Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Managing acute complications of sickle cell disease. In: Evidence-based management of sickle cell disease.

Bibliographic Source(s)

Managing acute complications of sickle cell disease. In: Evidence-based management of sickle cell disease. Bethesda (MD): National Heart, Lung, and Blood Institute (NHLBI); 2014. p. 31-54.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- August 31, 2016 – Opioid pain and cough medicines combined with benzodiazepines : A U.S. Food and Drug Administration (FDA) review has found that the growing combined used of opioid medicines with benzodiazepines or other drugs that depress the central nervous system (CNS) has resulted in serious side effects, including slowed or difficult breathing and deaths. FDA is adding Boxed Warnings to the drug labeling of prescription opioid pain and prescription opioid cough medicines and benzodiazepines.
- March 22, 2016 – Opioid pain medicines : The U.S. Food and Drug Administration (FDA) is warning about several safety issues with the entire class of opioid pain medicines. These safety risks are potentially harmful interactions with numerous other medications, problems with the adrenal glands, and decreased sex hormone levels. They are requiring changes to the labels of all opioid drugs to warn about these risks.

Recommendations

Major Recommendations

Definitions of the grades of recommendation (Strong, Weak), the quality of supporting evidence (High, Moderate, Low, Very Low), and consensus statements are presented at the end of the "Major Recommendations" field.

Note from the National Heart, Lung, and Blood Institute (NHLBI) and the National Guideline Clearinghouse (NGC): The evidence-based management of sickle cell disease (SCD) has been divided into five topic areas with individual summaries covering recommendations to assist health care professionals in various aspects of management. In addition to the current summary, the following are available:

- Health maintenance for people with sickle cell disease
- Managing chronic complications of sickle cell disease
- Hydroxyurea therapy in the management of sickle cell disease
- Blood transfusion in the management of sickle cell disease

Vaso-Occlusive Crisis (VOC)

Key Question 10

For adults and children with SCD-related acute pain, what are the most effective acute pain management strategies (including types of analgesics, dose and administration protocols, and other interventions such as inhaled nitrous oxide, oxygen, and transfusion)?

Recommendations

The recommendations labeled "consensus" in this section were based on recommendations developed by the American Pain Society (APS) or on panel expertise. The remaining recommendations are based on the evidence review conducted by the methodology team. These recommendations are intended to be for all settings where patients present with VOC.

1. In adults and children with SCD and pain
    - When indicated, initiate diagnostic evaluation of causes of pain other than a VOC while beginning to treat pain. (Consensus–Adapted)
2. In adults and children with SCD and a VOC
    - Determine characteristics, associated symptoms, location, and intensity of pain based on patient self-report and observation. If the VOC pain is atypical, investigate other possible etiologies of pain. (Consensus–Adapted)
    - Rapidly assess the patient's recent analgesic use (opioid and nonopioid). (Consensus–Adapted)
    - Rapidly initiate analgesic therapy within 30 minutes of triage or within 60 minutes of registration. (Consensus–Panel Expertise)
    - Base analgesic selection on pain assessment, associated symptoms, outpatient analgesic use, patient knowledge of effective agents and doses, and past experience with side effects. (Consensus–Adapted)
3. In adults and children with SCD and a VOC
    - Use an individualized prescribing and monitoring protocol (written by the patient's SCD provider) or an SCD-specific protocol whenever possible (see Exhibit 7 in the original guideline document) to promote rapid, effective, and safe analgesic management and resolution of the VOC. (Consensus–Panel Expertise)
4. In adults and children with SCD and a VOC associated with mild to moderate pain who report relief with NSAIDS in the absence of contraindications to the use of nonsteroidal anti-inflammatory drugs (NSAIDs), continue treatment with NSAIDs. (Moderate Recommendation, Low-Quality Evidence)
5. In adults and children with SCD and a VOC associated with severe pain, rapidly initiate treatment with parenteral opioids. (Strong Recommendation, High-Quality Evidence)
6. In adults and children with SCD and a VOC associated with severe pain
    - Calculate the parenteral (intravenous [IV] or subcutaneous) opioid dose based on total daily short-acting opioid dose currently being taken at home to manage the VOC. (Consensus–Panel Expertise)
    - Administer parenteral opioids using the subcutaneous route when IV access is difficult. (Consensus–Panel Expertise)
    - Reassess pain and re-administer opioids if necessary for continued severe pain every 15 to 30 minutes until pain is under control per patient report. (Consensus–Adapted)
    - Maintain or consider escalation of the dose by 25 percent until pain is controlled. (Consensus–Panel Expertise)
    - Reassess after each dose for pain relief and side effects. (Consensus–Panel Expertise)
    - Initiate around-the-clock opioid administration by patient-controlled analgesia (PCA) or frequently scheduled doses versus "as requested" (PRN) administration. (Moderate Recommendation, Low-Quality Evidence)
7. If ordering around-the-clock, continuous infusion of opioids via the PCA, carefully consider whether there is a need to withhold long-acting oral opioids to prevent over-sedation. (Consensus–Panel Expertise)
    - If demand dosing only is ordered via the PCA, continue use of long-acting oral opioids. (Consensus–Panel Expertise)
    - At discharge, evaluate inpatient analgesic requirements, wean parenteral opioids prior to conversion to oral opioids, and adjust home dose of long- and short-acting opioid prescriptions to prevent opioid withdrawal after discharge. (Consensus–Panel Expertise)
8. In adults and children with SCD and a VOC, do not use meperidine unless it is the only effective opioid for an individual patient.

