National Institute for Health and Clinical Excellence

Sickle cell

Scope Consultation Table

7th June - 5th July 2011

Type	Stakeholder	Order No	Section No	Comments Please insert each new comment in a new row.	Developer's Response Please respond to each comment
SH	Brent PCT	18.00	4.3.2	Should cover management by ambulance staff and other health professionals en route to hospital	Thank you for your comment. Although we recognise the importance of pre-hospital treatment, the remit provided by the Department of Health restricts the guideline to cover hospital settings.
SH	British Committee for Standards in Haematology / RCPath	11.00	4.1.2	It should be noted that sickle pain can precede life threatening sickle events eg chest syndrome even if not present on admission thus monitoring need to take this into account	Thank you for your comment. It is anticipated that the guideline will cover identification of clinical signs and symptoms of acute complications in patients with acute painful episodes. Pain due to causes other than acute painful episodes is beyond the scope of this guideline.
SH	British Committee for Standards in Haematology / RCPath	11.01	4.3.1.a	Patients attending hospital are unlikely to require a weak opioid if this has already failed. Guidance should focus on management of moderate-severe pain	Thank you for your comment. The evidence review will consider pain medications that are taken prior to attending hospital, however no specific guidance will be produced about managing pain at home. The focus of the guideline will be the management of pain in hospital settings and it is assumed that an acute painful episode, which cannot be controlled at home, will be of a moderate to severe nature. The evidence review will include all types of analgesia and recommendations will be based on the evidence reviewed and the expertise of the Guideline Development Group (GDG). Please see the guidelines manual for more information about the development of clinical guidelines http://www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines/clinicalguidelinedevelopme

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SH	British Committee for Standards in Haematology / RCPath	11.02	4.3.1.b	Guidance should take into account the wider range of analgesics and preparations which are now available including rapid onset oral/ sublingual/ intranasal formulations	Thank you. All analgesics will be considered for the evidence review.
SH	British Committee for Standards in Haematology / RCPath	11.03	4.3.2	Guidance should contain advice about fluids, oxygen, physiotherapy to avoid chest syndrome, laxatives, anti-emetics, antibiotics. Failure to address the severe complications of sickle cell which may accompany painful crisis is a missed opportunity and may make the guideline difficult to write particularly for the section relating to pregnancy.	Thank you. Thank you. Section 4.3.1 (a) has been amended to include oxygen and nitric oxide as pharmacological intervention for pain management. Section 4.3.1 has also been amended and all non-pharmacological interventions that are used specifically to manage acute painful episodes in hospital will be considered.
SH	British Committee for Standards in Haematology / RCPath	11.04	3.2.b	The majority of patients will given simple analgesics at home before attending hospital and this is optimal management. It is essential that this is recognised within the guideline and also that this is included into recommendations. One of the most frequent criticisms from patients is that the analgesia they have already taken at home is not taken into consideration and they are often given the same medication again at hospital, when it is clear that it is not working.	Thank you for your comment. Although we recognise the importance of managing pain at home, the remit is restricted to the management of pain in hospital settings. The evidence review will consider pain medications that are taken prior to attending hospital, however no specific guidance will be produced about managing pain at home.
SH	British Committee for Standards in Haematology / RCPath	11.05	3.2.c	This guidance is currently being rewritten.	Thank you for your comment.
SH	British Committee for Standards in Haematology / RCPath	11.06	4.3.1	Other issues which should be considered are - the role of other opioids (eg oxycodone) if there are side effects from morphine or diamorphine - the role of intra-nasal opioids - oral analgesia should be considered in all patients - the role of patient controlled or nurse controlled analgesia devices	Thank you for your comment. The role of other opioids, intra-nasal opioids, oral analgesia and patient controlled analgesia will be addressed in the pharmacological management of pain (please see section 4.3.1a-d.) The guideline will also cover the skills and knowledge required by healthcare professionals and teams providing care. The role of

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				- the role of protocols and patient held records - inclusion of the role of psychologist and Cognitive Behavioural Therapy	protocols and patient held records are beyond the scope of this guideline.
SH	British Committee for Standards in Haematology / RCPath	11.07	4.3.2	Prevention of an acute episode should be included Managing side effects of pharmacological interventions should be included as this will impact on quality of life Co-medications such as fluids, oxygen, laxatives, anti-histamines, heparin should be included as they are a vital part of holistic patient care	Thank you, however the prevention of acute painful episodes and the management of side-effects are outside the scope of this guideline. The evidence review will address the rates of adverse events however it is assumed that healthcare professionals providing care will manage these adverse events in an appropriate manner using their clinical expertise.
SH	British Pain Society	8.00	General	The British Pain Society welcomes the development of these guidelines and the acknowledgement of the need for good pain management in managing a Sickle cell acute episode in hospital	Thank you.
SH	British Pain Society	8.01	4.1.1.b	We welcome the consideration of specific subgroups. Pain assessment and management in children may need to be considered separately from that in Adults.	Thank you.
SH	British Pain Society	8.02	4.3.2	While we agree that Chronic pain should not be included in the scope it is important to note that for many pain may be a recurring intermittent pain and that this therefore needs to be taken into account particularly in relation to psychological aspects of treatment and assessment should include the persons' previous experiences.	Thank you, however the remit of this guideline is restricted to acute painful episodes.
SH	British Pain Society	8.03	General	In view of the complexities of pain management in these cases, and the need as acknowledged for specialist pain team involvement we would strongly recommend the inclusion of a pain specialist on the GDG.	Thank you for your comment. We agree and have advertised for a pain specialist to be a member of the GDG.
SH	British Pain Society	8.04	General	Oxygen therapy, hydration and simple measures have been omitted under Clinical issues that will be covered, and these are all important to pain relief.	Thank you. Section 4.3.1 (a) has been amended to include oxygen and nitric oxide as pharmacological intervention for pain management. Section 4.3.1 has also been amended and all non-pharmacological

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					interventions that are used specifically to manage acute painful episodes in hospital will be considered.
SH	British Pain Society	8.05	4.3.1.d	Includes adverse events associated with pain Management This seem ambiguous and need to be clarified	Thank you for your comment. This relates to any adverse events that are associated with any pharmacological or non-pharmacological interventions and may have an important impact on whether a specific drug is recommended for use or not. This has been removed from section 4.3.1
SH	British Pain Society	8.06	4.3.2.e	Excludes the management of side effects from pharmacological management. This seem ambiguous and need to be clarified	Thank you for your comment. The rate of adverse events that are associated with interventions will be considered as part of the evidence review and may have an important impact on whether a specific drug is recommended for use. However, the guideline will not produce any specific recommendations on how these side-effects should be managed. It is assumed that healthcare professionals providing care will manage these adverse events in an appropriate manner using their clinical expertise.
SH	British Pain Society	8.07	4.4.d	Risk factors associated with acute complications; does this mean complications of the acute sickle episode or of the treatment?	Thank you. The acute complications referred to here are complications of the acute painful episode. These may include acute chest syndrome, acute stroke and acute abdomen.
SH	British Psychological Society, The	1.00	4.3.1.e	'Distraction' is one of a range of strategies used as part of cognitive behaviour therapy to help manage pain and the related anxiety during an acute sickle crisis. Other strategies include thought identification and challenging, relaxation and visualisation. There is also growing evidence for the effectiveness of hypnosis in managing acute pain *(please see reference list below)* – this is perhaps more well known in hospital settings in the area of giving birth but we suggest it could be applied to managing acute painful sickle crises.	Thank you for your comment. Section 4.3.1 has been amended and all non-pharmacological interventions that are used specifically to manage acute painful episodes in hospital will be considered.

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				References: 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)*, 505-11. 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. Patterson D.R., Jensen, M.P. (2003). Hypnosis and Clinical Pain. *Psychological Bulletin*, *129(4)*, 495-521. Smith, C.A., Collins, C.T., Cyna, A.M. & Crowther, C.A. (2006). *Complementary and Alternative Therapies for Pain Management in Labour*. Adelaide, Australia: Cochrane Database of Systematic Reviews, Issue 4.	
SH	British Psychological Society, The	1.01	5.1	Related NICE guidance could also include clinical guideline 91 (2009) – Depression in adults with a chronic physical health problem[!]. [!] Accessed 16 June 2011 from: http://www.nice.org.uk/nicemedia/live/12327/45913/45913.pdf	Thank you. This guideline has been added.
SH	Department of Health	13.00	General	Department of Health has no substantive comments to make regarding this consultation.	Thank you.
SH	Institute of Biomedical Science	7.00	General	Acute management of acute pain should not only be addressed in hospital but also in ambulance and	Thank you for your comment. Although we recognise the importance of treatment within community

