceptions about patients presenting with an acute painful sickle cell episode. | Thank you for your comment |
| SH | NHS SICKLE CELL & THALASSAEMIA SCREENING PROGRAMME | 12 | Full | 11 | 227 | Patient representative has stressed that day care facilities should be used wherever possible. | Thank you for your comment |
| SH | The Royal College of Midwives (RCM) | 3 | Full | 11 | 236 | 1.1.26<br>It is important that pregnant women seek advice from the haematology as well as the obstetric team. There should be more emphasis on developing and utilising a clinical pathway for pregnant women with SC disease. The plans - in case of a crisis - need to be clearly documented in the notes emphasising that there should be support from the haematology team. This needs to have been discussed fully with | Thank you for your comment. It is assumed that haematology input will be used for all patients presenting with an acute painful sickle cell episode as haematology are considered to provide 'specialist support' (see recommendation 1.1.24). Therefore, pregnant women may require additional advice from obstetrics. The GDG discussed the management of pregnant women presenting with an acute painful sickle cell episode and agreed that their management would not differ compared with woman who are not pregnant (aside from the use of |

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| | | | | | | the woman and her family. | drugs, which are accounted for in the recommendations). |
| SH | NHS SICKLE CELL & THALASSAEMIA SCREENING PROGRAMME | 13 | Full | 11 | 238 | No mention of filling in patient records to record details of episode; details should also be entered on to the National Haemoglobinopathy Register. | Thank you for your comment. Although it is acknowledged that recording the results of observations and assessments are important, it is assumed that the completion of patient records will be carried out as part of routine clinical practice.<br><br>The guideline scope is focused on treating acute painful episodes and therefore we consider entering details onto the National Haemoglobinopathy Register a service deliver issue and therefore outside the scope of the guideline. |
| SH | The Sickle Cell Society | 7 | Full | 11 | 239-245 | No clear pathway reference in teams of aftercare<br>Given information to the carer and patient is great.<br>Community support should be included. Eg: Voluntary organisation, Community nurse, health visitor and social workers. | Thank you for your comment. Although management and support issues within the community are important issues, the scope of this guideline is restricted to in-hospital settings and specialist centres (see appendix C). |
| SH | Royal College of Paediatrics and Child Health | 8 | Full | 12-69 | | In evidence tables, many studies on children included dosages and these are variable. Does the guideline recommend dosages of drugs especially for opioid based on local guidelines? | Thank you for your comment. For all dosing information, healthcare professionals are advised to refer to up-to-date information from the BNF for both adults and children (see drug recommendations, page 4). |
| SH | British Psychological Society | 3 | Full | 70 | 1050 | The non-pharmacological management evidence review section specifically names 'distraction techniques' but not CBT, although | Thank you for your comment. Section 2.2.2 provides examples of some non-pharmacological interventions that may be |

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| | | | | | | CBT is mentioned later on page 75 ('… *although there are no studies assessing the use of CBT in an inpatient setting, there is evidence of beneficial effects associated with its use in patients with SCD in outpatient settings'*). The Guideline Development Group are reported as having considered that a recommendation supporting the provision of 'such interventions' is not supported by the evidence, and this is understandable as the evidence stands in terms of CBT for SCD acute pain in inpatient settings.<br><br>However, the BPS believes it is important that CBT is considered in further research as potentially useful in the management of acute pain as, in addition to 'distraction techniques'. This is because, CBT addresses how cognitions and behaviours can affect the pain experience, emphasises the role that patients can play in controlling their own pain, includes coping skills training such as relaxation, assertiveness and communication, and cognitive restructuring to manage negative pain-related thoughts (Keefe, 1996).<br><br>Furthermore, as mentioned on page 75, CBT has been shown to be effective in the management of SCD pain in the community (Thomas *et al*., 1999) and qualitative feedback | used in the management of an acute painful sickle cell episode in hospital. This list is not exhaustive as there are a wide range of interventions that may be included. The GDG discussed the importance of non-pharmacological interventions including CBT. The GDG made a specific research recommendation to assess the use of psychological interventions and standard care compared with standard care alone (see appendix B). |

