AHRQ Evidence-based Practice Center (EPC) Program Research Gaps Summary: Pain Management

An AHRQ EPC publication summarizing evidence gaps identified across recent EPC reviews for select healthcare topics addressing the treatment and management of acute and chronic pain

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This report is based on research conducted by AHRQ staff. The findings and conclusions in this document are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

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

The information in this report is intended to help healthcare researchers and funders of research make well-informed decisions in designing and funding research and thereby improve the quality of healthcare services. This report is not intended to be a substitute for the application of scientific judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical research and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances.

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of healthcare in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new healthcare technologies and strategies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

An important part of evidence reports is to not only synthesize the evidence, but also to identify the gaps in evidence that limited the ability to answer the systematic review questions. This information is provided for researchers and funders of research.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the healthcare system as a whole by providing important information to help improve healthcare quality. The evidence reports undergo public comment prior to their release as a final report.

If you have comments on this document, they may be sent by mail to the AHRQ staff named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov.

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Introduction

The AHRQ Evidence-based Practice Center (EPC) Program supports healthcare quality by providing the best available evidence on medications, devices, and healthcare services to help healthcare professionals, patients, policymakers, and healthcare systems make informed and evidence-based healthcare decisions. The EPC Program supports the overall AHRQ mission of producing evidence to make healthcare safer, higher quality, more accessible, equitable, and affordable, and to work within the U.S. Department of Health and Human Services and with other partners to make sure that the evidence is understood and used. The systematic synthesis of evidence reveals evidence gaps. These evidence gaps can inform future research studies, the findings from which can improve clinical practice, care delivery, and the Nation's overall health and well-being.

Pain is a significant public health challenge in the United States, affecting millions of individuals and impacting physical and mental function. To identify gaps in the evidence for treatment and management of pain, the EPC Program examined all reviews completed by an AHRQ EPC from September 2019 to September 2022, and included any review examining the treatment or management of acute and chronic pain.

The identified reviews are presented in this report in descending order by date, from newest to oldest. The purpose, key messages, and evidence gaps identified in each review are summarized. Evidence gaps are organized by population, intervention, outcomes, and study design to facilitate ease of use. Detailed descriptions of the gaps are also available in the original report as provided in hyperlinks.

A thematic analysis of evidence gaps identified across reports that addressed pain revealed the following research needs:

- **Population.** Improved recruitment is needed for older adults, individuals with pain-related diseases and chronic pain conditions (e.g., neuropathic pain, chronic migraine), individuals with comorbidities, individuals of diverse races and ethnicities (e.g., non-White individuals), and the medically underserved (e.g., rural populations, individuals with lower socioeconomic status).
- **Interventions.** Research needs to provide more details about the development and implementation of interventions (e.g., program structure, coordination, delivery, accessibility, acceptability, participant cost).
- **Outcomes.** More research should examine outcomes assessing quality of life, functionality, and others that are patient-centered (e.g., patient engagement).
- **Study design.** In general, longer followup periods, study expansion to multiple sites, and the recruitment of larger sample sizes can help address evidence gaps.

The evidence gaps identified in this report (Table 1) are provided to inform research funders, researchers, and policymakers about the types of issues that need to be addressed and the types of studies necessary to address these questions.

For more information, contact Angela.Carr@ahrq.hhs.gov or EPC@ahrq.hhs.gov or visit the Effective Health Care Program.

Table 1. Summary of reports

Report Category	Report	Number
Reports by Category	Acute Pain	5
	Chronic Pain	6
	Headaches/Migraines	2
Reports by Year	2022	6
	2021	2
	2020	1
	2019	2
Reports by Intervention Type	Pharmacological	7
	Nonpharmacological	6
	Comprehensive Pain Management	2
Reports by Target Audience	Professional Societies (Guideline panels)	9
	Clinicians	8
	Health Systems or Health Plans	3

Total Number of Reports = 11

Living Systematic Review on Cannabis and Other Plant-Based Treatments for Chronic Pain

September 20, 2022

https://effectivehealthcare.ahrq.gov/products/plant-based-chronic-pain-treatment/living-review

Purpose

The purpose of this systematic review, requested by the U.S. Congress, was to evaluate the evidence on benefits and harms of cannabinoids and similar plant-based substances with addiction potential (e.g., kratom) to treat chronic noncancer pain.