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				home where most of the painful episodes are managed by the patient and families.	settings and other pre-hospital settings, the remit of this guideline is restricted to pain management in hospital. The evidence review will consider pain medications that are taken prior to attending hospital, however no specific guidance will be produced about managing pain at home.
SH	Institute of Biomedical Science	7.01	3.1.a	Define Sickle cell disease, HbSC disease, Sickle beta (0) thalassaemia, Sickle beta (+) thalassaemia.	Thank you for your comment. A broad term has been used here to ensure that all genotypes of sickle cell disease are included.
SH	Institute of Biomedical Science	7.02	3.1.b	Require detailed pathophysiology leading to the acute painful sickle cell episodes.	Thank you for your comment. This section has been reworded to provide more information. A high level of detail about the pathophysiology was not considered necessary as the guideline will be focusing on the management of acute pain.
SH	Institute of Biomedical Science	7.03	3.1.c	Prevalence is increasing due to immigration and new births taking place every year.	Thank you. This has been added to section 3.1.
SH	Institute of Biomedical Science	7.04	4.1.1.a	Adult, children and young patients' diagnosis with **any genotype for sickle cell disease**…	Thank you for your comment. This has been amended in the scope.
SH	Institute of Biomedical Science	7.05	4.3.2.a	Guideline should consider the current treatment.	Thank you for your comment. The evidence review will consider pain medications that are taken prior to attending hospital, however no specific guidance will be produced about managing pain at home.
SH	Institute of Biomedical Science	7.06	4.3.11.g	The skill of healthcare professional is very important and it should address not only the knowledge, skills but also attitude.	Thank you, this has been amended to 'skills and knowledge'.
SH	Institute of Biomedical Science	7.07	4.3.1.h	Should also include information (eg complimentary therapy) that patient use to minimize the frequency of episodes of acute pain.	Thank you, however the prevention of acute painful episodes is outside the scope of this guideline. Although no guidance will be produced on how to prevent sickle cell crisis, this may be covered as part of the question on patient information and support needs. Recommendations will be based on the evidence review and the expertise of the GDG.

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SH	Institute of Biomedical Science	7.08	4.3.2.b	Should include information (eg special diet rich in antioxidants, complimentary therapies) for the prevention of acute painful sickle cell episode.	Thank you, however the prevention of acute painful episodes is outside the remit of this guideline. Although no guidance will be produced on how to prevent sickle cell crisis, this may be covered as part of the question on patient information and support needs. Recommendations will be based on the evidence review and the expertise of the GDG. Please see the guidelines manual for more information about the development of clinical guidelines http://www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines/clinicalguidelinedevelopmentmethods/GuidelinesManual2009.jsp
SH	Napp Pharmaceuticals	4.00	General	Napp supports the development of the guideline which should help improve patient care.	Thank you.
SH	Napp Pharmaceuticals	4.01	1	In relation to the term "in hospital" it may be necessary to clarify in the guideline that this refers to both the immediate treatment in emergency units and to in-patient stay in case the patient has to be admitted. Should it also include those patients who maybe managed in hospices?	Thank you for your comment. Section 4.2 refers to the healthcare settings that this guideline will cover and has been amended to include 'in hospital settings and specialist centres.' A&E departments and inpatient stay have not been mentioned specifically but will be included as part of 'in hospital.' Hospices are not included in hospital settings and will not be covered in this guideline.
SH	Napp Pharmaceuticals	4.02	3.2.b	Although morphine is often listed as the first line choice it is recognised that the clinical response is highly variable with up to 30% of patients not able to tolerate it and they may develop side-effects such as	Thank you for your comment. Section 3.2 of the scope provides an overview of the guidance available for the management of pain in hospital settings. It is also noted in section 3.2 (a) that this

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				hallucinations, confusion, nausea and vomiting.[1, 2]. Morphine metabolites are also known to accumulate in those with renal impairment and these metabolites may be associated with side-effects [2]. It is common practice to change to another opioid in these circumstances [3, 4]. Patients with a known prior history of morphine intolerance need to have access to alternative opioids for their pain control. Oxycodone has been shown to have similar efficacy to morphine and is used routinely as an alternative in pain management. Since all opioids are not the same it is therefore important that both health care professionals and patients have access to a range of injectable and oral opioids. Whilst morphine is regularly used in a number of UK hospitals oxycodone is also used (often ahead of diamorphine) as it can be used orally, in PCA and given s.c. [5]. Having a range of formulations also allows the HCP to continue care with the same drug. Given that the other two injectable opioids commonly used (morphine and diamorphine) have been clearly identified we would suggest that oxycodone should also be included as a further alternative (not a replacement) to morphine. 1. Riley, J. et al, Curr Med Res & Op 24, (1) 176-192, 2008.	management is variable across the UK. It is anticipated that this guideline will provide recommendations on which pharmacological interventions to use for acute painful sickle cell episodes, and will take into account adverse events.

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				2. Riley, J. et al, Supp Care Cancer, 14, 56-64, 2006. 3. Mercadante, S et al J. Clin Oncol 19 (11) 2898-2904 4. de Stoutz, N.D. et al, J. Pain Symptom Manage 10 (5) 378-384 5. Johnson, L. Journal of Pain & Palliative Care Pharmacotherapy, 22 (1) 51-54, 2008	
SH	Napp Pharmaceuticals	4.03	3.2.b	At the scoping workshop a much larger range of drugs (e.g. oxycodone (injection and oral formulations), fentanyl ("lollipops" and oral formulations), hydromorphone etc.) were identified as having value in managing pain and yet only two are quoted here. Will other drugs / formulations be included in the guideline? Adjuvant therapy to opioids was also mentioned but does not appear in the scope.	Thank you. Section 3.2 of the scope provides an overview of the guidance available for the management of pain in hospital. The evidence review will include any drugs that are used specifically for the management of acute painful episodes. Please see section 4.3.1 (a) and (e) for the specific pharmacological and non-pharmacological interventions that will be considered for the guideline.
SH	Napp Pharmaceuticals	4.04	3.2.b	There was some confusion at the scoping workshop over the terms opioid and opiate. It may be more appropriate to use the term opioid throughout.	Thank you for your comment. The scope now refers to 'opioid' when referring to the guideline under development. However, the terms used in other guidance (i.e.in section 3.2) may differ as this has been taken directly from their recommendations.
SH	Napp Pharmaceuticals	4.05	3.2.c	We agree that pain assessment is essential however using an appropriate pain scale and recording with a pain chart is important. Different pain scales need to be available for children and for those patients with communication issues.	Thank you for your comment. Section 3.2 of the scope relates to current practice within the NHS. This section is limited to the management of pain in hospital and provides an overview of the guidance available for this topic. Although we appreciate the importance of using appropriate pain scales to assess pain, it is anticipated that the guideline will be limited to producing recommendations on the timing and frequency of pain assessment (please see section

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					4.3.1c).
SH	Napp Pharmaceuticals	4.06	4.3.1.d and 4.3.2.e	A large number of patients (approximately 30%) may be intolerant to morphine. Adverse events associated with pain management may include hallucinations, confusion, nausea, vomiting and constipation. For patients to have their pain controlled successfully it may be necessary to give anti-emetics or laxatives with the opioid to alleviate or prevent these adverse events so that the patient may continue to take the medication. This does however seem at odds with the clinical issues that will not be covered.	Thank you for your comment. The rate of adverse events that are associated with interventions will be considered as part of the evidence review and may have an important impact on whether a specific drug is recommended for use. However, the guideline will not produce any specific recommendations on how these side-effects should be managed. It is assumed that healthcare professionals providing care will manage these adverse events in an appropriate manner using their clinical expertise.
SH	Napp Pharmaceuticals	4.07	4.4	Should length of stay be added as an outcome measure?	Thank you. Length of stay will be covered as part of 'resource use and cost'.
SH	NHS Bristol	10.00	General	Use of Plain English – the scoping document is written in fairly accessible language but, if you would like to secure real involvement of lay commentators, you will need to explain some complicated terms, perhaps in a glossary. Examples are "non-steroidal anti-inflammatory drugs", "pareneteral analgesia" and the difference between "acute" and "chronic".	Thank you. The final guidance will be produced in a number of formats including an 'Understanding NICE Guidance' version. This format is specifically written for patients and carers and provides plain English summaries of the recommendations. Please see the following link for more details http://www.nice.org.uk/patientsandpublic/index.jsp
SH	NHS Bristol	10.01	4.3.1	The existing guidelines referred to in section 3.2 do not mention the role of a clinical co-ordinator/specialist nurse in the multi-disciplinary team. The scope should include the exploration of this role, including the educational/practice development and patient advocacy aspects of the role.	Thank you for your comment. It is anticipated that this guideline will produce recommendations relating to the optimal settings for the management of acute pain and the skills and knowledge required by staff and teams providing care.
SH	NHS Bristol	10.02	4.3.1	If a patient is admitted to a non-haematology ward, s/he can feel that this is a suboptimal clinical setting for managing their painful episode, especially if staff appear to be non-responsive or unsure about how to proceed. The guidelines will need to explore good practice in bringing clinical expertise to bear on the	Thank you for your comment. It is anticipated that this guideline will produce recommendations relating to the optimal settings for the management of acute pain and the skills and knowledge required by staff and teams providing care.

