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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Agency for Healthcare Research and Quality

Supplemental Evidence and Data Request on Treatments for Acute Episodic Migraine

AGENCY: Agency for Healthcare Research and Quality (AHRQ), HHS.

ACTION: Request for Supplemental Evidence and Data Submissions

SUMMARY: The Agency for Healthcare Research and Quality (AHRQ) is seeking scientific information submissions from the public. Scientific information is being solicited to inform our review on *Treatments for Acute Episodic Migraine,* which is currently being conducted by the AHRQ's Evidence-based Practice Centers (EPC) Program. Access to published and unpublished pertinent scientific information will improve the quality of this review.

DATES: *Submission Deadline* on or before 30 days after date of publication in *Federal Register*.

ADDRESSES:

E-mail submissions: epc@ahrq.hhs.gov

Print submissions:

Mailing Address:

Center for Evidence and Practice Improvement

Agency for Healthcare Research and Quality

ATTN: EPC SEADs Coordinator

5600 Fishers Lane

Mail Stop 06E53A

Rockville, MD 20857

Shipping Address (FedEx, UPS, etc.):

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FOR FURTHER INFORMATION CONTACT:

Jenae Benns, Telephone: 301-427-1496 or Email: epc@ahrq.hhs.gov.

SUPPLEMENTARY INFORMATION:

The Agency for Healthcare Research and Quality has commissioned the Evidence-based Practice Centers (EPC) Program to complete a review of the evidence for Treatments for Acute Episodic Migraine. AHRQ is conducting this systematic review pursuant to Section 902(a) of the Public Health Service Act, 42 U.S.C. 299a(a).

The EPC Program is dedicated to identifying as many studies as possible that are relevant to the questions for each of its reviews. In order to do so, we are supplementing the usual manual and electronic database searches of the literature by requesting information from the public (e.g., details of studies conducted). We are looking for studies that report on *Treatments for Acute Episodic Migraine*, including those that describe adverse events. The entire research protocol is available online at: https://effectivehealthcare.ahrq.gov/products/migraine-treatments/protocol

This is to notify the public that the EPC Program would find the following information on *Treatments for Acute Episodic Migraine* helpful:

- A list of completed studies that your organization has sponsored for this indication. In the list, please *indicate whether results are available on ClinicalTrials.gov along with the ClinicalTrials.gov trial number*.
    - *For completed studies that do not have results on ClinicalTrials.gov*, a summary, including the following elements: study number, study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, primary and secondary outcomes, baseline characteristics, number of patients screened /eligible /enrolled /lost to follow-up /withdrawn /analyzed, effectiveness/efficacy, and safety results.
- *A list of ongoing studies that your organization has sponsored for this indication*. In the list, please provide the ClinicalTrials.gov trial number or, if the trial is not registered, the protocol for the study including a study number, the study period, design, methodology, indication and diagnosis, proper use instructions, inclusion and exclusion criteria, and primary and secondary outcomes.
- Description of whether the above studies constitute *ALL Phase II and above clinical trials* sponsored by your organization for this indication and an index outlining the relevant information in each submitted file.

Your contribution is very beneficial to the Program. Materials submitted must be publicly available or able to be made public. Materials that are considered confidential;

marketing materials; study types not included in the review; or information on indications not included in the review cannot be used by the EPC Program. This is a voluntary request for information, and all costs for complying with this request must be borne by the submitter.

The draft of this review will be posted on AHRQ's EPC Program website and available for public comment for a period of 4 weeks. If you would like to be notified when the draft is posted, please sign up for the e-mail list at: https://www.effectivehealthcare.ahrq.gov/email-updates.

The systematic review will answer the following questions. This information is provided as background. AHRQ is not requesting that the public provide answers to these questions.

Key Questions (KQ)

For patients with acute episodic migraine

KQ 1. Opioid therapy

KQ1a. What is the comparative effectiveness of opioid therapy versus: 1) nonopioid pharmacologic therapy (e.g., acetaminophen, nonsteroidal anti-inflammatory drugs [NSAIDs], triptans, ergots alkaloids, combination analgesics, muscle relaxants, anti-nausea medications, and marijuana/cannabis) or 2) nonpharmacologic therapy (e.g., exercise, cognitive behavioral therapy, acupuncture, biofeedback, neuromodulatory devices) for outcomes related to pain, function, pain relief satisfaction, and quality of life and after follow-up at the following intervals: < 1 day; 1 day to <1 week; 1 week to <2 weeks; 2 weeks to 4 weeks?