(Consensus–Adapted)

9. In adults and children with a VOC, administer oral NSAIDs as an adjuvant analgesic in the absence of contraindications. (Consensus—Adapted)
10. In adults and children with a VOC who require antihistamines for itching secondary to opioid administration, prescribe agents orally, and do not re-administer with each dose of opioid in the acute VOC management phase. Re-administer every 4 to 6 hours if needed. (Consensus–Panel Expertise)
11. To reduce the risk of acute chest syndrome in adults and children hospitalized for a VOC
    - Encourage use of incentive spirometry while awake. (Strong Recommendation, Moderate-Quality Evidence)
    - Encourage ambulation and activity as soon as possible. (Consensus–Panel Expertise)
12. In adults and children with VOC, use adjunctive nonpharmacologic approaches to treat pain such as local heat application and distraction. (Consensus–Adapted)
13. In euvolemic adults and children with SCD and a VOC who are unable to drink fluids, provide IV hydration at no more than maintenance rate to avoid over-hydration. (Consensus–Adapted)
14. In adults and children with SCD and a VOC being treated with opioids, monitor for excessive sedation by measuring sedation with an objective measurement sedation scale and oxygenation levels. (Consensus–Panel Expertise)
15. Gradually titrate down parenteral opioids as VOC resolves. (Consensus–Panel Expertise)
16. In adults and children with SCD and a VOC, do not administer a blood transfusion unless there are other indications for transfusion (see the NGC summary of the NHLBI guideline Blood transfusion in the management of sickle cell disease). (Moderate Recommendation, Low-Quality Evidence)
17. In adults and children with SCD and a VOC with an oxygen saturation <95 percent on room air, administer oxygen. (Consensus–Panel Expertise)

Fever

Recommendations

1. In people with SCD and a temperature ≥101.3°F (38.5°C), immediately evaluate with history and physical examination, complete blood count (CBC) with differential, reticulocyte count, blood culture, and urine culture when urinary tract infection is suspected. (Consensus–Panel Expertise)
2. In children with SCD and a temperature ≥101.3°F (38.5°C), promptly administer ongoing empiric parenteral antibiotics that provide coverage against *Streptococcus pneumoniae* and gram-negative enteric organisms. Subsequent outpatient management using an oral antibiotic is feasible in people who do not appear ill. (Consensus–Panel Expertise)
3. Hospitalize people with SCD and a temperature ≥103.1°F (39.5°C) and who appear ill for close observation and IV antibiotic therapy. (Consensus–Panel Expertise)
4. In people with SCD whose febrile illness is accompanied by shortness of breath, tachypnea, cough, and/or rales, manage according to the preceding recommendations and obtain an immediate chest x-ray to investigate for acute chest syndrome (ACS). (Consensus–Panel Expertise)
5. In febrile people with SCD who have localized or multifocal bone tenderness, especially when accompanied by erythema and swelling, include bacterial osteomyelitis in the differential diagnosis and manage accordingly. (Consensus–Panel Expertise)

Acute Renal Failure

Key Question 11

In people with SCD and acute renal failure (ARF), what are the most effective strategies to reduce mortality and the risk of developing end-stage renal disease (ESRD)?

Recommendations

1. In the setting of an acute rise in serum creatinine of ≥0.3 mg/dL
    - Monitor renal function daily, including serum creatinine and fluid intake/output. (Consensus–Panel Expertise)
    - Avoid potential nephrotoxic drugs and imaging agents. (Consensus–Panel Expertise)
    - Evaluate the patient thoroughly for all potential etiologies in consultation with a nephrologist as needed. (Consensus–Panel Expertise)
2. Do not give blood transfusions to treat ARF unless there are other indications for transfusion. (Consensus–Panel Expertise)
3. Use renal replacement therapy (e.g., hemodialysis) when needed for ARF. (Consensus–Panel Expertise)

Priapism

Key Question 12

In males with SCD presenting with acute priapism, what is the relative efficacy of conservative management, pharmacological management, transfusion, and surgery on the outcomes of detumescence and the incidence of future impotence?

Recommendations

1. For an episode of priapism lasting 4 hours or longer, initiate interventions to include:
    - Vigorous oral or IV hydration and oral or IV analgesia (Strong Recommendation, Low-Quality Evidence); and
    - Consultation with a urologist who can perform further evaluation and intervention for symptoms which do not remit with initial conservative medical management. (Consensus–Panel Expertise)
2. Do not use transfusion therapy for immediate treatment of priapism associated with SCD. (Moderate Recommendation, Low-Quality Evidence)
3. Consult with a hematologist for possible preoperative transfusion if surgical intervention is required.(Consensus–Panel Expertise)

Hepatobiliary Complications

Key Question 13

In people with SCD, what is the appropriate management of cholelithiasis and related cholecystitis to resolve symptoms and prevent perioperative complications? What is the most effective treatment strategy for people with SCD presenting with acute hepatic sequestration (AHS) and acute intrahepatic cholestasis (AIC) to reduce mortality and resolve symptoms?

Recommendations

1. Treat acute cholecystitis in children and adults with SCD with antibiotics and surgical consultation. (Consensus–Panel Expertise)
2. Treat asymptomatic gallstones with watchful waiting in children and adults with SCD. In those who develop symptoms specific to gallstones, treat with cholecystectomy. The laparoscopic approach is preferred if surgically feasible and available. (Strong Recommendation, Moderate-Quality Evidence)
3. Consult with a hematologist or sickle cell expert for possible preoperative transfusion if surgical intervention is required. (Consensus–Panel Expertise)
4. In children and adults with SCD and signs and symptoms of AHS or AIC, provide hydration, rest, close observation, and consult a sickle cell expert for further management. (Consensus–Panel Expertise)
5. In children and adults with SCD and signs and symptoms of possible AHS or severe AIC, obtain urgent consultation with a sickle cell disease expert for diagnosis confirmation. (Consensus–Panel Expertise)
6. In children and adults with SCD with confirmed AHS or severe AIC, perform simple or exchange transfusion. (Consensus–Panel Expertise)

Acute Anemia

Recommendations

1. During all acute illnesses in people with SCD, obtain a CBC and reticulocyte count, repeat daily in all hospitalized patients, and compare the results with the patient's prior measurements. (Consensus–Panel Expertise)
2. Assess people with SCD whose hemoglobin concentration is 2 g/dL or more below their baseline (or less than 6 g/dL when the baseline is unknown) for acute splenic sequestration, an aplastic episode, a delayed hemolytic transfusion reaction, ACS, and infection. (Consensus–Panel Expertise)
3. Use simple transfusion in people with SCD and acute anemia whose symptoms are due to anemia. (Consensus–Panel Expertise)
4. Perform a CBC and reticulocyte count promptly and again 7 to 10 days later in siblings and others with SCD who are exposed to a person with an aplastic episode. (Consensus–Panel Expertise)
5. Manage aplastic events with immediate red blood cell transfusion aimed at restoring the hemoglobin to a safe (not necessarily baseline) value. Isolation of hospitalized patients (droplet precautions) is required to prevent spread of the parvovirus B19 to pregnant women and others with SCD or compromised immunity. (Consensus–Panel Expertise)

Splenic Sequestration

Key Question 14

In people with SCD with acute anemia and splenic sequestration or hypersplenism, what are the most effective strategies to reduce mortality, correct anemia, and prevent recurrence?