Key Messages

- Oral spray with comparable amounts of THC and CBD in combination is probably associated with small improvements in pain severity and overall function. There may be a large increased risk of dizziness and sedation and a moderately increased risk of nausea.
- Synthetic THC may be associated with moderate improvement in pain severity, no effect on overall function, an increased risk of sedation, and large increased risk of nausea and dizziness.
- Extracted whole-plant products with higher THC than CBD may be associated with large increases in risk of study withdrawal due to adverse events and dizziness.
- Evidence on whole-plant cannabis products with lower THC than CBD levels (topical CBD), other cannabinoids (cannabidivarin), and comparisons with other active interventions was insufficient to draw conclusions.

Evidence Gaps

Study Population

- Studies to assess possible differential effects in different races, ethnicities, and age groups.
- Pain populations expanded to include persons with non-neuropathic chronic pain, specifically back pain, other musculoskeletal pain, and fibromyalgia.

Interventions

- Studies of high THC to CBD ratio products derived from whole-plant cannabis, with a clear description of extraction or purification process and consistent nomenclature regarding the final product.
- Studies to compare different routes of administration (e.g., oromucosal spray, oral oil, topical, oral capsule, smoked, etc.).
- Exploration of effects of different cannabinoids, and/or other plant-based products, including kratom.
- Studies comparing plant-based interventions with other plant-based treatments, opioids, nonopioid medications, or nonpharmacological interventions to evaluate active-control comparisons to provide direct evidence on comparative effectiveness.

Outcomes

- Future studies should include pain response, pain severity, measures of overall function, impact on opioid use and adverse events in addition to patient-reported outcomes (e.g., quality of life, depression, anxiety, and sleep).

Acute Treatments for Episodic Migraine

August 8, 2022

https://effectivehealthcare.ahrq.gov/products/migraine-treatments/research

Purpose

This systematic review, commissioned by the Centers for Disease Control and Prevention, assesses the comparative effectiveness and harms for acute migraine treatments, including opioid therapy, nonopioid pharmacologic therapy, and nonpharmacologic therapy.

Key Messages

- Compared with placebo, treatments such as triptans, NSAIDs (nonsteroidal anti-inflammatory drugs), dihydroergotamine, antiemetics, and acetaminophen, reduce pain but increase the risk of mild and transient adverse events.
- Only a small number of studies have evaluated opioids. Some opioids may reduce pain of episodic migraine. Some opioids may be less effective than other drugs.
- Newer therapies such as calcitonin gene-related peptide receptor antagonists and lasmiditan (5-HT1F receptor agonist) probably improve pain relief at 2 hours and increase the likelihood of being pain free at 2 hours, 1 day, and 1 week, and restore function. Serious adverse events are more common in patients who received lasmiditan than placebo.
- Although only studied in one or a few small trials, several other therapies available in the United States may improve migraine pain compared with placebo, including dexamethasone, dipyrone, lidocaine, magnesium sulfateoctreotide, and secobarbital. Evidence is insufficient to draw conclusions about serious adverse events.
- Although only studied in one or a few small trials, several nonpharmacological treatments for migraine may improve various measures of pain compared with placebo, including noninvasive neuromodulation devices such as remote electrical neuromodulation, magnetic stimulation, and external trigeminal nerve stimulation, as well as other therapies such as acupuncture, chamomile oil, and eye movement desensitization reprocessing. Evidence is insufficient to draw conclusions about serious adverse events.

Evidence Gaps

Study Populations

- Studies evaluating the efficacy of acute treatments in specific populations, including those with cardiovascular problems, cerebrovascular problems, hemiplegic migraine, and individuals over the age of 65.

Interventions

- Comparative trials between different acute medication choices to help clinicians decide among all of the available options and a combination of therapies.
- Studies on the acute treatment of migraine that compare relative risks of medication-overuse headaches with different classes of acute treatments.
- Research on noninvasive neuromodulation, including comparative studies with medications, to clarify their role as acute therapies for migraine
- Studies on behavioral pain management of migraine, such as cognitive behavioral therapy, mindfulness-based stress reduction, and others. Studies exploring strategies to overcome disparities such as race and socioeconomic status, in acute treatment of migraine.

Study Design

- Studies that compare the time it takes to reach clinically meaningful endpoints in addition to pain freedom, total migraine freedom, and freedom from other symptoms.

Outcomes

- Studies that emphasize patient-centric endpoints that reflect the quality of life impacted by migraine and its return to normal by acute treatment rather than only pain freedom or pain improvement.

