



Evidence-based Practice Center Technical Brief Protocol

Project Title: *Treatment of Acute Pain – An Evidence Map*

I. Background and Objectives for the Technical Brief

Addressing the opioid epidemic in the United States is a key priority of the United States Department of Health and Human Services. This will require a thorough understanding pain treatment with both pharmacologic and nonpharmacologic interventions. The treatment of acute pain is a topic in need of an up-to-date overview of available evidence. This technical brief will provide an evidence map summarizing current research on acute pain treatments and prioritizing future research needs relevant to select acute pain conditions.

Background

Pain has reemerged as a major public health issue. This reemergence primarily results from the sharp rise in opioid-related deaths in the United States over the last two decades. Opioids are a primary pharmacologic treatment for pain. Opioid related deaths have risen from 3 deaths per 100,000 people in 2000 to more than 13 per 100,000 in 2016.¹ Prescription opioids were involved in over 40 percent of all overdose deaths in 2016.¹ The urgency of the growing opioid epidemic has resulted in more attention and research funding for pain—especially, how to effectively prevent and manage acute and chronic pain with less reliance on highly addictive opioids.

In 2011, an Institute of Medicine (IOM) report described the “need for a cultural transformation in the way pain is viewed and treated.”² The IOM report spurred action across federal agencies and private organizations. The United States Department of Health and Human Services formed an Interagency Task Force aimed at updating best practices and identifying gaps in managing acute and chronic pain.³ The National Institutes of Health formed an Interagency Pain Research Coordinating Committee and published a Federal Pain Research Strategy.⁴ The Centers for Disease Control and Prevention issued guidelines on appropriate use of opioids.¹ The American Academy of Pain Medicine (AAPM) recognized the emergence of medical practice around acute pain and developed the Acute Pain Medicine Special Interest Group (APMSIG).⁵ A public private partnership, which included the United States Food and Drug Administration (FDA), [the Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities, and Networks (ACTION), American Pain Society (APS), and AAPM] developed a taxonomy for acute pain.⁶

AAPM’s working definition of acute pain as “the physiologic response and experience to noxious stimuli that can become pathologic, is normally sudden in onset, time limited, and motivates behaviors to avoid actual or potential tissue injuries.”⁵ Timing is a key element that distinguishes acute pain from subacute and chronic pain. The AAAPT further characterizes the working definition of acute pain with specific time-based specifications. Acute pain typically lasts up to 7 days but may last up to 30 days, with its duration determined in part by the mechanism and severity of the inciting event.⁶

Pain is extremely common, especially in the United States. The 2012 National Health Interview Survey (NHIS) showed that 56% of U.S. adults reported some pain during the previous three months.⁷ The high incidence and prevalence of pain leads to increased use of healthcare resources, poorer perception of health status, lower productivity, and increased antidepressant use.⁷ These high burdens of acute pain are dwarfed, however, by the burdens of chronic pain, which can result when acute pain is not effectively treated.⁸ Effective treatment of acute pain can minimize the sensitization of pain pathways and tissue damage that lead to chronic pain.⁸ Therefore, our ability to understand and manage acute pain is critical, both to minimize the length and severity of acute pain, and to prevent the transition to chronic pain.

Acute pain arises from a diverse array of conditions. The AAAPT makes a broad distinction between surgical/procedural pain and nonsurgical pain. It further classifies acute pain using five dimensions⁶: core criteria (the inciting event, timing, and location of pain), common features (symptoms and other features of the acute pain), modulating features (characteristics of the individual that affect the pain response), impact/functional consequences (recovery and other implications from the acute pain episode), and putative mechanisms (neurobiological mechanisms relevant to the acute pain episode).⁶

Accurately assessing acute pain is key to diagnosis and treatment. Improved understanding of individuals' pain experience has evolved, resulting in a shift in thinking about how pain is assessed. A comprehensive, multidimensional assessment that better characterizes the pain, the individual, and environment would likely improve acute pain diagnosis and treatment.^{2, 5} However, while current recommendations suggest a multidimensional approach,⁵ unidimensional assessments primarily measuring pain intensity remain widely used. Examples include the Numerical Rating Scale (NRS), Visual Analog Scale (VAS) and the Faces Pain Scale Revised (FPS-R).^{5, 9} These instruments provide a quick and simple method to assess and monitor pain intensity.⁹

