Effective Health Care

Management of Sickle Cell Pain

Results of Topic Selection Process & Next Steps

The nominator is interested in a new evidence review on management of sickle cell pain.

We identified two in-process systematic reviews, one in-process evidence map, and an in-process systematic review for a guideline by the American Society of Hematology covering the scope of the nomination. Therefore, a new review would be duplicative of an existing product. No further activity on this nomination will be undertaken by the Effective Health Care (EHC) Program.

Topic Brief

Topic Number and Name: Management of Sickle Cell Pain, #853

Nomination Date: 5/4/2019

Topic Brief Date: 5/17/2019

Authors
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Conflict of Interest: None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

Background

- Sickle cell disease are inherited red blood cell disorders. People with this condition have an abnormal protein in their red blood cells that can cause them to look like a C-shaped tool called a "sickle." [1]
- It is estimated that sickle cell disease affects 100,000 Americans. [2]
- There were about 75,000 hospitalizations for SCD between 1989 and 1993, costing about $475 million[2]
- The most complication of sickle cell disease is pain, called a vaso-occlusive crisis. This happens when the sickle cells get stuck in small blood vessels and clog the blood flow. This can happen suddenly, and can be very severe.[1]
- An acute sickle cell crisis can be treated with analgesics, such as ibuprofen and aspirin. When it is severe people are given opioid medications. Sometimes people are admitted to the hospital for treatment.[1]
- The nominator expresses concern with opioid prescribing for people with sickle cell disease based on guidelines intended to limit opioid prescriptions.
- A 2016 CDC guideline on opioid prescribing[3] specifically refers people who are managing patients with sickle cell disease to the NIH NHLBI Evidence based Management of Sickle Cell Disease Expert Panel Report[4] for the management of sickle cell disease.
    - The CDC guideline states that there are challenges with managing painful complications of sickle cell disease, and their recommendations do not apply.
- However policies and practices about opioid prescribing may have gone beyond the recommendations in the guideline, with misapplication to populations outside of its scope. [5]

Nominator and Stakeholder Engagement

Consultation with the nominator confirmed that the focus should be on pain management in people with sickle cell disease.

Key Questions and PICOs

The key questions for this nomination are:

1. What is the effectiveness and harms of pharmacologic pain treatments for chronic pain in people with sickle cell disease?
2. What is the effectiveness and harms of pharmacologic pain treatments for sickle cell crisis in people with sickle cell disease?

To define the inclusion criteria for the key questions, we specify the population, interventions, comparators, and outcomes (PICO) of interest (Table 1).

Table 1. Key Questions and PICO

Key Questions		
Population	Adults with sickle cell with chronic pain	Adults with sickle cell crisis
Interventions	Opioid medication	Opioid medications
Comparators	Usual care Nonopioid medications Other opioid medication	Usual care Nonopioid medications Other opioid medication
Outcomes	Pain Function Quality of life	Pain Function Quality of life

Abbreviations: none.

Methods

We assessed nomination for priority for a systematic review or other AHRQ EHC report with a hierarchical process using established selection criteria. Assessment of each criteria determined the need to evaluate the next one. See Appendix A for detailed description of the criteria.

1. Determine the *appropriateness* of the nominated topic for inclusion in the EHC program.
2. Establish the overall *importance* of a potential topic as representing a health or healthcare issue in the United States.
3. Determine the *desirability of new evidence review* by examining whether a new systematic review or other AHRQ product would be duplicative.
4. Assess the *potential impact* a new systematic review or other AHRQ product.
5. Assess whether the *current state of the evidence* allows for a systematic review or other AHRQ product (feasibility).
6. Determine the *potential value* of a new systematic review or other AHRQ product.

Appropriateness and Importance

We assessed the nomination for appropriateness and importance.

Desirability of New Review/Duplication

We searched for high-quality, completed or in-process evidence reviews published in the last three years on the key questions of the nomination. See Appendix B for sources searched.

Results

See Appendix A for detailed assessments of all EPC selection criteria.

Appropriateness and Importance

This is an appropriate and important topic.

Desirability of New Review/Duplication

A new evidence review would be duplicative of ongoing efforts. We found one in-process systematic review and an in-process systematic review to inform a guideline addressing KQ 1 on chronic pain; and one in-process systematic review, one in-process technical brief, and one in-process systematic review to inform a clinical practice guideline addressing KQ 2 on sickle cell crisis. See Appendix B for more details about these reviews.

Key Question 1: chronic pain

- Opioid treatments for chronic pain[6] The protocol for this in-process AHRQ systematic review was publicly posted on February 27, 2019. It will focus on opioid treatment for chronic pain in adults, with sickle cell as a specific subpopulation of interest.
- The American Society of Hematology (ASH) guideline is developing a set of five clinical practice guidelines.[7] One will focus on pain management, and is in-process. Publication is anticipated in 2019.