KQ1b. How does effectiveness of opioid therapy vary depending on: (1) patient demographics (e.g. age, race, ethnicity, gender, socioeconomic status (SES)); (2) patient medical comorbidities (previous opioid use, body mass index (BMI); (3) dose of opioids; (4) duration of opioid therapy, including number of opioid prescription refills and quantity of pills used?

KQ1c. What are the harms of opioid therapy versus nonopioid pharmacologic therapy, or nonpharmacologic therapy with respect to: (1) misuse, opioid use disorder, and related outcomes; (2) overdose; (3) medication overuse headache (MOH), (4) other harms including gastrointestinal-related harms, falls, fractures, motor vehicle accidents, endocrinological harms, infections, cardiovascular events, cognitive harms, and psychological harms (e.g., depression)?

KQ1d. How do harms vary depending on: (1) patient demographics (e.g., age, gender); (2) patient medical comorbidities; (3) the dose of opioid used; (4) the duration of opioid therapy?

KQ1e. What are the effects of prescribing opioid therapy versus not prescribing opioid therapy for acute episodic migraine pain on 1) short-term (<3 months) continued need for prescription pain relief, such as need for opioid refills, and 2) long-term opioid use (3 months or greater)?

KQ1f. For patients with acute episodic migraine being considered for opioid therapy, what is the accuracy of instruments for predicting risk of opioid misuse, opioid use disorder, or overdose?

KQ1g. For patients with acute episodic migraine being considered for opioid therapy, what is the effectiveness of instruments for predicting risk of opioid misuse, opioid use disorder, or overdose?

KQ1h. For patients with acute episodic migraine being considered for opioid therapy, what is the effect of the following risk mitigation strategies on the decision to prescribe opioids: (1) existing opioid management plans; (2) patient education; (3) clinician and patient values and preferences related to opioids; (4) urine drug screening; (5) use of prescription drug monitoring program data; (6) availability of close follow-up?

KQ 2. Nonopioid pharmacologic therapy

KQ2a. What is the comparative effectiveness of nonopioid pharmacologic therapy (e.g., acetaminophen, nonsteroidal anti-inflammatory drugs [NSAIDs], triptans, ergots alkaloids, combination analgesics, muscle relaxants, anti-nausea medications, and marijuana/cannabis) versus: 1) other nonopioid pharmacologic treatments, such as those in a different medication class; or 2) nonpharmacologic therapy for outcomes related to pain, function, pain relief satisfaction, and quality of life after follow-up at the following intervals: < 1 day; 1 day to <1 week; 1 week to <2 weeks; 2 weeks to 4 weeks?

KQ2b. How does effectiveness of nonopioid pharmacologic therapy vary depending on: (1) patient demographics (e.g. age, race, ethnicity, gender); (2) patient medical comorbidities; (3) the type of nonopioid medication; (4) dose of medication; (5) duration of treatment?

KQ2c. What are the harms of nonopioid pharmacologic therapy versus other nonopioid pharmacologic therapy, or nonpharmacologic therapy with respect to: (1) misuse,(2) overdose; (3) medication overuse headache (MOH), (4) other harms including gastrointestinal-related harms, cardiovascular-related harms, kidney-related harms, falls, fractures, motor vehicle accidents, endocrinological harms, infections, cognitive harms, and psychological harms (e.g., depression)?

KQ2d. How do harms vary depending on: (1) patient demographics (e.g. age, gender); (2) patient medical comorbidities; (3) the type of nonopioid medication; (4) dose of medication; (5) the duration of therapy?

KQ 3. Nonpharmacologic therapy

KQ3a. What is the comparative effectiveness of nonpharmacologic therapy versus sham treatment, waitlist, usual care, attention control, and no treatment after follow-up at the following intervals: < 1 day; 1 day to <1 week; 1 week to <2 weeks; 2 weeks to 4 weeks?

KQ3b. What is the comparative effectiveness of nonpharmacologic treatments (e.g. exercise, cognitive behavioral therapy, acupuncture, biofeedback, neuromodulatory devices) for outcomes related to pain, function, pain relief satisfaction, and quality of life?

KQ3c. How does effectiveness of nonpharmacologic therapy vary depending on: (1) patient demographics (e.g. age, gender); (2) patient medical comorbidities?

KQ3d. How do harms vary depending on: (1) patient demographics (e.g. age, gender); (2) patient medical comorbidities; (3) the type of treatment used; (4) the frequency of therapy; (5) the duration of therapy?