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				management of the episode. This might include securing admission to a specialist haematology/oncology ward where staff are able to develop enhanced competence/experience in providing care; as well as the advisory and advocacy roles of a clinical co-ordinator/specialist nurse, whatever the ward.	
SH	NHS Bristol	10.03	4.3.1	The role of hydration as part of the non-pharmacological element of managing acute pain should be included in the scope. This seems like a really important part of bringing a crisis to a speedier end, especially since the patient might present in a dehydrated state for a number of reasons.	Thank you for your comment. Section 4.3.1 has been amended and all non-pharmacological interventions that are used specifically to manage acute painful episodes in hospital will be considered.
SH	NHS Bristol	10.04	4.3.1	The importance of keeping the patient warm within the clinical setting should be included in the scope, since exposure to a cold environment might have been one of the triggers for a crisis and might present a risk of prolonging the painful episode.	Thank you for your comment. Section 4.3.1 has been amended and all non-pharmacological interventions that are used specifically to manage acute painful episodes in hospital will be considered.
SH	NHS Bristol	10.05	4.3.1	When referring to the skills of health care professionals and teams, the scope should be explicit that these include skills in cross-cultural communication and in understanding the health care-related needs of an ethnically diverse population. Issues arising during the management of an acute episode might include: the need to use interpreters; access to chaplaincy services representing different faiths; chaperones for female patients; and flexibility around accommodating prayer needs.	Thank you for your comment. It is anticipated that this guideline will produce recommendations relating to the optimal settings for the management of acute pain and the skills and knowledge required by staff and teams providing care. These recommendations will be based on the evidence reviewed and the expertise of the Guideline Development Group (GDG). Please see the guidelines manual for more information about the development of clinical guidelines http://www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines/clinicalguidelinedevelopmentmethods/GuidelinesManual2009.jsp
SH	NHS Bristol	10.06	4.3.2	Preventing an acute painful episode falls outside of the draft scope. Painful episodes can be triggered	Thank you, however the prevention of acute painful episodes is outside the remit of this guideline.

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				within an acute clinical setting (eg during an operation for a totally unrelated problem). It seems like a significant omission for the guidelines not to address ways of preventing such triggers or of minimising their effects.	Although no guidance will be produced on how to prevent sickle cell crisis, this may be covered as part of the question on patient information and support needs. Recommendations will be based on the evidence review and the expertise of the GDG. Please see the guidelines manual for more information about the development of clinical guidelines http://www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines/clinicalguidelinedevelopmentmethods/GuidelinesManual2009.jsp
SH	NHS Bristol	10.07	4.3.2	The guidelines should specifically signpost other guidelines/ good practice on managing side effects associated with pharmacological interventions or on co-medications which sickle cell disease patients are likely to taking.	Thank you. NICE is only able to refer to other NICE guidance and Department of Health publications. Other relevant guideline however will be presented to the GDG for discussion but will not form part of the evidence review.
SH	NHS Sickle Cell and Thalassemia Screening Programme	5.00	General	The guideline should emphasise "patient needs" and include:- - appropriate behavioural attitudes for medical staff; - age specific treatments eg paediatric guidelines should be suitable for specific age ranges; - management of sickle crises in community settings (eg at home, which patient may prefer) - multi-disciplinary team to provide holistic care eg the psychological and social needs of patients and their families/carers should also be considered and addressed - use of all expertise available eg might include pain expertise from terminal care - multidisciplinary team might also consider	Thank you for your comment. The guideline will cover the support needs of patients which are specifically related to pain management. The guideline will also cover the optimal settings for pain management and the skills and knowledge required for healthcare professionals and teams providing care. Recommendations will be based on the evidence reviewed and the expertise of the Guideline Development Group (GDG). Please see the guidelines manual for more information about the development of clinical guidelines http://www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines/clinicalguidelinedevelopmentmethods/GuidelinesManual2009.jsp

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				other critical situations with regard to sickle cell disease – eg the possibility of stroke incidence , particularly for children with SCD (may want to have TCD scan undertaken whilst child is in hospital once pain management has been sorted out) - recognition that a sickle cell crisis may be a single episode in NHS terms, but is part of a life-long condition for patients and so future reviews and plans to reduce frequency/severity of crises are very important for patients.	
SH	NHS Sickle Cell and Thalassemia Screening Programme	5.01	2. 4.2, 4.3.1.g & 4.5	Only relates to treatment of sickle cell crisis in hospital (secondary & tertiary care). It therefore ignores treatment in the community (including at home) which many patients may prefer and which , with good community care, may be possible. This may be relevant for cost effectiveness analysis.	Thank you for your comment. Although we recognise the importance of treatment within community settings, the remit provided by the Department of Health restricts the guideline to cover only in hospital settings.
SH	NHS Sickle Cell and Thalassemia Screening Programme	5.02	3.2	No reference to two relevant publications:- (i) the current standards for children with sickle cell disease – "Sickle Cell Disease in Childhood: Standards and Guidelines for Clinical Care" 2nd Edition October 2010 published by the NHS Sickle Cell and Thalassaemia Screening Programme in partnership with the Sickle Cell Society – (www.sct.screening.nhs.uk) (ii) RCN Competences – "Caring for people with sickle cell disease and thalassaemia syndromes : A framework for nursing staff " published by the Royal College of Nursing and NHS Sickle Cell and Thalassaemia Screening Programme in 2011. Competence 7 relates specifically to sickle cell disease pain. (http://sct.screening.nhs.uk/professional-resources)	Thank you for your comment. This section has been re-worded to include the sickle cell standards for children. The RCN competencies were not included here as this section is focusing on the management of acute pain in hospital. The RCN competences will be considered as part of the evidence review addressing the skills and knowledge of healthcare professionals and teams providing care (see section 4.3.1).

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SH	NHS Sickle Cell and Thalassemia Screening Programme	5.03	4.3.1.h	"Skills" should include training, experience and knowledge – the need for all healthcare professionals to have better training and understanding of Haemoglobinopathies was a key recommendation of the NCEPOD report "A Sickle Crisis ?" published in 2008.	Thank you, this has been amended to 'skills and knowledge.
SH	NHS Sickle Cell and Thalassemia Screening Programme	5.04	4.3.1	The clinical issues do not seem to mention specifically :- (i) psychological support for patient and their family/carers; (ii) multi-disciplinary team approaches and drawing on pain management experience from elsewhere e.g. from terminal care (iii) the need for clinical staff to work alongside the patient and their family/carers who may be "experts" in understanding their sickle crises (iv) behavioural attitudes of medical staff – the need for listening, empathy, non-judgemental etc	Thank you for your comment. Although (i) and (iii) will not be covered specifically, some aspects may be included as part of the specific information and support needs of patients (please see section 4.3.1i). Both (ii) and (iv) should be included as part of the optimal setting for managing acute painful episodes and the skills and knowledge of the healthcare professionals providing care.
SH	NHS Sickle Cell and Thalassemia Screening Programme	5.05	4.4.e	Patient satisfaction should also be extended to family/carers – particularly important for paediatric cases	Thank you. This has been amended to include carers/family.
SH	NHS Sickle Cell and Thalassemia Screening Programme	5.06	4.4.f	Health related quality of life – assume this includes psychological effects; hopefully will be child-specific for paediatric cases.	Thank you. We will consider any published data on both generic and age specific measures of Health related quality of life.
SH	NHS Sickle Cell and Thalassemia Screening Programme	5.07	4.4	No mention of follow up/review and plan to reduce frequency/severity of further episodes; this might also be part of cost-effectiveness analysis.	Thank you, however the prevention of acute painful episodes is outside the remit of this guideline and will not be a key economic consideration.

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				No mention of follow up/review to see if there are other medical conditions that might require further treatment eg has TCD scan been undertaken recently in all children with sickle cell disease (aged 2-16 years)	Although no guidance will be produced on how to prevent sickle cell crisis, this may be covered as part of the question on patient information and support needs. Recommendations will be based on the evidence review and the expertise of the GDG. Please see the guidelines manual for more information about the development of clinical guidelines http://www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines/clinicalguidelinedevelopmentmethods/GuidelinesManual2009.jsp
SH	NHS Wandsworth	14.00	4.2	We suggest further consideration is given to the roles of primary and acute care physicians and professionals in managing the acute crisis within the health care setting section. With the local developments we are proposing, based on virtual wards and Telehealth care systems development the role of these professionals is intrinsic to the management of acute painful crisis.	Thank you for your comment. The remit provided by the Department of Health is restricted to pain management in hospital settings. As a result we are unable to cover community settings and primary care. Section 4.2 has been amended to 'in hospital settings and specialist centres' and this includes acute trusts and A&E departments. It is anticipated that this guideline will produce recommendations relating to the optimal settings for the management of acute pain and the skills and knowledge required by staff and teams providing care.
SH	NHS Wandsworth	14.01	4.3.2	With a multi disciplinary team approach to care and moving care closer to the community and home for patients we are suggesting that the scope is expanded to include early interventions, crisis prevention including patient education and self management.	Thank you for your comment. Although we recognise the importance of treatment within community settings and other pre-hospital settings, the remit of this guideline is restricted to pain management in hospital. The evidence review will consider pain medications that are taken prior to attending hospital, however no specific guidance will be produced about managing pain at home.