Focusing solely on an individual self-reported pain intensity has several limitations. These instruments do not capture many dimensions of pain important to treatment decision-making. Some dimensions (e.g., anxiety and pain catastrophizing) are associated with longterm complications; others (e.g., pain with activity or movement) are equally important to pain at rest; and still other dimensions (e.g., overall health and well-being) that are crucial to understanding treatment effectiveness.⁵ Opioid treatment to achieve specific goals on pain assessment scales may not be the safest treatment strategy,⁵ given the misuse and abuse potential. The subjective nature of self-report and provider interpretation can lead to a wide range of treatment decisions.

Many unidimensional and multidimensional pain assessment scales are available including specific scales for a variety of pain conditions¹⁰⁻¹³ and for specific sub-populations.¹⁴⁻¹⁷ Multidimensional assessment moves beyond pain intensity and incorporates other attributes such as quality and character of pain, function, pain interference, and others.⁵ Examples of validated multidimensional assessment instruments include the Brief Pain Inventory and the McGill Pain Questionnaire.⁹ These instruments can be challenging to implement in settings typically seeing individuals with acute pain.⁹

Treatments for acute pain include pharmacologic and nonpharmacologic therapies. Ideally, providers customize therapy to the type and severity of pain, treatment setting, and patient characteristics. Some treatments are unique to the type of pain (e.g. triptans

for migraines), or setting (regional blocks used perioperatively to lessen postoperative pain and opioid use), but most treatments are used across a wide range of pain conditions. Length of treatment varies by acute pain condition. Multi-modal approaches to acute pain treatment are becoming more common in some settings.¹⁸⁻²⁰

Pharmacologic therapies for acute pain include drugs from several drug classes. Pain relieving analgesics include opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), and acetaminophen. Providers also elect to manage acute pain with benzodiazepines, muscle relaxants, antidepressants, alpha-2 agonists, gamma aminobutyric agonists, and cannabinoids.^{21, 22} Topical agents such as capsaicin and lidocaine are also used.²¹ Medications for pain management all have associated harms, some serious. Therefore, caution is necessary when prescribing pharmacologic pain treatment, especially in certain populations (such as older adults, individuals with comorbidities and/or polypharmacy or a history of substance abuse, pregnant and breastfeeding women, and children and adolescents).

Nonpharmacologic therapies for pain are becoming more widely used to avoid harms associated with pharmacologic therapies. Examples of nonpharmacologic therapies include acupuncture, psychological approaches (cognitive behavioral therapy, mindfulness-based stress reduction), chiropractic manipulation, physical therapy, transcutaneous electrical stimulation, massage therapy, exercise, and other complementary and alternative medicine therapies (CAM).

II. Guiding Questions

Our guiding questions provide a framework for us to identify, inventory, and organize the existing research on treatments for pain attributable to a set of priority acute pain conditions. The initial set of priority acute pain conditions were identified by AHRQ and includes:

- Musculoskeletal pain
- Postoperative pain after discharge from surgical facility
- Dental pain
- Kidney stones (episodic pain)
- Migraines (episodic pain)
- Sickle Cell crisis (episodic pain)
- Other episodic pain

We will address the following four Guiding Questions (GQs) with respect to the priority acute pain conditions listed above:

1. Which acute pain conditions are most commonly treated in select settings (emergency rooms; inpatient and outpatient surgical facilities; primary and specialty care clinics; and dental clinics and dental surgery centers)?
 - a. How is acute pain for these conditions assessed and monitored?
 - b. Which individual characteristics modify perceptions of pain severity, treatment options, and treatment response?
2. Which acute pain conditions have recent, high quality guidelines that address acute pain treatments?
3. Which acute pain conditions have recent, high quality systematic reviews evaluating acute pain treatments?

- a. Which populations, acute pain conditions, and treatments have been sufficiently systematically reviewed?
- b. What evidence gaps were identified in systematic reviews?
- 4. What original comparative effectiveness research is available evaluating acute pain treatments for priority acute pain conditions without recent high quality systematic reviews?
 - a. Which populations and settings have been studied?