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| | | | | | | from patients indicates that this intervention can have a positive impact on their ability to cope with acute sickle cell crisis and pain. In addition, cognitive coping skills training has also been shown to reduce pain reports of SCD patients during experimentally induced pain simulations (Gil *et al*., 1996).<br><br>*References:*<br><br>Gil, K.M., Wilson, J.J, Edens, JL, Webster, D, A., Abrams, M.A., Orringer, E. et al. (1996). Effects of Cognitive Coping Skills Training on Coping Strategies and Experimental Pain Sensitivity in African American Adults with Sickle Cell Disease. *Health Psychology*, *15(1)*, 3-10.<br><br>Keefe, F. J. (1996). Cognitive Behavioral Therapy for Managing Pain. *The Clinical Psychologist*, *49(3*), 4-5.<br><br>Thomas, V.J., Dixon, A.L. & Milligan, P. (1999). Cognitive-Behaviour Therapy for the Management of Sickle Cell Disease Pain: An evaluation of a community-based intervention. *British Journal of Health Psychology*, *4*, 209-229. | |
| SH | Royal College of Paediatrics and Child Health | 9 | Full | 76 | 1093 | Statement regarding "using own coping mechanism" needs expanding for children and families as they need specific guidance | Thank you for your comment. The GDG discussed the non-pharmacological management of an acute painful sickle cell |

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| | | | | | | regarding strategies and alternative methods for dealing with stress of pain. | episode and agreed that specific information could not be provided here due to the lack of evidence. The recommendation is not about educating patients on alternative methods of dealing with the stress of pain but encouraging those patients who are already aware of these alternatives and already have their own coping mechanisms in place for these times. The GDG agreed that this would not differ for children compared with adults. |
| SH | British Psychological Society | 4 | Full | 76 | 1096 | Research recommendation B3 states '*For patients with an acute painful sickle cell episode, are psychological interventions, in conjunction with standard care, effective in providing pain relief?*'. There is clearly a need for more research into psychological interventions for managing acute pain for patients with SCD in hospital and the BPS recommends that this should not only include traditional CBT, but also other psychological approaches such as hypnosis, mindfulness-based CBT, and acceptance and commitment therapy (ACT), given evidence for the effectiveness of these approaches in other relevant settings (see, for example, Cyna *et al*., 2004; Montgomery *et al*., 2000; Rosenswieg *et al*., 2010; and Veehof *et al*., 2011). | Thank you for your comment. |

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| | | | | | | *References:*<br><br>Cyna, A.M., McAuliffe, G.L. & Andrew, M.I. (2004). Hypnosis for Pain Relief in Labour and Childbirth: A systematic review. *British Journal of Anaesthesia*, *93(4)*, 505-511.<br><br>Montgomery, G.H., DuHamel, K.N. & Redd, W.H. (2000). A Meta-Analysis of Hypnotically Induced Analgesia: How effective is hypnosis? *International Journal of Clinical and Experimental Hypnosis*, *48(2)*, 138-153.<br><br>Rosenzweig, S., Greeson, J., Reibel, D., Green, J., Jasser, S.A. & Beasley, D. (2010). Mindfulness-Based Stress Reduction for Chronic Pain Conditions: Variation in treatment outcomes and role of home meditation practice. *Journal of Psychosomatic Research*, *68(1)*, 29-36.<br><br>Veehof, M.M., Oskam, M.-J., Schreurs, K.M.G. & Bohlmeijer, E.T. (2011). Acceptance-Based Interventions for the Treatment of Chronic Pain: A systematic review and meta-analysis. *Pain*, *152*, 533-542. | |
| SH | NW London Hospitals NHS Trust | 9 | Full | 107 | 1377 | <94% oxygen saturation should be interpreted in the context of previous results from the same patient. He or she may have chronically low oxygen saturations. | Thank you for your comment. . This issue was discussed at the post consultation GDG and has been amended to 95%. This cut-off level was agreed based on GDG consensus and expertise and was felt to be a widely agreed clinical threshold for treatment of hypoxia in |

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| | | | | | | | patients with an acute sickle cell episode. The GDG also agreed that baseline levels of oxygen saturation may not be available on presentation to hospital and agreed that this should not delay treatment. As a result, baseline levels are not specifically referred to in the final recommendations. |
| SH | RCOG | 5 | Full | 124 | 1609 | The RCOG Green-Top Guideline states that mild sickle cell crises can be managed in the community with early recourse to secondary care referral and therefore daycare management of sickle cell crises may be appropriate in pregnancy. | Thank you for your comment. Though community management of crisis is outside the scope, the results of our analysis suggest that treating acute painful sickle episodes in dedicated sickle cell daycare centres would be associated with cost savings, primarily as result of a reduction in the need for hospital ward admission – this appears to be in keeping with RCOG guideline. |
| SH | RCOG | 6 | Full | 126 | 1632 | The Green-Top Guideline agrees with the draft NICE guideline in stating that the management of sickle cell crises in pregnant women should follow the national recommendations for non-pregnant individuals given the lack of evidence of any comparison of the non-pregnant population to the pregnant population. | Thank you for your comment. |
| SH | Royal College of Paediatrics and Child Health | 10 | Full | 127 | 1637 | Need to specify setting for children and young people with recommended facilities and mental health professionals to reduce stress and anxiety. | Thank you for your comment. Recommendation 1.1.25 addresses the issue of ensuring that children are treated in an age-appropriate setting. This was a general recommendation as the GDG discussed that children should always be treated within a |