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SH	Nordic Pharma	12.00	General	As distributors of Siklos, the only form of hydroxycarbamide licensed for use in Sickle Cell Disease, our comments relate specifically to the use of this drug in the management of Sickle Cell Disease and prevention of recurrent, painful vaso-occulusive crisis in children, adolescents and adults.	Thank you for the information. Although we recognise the importance of preventing painful sickle cell episodes, this has been specifically excluded from this guideline (please see section 4.3.2b of the scope).
SH	Nordic Pharma	12.01	4.3 and 4.4	There are two sets of guidelines for the management of sickle cell disease ("Standards for the Clinical Care of Adults with Sickle Cell Disease in the UK", 2008 was published by the Sickle Cell Society and endorsed by the Department of Health and the UK Forum on Haemoglobin Disorders. Additionally "Sickle Cell Disease in Childhood: Standards and Guidelines for Clinical Care" October 2006 was published by the NHS Sickle Cell and Thalassaemia Screening Programme in partnership with the Sickle Cell Society) . Both recommend that hydroxycarbamide be considered for patients who experience 3 or more crises per year (or 2 acute chest crises), and that regular monitoring of patients taking hydroxycarbamide should be carried out. Patients should be clearly educated and informed about the risks and benefits associated with this medicine. Rather than symptomatic treatment of vaso-occlusive crisis it is possible to use Siklos (hydroxycarbamide). Hydroxycarbamide acts as a disease modifier in that it reduces the frequency and severity of painful crises the patient experiences, rather than simply managing the symptoms once they occur. From a patient care perspective this	Thank you for the information. Although we recognise the importance of preventing painful sickle cell episodes, this has been specifically excluded from this guideline (please see section 4.3.2b of the scope).

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				means a reduction in suffering, in disruption of normal life, and also potentially improves quality of life by reducing the anxiety associated with the knowledge that a crises can occur at any time without warning (Ref: Tachon G. *A new step in the management of sickle cell disease*. Hospital Pharmacy Europe (35): 58-64 (November/December 2007). Through treatment with hydroxycarbamide, patients with SCD experience fewer vaso-occlusive crises and acute chest syndromes. In a cross-over study involving 22 children, the mean r of hospitalisations was 12 in the treated group compar in the placebo group (p=0.0016) and the mean duratio hospitalisation was 5.3 days and 15.2 days respectivel (Reference: Ferster A, Vermylen C, Cornu G, Buyse M Corazza F, Devalck C et al. Hydroxyurea for treatment severe sickle cell anaemia: a paediatric clinical trial. Bl 1996 88:1960-4) A nine-year cohort follow-up study demonstrated a 40% fall in mortality in SCD patients treated with hydroxycarbamide (Reference: Steinberg MH, Barton F, Oswaldo C, Pegelow CH, Ballas SK, Kutlar A, et al. Effect of hydroxyurea on mortality and morbidity in adult sickle cell anaemia – risks and benefits up to 9 years of treatment. J Am Med Assoc 2003 289:1645-51).	
SH	Nordic Pharma	12.02	4.1.1	Siklos (hydroxycarbamide) is licensed for use in childen, adolescents and adults. Two formulations are now available: a 100mg film coated tablet can be dispersed easily and is particularly suitable for	Thank you for the information. Although we recognise the importance of preventing painful sickle cell episodes, this has been specifically excluded from this guideline (please see section 4.3.2b of the

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				paediatric use (being 6mm in diameter), and a 100mg tablet (scored to allow doses of 25mg to be administered). As such Siklos allows for accurate dosing titration which is important to prevent crisis, as well as to ensure safe use of a cytotoxic drug.	scope).
SH	Nordic Pharma	12.03	4.3	There are a number of key distinctions between Siklos and the unlicensed formulation (hydroxycarbamide capsules, marketed as Hydrea) particularly in terms of dosing accuracy. ***Of particular importance is the need to ensure children receive correct drug dosages.*** • The dosing regimen for hydroxycarbamide in sickle cell disease must be calculated according to a patient's weight. Siklos has been specifically designed to meet this requirement. • Siklos is available in a 1000 mg tablet which is scored so that it can be divided into 250 mg sections. This allows for greater dosing accuracy, thus meeting the needs of many patients who cannot achieve the required dosing of hydroxycarbamide using the 500 mg capsules. •In response to feedback from clinicians a 100mg tablet has just become available in the UK to enable patients to get even more accurate dosing intervals without the need to break up the tablet, thereby minimizing waste and avoiding the need for liquid even in young patients as it closely matches the dosing regimens. ***The dosing of Hydrea cannot be controlled in the same way*** • Hydrea is available as a capsule and is only	Thank you for the information. The main use of Siklos is for the prevention of painful sickle cell episodes and this has been specifically excluded from this guideline (please see section 4.3.2b of the scope).

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				available in a 500mg dose. This means that it is difficult to tailor the dosing to each individual patient. • In adults this can lead to slight over-dosing on one day managed by slight under-dosing the following day. The implications of this have not been formally studied. • For children, many of whom only need dosing between 250mg – 350mg, there is an increased risk of overdosing with Hydrea because doses smaller than 500 mg can only be achieved by breaking up the capsule and dissolving the powder in water. This practice is of concern because hydroxycarbamide is a type of drug known as a "cytotoxic", often used to treat types of cancer such as leukaemia. Cytotoxic medicines should be handled with great care. Furthermore the stability and bioavailability of these liquids cannot be guaranteed. They are also not available for patients to access in the community. •To overcome the patient safety issues associated with dissolving the product in water, some hospitals purchase an unlicensed liquid from a NHS owned body at the same price or similar to Siklos, however issues exist with this in terms of shelf life.	
SH	Nordic Pharma	12.04	4.3 and 4.4	Another important distinction between the use of unlicensed alternatives and Siklos is that Siklos contains a Risk Management Plan which was has been implemented as a result of discussions with the authorities. Within this risk management plan is a ten year monitoring programme. Although the benefits of treatment with hydroxycarbamide for certain groups	Thank you for the information. The main use of Siklos is for the prevention of painful sickle cell episodes and this has been specifically excluded from this guideline (please see section 4.3.2b of the scope).

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				of patients with sickle cell disease is well known, there are also certain known risks that have not been evaluated in long-term use in these people. This was the reason the regulatory authorities required the monitoring programme. It is known that treatment with hydroxycarbamide causes a reduction in the number of white blood cells (this is the mechanism for its use in leukaemia). However, in sickle cell disease this is not the primary medicinal effect but a side effect (the therapeutic effect in sickle cell disease comes from its effect on haemoglobin). Lowered white blood cell counts may mean that a patient is vulnerable to infection and this needs to be regularly monitored and managed. It is possible that hydroxycarbamide affects the ability of the body to produce sperm. It is not known what the long term effect is however, as this has never been studied in patients with sickle cell disease who are taking hydroxycarbamide long term. This is another important reason for the monitoring programme, and was a specific concern raised by the regulatory authorities when considering grating this licence. Hydroxycarbamide has been shown to significantly reduce the frequency and severity of crises experienced over a period of just less than two years (Reference: MSH Study, Charache, NEJM 1995). However, there is no large-scale, long-term data that clearly demonstrates the therapeutic outcomes such as organ damage, incidence of stroke (common in severe sickle cell disease at young age) and other	

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				factors that can affect the health of those with this condition. All this information, collected on a multi-centre long term systematic basis, will help inform best practice for the management of this debilitating, painful and sometimes life-limiting condition. It could be used to help the NHS design optimal and cost-effective services for this group of patients. The Risk Management Plan is leading to further research into Sickle Cell Disease and will translate into more treatment options for patients. Even though the NHS has been treating these patients for many years, none of this data has been collected, which is the reason that the regulatory authorities have asked Nordic to carry out the monitoring programme. Without such systems in place the NHS can never hope to improve treatment and quality of life for these patients. The Risk Management Plan presents an idea model of outcomes data collection for the NHS. This 10 year Monitoring Programme is conducted by Nordic at no cost to the NHS. But the programme allows for greater joined-up working and collaboration between the NHS and pharmaceutical companies to ensure future R&D meets the needs of the healthcare system.	
SH	Nordic Pharma	12.05	4.3.1	Licensing is mentioned in the scope of these guidelines. Nordic Pharma would like to raise the following points:	Thank you for the information. The main use of Siklos is for the prevention of painful sickle cell episodes and this has been specifically excluded from this guideline (please see section 4.3.2b of the

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				Prior to the launch of Siklos there was no licensed treatment for this small group of patients Siklos has been specially developed for the treatment of Sickle Cell Disease in adults and children. There is no risk management programme in place for the off-label use of Hydrea. The license holders of Hydrea are not obliged to accept liability for the potential serious side effects if used off-label. ***The licensing process is complex and is designed to ensure patient safety*** The EU has a rigorous regulatory system to ensure the safety, efficacy and quality of medicines licensed for human use. This is matched by national regulatory bodies, such as the Medicines and Healthcare Products Regulatory Agency (MHRA) in the UK. Using drugs off-label where licensed product exists undermines this process which the Government itself has invested significant funds in.	scope).
SH	Nordic Pharma	12.06	4.5	Siklos 100mg is priced at £100 for a box of 60 tablets, with the 1000mg tablets being dose per dose equivalent. In hospitals where an unlicensed liquid formulation is in use (particularly for paediatrics) the switch to Siklos will likely not incur any additional costs [calculated using list prices]. Hydroxycarbamide is dosed according to BMI and therefore the cost of Siklos for a UK patient is projected at being between £3,000-£6,000 per year. This price takes into account the requirement for a 10-year monitoring programme. In addition, there	Thank you for the information. Although we recognise the importance of preventing painful sickle cell episodes, this has been specifically excluded from this guideline (please see section 4.3.2b of the scope).

