Management of Sickle Cell Disease: Workgroup Meeting Summary

Overview

On March 7, 2016, the Patient-Centered Outcomes Research Institute (PCORI) convened a multi-stakeholder workgroup in Washington, DC to identify patient-centered, clinical comparative effectiveness research (CER) questions that, if addressed, could help to fill evidence gaps and improve outcomes for individuals with sickle cell disease (SCD). To ensure a focus on important evidence gaps that can influence clinical practice, representatives from a wide range of stakeholder groups attended. While in-person attendance was by invitation only, the public was welcome to listen in via teleconference.

Prior to the meeting, participants submitted up to two key CER questions each relevant to improving outcomes for those with SCD, with a focus on care transitions and pain management. PCORI received a total of 59 questions prior to the meeting. During the meeting, participants split into one of the two breakout groups to refine and gain consensus on the top two to three CER questions whose findings could improve patient-centered outcomes.

The *care transitions* breakout group prioritized three topics for potential CER trials:

1) What is the comparative effectiveness of evidence-based transition models that link a multidisciplinary SCD expert team and primary care clinician (e.g. Project ECHO) vs. other transition models on patient-reported outcomes, satisfaction and experience of care, hospitalizations, and emergency department and ambulatory ratios (ED and ambulatory care) among emerging adults with SCD transitioning to adult care?
2) What is the comparative effectiveness of virtual provider consultation models vs. in-person basic decision support vs. electronic decision support on QOL, patient self-efficacy, healthcare utilization, missed days from school or work, and other patient-reported outcomes among emerging adults with SCD transitioning to adult care?
3) What is the comparative effectiveness of patient activation models on patient-reported and other clinical outcomes among emerging adults with SCD transitioning to adult care?

The *pain management* breakout group prioritized three topics for potential CER trials:

1) What is the comparative effectiveness of evidence-based self-efficacy and/or care models on improved functionality, school/work attendance, reduction in admission to ER/hospitals, and reduced pain outside of the health care setting for individuals with SCD?
2) What is the comparative effectiveness of standardized vs. individualized pain management plans on improved pain relief and patient experience of care, stress and conflict reduction, and increase in standardization of care inside the healthcare setting for individuals with SCD?
3) What is the comparative effectiveness of various provider education plans to improve pain relief and patient experience of care for individuals with SCD, particularly related to reducing stress and improving timeliness of care?

PCORI staff will discuss the workgroup's deliberations, refine the CER questions, and present the results of the discussion to leadership to determine future steps regarding funding in this area.

Related Information

- Management of Sickle Cell Disease Topic Brief
- Management of Sickle Cell Disease Workgroup: Main Presentation
- Participant List
- Submitted Stakeholder Questions
- Consolidated CER Themes and Questions

The Patient-Centered Outcomes Research Institute (PCORI) is an independent organization created to help people make informed healthcare decisions.

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Setting the Stage

Dr. Romana Hasnain-Wynia, Director of PCORI's Addressing Disparities (AD) program, opened the meeting by setting the stage for the day, discussed the significance of improving care for individuals with SCD as an important issue to multiple stakeholders, and provided an overview of PCORI's current investment in SCD funding. She noted that the topic of SCD is a high priority for PCORI's scientific programs and offers a unique opportunity for collaboration across four of PCORI's National Research Priorities (Addressing Disparities, Improving Health Systems, Communication and Dissemination, and Clinical Comparative Effectiveness Research).

The participants raised a question regarding the need for strong efficacy data for all study comparators, per PCORI's requirements, particularly since such data can be sparse in the study of rare diseases. While acknowledging this challenge, staff noted that for high-priority, understudied topics, PCORI is interested in funding studies that employ evidence-based comparators to answer compelling questions ready for CER. In cases where such data are lacking, it is acceptable for efficacy data to be from a study conducted in a different population or disease cohort, as long as it can be applied to the study in question.

The Chair of the workgroup, Dr. W. Keith Hoots, Director, Blood Diseases Branch, Division of Blood Diseases and Resources at the National Heart, Lung, Blood Institute (NHLBI) at the National Institutes of Health (NIH), discussed the landscape of NIH-funded SCD research. In addition, he provided an overview of a funding announcement NHLBI released in July 2015 for T4 (translational) research that will support the use of implementation science to optimize care for adolescents and older adults with SCD. The goal of this investment is to create a geographic consortia (SCD neighborhoods), an integrated care system that can be followed longitudinally, and to create a registry of SCD patients.