Treatments for Acute Pain: A Systematic Review

June 22, 2022

https://effectivehealthcare.ahrq.gov/products/treatments-acute-pain/research

Purpose

The purpose of this report, commissioned by the Centers for Disease Control and Prevention, is to evaluate the effectiveness and comparative effectiveness of opioid, nonopioid pharmacologic, and nonpharmacologic therapy in patients with specific types of acute pain (back pain, neck pain, other musculoskeletal pain, neuropathic pain, postsurgical pain, dental pain, and pain associated with renal colic and sickle cell disease), including effects on pain, function, quality of life, adverse events, and long-term use of opioids.

Key Messages

- Opioids are probably less effective than nonsteroidal anti-inflammatory drugs (NSAIDs) for surgical dental pain and kidney stone pain and might be similarly effective to NSAIDs for low back pain.
- Opioids might be and NSAIDs are probably more effective than acetaminophen for surgical dental pain, but opioids are probably less effective than acetaminophen for kidney stone pain.
- An opioid might be more effective than gabapentin for acute neuropathic pain.
- Opioids are probably associated with increased risk of short-term adverse events versus nonopioid pharmacologic therapy for acute pain, including any adverse event, study withdrawal due to adverse events, nausea, dizziness, and somnolence, but serious adverse events are uncommon in randomized trials.
- Being prescribed an opioid for acute low back pain or postoperative pain might be associated with increased likelihood of use of opioids at long-term followup versus not being prescribed.
- Heat therapy is probably effective for acute low back pain, spinal manipulation might be effective for acute back pain with radiculopathy, massage might be effective for postoperative pain, and a cervical collar or exercise might be effective for acute neck pain with radiculopathy.

Evidence Gaps

Study Populations

- Research benefits and harms in patients with a history of or current opioid use/misuse disorder, mental health, and medical comorbidities (including sickle cell pain, neuropathic pain, and neck pain).

Interventions

- Research to identify effective nonpharmacologic therapies for neuropathic pain.
- Studies exploring the association between use of opioid and nonopioid therapies and risk of misuse and opioid use disorder using standardized methods.
- Research to develop and validate instruments for accurately predicting risk of opioid use disorder or misuse in persons with acute pain.

Study Design

- Research to better understand how patients value different outcomes (beneficial and harmful).
- Longitudinal studies on opioids to evaluate longer-term outcomes, including associated harms (e.g., opioid use disorder, overdose, impaired social and emotional cognition, and workforce nonparticipation).

Outcomes

- Studies that measure sleep and mental health outcomes, in addition to pain, function, and quality of life.
- Studies that address how policies aimed at reducing the duration or dose of opioid prescribing impact patient outcomes such as pain and quality of life and the effectiveness of interventions to mitigate such effects.
- Determine how using risk prediction instruments impact treatment decisions and, ultimately, patient outcomes.

Noninvasive Nonpharmacological Treatment for Chronic Pain

June 22, 2022

https://effectivehealthcare.ahrq.gov/products/noninvasive-nonpharm-pain-update/research

Purpose

This report, commissioned by the Centers for Disease Control and Prevention, assesses noninvasive nonpharmacological treatments for common chronic pain conditions.

Key Messages

Interventions that improved function and/or pain for at least month:

- Low back pain: Exercise, psychological therapy, spinal manipulation, low-level laser therapy, massage, mindfulness-based stress reduction, yoga, acupuncture, multidisciplinary rehabilitation (MDR).
- Neck pain: Exercise, low-level laser, mind-body practices, massage, acupuncture.
- Knee osteoarthritis: Exercise, cognitive behavioral therapy (CBT).
- Hip osteoarthritis: Exercise, manual therapies.
- Fibromyalgia: Exercise, CBT, myofascial release massage, mindfulness practices, tai chi, qigong, acupuncture, MDR.
- Tension headache: Spinal manipulation.

Evidence Gaps

Interventions

- Trials comparing interventions with pharmacological treatments with outcome reports that include patients achieving a clinically meaningful improvement in pain, function, or quality of life.

Study Design

- Explanatory and pragmatic trials with long-term follow up to evaluate differential effectiveness and safety of treatments in subpopulations of interest, including age and social determinants of health.
- Studies with documentation of coexisting conditions and factors in trials with sufficient sample size to evaluate the differential impact of conditions and factors. These should include studies in pregnant and breastfeeding women with chronic pain and comparison of treatment effects between patients with nociplastic pain (e.g., fibromyalgia) and those with other types of pain.