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				are significant demands placed on companies seeking to license medicines, to conform to the requirements of the licensing authorities. The costs of these are spread between the numbers of patients prescribed the drug. For an orphan disease, the number of patients is by definition small, so the proportionate cost per patient of meeting the regulatory requirement is greater. However, because of the small number of patients involved, the overall cost to the NHS is less likely to have a significant budget impact than a drug widely prescribed in the general population, despite the cost per individual being lower in the latter case. Compared to symptomatic treatment of pain the cost needs to be balanced against pain and the use of drugs coupled with in-patient hospital stays. Alternatively blood transfusions could be used but these too carry risks and costs. The price of Siklos was approved following scrutiny by the UK Department of Health under the terms of the Pharmaceutical Price Regulation Scheme (PPRS).	
SH	Northwest London Hospitals NHS Trust	6.00	3.2.c	We suggest the recognition of nurses within the multidisciplinary team; playing a pivotal role in the management of acute pain including use of assessment tools, administration of pain relief etc.	Thank you for your comment. Section 3.2 of the scope relates to current practice within the NHS. This section provides an overview of the guidance available for this topic. It is anticipated that this guideline will produce guidance on optimal setting for managing acute painful episodes and the skills and knowledge required by the healthcare professionals and teams

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					providing care.
SH	Northwest London Hospitals NHS Trust	6.01	3.2.c	We suggest that the guidelines specifying 2 hourly monitoring for pain control may be too prescriptive. In the clinical setting, more frequent assessment may be warranted and will depend on a variety of factors such as presenting symptoms, changes to analgesia and specific concerns about side effects. The guidelines should avoid being overly limited in scope and would need to include allowance for these considerations, emphasising the importance of professional judgement when clinically evaluating patient care and determining the most appropriate observation frequency.	Thank you for your comment. Section 3.2 of the scope relates to current practice within the NHS. This section is limited to the management of pain in hospital and provides an overview of the guidance available for this topic. It is anticipated that the guideline will produce recommendations on the timing and frequency of pain assessment (please see section 4.3.1c) and these recommendations will be based on the evidence reviewed and the expertise of the Guideline Development Group (GDG). Please see the guidelines manual for more information about the development of clinical guidelines http://www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines/clinicalguidelinedevelopmentmethods/GuidelinesManual2009.jsp
SH	Northwest London Hospitals NHS Trust	6.02	4.2.a	Consideration should be given to the pre-hospital healthcare setting provided by paramedic services during the period of transfer to the secondary or tertiary setting. Specifically the role of Entenox out of hospital and the transition to in-hospital pain evaluation and management and the provision of analgesia at the appropriate next step in the ladder.	Thank you for your comment. Although we recognise the importance of pre-hospital treatment, the remit provided by the Department of Health restricts the guideline to cover in hospital settings. The evidence review will consider pain medications that are taken prior to attending hospital, however no specific guidance will be produced about managing pain in these settings.
SH	Northwest London Hospitals NHS Trust	6.03	4.3.1.b	Consideration of other agents or preparations such as the role of intravenous paracetamol in the analgesic ladder.	Thank you. All analgesics will be considered for the evidence review
SH	Northwest London Hospitals NHS Trust	6.04	4.3.1.c	We suggest that guidelines should include some elaboration of what the term 'pain control' should mean in clinical practice. Clinical experience	Thank you for your comment. Although we appreciate the importance of using appropriate pain scales to assess pain, it is anticipated that the

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				indicates that good pain control should be related to the patients ability to gently mobilise however there is little understanding or agreement whether this would mean a mobilisation pain score of zero (pain free) or what pain score on mobilisation would constitute adequate pain control (ie: not necessarily entirely pain free). Use of pain relief scores (in addition to pain intensity scores) should also be considered in terms of assessing pain control.	guideline will be limited to producing recommendations on the timing and frequency of pain assessment Please see section 4.4 for the main outcomes that will be extracted from the evidence. The number of outcomes will be restricted to those that are considered most important and will be discussed with the Guideline Development Group (GDG). Reduction in pain will be included as part of section 4.4 (b).
SH	Northwest London Hospitals NHS Trust	6.05	4.3.1.e	Suggest that inclusion of non - pharmacological/complementary approaches should be restricted to those with good evidence for use in acute sickle cell pain.	Thank you for your comment. Section 4.3.1 has been amended and all non-pharmacological interventions that are used specifically to manage acute painful episodes in hospital will be considered. All evidence will be critically appraised and will need to reach a pre-specified inclusion criteria to be included as part of the evidence review. Please see the guidelines manual for more information about the development of clinical guidelines http://www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines/clinicalguidelinedevelopmentmethods/GuidelinesManual2009.jsp
SH	Northwest London Hospitals NHS Trust	6.06	4.3.1.f	We suggest that the guideline should specifically mention the need to optimise pain control when affecting chest or abdominal sites as a means of preventing hypoventilation secondary to pain and the subsequent risk of developing an acute chest crisis. We suggest the guidelines include reference to use of chest physiotherapy, deep breathing exercise or use of incentive spirometry alongside good pain control to enable these interventions and to thus	Thank you for your comment. The guideline will cover the management of pain in all patients with acute painful episodes. Any specific sub-groups that arise from the research will be addressed appropriately and will be discussed with the GDG. Section 4.3.1 has also been amended and all non-pharmacological interventions that are used specifically to manage acute painful episodes in hospital will be considered

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				minimise risk of further and significant complications in this patient cohort.	
SH	Northwest London Hospitals NHS Trust	6.07	4.3.1.f	Suggest specific mention of the need to re-evaluate patients with uncontrolled pain case of: i) escalating pain due to an unsuspected sickle related clinical deterioration or life threatening complication such as acute chest crisis or ii) ii) escalating or uncontrolled pain due to an unsuspected non-sickle related episode such as a surgical or medical emergency. Uncontrolled or escalating sickle pain despite apparent appropriate and analgesic control should prompt clinical re-evaluation. This would not require specific mention of managing such emergencies which are out of scope within these guidelines.	Thank you. The guideline will cover the possibility of acute complications but surgical or medical emergencies are outside the scope of this guideline.
SH	Northwest London Hospitals NHS Trust	6.08	General	We suggest guidelines should recognise patients are important partners in the management of their pain the scope need to incorporate the role of the patient in their pain management and development of national strategies. Consideration that guidelines include advice on the use of individualised pain protocols (which may also be patient/parent held) to facilitate appropriate and prompt administration of analgesia for these patient groups with specifically identified needs in the secondary or tertiary hospital setting.	Thank you for your comment. The guideline will cover the support needs of patients which are specifically related to pain management. Recommendations will be based on the evidence reviewed and the expertise of the Guideline Development Group (GDG). Please see the guidelines manual for more information about the development of clinical guidelines http://www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines/clinicalguidelinedevelopmentmethods/GuidelinesManual2009.jsp
SH	Northwest London Hospitals NHS Trust	6.09	General	Suggest scope should include a management approach to those individuals who have developed opioid tolerance and/or dependency or drug seeking behaviour in addition to having genuine pain control	Thank you for your comment. All patients with acute sickle cell painful episodes will be included and subgroups will be considered as they emerge from the research.

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				requirements. Also should include those who have developed hyperalgesia (ie. heightened sensitivity to pain). These groups of patients may have specific pain control needs that are easily overlooked or discriminated against in the clinical setting.	
SH	Northwest London Hospitals NHS Trust	6.10	General	We suggest guidelines should include a statement regarding the clinical need to make a distinction between acute pain crisis and an acute exacerbation of a chronic pain problem that may require a different clinical approach.	Thank you for your comment. The relevant definitions will be added to a glossary within the clinical guideline. The management of chronic pain is outside the scope of this guideline.
SH	RCGP	9.00	General	The scope seems comprehensive and relevant	Thank you.
SH	Royal College of Nursing	16.00	General	The Royal College of Nursing welcomes proposals to develop this guideline. It is timely. The draft scope is comprehensive.	Thank you.
SH	Royal College of Nursing	16.01	3.2.b	There is a statement about the use of opiates analgesia - many clinicians do not or no-longer use Diamorphine in adults but in children nasal Diamorphine is used. Oxynorm (Oxycodone) is analgesia of choice. We therefore consider that Diamorphine is not a first drug of choice but only if patients are already on it and prefer to remain on it.	Thank you for your comment. Section 3.2 of the scope relates to current practice within the NHS. This section is limited to the management of pain in hospital and provides an overview of the guidance available for this topic. It is also noted in section 3.2 (a) that this management is variable across the UK. It is anticipated that this guideline will provide recommendations on which pharmacological interventions to use in hospital for acute painful sickle cell episodes, and will take into account adverse events.
SH	Royal College of Nursing	16.02	3.2.c	A multidisciplinary approach / at the end of the sentence it reads- 'counsellors'. One does not get counsellors in hospitals for this but specialist nurses; therefore, this should be replaced with 'specialist nurses'.	Thank you for your comment. Section 3.2 of the scope relates to current practice within the NHS. This section is limited to the management of pain in hospital and provides an overview of the guidance available for this topic. The wording has been taken directly from the guideline and has not been changed.