Recommendations

1. In people with hypovolemia due to severe acute splenic sequestration, immediately provide IV fluid resuscitation. (Strong Recommendation, Low-Quality Evidence)
2. In consultation with a sickle cell expert, transfuse people who have acute splenic sequestration and severe anemia to raise the hemoglobin to a stable level, while avoiding over-transfusion. (Strong Recommendation, Low Quality Evidence)
3. In consultation with a sickle cell expert, address the performance and timing of splenectomy in people with recurrent acute splenic sequestration or symptomatic hypersplenism. (Moderate Recommendation, Low-Quality Evidence)

Acute Chest Syndrome (ACS)

Key Question 15

In people with SCD and ACS, what is the most effective treatment (among transfusion, exchange transfusion, supportive therapy, steroids, and/or antibiotics) to reduce mortality, resolve pain, and prevent clinical deterioration?

Recommendations

1. Evaluate people with SCD who develop acute onset of lower respiratory tract disease signs and/or symptoms (cough, shortness of breath, tachypnea, retractions, or wheezing) with or without fever for ACS. This should include a chest x-ray and measurement of oxygen saturation by pulse oximetry. (Consensus–Panel Expertise)
2. Hospitalize people with ACS. (Consensus–Panel Expertise)
3. Treat people with SCD who have ACS with an IV cephalosporin, an oral macrolide antibiotic, supplemental oxygen (to maintain oxygen saturation of greater than 95 percent), and close monitoring for bronchospasm, acute anemia, and hypoxemia. (Strong Recommendation, Low-Quality Evidence)
4. In people with sickle cell anemia (SCA), give simple blood transfusion (10 mL/kg red blood cells) to improve oxygen carrying capacity to people with symptomatic ACS whose hemoglobin concentration is >1.0 g/dL below baseline. If baseline hemoglobin is 9 g/dL or higher, simple blood transfusion may not be required. (Weak Recommendation, Low-Quality Evidence)
5. In people with HbSC disease or HbSβ^+-thalassemia with ACS, decisions about transfusion should be made in consultation with an SCD expert. (Strong Recommendation, Low-Quality Evidence)
6. In all persons with SCD, perform urgent exchange transfusion—with consultation from hematology, critical care, and/or apheresis specialists—when there is rapid progression of ACS as manifested by oxygen saturation below 90 percent despite supplemental oxygen, increasing respiratory distress, progressive pulmonary infiltrates, and/or decline in hemoglobin concentration despite simple transfusion. (Strong Recommendation, Low-Quality Evidence)
7. Encourage use of incentive spirometry while awake. (Strong Recommendation, Moderate-Quality Evidence)

Acute Stroke

Key Question 16

In people with SCD presenting with acute stroke, what is the most effective treatment strategy (transfusion, thrombolytics, hydroxyurea, or other therapies) to reduce mortality, preserve neurological function, and reduce recurrence rates?

Recommendations

1. In people with SCD who present with severe headache, altered level of consciousness, seizures, speech problems, and/or paralysis, evaluate for acute stroke by seeking neurologic consultation and performing an urgent head computerized tomography (CT) scan followed by magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) if available. (Consensus–Panel Expertise)
2. In consultation with a sickle cell expert, perform exchange transfusion in people with SCD who develop acute stroke confirmed by neuroimaging. (Consensus–Panel Expertise)
3. Initiate prompt evaluation, including neurologic consultation and neuroimaging studies, in people with SCD who have mild, subtle, or recent history of signs or symptoms consistent with transient ischemic attack. (Consensus–Panel Expertise)
4. In children and adults who have had a stroke, initiate a program of monthly simple or exchange transfusions. (Moderate Strength, Low-Quality Evidence)
5. In children and adults who have had a stroke, if it is not possible to implement a transfusion program, initiate hydroxyurea therapy. (Moderate Strength, Low-Quality Evidence)

Multisystem Organ Failure (MSOF)

Recommendations

1. In people with SCD who exhibit severe deterioration during a VOC, immediately evaluate for potential MSOF. (Consensus–Panel Expertise)
2. In people with SCD and respiratory failure, support respiratory status with supplemental oxygenation and mechanical ventilation when needed. (Consensus–Panel Expertise)
3. Use renal replacement therapy (e.g., hemodialysis) when needed for acute renal failure. (Consensus–Panel Expertise)
4. In people with SCD and MSOF, immediately initiate either simple or exchange transfusion in consultation with a sickle cell expert or hematologist. (Consensus–Panel Expertise)

Acute Ocular Conditions

Key Question 17

In people with SCD and acute eye symptoms, what is the optimal management strategy to preserve vision and prevent long-term ocular complications?

Recommendations

1. Immediately examine for hyphema anyone with SCD who presents with eye trauma. If hyphema is present, immediately refer to an ophthalmologist for further management. (Consensus–Panel Expertise)
2. Promptly refer anyone with SCD exhibiting signs and symptoms such as protrusion of the eye, changes in visual acuity (flashers or floaters), and unilateral or bilateral loss of vision to an eye specialist capable of performing a dilated eye exam to assess visual acuity, intraocular pressure, and the peripheral retina. (Consensus–Panel Expertise)
3. Manage acute ocular complications in consultation with an ophthalmologist, hematologist, and other specialists with expertise in SCD. (Consensus–Panel Expertise)

Definitions:

Grading of Recommendations Assessment, Development and Evaluation (GRADE) Recommendations