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| | | | | | | | pediatric setting, regardless of what condition they are being treated for. |
| SH | Royal College of Paediatrics and Child Health | 11 | Full | 144 | 1757 | "clinical and psychological support" needs clarifying and specifying for children and young people. | Thank you for your comment. This section relates to evidence statements and are summaries of the evidence reviewed. The included studies for the review question on patient information and support was largely based on adult populations (see section 2.5.2). |
| SH | NHS Direct | 1 | Full | General | | NHS Direct have considered the content and have no comments as part of the consultation. | Thank you for your comment. |
| SH | The Royal College of Midwives (RCM) | 1 | Full | General | | As documented in the evidence, there is a significant need for on-going education in this area. The RCM would suggest that that there should be a clear recommendation about this. | Thank you for your comment. The GDG discussed the issue of training and felt that this would differ according to settings and clinical need. As a result a general recommendation setting out important topics that should be covered by all training programmes was included (see 1.1.22). |
| SH | The Royal College of Midwives (RCM) | 2 | Full | General | | The guidelines needs to include advice to GPs about what should be done in the postnatal period as this is a period which may trigger a crisis and Sickle Cell Disease (SCD) sufferers are significantly disadvantaged. GPs are often not fully versed in this area.<br><br>This can be when SCD sufferers may develop dependence on the strong | Thank you for your comment. Although we understand the important of preventing an acute painful sickle cell episode in primary care settings, this is outside the scope of the guideline (see appendix C). |

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| | | | | | | analgesia that is commonly distributed. | |
| SH | The Royal College of Midwives (RCM) | 4 | Full | General | | There are obstetricians who are knowledgeable in SC disease and these women tend to book with them if they can. However, these obstetricians are predominantly based in London. It is important to include advice about developing and sharing knowledge and expertise in caring for pregnant women. | Thank you for your comment. The guideline aims to provide recommendations on the management of an acute sickle cell episode, not on managing pregnancy in women with sickle cell. The GDG discussed the management of pregnant women presenting with an acute painful sickle cell episode and agreed that their management would not differ compared with woman who are not pregnant (aside from the use of drugs, and advice from an obstetrics team). |
| SH | The Royal College of Midwives (RCM) | 5 | Full | General | | There should be a clear recommendation that hospitals desist from the practice of admitting these patients on to cancer wards. | Thank you for your comment. Recommendations 1.1.22 to 1.1.26 relate to the optimal settings to treat patients presenting to hospital with an acute painful sickle cell episode. |
| SH | The Royal College of Midwives (RCM) | 6 | Full | General | | There is too much emphasis on acute management on sickle treatment and insufficient stress on community engagement or community treatment, which is so important to the management of this disease. There are specialist nurses and counsellors such as | Thank you for your comment. The management of an acute painful sickle cell episode within community settings is outside the scope of this guideline (see appendix C). |

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| | | | | | | Roald Dahl Specialist Nurses and their contribution in community settings | |
| SH | British Psychological Society | *1* | Full | General | | The BPS considers the draft guideline to have a number of strengths, as outlined below:<br><br>The guidelines take account of some relevant psychological factors, including consideration of some non-pharmacological interventions and support needs of patients. Common problems encountered by patients with sickle cell disease (SCD) in hospital, such as delays in receiving analgesia and stigmatising patients as drug seeking, are noted. This is important since such factors can cause emotional distress and thus exacerbate the patient's pain experience and undermine relationships with health care professionals. The BPS therefore welcomes the recommendation that healthcare professionals' training should include attitudes towards, and preconceptions about, patients who present with an acute painful sickle cell episode. We also welcome the recommendation that, during assessment, patients (and/or their carers) should be regarded as expert in their condition, and that discussion should take place regarding any concerns about their current painful episode as well as any | Thank you for your comment. |