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					It is anticipated that this guideline will produce recommendations relating to the optimal settings for the management of acute pain and the skills and knowledge required by staff and teams providing care.
SH	Royal College of Nursing	16.03	3.2.c	Pethidine is no longer used unless it is a patient's preference and there is specific instruction that it is appropriate from the haematologist who treats the individual patient. We would therefore suggest that at the end of that statement it should read; 'only if it is known as the patient's preference and the haematologist considers it appropriate.'	Thank you for your comment. Section 3.2 of the scope relates to current practice within the NHS. This section is limited to the management of pain in hospital and provides an overview of the guidance available for this topic. It is anticipated that this guideline will provide recommendations on which pharmacological interventions to use in hospital for acute painful sickle cell episodes, and will take into account adverse events.
SH	Royal College of Nursing	16.04	3.2.c	Diamorphine is mentioned however it is only very rarely considered appropriate and one rarely sees adult patients on it. Oxynorm is the drug of choice.	Thank you for your comment. Section 3.2 of the scope relates to current practice within the NHS. This section is limited to the management of pain in hospital and provides an overview of the guidance available for this topic. It is anticipated that this guideline will provide recommendations on which pharmacological interventions to use in hospital for acute painful sickle cell episodes, and will take into account adverse events. These recommendations will be based on the evidence reviewed and the expertise of the Guideline Development Group (GDG). Please see the guidelines manual for more information about the development of clinical guidelines http://www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines/clinicalguidelinedevelopmentmethods/GuidelinesManual2009.jsp

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SH	Royal College of Nursing	16.05	4.3.c	Oral fluid, massage and oxygen can be added because these three things tend to make patients feel better.	Thank you. Thank you. Section 4.3.1 (a) has been amended to include oxygen and nitric oxide as pharmacological intervention for pain management. Section 4.3.1 has also been amended and all non-pharmacological interventions that are used specifically to manage acute painful episodes in hospital will be considered
SH	Royal College of Paediatrics and Child Health	3.00	General	The College notes that this is a remarkably restricted remit. The most cost effective way of dealing with crises is prevention but this is excluded from consideration. It appears to concentrate on pain relief alone. The restricted nature of the scope does imply that NICE consider acute pain relief to be the critical issue for SCD sufferers. The key is that failure to identify the trigger for the pain will mean a far higher probability of recurrence and therefore greater cost. Specialist investigation is required which now must include assessment of respiratory status. It would be far better to broaden the remit of this short guideline.	Thank you for your comment. Although we recognise the importance of all the issues that have been raised, the remit of the guideline is to produce a short clinical guideline on the management of sickle cell crisis in hospital. The prevention of acute painful episodes is outside the scope of this guideline.
SH	Royal College of Paediatrics and Child Health	3.01	General	There is no mention of oxygen which is essential treatment for crises. Furthermore, one of the commonest triggers is infection and this also requires treatment. If the infection is pneumonia then opioids may cause respiratory suppression and increase hypoxaemia.	Thank you. Section 4.3.1 (a) has been amended to include oxygen and nitric oxide as pharmacological intervention for pain management.
SH	Royal College of Paediatrics and Child Health	3.02	General	The National Institutes of Health (NIH) have funded a large study of co-morbid respiratory problems in sickle cell disease (SCD) and the way they affect the risk of crises. This is based in St Louis, USA and London. It has highlighted that asthma is a common	Thank you for your comment. The identification of co-morbidities is beyond the scope of this guideline.

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				problem which significantly increases the risk of crises but is rarely recognised or appropriately treated.	
SH	Royal College of Paediatrics and Child Health	3.03	General	We note there are very important clinical aspects, but have concerns about this scope. We note it is difficult to deal with health economics when it is confined to a very specific aspect of SCD (acute pain only); the risk of accumulating isolated health economics data in this way is that they may be used in the future to justify changes in service provision. In particular, we think there is a risk of moving the emphasis too far from specialist centres out into the community (for economic reasons). The risk attached to this is that it would require a continuous, very intensive 'rolling' education programme to maintain enough permanent, up to date SCD knowledge over a very wide community/DGH network. Up to date management and knowledge about advances is only normally maintained in the specialist centres.	Thanks for your comment. However community care is outside the remit of this guideline and as such the health economic considerations will be addressed with respect to management of an acute sickle cell episode in hospitals/specialist centres.
SH	Royal College of Paediatrics and Child Health	3.04	4.2	We note that the draft scope excludes primary health care settings. We suggest the guideline include a recommendation that SCD patients have facility to self-refer to hospital service (secondary or tertiary depending on nearest appropriate facility) and not to have to go via GP or routine Emergency Department visit.	Thank you for your comment. The remit provided by the Department of Health is restricted to pain management in hospital settings. As a result we are unable to cover community settings and primary care.
SH	Royal College of Paediatrics and Child Health	3.05	4.3.1	Before treatment of painful crisis is discussed, we think there should be a recommendation that all secondary and tertiary services treating such patients set up appropriate fast-track access systems so as to meet the timeline for first administration of analgesia and effective analgesia.	Thank you for your comment. Although we recognise the importance of appropriate access systems, this guideline will begin with patients who are suspected of having an acute painful episode in hospital. The specific method of accessing the service is outside the scope of this guideline.

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SH	Royal College of Paediatrics and Child Health	3.06	4.3.1 (e), (g) and (i)	In other respects, the scope seems fairly inclusive, in particular more or less including the psychosocial aspects (4.3.1 (e), (g) and (i)).	Thank you for your comment.
SH	Royal College of Paediatrics and Child Health	3.07	4.3.2.d	We think this guideline will be more helpful if it did include the management of acute complications, including acute chest syndrome.	Thank you for your comment. Although the guideline will cover the clinical signs and symptoms to identify patients who are likely to have an acute complication, no guidance will be produced on how to manage these complications as this is outside the remit.
SH	Royal College of Paediatrics and Child Health	3.08	4.3.2.g	While non-pain relief medication is not to be covered, we recommend the guideline make mention of continuing appropriate pneumococcal prophylaxis (penicillin or suitable alternative antibiotic, if one needed).	Thank you for your comment, however the prevention of infection is outside the remit of this guideline.
SH	Royal College of Paediatrics and Child Health	3.09	4.4.b	We note that specific mention is not made that the guideline will have an expectation of timeline from arrival to first administration of analgesia and effective analgesia. This is inferred in 4.4(b) but we think needs to be clearly stated as expectation of standard.	Thank you. The evidence will be reviewed before recommendations about timeframes are made. Recommendations will be based on the evidence reviewed and the expertise of the Guideline Development Group (GDG). Please see the guidelines manual for more information about the development of clinical guidelines http://www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines/clinicalguidelinedevelopmentmethods/GuidelinesManual2009.jsp
SH	Sickle Cell Society	17.00	General	It is important that reference is made to the National Standards and Guidelines developed by Sickle Cell Society, UK Forum, BCSH & UKTS. The guidelines should take the following into consideration The management of acute sickle cell pain should not only be in a hospital settings but to include a. self management b. carers, families c: Community eg: local GP and specialist	Thank you for your comment. NICE is only able to refer to other NICE guidance and Department of Health publications within the guideline. Although we recognise the importance of all the issues that have been raised, the remit of the guideline is to produce a short clinical guideline on the management of sickle cell crisis in hospital.