Dr. Parag Aggarwal, Senior Program Officer with the AD program, briefly reviewed the main points in the PCORI topic brief, Management of Sickle Cell Disease, and walked the group through the day's agenda. In preparation for the workgroup, participants received the topic brief and were asked to submit up to two CER questions with the potential to fill evidence gaps and improve outcomes for patients with SCD. PCORI received a total of 59 questions. Prior to the meeting, PCORI staff consolidated these into 38 questions and 10 themes for further refinement and prioritization during the workgroup.

Participants split into two breakout groups (*care transitions* and *pain management*) to refine and gain consensus on the top two to three questions in each topic using the "PICOTS" framework:

- **P**atients
- **I**nterventions
- **C**omparators
- **O**utcomes
- **T**iming
- **S**ettings

Breakout Group: Care Transitions

The first breakout group, moderated by Dr. Hoots, focused on transitions from pediatric to adult care for SCD patients. Dr. Hoots began by re-emphasizing the importance of PCORI's research prioritization criteria—specifically, patient-centeredness, assessment of current options, and the likelihood of implementation in practice. Dr. Hasnain-Wynia reminded participants that interventions should have a clear health system component.

PCORI staff organized the 19 stakeholder-submitted questions into the following themes prior to the meeting:

- **Care delivery models**
    - Personnel-focused
    - Care-setting focused
- **Clinician training**
- **Self-care management**
    - Peer navigator vs. technology-based interventions
    - Patient activation interventions

During discussion of the questions within each of the above themes, participants identified the following important considerations for selecting CER questions in this topic area: 1) distinguishing between *transition*, the process of planning and preparing for health care as an adult, and *transfer*, the actual movement from a pediatric to adult clinic or model of care; 2) acknowledging the differences between urban and non-urban settings in available resources and access to health care; and 3) determining if the transition process should begin at a certain age or level of psychosocial/developmental maturity. Participants decided to consolidate multiple themes to develop CER questions rather than choosing from among the previously submitted questions, especially given the considerable overlap in the questions.

After the lunch break, participants identified four CER questions that were patient-centered, had comparators with efficacy data either within SCD or that could be applied to SCD, and had potential for changing practice. Discussion focused on identifying advantages and limitations of each question prior to voting on top research priorities in care transitions for individuals with SCD.

By consensus, the following three questions emerged:

1. What is the comparative effectiveness of evidence-based transition models that link a multidisciplinary SCD expert team and primary care clinician (e.g. Project ECHO) vs. other transition models on patient-reported outcomes, satisfaction and experience of care, hospitalizations, and emergency department and ambulatory ratios (ED and ambulatory care) among emerging adults with SCD transitioning to adult care?
2. What is the comparative effectiveness of virtual provider consultation models vs. in-person basic decision support vs. electronic decision support on QOL, patient self-efficacy, healthcare

utilization, missed days from school or work, and other patient-reported outcomes among emerging adults with SCD transitioning to adult care?

3. What is the comparative effectiveness of patient activation models on patient-reported and other clinical outcomes among emerging adults with SCD transitioning to adult care?

Breakout Group: Pain Management

Dr. Harvey Luksenberg, Special Advisor to the Director, Blood Diseases Branch, Division of Blood Diseases and Resources at NHLBI, moderated the second breakout group, focusing on management of acute pain crises. Dr. Luksenberg began by establishing consensus that the CER questions under discussion were supported by varying levels of efficacy data. Participants also agreed that reasonable models for treating SCD pain currently exist. Participants pointed out that important research questions in pain management for patients with SCD should consider the nature of the pain itself, the nature of pain research, and the problems associated with SCD care in general. Because all these factors have similar gaps in evidence, the group agreed that they would need to make assumptions as they refined research questions and that some assumptions might extrapolate from management models for other pain syndromes

PCORI staff organized the 19 stakeholder-submitted questions into the following themes prior to the meeting:

- **Self-care management**
- **Pharmacologic pain management**
- **Pharmacologic vs. non-pharmacologic therapies**
- **Improving health care processes**
    - Among care settings
    - Within care settings

After discussion, participants unanimously voted for self-care management and improving healthcare processes as the highest-priority themes.