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| | | | | | | psychological and/or social support they may need.<br><br>It is a further strength of the draft guideline that it refers to evidence of the beneficial effects of cognitive behavioural therapy (CBT) with patients with SCD in outpatient settings and states that patients should be encouraged to use ideas learnt in such settings.<br><br>The BPS welcomes the inclusion, within the research recommendations, of considering if psychological interventions, in conjunction with standard care, are effective in providing pain relief for patients with acute painful sickle cell episodes.<br><br>The BPS also welcomes the inclusion of a reference to the related NICE guidance on depression in adults with a chronic physical health problem (NICE, 2009).<br><br>*Reference:*<br><br>NICE (2009). Depression in Adults with a Chronic Physical Health Problem. NICE clinical guideline 91. www.nice.org.uk/guidance/cg91. Accessed 1 March 2012. | |

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| SH | NW London Hospitals NHS Trust | 1 | Full | General | | The summary of recommendations is sensible and in line with our current practice.<br>It is a comprehensive review with critical evaluation of the evidence for the recommendations. It is impressive and looks very useful for not just current care but also future research projects. | Thank you for your comment. |
| SH | NW London Hospitals NHS Trust | 2 | Full | General | | Perhaps include the goals for effective pain management in an episode of acute sickle pain in the guidelines introduction | Thank you for your comment. The introduction section has been amended to include the goals of effective pain management. |
| SH | RCOG | 1 | Full | General | | We would like to commend NICE on an excellent and very thorough guideline which we have read alongside RCOG Green-Top Guideline 61 – Management of Sickle Cell Disease in Pregnancy | Thank you for your comment. |
| SH | NHS SICKLE CELL & THALASSAEMIA SCREENING PROGRAMME | 1 | Full | General | | The Sickle Cell & Thalassaemia (SC&T) Screening Programme strongly supports issuance of NICE clinical guidelines on sickle cell acute painful episode. The guidance rightly recognises that painful episodes can form a major part of many sickle cell patients' lives and that these patients deserve optimum treatment and care, with access to specialised care when appropriate, wherever and whenever a painful episode occurs. The NCEPOD report highlighted failures of care in painful crises and poor monitoring of patients with high doses of opiates leading in some cases to avoidable deaths and these | Thank you for your comment. |

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| | | | | | | guidelines should improve clinical management. We hope that this guidance will be actively implemented and audits of any deaths of sickle cell disease carefully reviewed internally including a review of the approach to management of painful crises and opiates. | |
| SH | NHS SICKLE CELL & THALASSAEMIA SCREENING PROGRAMME | 2 | Full | General | | The SC&T Screening Programme has only commented on general aspects of the draft guidance as detailed aspects of clinical care are outside the remit of the Programme. Comments have also be included on behalf of an expert patient representative. | Thank you for your comment. |
| SH | NHS SICKLE CELL & THALASSAEMIA SCREENING PROGRAMME | 14 | Full | General | 238 | As we commented on the draft scope, we feel that:-<br>- These guidelines should be extended to community settings as many patients may prefer to deal with sickle cell acute painful episodes locally and/or at home; this may be especially important for parents who may find it difficult to rush off to hospital, particularly at night;<br>- These guidelines should recognise that a painful crisis may be a single episode in NHS terms, but it may be a major part of the patient's life and thus future reviews/follow up and plans to reduce frequency/severity of painful crises are very important for patients. | Thank you for your comment. Although we understand the importance of managing an acute painful sickle cell episode within community settings and prevention of future episodes, this issue is outside the scope of this guideline (see appendix C). |
| SH | NHS SICKLE CELL & | 15 | Full | Gener | | The Guidelines as drafted appear to assume | Thank you for your comment. The guideline |

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| | THALASSAEMIA SCREENING PROGRAMME | | | al | | that the patient is not known to the hospital. Where the patient is known, very possibly through frequent admissions for sickle cell acute painful episodes, patient preferences and needs should routinely be recorded and easily and widely accessible to staff who require such information such as A&E staff. | aims to provide guidance for hospitals and settings that provide regular management for patients with sickle cell disease, but also for hospitals in low prevalence areas, where patients may not be known as healthcare professionals in these areas may lack experience in the management of an acute sickle cell episode. |
| SH | The Royal College of Pathologists (RCPath) and The British Society for Haematology (BSH) | 1 | Full | General | | This is a thorough examination of the available evidence relating to the management of sickle cell painful crisis. Sadly it highlights the paucity of high quality evidence and particularly the lack of appropriate trials of analgesia. In this respect sickle cell disease lags behind other areas. No attempt has been made to examine results obtained in other areas that may be of use to those caring for patients with sickle cell disease.<br><br>The summary guidance (which is what most individuals will read) offers sound general advice, however as a consequence of the poor quality evidence this offers little more than can be found in many texts on medical emergencies. For doctors with limited experience in low prevalence areas this guidance is unlikely to meet the objective of improving or unifying quality of care. Although fully cognisant of the reasons why | Thank you for your comments. There are problems associated with using evidence from different disease conditions in terms of applicability, therefore studies that did not meet the inclusion criteria were not considered (see appendix D). However, the recommendations were also produced using the expertise and consensus of the GDG members.<br><br>The GDG considered hospitals in low prevalence areas when making recommendations. The guideline aims to provide guidance for hospitals and settings that provide regular management for patients with sickle cell disease, but also for hospitals in low prevalence areas, where patients may not be known. Because the group were working within a specified scope and as there was a lack of evidence overall, |