Grade of Recommendation	Clarity of Risk/Benefit	Quality of Supporting Evidence	Implications
Strong recommendation **High-quality evidence**	Benefits clearly outweigh harms and burdens, or vice versa	Consistent evidence from well-performed randomized controlled trials (RCTs) or exceptionally strong evidence from unbiased observational studies*	Recommendation can apply to most patients in most circumstances. Further research is very unlikely to change confidence in the estimate of effect.
Strong recommendation **Moderate-quality evidence**	Benefits clearly outweigh harms and burdens, or vice versa	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect or imprecise evidence), or unusually strong evidence from unbiased observational studies	Recommendation can apply to most patients in most circumstances. Further research (if performed) is likely to have an impact on confidence in the estimate of effect and may change the estimate.
Strong recommendation **Low-quality evidence**	Benefits clearly outweigh harms and burdens, or vice versa	Evidence for at least one critical outcome from observational studies, from RCTs with serious flaws, or indirect evidence	Recommendation may change when higher quality evidence becomes available. Further research (if performed) is likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Strong recommendation **Very low-quality evidence (very rarely applicable)**	Benefits clearly outweigh harms and burdens, or vice versa	Evidence for at least one of the critical outcomes from unsystematic clinical observations or very indirect evidence	Recommendation may change when higher quality evidence becomes available; any estimate of effect, for at least one critical outcome, is very uncertain.
Weak recommendation **High-quality**	Benefits closely balanced with harms and burdens	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies	The best action may differ depending on circumstances or patient or societal values. Further research is very unlikely to change confidence in the estimate of effect.

Grade of Recommendation	Clarity of Risk/Benefit	Quality of Supporting Evidence	Implications
Weak recommendation **Moderate-quality evidence**	Benefits closely balanced with harms and burdens	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect or imprecise evidence), or unusually strong evidence from unbiased observational studies	Alternative approaches likely to be better for some patients under some circumstances. Further research (if performed) is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Weak recommendation **Low-quality evidence**	Uncertainty in the estimates of benefits, harms, and burdens; benefits may be closely balanced with harms and burdens	Evidence for at least one critical outcome from observational studies, from RCTs with serious flaws, or indirect evidence	Other alternatives may be equally reasonable. Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Weak recommendation **Very low-quality evidence**	Major uncertainty in the estimates of benefits, harms, and burdens; benefits may or may not be balanced with harms and burdens	Evidence for at least one critical outcome from unsystematic clinical observations or very indirect evidence	Other alternatives may be equally reasonable. Any estimate of effect, for at least one critical outcome, is very uncertain.

Source: Reprinted with permission of the American Thoracic Society. Copyright © 2012 American Thoracic Society. Schünemann HJ, Jaeschke R, Cook DJ, Bria WF, El-Solh AA, Ernst A, Fahy BF, Gould MK, Horan KL, Krishnan JA, Manthous CA, Maurer JR, McNicholas WT, Oxman AD, Rubenfeld G, Turino GM, Guyatt G; ATS Documents Development and Implementation Committee. An official ATS statement: grading the quality of evidence and strength of recommendations in ATS guidelines and recommendations. *Am J Respir Crit Care Med*. 2006 Sep 1;174(5):605-14. Official Journal of the American Thoracic Society.

*Exceptionally strong evidence from unbiased observational studies includes: (1) evidence from studies that yield estimates of the treatment effect that are large and consistent; (2) evidence in which all potential biases may be working to underestimate an apparent treatment effect, and therefore, the actual treatment effect is likely to be larger than that suggested by the study data; and (3) evidence in which a dose-response gradient exists.

Consensus Statements

The panel believed that, for this guideline document to be most helpful to primary care providers and specialty health care professionals, it needed to be comprehensive. This required that, in areas with minimal existing direct evidence, the panel would provide recommendations based on their and others' expert opinions. Those recommendations are labeled as "consensus." Several different situations, outlined below, led to the use of consensus statements.

Consensus–Panel Expertise

- Systematic reviews conducted by the methodology team revealed minimal or no supporting evidence (e.g., management of acute hepatic sequestration).
- An adequate systematic review of the literature was not feasible because of anticipated low yield or no yield (e.g., comparative effectiveness of management approaches for individuals with SCD presenting with fever or worsening anemia).
- Recommendations were based on the panel's expert knowledge, practice experience, and ability to extrapolate evidence from non-SCD populations (e.g., management of chronic opioid therapy in chronic SCD pain).

Consensus–Adapted

- These recommendations were based on the panel's expert knowledge to adapt recommendations derived from existing guidelines and synthesized evidence developed by other professional societies (e.g., management of acute and chronic pain in SCD). The panel clearly identified these statements as consensus recommendations and acknowledges that these areas represent gaps in the evidence base and areas for future research.

Clinical Algorithm(s)

An algorithm titled "Acute Pain Algorithm" is provided in the original guideline document.

Scope

Disease/Condition(s)

Acute complications of sickle cell disease (SCD) including:

- Vaso-occlusive crisis (VOC)
- Fever
- Acute renal failure (ARF)
- Priapism
- Hepatobiliary complications (cholelithiasis, acute cholecystitis, acute hepatic sequestration [AHS], acute intrahepatic cholestasis [AIC])
- Acute anemia
- Splenic sequestration
- Acute chest syndrome (ACS)
- Acute stroke
- Multisystem organ failure (MSOF)
- Acute ocular conditions

Guideline Category

Evaluation

Management

Treatment

Clinical Specialty

Critical Care

Emergency Medicine

Family Practice

Gastroenterology

Hematology

Infectious Diseases

Internal Medicine

Nephrology

Neurology

Nursing

Ophthalmology

Pediatrics

Pulmonary Medicine

Surgery

Urology

Intended Users

Advanced Practice Nurses

Health Care Providers

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To synthesize the available scientific evidence on sickle cell disease (SCD) and offer guidance to busy primary care clinicians
- To help people living with SCD receive appropriate care by providing the best science-based recommendations to guide practice decisions
- To assist health care professionals in the management of common issues, including routine health maintenance, the recognition and treatment of common acute and chronic complications and comorbidities of SCD, as well as the indications for and monitoring of hydroxyurea and blood transfusion therapy
- To help provide the latest evidence-based recommendations to manage this condition and to help engage health care professionals in supporting their implementation at the practice level
- To present recommendations for the evaluation and management of common acute SCD complications, as well as information regarding their frequency, common presentation, usual evaluation, and treatment