III. Methods

GQ1 and GQ2 will be informed by a narrative review and KI discussions. We will conduct a search to identify systematic reviews on pain treatments for acute pain for the priority acute pain conditions mentioned in the statement of work (SOW). GQ4 will assess the findings from GQ1 through GQ3 to identify future research needs.

1. Data Collection:

A. Discussions with Key Informants

We have developed a preliminary list of Key Informants (KIs) with diverse experiences and perspectives on assessment and treatment of acute pain. Discussions will be timed early in the project and occur throughout the project timeline. We identified KIs in several ways. First, team members with experience and expertise on treating pain recommended experts and professional associations/subspecialties who treat acute pain. We also identified KIs and Technical Expert Panel (TEP) members who served on past EPC projects who could also provide constructive and valuable input on this topic. We then reviewed committee and workgroup members on various public and private endeavors aimed at strengthening the evidence base on the assessment and treatment of acute pain. This initial KI list was developed to recruit expertise on a wide variety of issues and perspectives with respect to the assessment and treatment of acute pain.

We will use a set of questions to facilitate discussions with KIs (Appendix A). We will ask questions of the KIs to facilitate a conversation about which types of acute pain conditions are frequent, which guidelines there were aware of with regard to acute pain treatments.

B. Grey Literature search.

We will conduct grey literature searching to identify guidelines not found through bibliographic database searching. We will search the ECRI Guidelines Trust resource²³ provider point of care tools (e.g., DynaMed, UpToDate), and websites of relevant agencies and professional associations.

C. Published Literature search.

A search strategy will be developed to identify systematic reviews evaluating treatments for the acute pain attributable to the priority acute pain conditions. We will search MEDLINE and the Cochrane Library. We will construct search strategies to identify original research on specific acute pain conditions without recent high quality systematic reviews. As a proxy for sufficient quality, we will require systematic reviews to have conducted and reported risk of bias assessments on eligible studies.

When priority acute pain conditions without relevant high quality systematic reviews are identified, we will supplement specific bibliographic database searches with targeted searches for original research published since the systematic review search dates.

D. Study Selection

We will include clinical practice guidelines developed by key national societies relevant to our priority acute pain conditions. Our assessment of clinical practice guideline quality will be guided by AGREE II.²⁴

Search results (GQ3) will be screened for eligibility. Inclusion/exclusion criteria will be designed to select recent systematic reviews published 2016 forward in English, aim to evaluate treatment for the acute pain conditions mentioned in the SOW, and of sufficient quality. We selected 2016 to capture systematic review with search end dates less than three years old. For acute pain conditions with low volumes of literature, we may extend the publication year to 2014. Our assessment of sufficient quality will be guided by AMSTAR II.²⁵ The review must include a systematic search strategy and a risk of bias assessment of eligible studies.

We will conduct additional searches for original research for topics not addressed by published systematic reviews. These search results will be title and abstract screened by one investigator to summarize the number of studies potentially available for systematic review. We will use bibliographic management software to catalog these studies.

Data Organization and Presentation:

Our initial approach to organizing the identified research studies will begin with broad acute pain categories as described in the ACTION-APS-AAPM pain taxonomy to classify acute pain conditions.⁶ This broad classification separates acute pain conditions into surgical/procedural and nonsurgical. Within these broad categories are many subcategories based upon the type of surgery, illness, or injury.

A. Information Management

Evidence tables specific to each priority acute pain condition will be created from data abstracted from eligible clinical practice guidelines and systematic reviews. We will abstract author, publication year, search dates, and number and type of included studies, populations, interventions, comparisons, and outcomes reported from systematic reviews.

We will abstract descriptive data necessary to categorize studies and assess feasibility for systematic review from original research. Feasibility will be determined by the number and sample size of clinical trials available per topic.