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| | | | | | | the guidance is written in this manner I feel it needs to offer more specific advice specifically in relation to analgesic choice.<br><br>I agree with the guideline group in its support of the role of oral analgesia, use of day case models of care and stance taken on pethidine use. Following the NCEPOD report this guidance should attempt to strengthen the links between pain services and sickle cell care. There is no mention of the need to taper analgesia, failure to do this may precipitate more pain in certain patients.<br><br>Guidelines for audit should be included. | the GDG made general recommendations for some of the review questions. However it is assumed that local protocols will be in place to provide detailed information that are in-line with the guideline recommendations.<br><br>For analgesic choice, it is assumed that healthcare professionals will use the recommendations together with clinical judgement and patient's responses to assessment and reassessment of pain to escalate and step-down pharmacological treatment as appropriate. The GDG agreed that the use of strong opioids on presentation to hospital should not be delayed and this is reflected in recommendations 1.1.4, 1.1.7 and 1.1.10<br><br>Audit tools will accompany the full guideline when it is published |
| SH | The Sickle Cell Society | 1 | Full | General | | The Sickle Cell Society is please about the guideline on sickle cell acute painful episode: management of an acute painful sickle cell episode in hospital. As a patient, focus organisation. We want only the best for our patients. The guidelines are very comprehensive. | Thank you for your comment. |
| SH | The Sickle Cell Society | 2 | Full | General | | The Society has commented on the general; aspects of the consultation. | Thank you for your comment. |
| SH | The Sickle Cell Society | 8 | Full | Gener | | We hope that all hospitals will adapt these | Thank you for your comment. |

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| | | | | al | | guidelines and ensure they are protocol | |
| SH | The Sickle Cell Society | 9 | Full | General | | G.P. should be more aware of these guidelines so that they can be more engaged with patient care. | Thank you for your comment. We have passed this onto our Implementation and Comms Directorate |
| SH | The Sickle Cell Society | 10 | Full | General | | The Sickle Cell Society will ensures that patients and carers are aware of these new guidelines | Thank you for your comment. |
| SH | Royal College of Paediatrics and Child Health | 1 | Full | General | | The document should mention use of intranasal diamorphine (and appraise the literature). The half-hour timescale to start pain relief is made much more realisable if intranasal diamorphine can be used as first treatment and then proceed to IV cannulation and intravenous on-going treatment. | Thank you for your comment. No evidence was identified that assessed the use of intra nasal diamorphine in the management of an acute painful sickle cell episode and met the inclusion criteria. |
| SH | Royal College of Paediatrics and Child Health | 2 | Full | General | | We could find no mention of the use of incentive spirometry during a painful crisis as a measure to protect against the development of acute chest syndrome. There is some evidence that this is helpful (eg J Pediatr Hematol Oncol. 2011 Aug;33(6):415-20) and it is widely used.<br><br>We could also find no discussion on the use of antibiotics in children with respiratory problems (eg hypoxemia) which is also widely recommended (particularly in children who are functionally asplenic).<br><br>There are no recommendations on the use of | Thank you for your comments. The prevention and management of acute complications is outside the scope of this guideline (see appendix C).<br><br>Thank you, the prevention and management of acute complications is outside the scope of this guideline (see appendix C). |