Target Population

Infants, children, adolescents, and adults with sickle cell disease (SCD)

Interventions and Practices Considered

1. Evaluation and treatment of acute pain (vaso-occlusive crisis [VOC]): pain assessment, types of analgesics (nonsteroidal anti-inflammatory drugs [NSAIDs] or opioids), dose and administration protocols, nonpharmacologic interventions such as heat
2. Evaluation and management of fever: parenteral antibiotics and hospitalization
3. Evaluation and management of acute renal failure (ARF): monitoring serum creatinine and fluid intake/output, avoiding nephrotoxic drugs, hemodialysis when needed
4. Management of priapism: vigorous hydration, analgesia, urology and hematology consultation
5. Management of hepatobiliary complications
    - Antibiotics and surgical consultation for acute cholecystitis
    - Cholecystectomy for symptomatic gallstones
    - Consultation with hematologist and sickle cell expert for possible acute hepatic sequestration (AHS) and acute intrahepatic cholestasis (AIC)
    - Simple or exchange transfusion for confirmed AHS or severe AIC
6. Evaluation and management of acute anemia: complete blood count (CBC), reticulocyte count, hemoglobin concentration, and transfusion
7. Management of acute splenic sequestration: intravenous (IV) fluid resuscitation, transfusion, consult with sickle cell expert, and splenectomy
8. Evaluation and management of acute chest syndrome (ACS): chest x-ray, measurement of oxygen saturation, hospitalization, antibiotics, supplementation oxygen, blood transfusion, exchange transfusion, incentive spirometry (steroids were considered but not recommended)
9. Evaluation and management of acute stroke: neurologic consultation, head computerized tomography (CT) and magnetic resonance imaging (MRI), sickle cell expert consultation, simple or exchange transfusion, hydroxyurea therapy
10. Evaluation and management of multisystem organ failure (MSOF): supplemental oxygenation, mechanical ventilation, renal replacement therapy (hemodialysis), simple or exchange transfusion, consultation with sickle cell expert or hematologist
11. Evaluation and management of acute ocular conditions: examination for hyphema, prompt consultation with ophthalmologist, hematologist, or other expert

Major Outcomes Considered

- Complication-specific outcomes including resolution of complication
- General sickle cell disease (SCD) outcomes if relevant (death, stroke, pain crises, need for transfusion, hemoglobin and hemoglobin F

levels)
- Outcomes of diagnostic studies: accuracy of diagnosis if reported

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

General Literature Search

Due to the comprehensive scope of the guidelines, the search strategies for the systematic reviews were designed to have high sensitivity and low specificity; hence, the strategies were often derived from population and condition terms (e.g., people with sickle cell disease [SCD] who have priapism) and not restricted or combined with outcome or intervention terms. To be inclusive of the available literature in the field, searches included randomized trials, nonrandomized intervention studies, and observational studies. Case reports and small case series were included only when outcomes involved harm (e.g., the adverse effects of hydroxyurea) or when rare complications were expected to be reported.

Literature searches involved multiple databases (e.g., Medline® In-Process & Other Non-Indexed Citations, MEDLINE®, EMBASE, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Cumulative Index to Nursing and Allied Health Literature [CINAHL®], TOXLINE®, and Scopus) and used controlled vocabulary (prespecified) terms supplemented with keywords to define concept areas.

An updated search was performed to span the time from June 1, 2010 through July 11, 2014.

Guideline-specific Literature Search

A comprehensive study of several databases was conducted, and all human studies in English published from 1970 to July 2010 that addressed each Patient, Intervention, Comparison, Outcomes, and Study Design (PICOS) question were identified. When the literature search found insufficient evidence on a topic (e.g., vaso-occlusive crisis), these topics were supplemented with recommendations derived from other published guidelines by professional organizations, which were based on systematic reviews of broader population groups; these recommendations are labeled "Consensus–Adapted." In the instances of fever, acute anemia, and multisystem organ failure (MSOF), a literature search was not conducted, so the panel relied on their cumulative expertise and knowledge to make recommendations; these recommendations are labeled "Consensus–Panel Expertise."

Detailed information on the search questions, search strategy, study selection process, and list of excluded studies used in this guideline can be found in the systematic review (see the "Availability of Companion Documents" field).

Number of Source Documents

General Literature Search

The initial literature searches performed to support these guidelines yielded 12,532 references. The expert panel also identified an additional 1,231 potentially relevant references. An updated search of randomized controlled trials (RCTs) added eight trials. All abstracts were reviewed independently by two reviewers using an online reference management system (DistillerSR—http://systematic-review.net) until reviewers reached adequate agreement (kappa ≥0.90). A total of 1,575 original studies were included in the evidence tables.

Guideline-specific Literature Search

A total of 549 studies of complications were included.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

See the "Rating Scheme for the Strength of the Recommendations" field.

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

General Methodology

Evidence Synthesis

Methodologists developed evidence tables to summarize individual study findings and present the quality of evidence (i.e., confidence in the estimates of effect). The tables included descriptions of study population, sickle cell disease (SCD) genotypes, interventions, and outcomes. Additional methodological details are discussed in each evidence table, including the search question, search strategy, study selection process, and list of excluded studies (see the "Availability of Companion Documents" field).

Evidence Framework

The methodology team used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework to grade the quality of evidence, and, in concert with the panel, determine the strength of recommendations. The GRADE framework is accepted by more than 75 national and international organizations (see exhibit 3 in the original guideline document). It provides the advantages of: (a) separately judging the quality of supporting evidence and strength of recommendations, and (b) incorporating factors other than evidence in decisionmaking (e.g., the balance of benefits and harms; the perceived values and preferences of those with SCD; resources; and clinical and social context). GRADE emphasizes the use of patient-important outcomes (i.e., outcomes that affect the way patients feel, function, or survive) over laboratory and physiologic outcomes.