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				community nurse d: Comprehensive care, taking holistic approaches when treating the patient eg: the psychological, social needs of the patient as well as the carers. e: The age, gender, culture, faith of the patients should be considered. Access to interpreters f: Patient need to be involved in the choice of treatment. Patient's involvement in the development of the guidelines should take in consideration of those individuals who have no access to internet. g: The word episode should be replaced by crisis and this must be consistent h: The use of plain English language is essential. Add glossary for complicated terms. Eg: "non-steroidal anti-inflammatory drugs, parental analgesia as well as the difference between " acute and chronic. I: 30mins maximum delay to patients at the A&E	
SH	Sickle Cell Society	17.01	3.1a.b.c	The disease is the commonest most inherited genetic disorder in the UK. New research has pointed to other causes of sickling such as lack of nitric oxide. The numbers of sufferers are increasing around the country though with high concentration in some areas (the increase is not only through immigration). • Please add, the red blood cell changes shape when the red blood cell gives up the oxygen.	Thank you for your comment. This section has been reworded to provide more information. A high level of detail about the pathophysiology was not considered necessary as the guideline will be focusing on the management of acute pain.
SH	Sickle Cell Society	17.02	3.2 a.b.c	Care must be taken to avoid overdosing of analgesia as some patients are likely to have self	Thank you for your comment. Although we recognise the importance of managing pain at home, the remit

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				medication to alleviate the pain at home before coming to hospital. Some patients effectively manage the pain at home.	is restricted to the management of pain in hospital settings. The evidence review will consider pain medications that are taken prior to attending hospital, however no specific guidance will be produced about managing pain at home.
SH	Sickle Cell Society	17.03	4.3.1	The guidelines recommendation to be adhered to by advising the patient if the drugs are licensed or not before a decision is taken. There should be recommendation for sufficiently trained GPs to manage acute complications associated with sickle cell. There is the need to train and engage more specialist sickle cell nurses for A&E and the wards for effective and satisfactory outcome. The current scope does not mention specialist team. Patients should be put in separate room because of distress they at times shout and cry can be disturbing to others. (None – Pharmacological treatment), head massages should be included along with reflexology hydration and Psychological intervention. Keeping the patient warm within the clinical setting.	Thank you for your comment. This guideline is restricted to hospital settings and specialist care. Primary care is outside the scope of this guideline and the management of acute complications will also not be covered. It is anticipated that this guideline will produce recommendations relating to the optimal settings for the management of acute pain and the skills and knowledge required by healthcare professionals and teams providing care. These recommendations will be based on the evidence reviewed and the expertise of the Guideline Development Group (GDG). Please see the guidelines manual for more information about the development of clinical guidelines http://www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines/clinicalguidelinedevelopmentmethods/GuidelinesManual2009.jsp
SH	Sickle Cell Society	17.04	4.3.2	Sickle cell episodes are associated with acute pain which can lead eventually to chronic pain. It is important to monitor side effects associated with pharmacological interventions.	Thank you for your comment. The rate of adverse events that are associated with interventions will be considered as part of the evidence review and may have an important impact on whether a specific drug is recommended for use. However, the guideline will not produce any specific recommendations on how these side-effects should be managed. It is assumed that healthcare professionals providing care will manage these adverse events in an appropriate

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					manner using their clinical expertise.
SH	Sickle Cell Society	17.05	4.4	The main outcome should include reduction of pain as a priority as well as quality of life. Improved life expectancy. Patients improved knowledge of pain management techniques. The main outcome should be divided into categories.	Thank you for your comment. The reduction of pain will be included as part of 'intensity and duration of pain'. Patients improved knowledge of pain management was not considered as important as patient and carer satisfaction or experience of pain management in order to address the clinical issue information and support needs (see section 4.3.1g)
SH	Sickle Cell Society	17.06	4.5	Economic issues at this stage of the scoping process should be avoided for a fair conclusion. There should be investment in different pharmacological strategies for managing acute pain, including alternative medicine.	Thank you for your comment. It is however important at this early stage to identify the key economic areas in the management of pain during an acute sickle cell episode. Further economic analysis will be considered if any additional questions are identified during guideline development.
SH	Sickle Cell Society	17.07	General	It is important that reference is made to the National Standards and Guidelines developed by Sickle Cell Society, UK Forum, BCSH & UKTS. The guidelines should take the following into consideration The management of acute sickle cell pain should not only be in a hospital settings but to include a. self management b. carers, families c: Community eg: local GP and specialist community nurse d: Comprehensive care, taking holistic approaches when treating the patient eg: the psychological, social needs of the patient as well as the carers. e: The age, gender, culture, faith of the patients should be considered. Access to interpreters f: Patient need to be involved in the choice of treatment.	Thank you for your comment. NICE is only able to refer to other NICE guidance and Department of Health publications within the guideline. Although we recognise the importance of all the issues that have been raised, the remit of the guideline is to produce a short clinical guideline on the management of sickle cell crisis in hospital.

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				Patient's involvement in the development of the guidelines should take in consideration of those individuals who have no access to internet. g: The word episode should be replaced by crisis and this must be consistent h: The use of plain English language is essential. Add glossary for complicated terms. Eg: "non-steroidal anti-inflammatory drugs, parental analgesia as well as the difference between " acute and chronic. I: 30mins maximum delay to patients at the A&E	
SH	UK Forum on Haemoglobin Disorders	15.00	General	1] It is understood that the purpose of this short guideline is to improve safety and effectiveness of management of acute sickle cell pain episodes in hospitals, but nonetheless we feel that so narrow a scope misses the opportunity to improve the safety and effectiveness of managing acute pain problems in sickle cell more broadly. Most uncomplicated, even severe, acute painful sickle cell episodes are managed by patients and families at home, sometimes with the support of outreach or community nurses. It is largely an individual patient 'threshold' which determines presentation to hospital for escalated management. Some patients use a full range of analgesics, including morphine, at home to manage acute severe pain, so that many of the same issues apply. 2] An acute painful sickle cell episode should not be managed as an isolated 'hospital event'. These are lifelong conditions, and the necessity for addressing relevant aspects long-term condition management must be stressed.	Thank you for your comments. 1) Although we recognise the importance of treatment within community settings, the remit of this guideline is restricted to in hospital settings. The evidence review will consider pain medications that are taken prior to attending hospital, however no specific guidance will be produced about managing pain at home. 2) The remit of this guideline specifically addresses acute painful episodes and the long-term management is outside the scope. 3) The guideline will cover the optimal settings for pain management and the skills and knowledge required by the health care professionals and teams providing care. 4) This guideline focuses on the management of acute painful episodes and long-term management including the prevention of painful episodes is outside the scope.

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				3] Continuity of care by familiar care-givers is important. Patients being managed by a different acute admitting team for every presentation leads to fragmented and inconsistent care, and lack of confidence. 4] Not to cover ways of minimising painful crisis [4.3.2 b)] seems an important omission, which we feel should be re-considered. 5] The importance of involving patients and families about care decisions is not sufficiently emphasised.	5) The guideline will cover the support needs of patients which are specifically related to pain management. Recommendations will be based on the evidence reviewed and the expertise of the Guideline Development Group (GDG). Please see the guidelines manual for more information about the development of clinical guidelines http://www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines/clinicalguidelinedevelopmentmethods/GuidelinesManual2009.jsp
SH	UK Forum on Haemoglobin Disorders	15.01	3.1.a	Where is the evidence that 'life expectancy has improved in recent years..'? If this relates to the UK, we have no data about overall life expectancy. We now have the tool to collect such data, the National Haemoglobinopathy Registry, and it would be helpful to include mention of this in the document. We do know that good care in the early years improves outcomes to age 16 [Telfer et al, Haematologica. 2007 Jul;92(7):905-12], and it is reasonable to hope that continued good care into adulthood improves survival, but this is not yet evidenced.	Thank you, this has been removed from section 3.1 and a section about the National Haemoglobinopathy Registry has been added to section 3.1 (c).
SH	UK Forum on Haemoglobin Disorders	15.02	3.1.b	The description of the pathophysiology of the painful episodes – red cells changing shape and leading to vessel blockage – is an over simplification. It is now known that the process is a good deal more complex, involving over expression of adhesion molecules, and vasomotor abnormalities relating to nitric oxide metabolism. We don't think detail is important, but perhaps could read *'the red cells in people with sickle cell disease behave differently under a variety of conditions, including dehydration, low oxygen, elevated temperature, which causes*	Thank you for your comment. This section has been reworded to provide more information.

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				them to block small vessels and cause tissue infarction'.	
SH	UK Forum on Haemoglobin Disorders	15.03	3.1.b	'Crises are often unpredictable and pain may vary in intensity' is true, but should perhaps be emphasised by continuing '*but can be of excruciating severity'.*	Thank you. This has been added to section 3.1.
SH	UK Forum on Haemoglobin Disorders	15.04	3.1.c	The prevalence is increasing not only because of immigration to the UK, but also because of around 350 new births per year [NHS sickle cell and thalassaemia screening programme].	Thank you. This has been added to section 3.1.
SH	UK Forum on Haemoglobin Disorders	15.05	3.1.d	Numbers collected during the peer review programme visits to centres managing children with sickle cell disease and thalassaemia during 2010 – 11 indicated that over 80% of affected children are managed by the London centres. Thus under prevalence, '*at least* two thirds of people with s c d live in London' might be better.	Thank you. These figures are estimated and a section about the National Haemoglobinopathy Registry has been added to section 3.1 (c) to show that reporting of the number and geographical distribution of patients will be improved in the future.
SH	UK Forum on Haemoglobin Disorders	15.06	3.2.b	We think it worth stressing that while it is true that treatment begins with a simple oral analgesic in conjunction with NSAIDs, by the time of presentation to hospital a great majority will have already been trying these at home, and present because they have proved insufficient. Many will have tried at least 'middle strength' analgesics also.	Thank you for your comment. Section 3.2 of the scope relates to current practice within the NHS. This section is limited to the management of pain in hospital and provides an overview of the guidance available for this topic. The evidence review will consider pain medications that are taken prior to attending hospital, however no specific guidance will be produced about managing pain at home.
SH	UK Forum on Haemoglobin Disorders	15.07	3.2.c penultimate bullet point	Evidence for that statement is lacking, and in units which use appropriate weight related doses of oral morphine initial control can often be achieved with oral analgesia. The assumption that severe pain always needs parenteral analgesia is to be avoided, as it means that severe pain episodes always need hospital care, which we know is not the case. Some	Thank you for your comment. Section 3.2 of the scope relates to current practice within the NHS. This section has been taken directly from published guidance, although it is also noted in section 3.2 (a) that current practice in the UK is variable. It is anticipated that this guideline will provide recommendations on which pharmacological