PICOTS (Populations, Interventions, Comparators, Outcomes, Timing, Settings)

PICOTS Elements	Inclusion Criteria	Exclusion Criteria
Population	• Patients with acute episodic migraine seeking abortive treatment • Adults 18 years and older *Special populations: ○ General adult ○ Older populations >65 years ○ Patients with history of substance use disorder ○ Patients currently under treatment for opioid use disorder with opioid agonist therapy or naltrexone ○ Patients with a history of mental illness ○ Patients with history of overdose ○ Pregnant/breastfeeding women ○ Patients with comorbidities (e.g., kidney disease, sleep disordered breathing)	• Animals • Children (age < 18 years)

PICOTS Elements	Inclusion Criteria	Exclusion Criteria
Interventions	KQ 1 a-e: Any systemic opioid abortive therapy, include: • Codeine • Fentanyl (Actiq, Duragesic, Fentora, Abstral, Onsolis) • Hydrocodone (Hysingla, Zohydro ER) • Hydrocodone/acetaminophen (Lorcet, Lortab, Norco, Vicodin) • Hydromorphone (Dilaudid, Exalgo) • Meperidine (Demerol) • Methadone (Dolophine, Methadose) • Morphine (Kadian, MS Contin, Morphabond) • Oxycodone (OxyContin, Oxaydo) • Oxycodone and acetaminophen (Percocet, Roxicet) • Oxycodone and naloxone • And other agonists, partial agonists and mixed mechanism opioids KQ 1 f-g: Instruments and genetic/metabolic tests for predicting risk of misuse, opioid use disorder, and overdose KQ 1 h: Risk mitigation strategies, including • Existing opioid management plans • Patient education • Clinician and patient values and preferences related to opioids • Urine drug screening	For all KQs, exclude Invasive treatments, and preventive (prophylactic) treatment For KQ2, exclude NSAIDs vs placebo and triptans vs placebo

PICOTS Elements	Inclusion Criteria	Exclusion Criteria
	• Use of prescription drug monitoring program data • Availability of close follow-up • And others KQ 2: Any oral, injection, infusion, topical nonopioid abortive drug, including: • Acetaminophen • Nonsteroidal anti-inflammatory drugs [NSAIDs] (if compared against active treatment) • Triptans (if compared against active treatment) • Ergots alkaloids • Combination analgesics • Muscle relaxants • Anti-nausea medications • Marijuana/cannabis • And others KQ 3: Any non-invasive nonpharmacologic abortive therapy, including: • Exercise • Cognitive behavioral therapy • Acupuncture • And others	
Comparators	KQ 1: a-e. Usual care, another opioid therapy, nonopioid pharmacologic therapy, nonpharmacologic therapy	None

PICOTS Elements	Inclusion Criteria	Exclusion Criteria
	KQ 1 f. Reference standard for misuse, opioid use disorder, or overdose; or other benchmarks KQ g-h. Usual care KQ 2: Another nonopioid pharmacologic therapy, nonpharmacologic therapy KQ3: Sham treatment, waitlist, usual care, attention control, and no treatment, another non-invasive nonpharmacologic therapy	
Outcomes	KQ 1. Opioid Therapy: KQ 1a-e. Pain, function, pain relief satisfaction and quality of life, harms/adverse events (including withdrawal, risk of misuse, opioid, OUD, overdose, MOH). KQ 1f. Measures of diagnostic accuracy KQ 1g-h. Misuse, opioid use disorder, overdose and other harms KQ 2. Non-Opioid Therapy: Pain, function, pain relief satisfaction, quality of life, and quality of life, harms/adverse events KQ 3: Non-invasive non-pharm Therapy: Pain, function, pain relief satisfaction, quality of life and quality of life, harms, adverse events	None
Timing	At the following intervals: < 1 day; 1 day to <1 week; 1 week to <2 weeks; 2 weeks to 4 weeks	None
Settings	ER, physician's office, hospital	None
Study design	• Original studies o RCTs o Comparative observational studies	In vitro studies, non-original data (e.g. narrative

PICOTS Elements	Inclusion Criteria	Exclusion Criteria
	• Any sample size • Relevant systematic reviews, or meta-analyses (used for identifying additional studies)	reviews, editorials, letters, or erratum), single-arm observational studies, case series, qualitative studies, cost-benefit analysis, cross-sectional (i.e., non-longitudinal) studies, before-after studies, survey
Publications	Studies published in English only.	Foreign language studies

Abbreviations: RCT = randomized controlled trial

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