Determining Evidence Quality

In the GRADE framework, the quality of evidence (in this case, the body of evidence) is rated as high, moderate, low, or very low. The quality of evidence derived from randomized trials starts as "high," and the quality of evidence derived from observational studies starts as "low." The quality of evidence can then be lowered due to methodological limitations in individual studies (risk of bias), inconsistency across studies (heterogeneity), indirectness (the extent to which the evidence fails to apply to the specific clinical question in terms of the patients, interventions, or outcomes), imprecision (typically due to a small number of events or wide confidence intervals), and the presence of publication and reporting biases. Conversely, the quality of evidence can be upgraded in certain situations such as when the treatment effect is large or a dose-response relationship is evident.

Existing Systematic Reviews and Clinical Practice Guidelines

The expert panel and methodology team identified existing systematic reviews and clinical practice guidelines that were relevant to the topics of this guideline, even though they were not necessarily specific to people with SCD. If the methodological quality of these resources was found to be appropriate by the methodology team, they were used. Using this external evidence was considered helpful because well-conducted systematic reviews made the process of identifying relevant studies more feasible. In addition, using existing guidelines developed by professional organizations enabled the panel to develop more comprehensive recommendations that addressed specific aspects of care in individuals with SCD. Usually, this external evidence was derived from studies in non-sickle cell patient cohorts because it was felt that they offered more precise and useful inferences than evidence derived from sickle cell patient studies. For example, comparative evidence in the area of pain management in people with SCD was sparse. In this situation, pain management guidelines from individuals with other pain-related conditions proved to be helpful.

The methodology team used the AMSTAR tool to assess the methodological quality of systematic reviews. Recent well-conducted systematic reviews were identified that addressed hydroxyurea therapy in pediatric and adult patients. The expert panel and methodology team appraised

these reviews and conducted additional searches to update the existing systematic review through May 2010 to find evidence for the benefits, harms, and barriers of using hydroxyurea. Regarding the management of children with SCD complications, the panel also used recent evidence that had been systematically reviewed.

Existing clinical practice guidelines were considered acceptable if they had prespecified clinical questions, were developed after a comprehensive literature search, had explicit and clear criteria for the inclusion of evidence, and included recommendations that were explicitly linked to the quality of supporting evidence. The expert panel and methodology team used relevant recommendations from the U.S. Preventive Services Task Force (USPSTF), the Advisory Committee on Immunization Practices (ACIP), the Centers for Disease Control and Prevention's (CDC) adaptation of the World Health Organization's (WHO) "Medical Eligibility Criteria for Contraceptive Use," and the American Pain Society's "Guideline for the Management of Acute and Chronic Pain in Sickle-Cell Disease," and "Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain."

Guideline-specific Methodology

Detailed information on the evaluated studies as well as the observational and case studies/series referenced can be found in the evidence table in the systematic review (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

These guidelines were developed by an expert panel composed of health care professionals with expertise in family medicine, general internal medicine, adult and pediatric hematology, psychiatry, transfusion medicine, obstetrics and gynecology, emergency department nursing, and evidence-based medicine. Panel members were selected by the National Heart, Lung, and Blood Institute's (NHLBI's) leadership.

Process and Methodology

The expert panel first convened in the spring of 2009 to establish the vision and purpose of the panel, discuss the process and schedule for producing the guidelines, and determine the critical areas to be addressed. Prior to this meeting, the expert panel participated in a conference call to introduce the panel's work and discuss the overarching questions that should be answered by the guidelines. Before beginning the writing of the guidelines report, the expert panel divided its work into sections dealing with preventive care or health maintenance, recognition and management of acute sickle-cell disease (SCD)-related complications, recognition and management of chronic SCD-related complications, and the two most broadly assessed and available disease-modifying therapies for SCD, hydroxyurea and chronic blood transfusions.

With the assistance of the methodology team and the supporting evidence center, the panel then developed key questions and literature search terms to identify evidence. The field of SCD has a limited number of randomized controlled trials (RCTs) or large prospective cohort studies to guide clinical decisionmaking; therefore, few of the recommendations in this document are based on this highest quality evidence. For common health issues, the panel included the evidence-based recommendations of the United States Preventive Services Task Force (USPSTF) as well as vetted recommendations of other groups. These recommendations include the SCD reproductive-related recommendations of the World Health Organization (WHO), the immunization recommendations of the Advisory Committee on Immunization Practices (ACIP), and the acute and chronic pain management recommendations of the American Pain Society (APS). These recommendations are denoted as "Consensus–Adapted."

Recognizing the need to provide practical guidance for common problems that may lie outside of the panel's evidence reviews or available science, in many areas the published evidence was supplemented by the expertise of the panel members, who have many years of experience in managing and studying individuals with SCD. Recommendations based on the opinions of the expert panel members are labeled as "Consensus–Panel Expertise." Each is clearly labeled with the strength of the recommendation and the quality of evidence available to support it.

Determining the Strength of Recommendations

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework rates the strength of recommendations as "strong" or "weak." However, the panel modified the GRADE system and used a third category—moderate—when they determined that patients would be better off if they followed a recommendation, despite there being some level of uncertainty about the magnitude of benefit of the intervention or the relative net benefit of alternative courses of action. The panel intends for these moderate-strength recommendations to be used to populate protocols of care and provide a guideline based on the best available evidence. The panel does not intend for weak- or moderate-

strength recommendations to generate quality-of-care indicators or accountability measures or affect insurance reimbursement. Variation in care in the areas of weak- or moderate-strength recommendations may be acceptable, particularly in ways that reflect patient values and preferences. Conversely, strong recommendations represent areas in which there is confidence in the evidence supporting net benefit, and the recommendations likely apply to most individuals with sickle cell anemia. For more information, see the "Rating Scheme for the Strength of the Recommendations" field.