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				patients certainly manage uncomplicated, severe pain episodes – ie those that are not accompanied by fever, chest pain, other unusual features - at home with oral morphine [see general point above].	interventions to use in hospital for acute painful sickle cell episodes. This specifically includes the choice, timing and route of analgesia (please see section 4.3.1 for other clinical issues that will be covered).
SH	UK Forum on Haemoglobin Disorders	15.08	4.1.1.a	'with diagnosed sickle cell disease' should perhaps read '*with any genotype of sickle cell disease*' to ensure inclusion of those with HbSC, S□thalassaemia etc as well as HbSS.	Thank you for your comment. This has been amended in the scope.
SH	UK Forum on Haemoglobin Disorders	15.09	4.3.1.e	Ist bullet point – 'distraction techniques' should address also other Cognitive Behavioural Therapy inputs.	Thank you for your comment. Section 4.3.1 has been amended and all non-pharmacological interventions that are used specifically to manage acute painful episodes in hospital will be considered
SH	UK Forum on Haemoglobin Disorders	15.10	4.3.1.h	The skills of healthcare professionals – should be widened to address attitudes, as well as knowledge.	Thank you, this has been amended to 'skills and knowledge'
SH	UK Forum on Haemoglobin Disorders	15.11	4.3.1.i	Should include information about how people can take steps to reduce the risk of acute pain episodes.	Thank you, however the prevention of acute painful episodes is outside the scope of this guideline. Although no guidance will be produced on how to prevent sickle cell crisis, this may be covered as part of the question on patient information and support needs. Recommendations will be based on the evidence review and the expertise of the GDG. Please see the guidelines manual for more information about the development of clinical guidelines http://www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines/clinicalguidelinedevelopmentmethods/GuidelinesManual2009.jsp
SH	UK Forum on Haemoglobin Disorders	15.12	4.3.2.b	We feel that ways of trying to minimise acute painful episodes should be included.	Thank you, however the prevention of acute painful episodes is outside the remit of this guideline. Although no guidance will be produced on how to prevent sickle cell crisis, this may be covered as part

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					of the question on patient information and support needs. Recommendations will be based on the evidence review and the expertise of the GDG. Please see the guidelines manual for more information about the development of clinical guidelines http://www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines/clinicalguidelinedevelopmentmethods/GuidelinesManual2009.jsp
SH	UK Forum on Haemoglobin Disorders	15.13	4.3.2.e	It seems incomplete to address a range of treatment agents and then not to cover how to deal with their adverse effects. Indeed adverse events associated with pain management appears to be a Main Outcome [4.4 c)	Thank you for your comment. The rate of adverse events that are associated with interventions will be considered as part of the evidence review and may have an important impact on whether a specific drug is recommended for use. However, the guideline will not produce any specific recommendations on how these side-effects should be managed. It is assumed that healthcare professionals providing care will manage these adverse events in an appropriate manner using their clinical expertise.
SH	UK Forum on Haemoglobin Disorders	15.14	5.1	Refers only to relevant NICE guidance but omits a range of relevant other documents. We are sure that the Guidelines Group will include professionals familiar with these and so do not include them here, but would be happy to if helpful.	Thank you. NICE is only able to refer to other NICE guidance and Department of Health publications. Other relevant guideline however will be presented to the GDG for discussion but will not form part of the evidence review.
SH	Wockhardt UK	2.00	3.2.c	According to the seventh bullet point in this section, The British Committee for Standards in Haematology (2003) recommends the use of oral analgesia, if possible, in children, although "very severe pain may require initial control with parenteral analgesia". If effective analgesia is to be achieved by 60 minutes, as also recommended by the British Committee for Standards in Haematology (2003), oral analgesia will not be appropriate for a distressed child in severe pain and parenteral – preferably non-invasive –	Thank you for your comment. Section 3.2 of the scope relates to current practice within the NHS. This section is limited to the management of pain in hospital and provides an overview of the guidance available for this topic. It is anticipated that this guideline will provide recommendations on which pharmacological interventions to use in hospital for acute painful sickle cell episodes. This specifically includes the

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				analgesia should be given initially (e.g. nasal diamorphine).	choice, timing and route of analgesia (please see section 4.3.1 for other clinical issues that will be covered).
SH	Wockhardt UK	2.01	3.2.e	This is blank.	Thank you.
SH	Wockhardt UK	2.02	4.4.d	This outcome should simply be "Development of acute complications". "Risk factors" are not outcomes but contributors to outcomes.	Thank you. In order to fully address 4.3.1f (i.e. the clinical signs and symptoms to identify patients who are likely to have acute complications associated with a painful sickle cell episode) it was considered important to have 'risk factors for the development of acute complications' as it is the risk factors or predictors of acute complications that will be extracting from the research papers.
SH	Wockhardt UK	2.03	4.5	It is difficult to see how the Quality-Adjusted Life Year can be used as the preferred unit of effectiveness in the management of **an** acute episode, for which the guideline is intended to cover management only until the pain is under control (as per the third introductory paragraph to section 4). For a single episode, the preferred unit of effectiveness should be a measure of the speed and degree of pain relief – e.g. the time to achieve complete pain relief.	Thank you for your comment. NICE has a preference for expressing health gain in QALYs in order to capture the effects that therapy may have on both duration and quality of life, and also to facilitate comparability between clinically unrelated topics. We appreciate the difficulty in measuring QALYs for an acute event. In addition to using speed and degree of pain relief as a measure of effectiveness in this case, it is also important to extrapolate long term consequences in terms of morbidity and mortality.

These organisations were approached but did not respond:

African Health Policy Network
Alder Hey Children's NHS Foundation Trust
Association of Paediatric Anaesthetists of Great Britain and Ireland
Association of Paediatric Emergency Medicine
BMJ
BOC Healthcare

British Medical Association (BMA)
British National Formulary (BNF)
British Society for Haematology
Cambridge University Hospitals NHS Foundation Trust (Addenbrookes)
Care Quality Commission (CQC)
Central North West London NHS Trust
College of Emergency Medicine
Connecting for Health
Department for Communities and Local Government
Department of Health Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI)
Department of Health, Social Services & Public Safety, Northern Ireland (DHSSPSNI)
Dudley PCT
Faculty of Pain Medicine of the Royal College of Anaesthetists
George Elliot Hospital Trust
GlaxoSmithKline UK
Gloucestershire Hospitals NHS Trust
Great Western Hospitals NHS Foundation Trust
Guy's and St Thomas NHS Foundation Trust
Healthcare Improvement Scotland
Healthcare Quality Improvement Partnership
Lambeth Community Health
Launch Diagnostics Limited
Liverpool Community Health
London Ambulance Service NHS Trust
Luton & Dunstable Hospital NHS Foundation Trust
Manchester Sickle Cell & Thalassaemia Centre
Medicines and Healthcare Products Regulatory Agency (MHRA)
Ministry of Defence (MoD)
National Patient Safety Agency (NPSA)
National Treatment Agency for Substance Misuse
Neonatal & Paediatric Pharmacists Group (NPPG)
NETSCC, Health Technology Assessment
NHS Blood and Transplant
NHS Clinical Knowledge Summaries Service (SCHIN)
NHS Direct
NHS Plus
NHS Sheffield
NHS Western Cheshire

Nottingham University Hospitals NHS Trust
Paediatric Intensive Care Society
PERIGON Healthcare Ltd
Public Health Wales
Rotherham NHS Foundation Trust
Royal Berkshire NHS Foundation Trust
Royal College of Anaesthetists
Royal College of General Practitioners Wales
Royal College of Midwives
Royal College of Obstetricians and Gynaecologists
Royal College of Physicians London
Royal College of Psychiatrists
Royal College of Radiologists
Royal College of Surgeons of England
Royal Pharmaceutical Society of Great Britain
Royal Society of Medicine
Scarborough and North Yorkshire Healthcare NHS Trust
Scottish Intercollegiate Guidelines Network (SIGN)
Sheffield Teaching Hospitals NHS Foundation Trust
Sky Medical Technology Ltd
Social Care Institute for Excellence (SCIE)
Social Exclusion Task Force
Society and College of Radiographers
Society for Acute Medicine
Society for Vascular Technology of Great Britain and Ireland
South East Coast Ambulance Service
UCLH NHS Foundation Trust
UNITE THE UNION-CPHVA
Welsh Assembly Government
Welsh Scientific Advisory Committee (WSAC)
West Midlands Ambulance Service NHS Trust
Western Health and Social Care Trust
Whittington Hospital Trust
Wirral University Teaching Hospital NHS Foundation Trust
York Teaching Hospital NHS Foundation Trust