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| | | | | | | intravenous hydration (again widely practiced)<br><br>There are no recommendations on the indications for transfusion or exchange transfusion in children who have persistent hypoxemia.<br><br>Although the evidence for use of nitric oxide is considered, it does not lead to any guidance. | No evidence was identified to assess the effectiveness of IV hydration in the management of acute painful sickle cell episodes.<br>No evidence was identified to assess the effectiveness of transfusion in the management of acute painful sickle cell episodes.<br><br>The GDG did not feel that there was strong evidence of a beneficial effect to support a recommendation about nitric oxide. |
| SH | Royal College of Paediatrics and Child Health | 3 | Full | General | | General lack of detail regarding established mental health supports and treatments for pain treatment in children and young people in sickle cell crises. Need for detailing of mental health antecedents to pain experience and relief in children. Identify paediatric liaison services. | Thank you for your comment. There is a review question covering patient's information and support needs. However, this question did not include use of psychosocial interventions for the management of an acute painful sickle cell episode. The review question assessing the use of non-pharmacological interventions to manage an acute episode did not identify any evidence relating to psychosocial interventions in hospital. As a result, general recommendations have been made and a research recommendation has been made in appendix B. |
| SH | Napp Pharmaceutical Holdings Limited | 1 | Full | General | | Napp supports the development of the guideline and is grateful for the opportunity to comment on the draft document. | Thank you for your comment. |
| SH | Napp Pharmaceutical | 3 | Full | Gener | | Napp suggests that a recommendation should | Thank you for your comment. The |

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| | Holdings Limited | | | al | | be given for those patients who are unable to tolerate analgesia with morphine during acute Sickle Cell crisis.<br><br>Not all patients respond in the same way to all opioids and for those who may not have adequate pain relief or have intolerable side-effects alternatives are needed.<br><br>Riley[1] has demonstrated that 25% of patients did not respond to morphine and of these about 78% responded to oxycodone.<br>1. http://www.ncbi.nlm.nih.gov/pubmed/15952009 | recommendations set out in NICE clinical guidelines do not cover all possible situations and does not replace clinical judgement. It is assumed that healthcare professionals will use clinical judgement to use alternative analgesia when patients present with intolerance and other issues. More over no recommendation has been made on specific opioids. |
| SH | Napp Pharmaceutical Holdings Limited | 4 | Full | General & 65 | | There appears to be little high-grade evidence for the use of opioids in Sickle Cell painful crises. Indeed, the guideline briefly mentions that there are a number of evidence gaps for treatments such as oxycodone and other analgesics commonly used in clinical practice.<br><br>We would like to present the following case studies and audits as examples of the use of opioids including oxycodone.<br><br>**1. Shaiova L, Wallenstein D. Outpatient management of sickle cell pain with chronic opioid pharmacotherapy. J Natl Med Assoc** | Thank you for your comments. However the listed references do not meet the inclusion criteria for the included review question (see appendix D). |

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| | | | | | | **2004;96(7)984-6.**<br>We report our experience of providing chronic opioid pharmacotherapy on an outpatient basis to selected patients with frequent episodes of moderate-to-severe pain from sickle cell disease (SCD). Three cases illustrate our clinical experience in approximately 40 patients with sickle cell pain. Patients were seen at our sickle cell pain clinic at Beth Israel Hospital once each month for a three-hour visit. Visits included group music therapy and individual medical care, including comprehensive blood work and scheduling of medical tests when appropriate. Between visits, the pain and palliative care physicians followed patients on an as-needed basis. The SCD pain opioid pharmacotherapy protocol was modeled on a regimen used to treat malignant pain-typically a long-acting opioid in combination with a short-acting opioid, such as oral transmucosal fentanyl citrate (OTFC; Actiq) for breakthrough pain (BTP). Emergency department (ED) visits and hospital admissions were dramatically reduced in the three patients whose pain was managed by adapting the cancer pain model. During the year before their first visit to our pain clinic, the patients each had between six and 18 ED visits, which resulted in six- to 13 hospital admissions amounting to 32-182 | |

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| | | | | | | inpatient days per patient. Each of the patients was prescribed a long-acting opioid (methadone, control-release oxycodone, or transdermal fentanyl) with a short-acting opioid for BTP from crises (oral transmucosal fentanyl citrate for two patients; short-acting oxycodone for one patient). Pain was well controlled. For each patient, hospital admissions were reduced to < or = 1 visit per year. These reduced levels of ED visits and hospital admissions have remained constant for more than three years.<br><br>**2. Johnson L. Management of sickle cell disease. Journal of Pain & Palliative Care Pharmacotherapy 2008;22(1):51-4.**<br>Assessment of pain in sickle cell disease is briefly described and a case of a 32-year-old Nigerian woman who had sickle cell pain is presented. The management and outcomes of her care in the UK are described and commentaries are presented on this case of sickle cell pain by specialists from Spain and The Netherlands.<br><br>**3. Ballas SK, Barton F, Castro O et al. Narcotic analgesic use among adult patients with sickle cell anaemia. Blood 1995;86:S642a**<br><br>**4. Silbergleit R, Jancis MO, McNamara RM.** | |