The discussion of self-care management focused on individualized pain plans. Participants noted that while individualized pain plans are not backed by strong efficacy data, they are highly patient-centered and make intuitive sense for managing SCD pain. One caveat, however, is that individualized pain plans are often not specific to patients, but instead inadvertently aligned with provider needs. Participants noted that the two themes involving pharmacologic and non-pharmacologic therapies could be rolled into the self-care management theme. The therapies that are deemed important by the community (such as the use of hydroxyurea) could be (and should be) incorporated into a pain management plan.

In discussing the theme of improving health care processes, participants agreed that system-level interventions is a ripe area to address for improving the management of SCD pain crises. Questions could include why pain management strategies, such as those for chronic lower back pain, do not transfer to SCD pain crises. Participants agreed that systems questions should address interventions and

comparators within care settings, and emphasized the importance of distinguishing among settings, such as hospital, emergency department, and ambulatory sites.

Participants proposed focusing on adolescent and adult patients as the target population for a CER study, as adolescence represents the fulcrum where transitions in care are about to occur. However, young children should not be excluded in the target population, as they experience episodes of pain similar to adolescents. Participants suggested the following outcomes: rapidity of pain resolution, which can prevent other complications; patient experience of care; reducing patient conflict and stress; understanding what to expect in the emergency department; and reducing variability of care. For adolescents, outcomes could also include ability to participate fully in activities such as sports, while for adults, outcomes could include ability to function at work.

By consensus, the following three questions emerged:

1. What is the comparative effectiveness of evidence-based self-efficacy and/or care models on improved functionality, school/work attendance, reduction in admission to ER/hospitals, and reduced pain outside of the health care setting for individuals with SCD?
2. What is the comparative effectiveness of standardized vs. individualized pain management plans on improved pain relief and patient experience of care, stress and conflict reduction, and increase standardization of care inside the healthcare setting for individuals with SCD?
3. What is the comparative effectiveness of various provider education plans to improve pain relief and patient experience of care for individuals with SCD, particularly related to reducing stress and improving timeliness of care?

Report Out and Wrap-up Discussion

In the day's final session, the two breakout groups reconvened together to report back on their respective CER questions. Participants raised the following contextual points about each of the topic areas.

Pain Management

- Reiterated the importance of standardization in reducing variability of care for SCD patients and suggested including reducing variability as a potential outcome.
- Suggested that all age groups (children, adolescents, and adults) be included in potential studies and no patient with SCD should be excluded.
- Underscored the need to improve general processes and provide educational tools to providers and/or patients to help improve patient satisfaction and break-down stigmas and pre-conceptions around pain management for patients with SCD.
- Agreed that a focus on use of different opioids or other pharmacological interventions was not prioritized because there would be minimal information gained from conducting a comparative effectiveness study on this topic. Strong evidence suggests that differences in efficacy among the various opioids would most likely be minimal, as would the differences in patient-satisfaction.

Care Transitions

- Suggested that a modified version of the ECHO hub and spoke platform may serve as a model intervention with one or two comparator group(s). ECHO Hub is currently used to share hepatitis C expertise with rural communities. This is a virtual peer mentoring and telemedicine model that brings various providers ("spokes") to a "hub," where experts in hepatitis C care answer their queries. These models help to accommodate differences that may exist in different practices.
- Suggested that CER questions include more patient-reported outcomes, such as patient experience of care that go beyond patient satisfaction measures.
- Agreed to identify the group of young adults and adolescents as "emerging adults."
- Recognized that an important component of the transition process is "breaking the bond" with parental/caregiver units as a patient moves from adolescence to emerging adulthood and beyond.
- Agreed that evidence-based shared decision-making models should be included as a component of potential interventions.
- Agreed that from a timing perspective, studies should focus more on the middle of the transition period, rather than on the beginning, since studies focusing on early adulthood could have the greatest impact.

Next Steps

PCORI program staff from the Addressing Disparities team will work with colleagues from the Improving Health Systems, Communication and Dissemination, and Clinical Comparative Effectiveness Research programs, as well as NHLBI, to conduct further refinement of the CER questions resulting from the workgroup. The workgroup questions will be presented to the PCORI Science Oversight Committee, which will make a recommendation to PCORI's Board of Governors regarding PCORI's role in this area.