B. Data Presentation

We will summarize the research on the treatment of acute pain attributable to the acute pain conditions. Mapping evidence requires a high degree of aggregation and graphical depictions using a limited number of variables. Our evidence maps will present and summarize the data using key variables. Likely variables include acute pain category, acute pain condition, population, number of systematic reviews, and number of studies and individuals included in systematic reviews. We will investigate options for organizing and presenting the evidence map (likely a combination of tables, charts, and diagrams following examples from previous evidence maps).²⁶⁻²⁸

We will organize results to demonstrate the acute pain conditions, populations, treatments, and outcomes addressed by recent high quality systematic reviews by setting.

IV. References

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V. Definition of Terms

NA

VI. Summary of Protocol Amendments

NA

VII. Key Informants

Within the Technical Brief process, Key Informants serve as a resource to offer insight into the clinical context of the technology/intervention, how it works, how it is currently used or might be used, and which features may be important from a patient of policy standpoint. They may include clinical experts, patients, manufacturers, researchers, payers, or other perspectives, depending on the technology/intervention in question. Differing viewpoints are expected, and all statements are crosschecked against available literature and statements from other Key Informants. Information gained from Key Informant interviews is identified as such in the report. Key Informants do not do analysis of any kind nor contribute to the writing of the report and have not reviewed the report, except as given the opportunity to do so through the public review mechanism.

Key Informants must disclose any financial conflicts of interest greater than \$5,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals are invited to serve as Key Informants and those who present with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

VIII. Peer Reviewers

Peer reviewers are invited to provide written comments on the draft report based on their clinical, content, or methodologic expertise. Peer review comments on the preliminary draft of the report are considered by the EPC in preparation of the final draft of the report. Peer reviewers do not participate in writing or editing of the final report or other products. The synthesis of the scientific literature presented in the final report does not necessarily represent the views of individual reviewers. The dispositions of the peer review comments are documented and will be published three months after the publication of the evidence report.

Potential Reviewers must disclose any financial conflicts of interest greater than \$5,000 and any other relevant business or professional conflicts of interest. Invited Peer Reviewers may not have any financial conflict of interest greater than \$5,000. Peer reviewers who disclose potential business or professional conflicts of interest may submit comments on draft reports through the public comment mechanism.

IX. EPC Team Disclosures

EPC core team members must disclose any financial conflicts of interest greater than \$1,000 and any other relevant business or professional conflicts of interest. Related financial conflicts of interest that cumulatively total greater than \$1,000 will usually disqualify EPC core team investigators.

X. Role of the Funder

This project was funded under Contract No. xxx-xxx from the Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services. The Task Order Officer reviewed contract deliverables for adherence to contract requirements and quality. The authors of this report are responsible for its content. Statements in the report should not be construed as endorsement by the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

Appendix A. Key Informant Call Topics and Potential Questions

Topic	Questions
Acute Pain Conditions/Assessment/ Guidelines	<ul style="list-style-type: none"> • Which acute pain conditions are of highest priority in terms of identifying alternatives to opioids? • Which settings are of highest priority in terms of identifying alternatives to opioids? • Which acute pain conditions are most often treated in each setting: <ul style="list-style-type: none"> ○ Emergency Departments ○ Inpatient and outpatient surgical facilities ○ Primary care clinics ○ Specialty care clinics ○ Dental clinics ○ Oral surgery facilities • How is acute pain assessed before and during treatment? <ul style="list-style-type: none"> ○ How does the assessment modify treatment? ○ Does this differ by setting? • Which individual characteristics modify: <ul style="list-style-type: none"> ○ Perception of pain? ○ Treatment options? ○ Treatment response?
Acute Pain Treatment: Guidelines	<ul style="list-style-type: none"> • Are you aware of clinical practice guidelines addressing acute pain in general? • Are you aware of clinical practice guidelines addressing reducing the use of opioids? • Are you aware of clinical practice guidelines addressing specific common acute pain conditions? • Is treatment of acute pain guided by these guidelines in your organization? • What other guidance informs treatment for acute pain in your organization? • We are compiling a list of clinical practice guidelines for treatment of acute pain; do you believe that clinical practice guidelines developed for use in other countries be useful? If so, which countries or organizations?
Knowledge Gaps	<ul style="list-style-type: none"> • Which areas do you feel need additional research to inform the treatment for acute pain?