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| | | | | | | **Management of sickle cell pain crisis in the emergency department at teaching hospitals. J Emerg Med. 1999 Jul-Aug;17(4):625-30.** | |
| SH | UK Forum on Haemoglobin Disorders | 1 | Full | General | | This is a most comprehensive review of available evidence to guide treatment of acute sickle pain presentations and some of their complications, in a hospital setting. The immense amount of work which must have gone into such a detailed analysis and consideration of all available material is acknowledged.<br>There is, however, a sense that the document will speak most comfortably to those already well versed with treating these conditions, rather than those who might refer to these guidelines because they are unfamiliar with the problem in daily practice. For example, the advice to 'refer to local guidelines or policies' in regard to choosing analgesic type and route, and to 'be aware of the possibility of aplastic or splenic sequestration crisis' without indicating what might alert the clinician to these possibilities may not be helpful. Those referring to the guidance might reasonably expect to be given specific guidance as to approved or suitable types / routes / for analgesia, including dose ranges for those who are opiate naïve and for more | Thank you for your comments. The guideline aims to provide guidance for hospitals and settings that provide regular management for patients with sickle cell disease, but also for hospitals in low prevalence areas, where patients may not be known. Because the group were working within a specified scope and as there was a lack of evidence overall, the GDG made general recommendations for some of the review questions. However it is assumed that local protocols will be in place to provide detailed information that are in-line with the current recommendations. |

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| | | | | | | regular users. Possible warning signs for the other acute complications would be useful also.<br>If such detailed guidance for the 'less initiated' is not to be included, it would perhaps be worth including a note in any introduction that the document is not intended to offer practical guidance for management of the acute presentation. | |
| SH | UK Forum on Haemoglobin Disorders | 2 | Full | General | | In the absence of such specific clinical guidance, reference to local protocols should stress the importance of functioning Clinical Networks, so that all local protocols are shared with, or at least approved by, a Specialist Centre team with which all treating hospitals should have a direct and formalised link. The need for agreed indications for consultation with the Specialist Centre about a patient during an acute presentation, and / or immediate transfer to the Specialist Centre should also be included. | Thank you for your comment.The use of networked links is outside the scope of this guideline (see appendix C). Some recommendations have been provided to ensure that patients are treated within optimal settings and by healthcare professionals with the appropriate skills (see recommendations 1.1.22 to 1.1.26). Specifically, recommendation 1.1.24 suggests that all healthcare professionals within emergency departments should have access to specialist support. |
| SH | UK Forum on Haemoglobin Disorders | 3 | Full | General | | As expressed in an earlier stage consultation, we regret that the opportunity was not taken to include appropriate management of pain crises at home, and also descriptions of what features should prompt patients / families to seek hospital assessment rather than attempt to manage at home [associated fever, chest pain, breathing difficulty, limb weakness, etc]. The reference to Day Care management, | Thank you for your comment. Although we understand that the management of an acute painful sickle cell episode in the community is an important issue, this is outside the scope of the current guideline (see appendix C). |

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| | | | | | | however, is welcomed. | |
| SH | UK Forum on Haemoglobin Disorders | 4 | Full | General | | It is suggested that there might usefully be some description of the evolution of the painful crisis, and need to mirror this with immediate analgesia, background and breakthrough analgesia, and withdrawal of opiates as the pain crisis resolves. It is acknowledged that there is little published evidence on how to manage a pain crisis, but a large literature on acute pain management in other settings which could be referenced. | Thank you for your comment. The introduction section of the guideline has been amended to include some additional aspects of the evolution of the painful episode and the goals of pain management. In addition, following GDG discussion a further recommendation has been added to the guideline to address the step down of pharmacological treatment. |
| SH | UK Forum on Haemoglobin Disorders | 5 | Full | General | | The recommendations for research and development issues to be addressed are most useful. It is hoped these will be taken up to inform future research plans, in order to further the evidence we have on which to base clinical management of these patients. | Thank you for your comment. |
| SH | RCGP | 1 | Full | General | | My main concern is that the acute sickle episode is seen to occur and be managed entirely within the hospital setting. There is a comment 1.1.27 about discharge planning which advised that how to obtain specialist advice and additional medication. This is not discussed further. What are the resources available in the community and within what time frame can they be mobilised. How do patients get new medication from GPs, how long does it take and what is the mechanism? Similarly with community pharmacists and stock levels and opening hours. This may not | Thank you for your comment. Management of an acute painful sickle cell episode in the community and within primary care is outside the scope of this guideline (see appendix C). |