Rating Scheme for the Strength of the Recommendations

Grading of Recommendations Assessment, Development and Evaluation (GRADE) Recommendations

Grade of Recommendation	Clarity of Risk/Benefit	Quality of Supporting Evidence	Implications
Strong recommendation **High-quality evidence**	Benefits clearly outweigh harms and burdens, or vice versa	Consistent evidence from well-performed randomized controlled trials (RCTs) or exceptionally strong evidence from unbiased observational studies*	Recommendation can apply to most patients in most circumstances. Further research is very unlikely to change confidence in the estimate of effect.
Strong recommendation **Moderate-quality evidence**	Benefits clearly outweigh harms and burdens, or vice versa	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect or imprecise evidence), or unusually strong evidence from unbiased observational studies	Recommendation can apply to most patients in most circumstances. Further research (if performed) is likely to have an impact on confidence in the estimate of effect and may change the estimate.
Strong recommendation **Low-quality evidence**	Benefits clearly outweigh harms and burdens, or vice versa	Evidence for at least one critical outcome from observational studies, from RCTs with serious flaws, or indirect evidence	Recommendation may change when higher quality evidence becomes available. Further research (if performed) is likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Strong recommendation **Very low-quality evidence (very rarely applicable)**	Benefits clearly outweigh harms and burdens, or vice versa	Evidence for at least one of the critical outcomes from unsystematic clinical observations or very indirect evidence	Recommendation may change when higher quality evidence becomes available; any estimate of effect, for at least one critical outcome, is very uncertain.
Weak recommendation **High-quality evidence**	Benefits closely balanced with harms and burdens	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies	The best action may differ depending on circumstances or patient or societal values. Further research is very unlikely to change confidence in the estimate of effect.
Weak recommendation **Moderate-quality evidence**	Benefits closely balanced with harms and burdens	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect or imprecise evidence), or unusually strong evidence from unbiased observational studies	Alternative approaches likely to be better for some patients under some circumstances. Further research (if performed) is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Weak recommendation **Low-quality evidence**	Uncertainty in the estimates of benefits, harms, and burdens; benefits may be closely balanced with harms and burdens	Evidence for at least one critical outcome from observational studies, from RCTs with serious flaws, or indirect evidence	Other alternatives may be equally reasonable. Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Weak recommendation **Very low-quality evidence**	Major uncertainty in the estimates of benefits, harms, and burdens; benefits may or may not be balanced with harms and burdens	Evidence for at least one critical outcome from unsystematic clinical observations or very indirect evidence	Other alternatives may be equally reasonable. Any estimate of effect, for at least one critical outcome, is very uncertain.

Source: Reprinted with permission of the American Thoracic Society. Copyright © 2012 American Thoracic Society. Schünemann HJ, Jaeschke R, Cook DJ, Bria WF, El-Solh AA, Ernst A, Fahy BF, Gould MK, Horan KL, Krishnan JA, Manthous CA, Maurer JR, McNicholas WT, Oxman AD, Rubenfeld G, Turino GM, Guyatt G; ATS Documents Development and Implementation Committee. An official ATS statement: grading the quality of evidence and strength of recommendations in ATS guidelines and recommendations. *Am J Respir Crit Care Med*. 2006 Sep 1;174(5):605-14. Official Journal of the American Thoracic Society.

*Exceptionally strong evidence from unbiased observational studies includes: (1) evidence from studies that yield estimates of the treatment effect that are large and consistent; (2) evidence in which all potential biases may be working to underestimate an apparent treatment effect, and therefore, the actual treatment effect is likely to be larger than that suggested by the study data; and (3) evidence in which a dose-response gradient exists.

Consensus Statements

The panel believed that, for this guideline document to be most helpful to primary care providers and specialty health care professionals, it needed to be comprehensive. This required that, in areas with minimal existing direct evidence, the panel would provide recommendations based on their and others' expert opinions. Those recommendations are labeled as "consensus." Several different situations, outlined below, led to the use of consensus statements.

Consensus–Panel Expertise

- Systematic reviews conducted by the methodology team revealed minimal or no supporting evidence (e.g., management of acute hepatic sequestration).
- An adequate systematic review of the literature was not feasible because of anticipated low yield or no yield (e.g., comparative effectiveness of management approaches for individuals with sickle cell disease [SCD] presenting with fever or worsening anemia).
- Recommendations were based on the panel's expert knowledge, practice experience, and ability to extrapolate evidence from non-SCD populations (e.g., management of chronic opioid therapy in chronic SCD pain).

Consensus–Adapted

- These recommendations were based on the panel's expert knowledge to adapt recommendations derived from existing guidelines and synthesized evidence developed by other professional societies (e.g., management of acute and chronic pain in SCD). The panel clearly identified these statements as consensus recommendations and acknowledges that these areas represent gaps in the evidence base and areas for future research.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Prior to publication, these guidelines were reviewed by the National Heart, Lung, and Blood Institute (NHLBI) Advisory Council, a separate panel of sickle cell disease (SCD) experts, and the National Blood Disorders Program Coordinating Committee. The guidelines were also posted to the NHLBI Web site for an extensive public review and comment period, which resulted in the submission of more than 1,300 comments from individuals and professional societies. The expert panel and NHLBI staff reviewed each comment or recommendation, many of which resulted in a revision to the guidelines. The guidelines were then reviewed by SCD experts representing three professional societies.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of acute complications of sickle cell disease (SCD)

Potential Harms

- Adverse effects associated with opioid therapy, including sedation and itching, and effects of opioid withdrawal
- Adverse effects related to steroids

Qualifying Statements

Qualifying Statements

The purpose of the "Evidence-Based Management of Sickle Cell Disease: Expert Panel Report (EPR), 2014" is to synthesize the available scientific evidence on sickle cell disease and offer guidance to busy primary care clinicians. Readers of this report should remember that this document is intended to provide guidance for management, not to be rigidly prescriptive. The panel recognizes that the responsible clinician's judgment regarding the management of patients remains paramount. Therefore, the Expert Panel Report is a tool to be adopted and implemented in local and individual settings, and to provide an opportunity for shared decisionmaking in which providers and patients are both fully engaged.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Clinical Algorithm

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Timeliness

Identifying Information and Availability

Bibliographic Source(s)

Managing acute complications of sickle cell disease. In: Evidence-based management of sickle cell disease. Bethesda (MD): National Heart, Lung, and Blood Institute (NHLBI); 2014. p. 31-54.

Adaptation

The panel adapted selected recommendations from the American Pain Society (APS) guidelines for treatment of sickle cell disease (SCD) pain:

- Benjamin LJ, Dampier CD, Jacox A, Odesina V, Phoenix D, Shapiro BS, et al. Guideline for the management of acute and chronic pain in sickle-cell disease. Glenville, IL: APS Clinical Practice Guideline Series, No. 1, 1999.