Key question 2: sickle cell crisis

- Cooper et al. Pharmacological interventions for painful sickle cell vaso-occlusive crises in adults.[8] This in-process Cochrane systematic review focuses on opioid and non-opioid analgesics in vaso-occlusive crises in adults with sickle cell.
- Treatment of acute pain: an evidence map.[9] This in-process AHRQ technical brief will provide an evidence map for acute pain treatment for selected acute pain conditions. One of the conditions is sickle cell crisis. This document will identify high-quality systematic reviews, high quality guidelines, and primary research that addresses acute pain management of sickle cell crisis.

- The American Society of Hematology (ASH) guideline is in-process.[7] As noted above, ASH is developing clinical practice guidelines on the acute and chronic complications of sickle cell disease.

Other Information

This information is not directly related to the nomination question, but may address concerns raised by the nominator.

- Clinical Decision Support from AHRQ's CDS Connect. Factors to consider in managing chronic pain: a pain management summary.[10] CDS Connect demonstrates a web-based Repository for clinical decision support resources, known as artifacts. These can improve quality of care through clinical decision support and identify evidence-based standards of care.
- Haywood et al. A systematic review of barriers and interventions to improve appropriate use of therapies for sickle cell disease.[11]

Summary of Findings

- Appropriateness and importance: The topic is both appropriate and important.
- Duplication: A new review would be duplicative of ongoing efforts. We found two in-process systematic reviews, an in-process technical brief, and in-process systematic review for a guideline that directly address the scope of this topic.

References

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11. Haywood C, Jr., Beach MC, Lanzkron S, et al. A systematic review of barriers and interventions to improve appropriate use of therapies for sickle cell disease. J Natl Med Assoc. 2009 Oct;101(10):1022-33. PMID: 19860302. https://www.ncbi.nlm.nih.gov/pubmed/19860302

Appendix A. Selection Criteria Assessment

Selection Criteria	Assessment
1. Appropriateness	
1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the U.S.?	Yes
1b. Is the nomination a request for a systematic review?	Unclear
1c. Is the focus on effectiveness or comparative effectiveness?	No
1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?	Yes
2. Importance	
2a. Represents a significant disease burden; large proportion of the population	Approximately 100,000 Americans have sickle cell disease. Serious complications are common, and include pain crisis, stroke, leg ulcers, vision loss, and splenic sequestration.
2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population	People with sickle cell disease commonly experience pain. The concern around opioid use may impact their ability to receive appropriate pain management. The evidence for the effectiveness of analgesics, including opioids, will inform decisions around pain management.
2c. Represents important uncertainty for decision makers	Yes, there is uncertainty about balancing the need for appropriate pain management and avoiding opioid use disorder.
2d. Incorporates issues around both clinical benefits and potential clinical harms	Yes
2e. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers	Yes. People with sickle cell disease may be seen at the emergency department and admitted for pain management. There were about 75,000 hospitalizations for sickle cell disease between 1989 and 1993, costing about $475 million[2]
3. Desirability of a New Evidence Review/Duplication	

Selection Criteria	Assessment
3. Would not be redundant (i.e., the proposed topic is not already covered by available or soon-to-be available high-quality systematic review by AHRQ or others)	Yes. We found multiple systematic reviews that cover the scope of the nomination questions. Key Question 1: chronic pain • Opioid treatments for chronic pain.[6] o This is an update of a 2015 AHRQ systematic review. A subquestion asks about how effectiveness and harms vary depending on the cause of pain, and specifically mentions sickle cell disease. • The American Society of Hematology (ASH) guideline is in-process.[7] o ASH is developing clinical practice guidelines on the acute and chronic complications of sickle cell disease. One of the guidelines will address pain management. Publication is anticipated in 2019. Key question 2: sickle cell crisis • Cooper et al. Pharmacological interventions for painful sickle cell vaso-occlusive crises in adults.[8] o This in-process Cochrane systematic review focuses on opioid and non-opioid analgesics in vaso-occlusive crises in adults with sickle cell. • Treatment of acute pain: an evidence map.[9] o This technical brief will provide an evidence map for acute pain treatment for selected acute pain conditions. One of the conditions is sickle cell crisis. o This document will identify high-quality systematic reviews, high quality guidelines, and primary research that addresses sickle cell crisis. • The American Society of Hematology (ASH) guideline is in-process.[7] o ASH is developing clinical practice guidelines on the acute and chronic complications of sickle cell disease. One of the guidelines will address pain management. Publication is anticipated in 2019.

Abbreviations: AHRQ=Agency for Healthcare Research and Quality; ASH=American Society of Hematology; KQ=Key Question

Appendix B. Search for Evidence Reviews (Duplication)

Listed below are the sources searched, hierarchically

Primary Search
AHRQ: Evidence reports and technology assessments https://effectivehealthcare.ahrq.gov/; https://www.ahrq.gov/research/findings/ta/index.html; https://www.ahrq.gov/research/findings/evidence-based-reports/search.html
VA Products: PBM, and HSR&D (ESP) publications, and VA/DoD EBCPG Program https://www.hsrd.research.va.gov/publications/esp/
Cochrane Systematic Reviews http://www.cochranelibrary.com/
PROSPERO Database (international prospective register of systematic reviews and protocols) http://www.crd.york.ac.uk/prospero/
PubMed https://www.ncbi.nlm.nih.gov/pubmed/