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| | | | | | | be for pain killer but for more mundane post opiate laxatives.<br>What does the out of hours centre know about the patient? There is a mention made of withdrawal symptoms but these may continue outside the hospital.<br>How is the community staff to be notified of discharge? | |
| SH | British Pain Society | 1 | Full | General | | We welcome the guidance as a pragmatic approach to the management of an acute painful sickle cell episode.<br>We welcome the advice not to use pethidine as an analgesic | Thank you for your comment. |
| SH | British Pain Society | 5 | Full | General | | You have not mentioned specific opioid analgesics or dose ranges. We recommend that the prescriber is careful to refer to equivalent analgesic dosing information when switching opioids. | Thank you for your comment. For all dosing information, healthcare professionals are advised to refer to up-to-date information from the BNF for (see drug recommendations, page 4). |
| SH | British Pain Society | 6 | Full | General | | Pain specialists and hospital based pain teams can also supply useful advice for pain that is difficult to control | Thank you for your comment. Pain specialists are included as healthcare professionals who provide specialist knowledge. |
| SH | Leeds Teaching Hospital | 1 | Full | General | | We welcome the recommendations set out in this guideline.<br><br>An established acute painful episode may last 5-7 days and during that time, there is a "chronic" element to the pain. Some hospitals have found long acting as well as short acting strong oral opiates to be helpful in an established crisis. Although there is | Thank you for your comment. There was no specific review question addressing short acting opioids compared with longer acting opioids therefore no specific recommendations were made. |

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| | | | | | | little published evidence, an expert consensus view on long acting opiates might be helpful. | |
| SH | Department of Health | 1 | Full | General | | The importance of networked working links and leadership of designated specialist haemoglobinopathy centres needs to be strengthened beyond the care in emergency departments. Where SCD patients are being treated as an emergency, admitted patient or outpatient all care needs to be in line with local protocol and policy which has been agreed by and has the support of a designated specialist centre. These protocols should include clear transfer protocols to the specialist centre when required and communication with primary care and community service at discharge. | Thank you for your comment. The use of networked links and transfer to primary or community care is outside the scope of this guideline (see appendix C). Some recommendations have been provided to ensure that patients are treated within optimal settings and by healthcare professionals with the appropriate skills (see recommendations 1.1.22 to 1.1.26). Specifically, recommendation 1.1.24 suggests that all healthcare professionals within emergency departments should have access to specialist support. |
| SH | Faculty of Pain Medicine | 1 | Full | General | | The Faculty of Pain Medicine does not wish to make any suggestions for changes to the Sickle Cell Guidance. Many thanks for the opportunity to comment | Thank you for your comment. |
| SH | Napp Pharmaceutical Holdings Limited | 2 | Full | General & 1.17 | | Napp supports the general recommendation that strong opioids should be used to provide primary analgesia for patients presenting with severe acute pain due to Sickle Cell Crisis. | Thank you for your comment. |
| SH | Royal College of Paediatrics and Child Health | 12 | Full | General & 144 | 1758 | Although many of the research papers cited mention client dissatisfaction with psychosocial management - and the chair of the GDG is a psychiatrist - there is very little | Thank you for your comments. This review questions aimed to cover patient's information and support needs. This question did not include the use of |

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| | | | | | | mention of: psychosocial interventions; the mental health component of painful sickling crises; or the need for attention to emotional health and well-being. The little mention there is seems to be confined to a small paragraph at the bottom of page 144: **2.5.3.8.**<br><br>"Evidence from five studies showed that patients had various support needs (including both clinical and psychosocial support), although some patients reported satisfaction in their ability to discuss concerns with a nurse or consultant."<br><br>This does not do the issue justice. The guideline could be improved by the addition one or two paragraphs describing what kind of psychosocial input would be most helpful for this group of patients - preferably describing adults and children separately. | psychosocial interventions for the management of an acute painful sickle cell episode. The review question assessing the use of non-pharmacological interventions to manage an acute episode did not identify any evidence relating to psychosocial intervention in hospital and a research recommendation has been made in appendix B. |
| SH | RCN | 1 | General | | | The Royal College of Nursing welcomes this guideline. It is comprehensive. There are no additional comments to make on this document. | Thank you for your comment. |