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2014

Guideline Developer(s)

National Heart, Lung, and Blood Institute (U.S.) - Federal Government Agency [U.S.]

Source(s) of Funding

United States Government

Guideline Committee

Expert Panel

Composition of Group That Authored the Guideline

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Refer to the original guideline document for members of the National Heart, Lung, and Blood Institute staff and the contractor support.

Financial Disclosures/Conflicts of Interest

The National Heart, Lung, and Blood Institute (NHLBI) established the expert panel and invited the panel members. All members served as volunteers and received no compensation from NHLBI or any other entity for their participation.

During the development of these guidelines, measures were taken to ensure the transparency of the evidence review process and to manage all potential or perceived conflicts of interest. At the initial expert panel meeting, expert panel members were asked by the panel co-chairs to disclose interests and relationships that could potentially influence their participation or pose a potential conflict of interest. The responses are provided below.

- Araba N. Afenyi-Annan, M.D., M.P.H.—Consultant, Transfusion Safety Summit: Risks Associated with Iron Toxicity in Transfusional Medicine—Novartis Pharmaceuticals Corporation (November 2008); Duke University Comprehensive Sickle Cell Center, Mentored Research Training Supplement (April 2005–April 2006); Expert Witness for Hall, Booth, Smith & Slover, P.C. (2010–present)
- Samir K. Ballas, M.D.—Speaker's Bureau, Novartis; Sickle Cell Advisory Board, HemaQuest; U.S. Sickle Cell Advisory Board, Sangart
- Kathryn L. Hassell, M.D.—Advisory Board, ApoPharma; Consultant, AGA Medical Corp.; Consultant and Principal Investigator of Local Site Multicenter Sickle Cell Study, Terumo, Inc.; Principal Investigator of Local Site Multi-Center Sickle Cell Study, GlycoMimetics, Inc.; Principal Investigator of Local Site Multi-Center Sickle Cell Study, Emmaus, Inc.; Board of Directors, Mount Evans Home Health & Hospice; Medical Advisory Board, Foundation for Women and Girls with Blood Disorders; Medical Advisory Board, PFO Research Foundation
- Andra H. James, M.D., M.P.H.—Consultancy for the von Willebrand Disease Medical Advisory Board for CSL Behring; Research study of antithrombin levels in pregnancy for Grifols/Talecris; Study of von Willebrand factor levels and fibrinogen levels post partum for CSL Behring; Expert witness for Johnson & Johnson and Sanofi-Aventis
- Lanetta Jordan, M.D., M.P.H., M.S.P.H.—National Heart, Lung, and Blood Advisory Council; Faculty Chair, Sickle Cell Disease Association of America, Inc. (SCDAA) and National Initiative for Children's Healthcare Quality (NICHQ) for Health Resources and Services Administration-funded Sickle Cell Disease Treatment Demonstration Program; AESRx Medical Advisory Council; Prolong Pharmaceutical Medical Advisory Board; Consultant for NKT Therapeutics, TriStem, Pfizer, and Novartis; Board Member, Foundation for Women and Girls with Blood Disorders and Miami YWCA
- Sophie M. Lanzkron, M.D., M.H.S.—Scientific Advisory Board for HemaQuest; Principal investigator on studies sponsored by Emmaus, GlycoMimetics, Inc., and Novartis
- Paula J. Tanabe, Ph.D., R.N., M.S.N., M.P.H.—Partner, ESI Triage Research Team, LLC; Principal investigator on Agency for Healthcare Research and Quality research grant; Subcontractor to the Michigan Public Health Institute and the Health Resources and Services Administration (HRSA) to conduct a project in SCD, pediatrics, emergency department (ED) research; recipient of Duke School of Nursing grant to complete a project to measure the effect of a high dose opioid protocol to treat adults with a vaso-occlusive crisis (VOC) in the ED; Expert witness consultant on one SCD legal case
- Russell E. Ware, M.D., Ph.D.—Consultant for Bayer, Novartis Pharmaceuticals, and Sobi

No relationships to disclose: George R. Buchanan, M.D.; Richard Lottenberg, M.D.; William J. Savage, M.D., Ph.D.; Barbara P. Yawn, M.D., M.Sc., M.S.P.H.

Guideline Endorser(s)

American Academy of Emergency Medicine - Medical Specialty Society

American Academy of Pediatrics - Medical Specialty Society

American Academy of Physician Assistants - Professional Association

American Osteopathic Association - Professional Association

American Society of Hematology - Medical Specialty Society

American Society of Pediatric Hematology/Oncology - Professional Association

International Association of Sickle Cell Nurses and Physician Assistants - Professional Association

National Black Nurses Association, Inc - Professional Association

National Institute for Children's Health Quality - Professional Association

National Medical Association - Professional Association

Sickle Cell Disease Association of America - Disease Specific Society

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Electronic copies: Available from the National Heart, Lung, and Blood Institute (NHLBI) Web site .

Print copies: Available from the NHLBI Information Center, P.O. Box 30105, Bethesda, MD 20824-0105; e-mail: nhlbiic@dgsys.com.

Availability of Companion Documents

The following are available:

- Evidence-based management of sickle cell disease. Expert panel report quick guide. Bethesda (MD): National Heart, Lung, and Blood Institute (NHLBI); 2014. 45 p. Electronic copies: Available from the National Heart, Lung, and Blood Institute (NHLBI) Web site .
- Management of sickle cell disease. Summary of the 2014 evidence-based report by expert panel members. JAMA. 2014 Sep 10;312(10):1033-1048. Electronic copies: Available from the Journal of the American Medical Association (JAMA) Network Web site .
- Hazem A, Mullan R, Lane M, Elraiyah T, Shahrour A, Gupta S, Prokop L, Montori VM, Murad MH. The management of sickle cell disease complications: a systematic review, 2012. 353 p. Electronic copies: Available from the NHLBI Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on October 24, 2014. This summary was updated by ECRI Institute on September 21, 2015 following the U.S. Food and Drug Administration advisory on non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI Institute on June 2, 2016 following the U.S. Food and Drug Administration advisory on opioid pain medicines. This summary was updated by ECRI Institute on October 21, 2016 following the U.S. Food and Drug Administration advisory on opioid pain and cough medicines combined with benzodiazepines.

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