Nonopioid Pharmacologic Treatments for Chronic Pain

June 21, 2022

https://effectivehealthcare.ahrq.gov/products/nonopioid-chronic-pain/research

Purpose

This report, commissioned by the Centers for Disease Control and Prevention, evaluates the benefits and harms of nonopioid drugs in randomized controlled trials of patients with specific types of chronic pain, considering the effects on pain, function, quality of life, and adverse events.

Key Messages

- In the short term, improvement in pain and function was small with specific anticonvulsants, moderate with specific antidepressants in diabetic peripheral neuropathy/post-herpetic neuralgia and fibromyalgia, and small with nonsteroidal anti-inflammatory drugs (NSAIDs) in osteoarthritis and inflammatory arthritis.
- In the intermediate term, evidence was limited, with evidence of benefit for memantine in fibromyalgia and for serotonin norepinephrine reuptake inhibitor (SNRI) antidepressants in low back pain and fibromyalgia.
- In the long term, evidence was too limited to draw conclusions. In general, evidence on quality of life was limited and no treatment achieved a large improvement in pain or function.
- Small to moderate, dose-dependent increases in withdrawal due to adverse events were found with SNRIs duloxetine and milnacipran, anticonvulsants pregabalin and gabapentin, and NSAIDs. Large increases in withdrawal due to adverse events were seen with oxcarbazepine. NSAIDs have increased risk of serious gastrointestinal, liver dysfunction, and cardiovascular adverse events.

Evidence Gaps

Study Populations

- Trials in older patients to better understand possible age-related difference in treatment effect and in patients of non-White races.
- Trials in patients with chronic headache, low back pain, and sickle cell disease.

Interventions

- Comparative effectiveness trials that evaluate intermediate and long-term treatment duration, and make direct comparisons among key interventions both within and across drug classes.

Study Design

- Study designs need a consistent use of recognized standard measures of pain and function to facilitate comparisons across trials.
- Explanatory and pragmatic trials with long-term followup to evaluate differential effectiveness and safety of treatments in subpopulations of interest, including age and social determinants of health.

Outcomes

- Long-term health outcomes (including quality of life).

Opioid Treatments for Chronic Pain

May 17, 2022

https://effectivehealthcare.ahrq.gov/products/opioids-chronic-pain/research

Purpose

This report, commissioned by the Centers for Disease Control and Prevention, assesses the effectiveness and harms of opioid therapy for chronic noncancer pain, alternative opioid dosing strategies, and risk mitigation strategies.

Key Messages

- Opioids are associated with small improvements versus placebo in pain and function, and increased risk of harms at short-term (1 to <6 months) followup; evidence on long-term effectiveness is very limited, and there is evidence of increased risk of serious harms that appear to be dose dependent.
- At short-term followup, evidence showed no differences between opioids versus nonopioid medications in improvement in pain, function, mental health status, sleep, or depression.
- Provision of naloxone to patients might reduce the likelihood of opioid-related emergency department visits.
- No instrument has been shown to be associated with high accuracy for predicting opioid overdose, addiction, abuse, or misuse.

Evidence Gaps

Study Populations

- Trials with patients characterized by nociplastic pain (e.g., fibromyalgia) that measure multiple important outcomes, including pain, function, quality of life, sleep, mental health outcomes, misuse, and opioid use disorder.

Interventions

- Studies to understand how underlying pain mechanisms, presence of specific pain conditions (e.g., autoimmune, congenital, sickle cell) and presence of genetic polymorphisms affecting opioid metabolism impact effectiveness of therapies.
- Longitudinal studies on the comparative benefits and harms of different opioids or formulations and different prescribing methods.
- Studies on the effects of risk mitigation strategies (use of naloxone, urine drug screening, prescription drug monitoring programs, and abuse deterrent formulations) on clinical outcomes.
- Comparative effectiveness studies on alternative tapering strategies and concomitant use of cannabis or gabapentinoids with opioids.
- Studies to develop and validate instruments to accurately predicting risk of opioid use and determine use of risk prediction instruments impacts treatment decisions and outcomes.

Study Design

- Longitudinal explanatory and pragmatic trials to evaluate effectiveness and safety of treatments

Outcomes

- Research to understand how patients value different outcomes (beneficial and harmful) associated with opioid prescribing.
- Longitudinal outcome studies on opioids, including harms (e.g., refractory opioid dependence, impaired social and emotional cognition, workforce nonparticipation, and effects on functions of the endogenous opioid system).

Integrated and Comprehensive Pain Management Programs: Effectiveness and Harms

October 29, 2021

https://effectivehealthcare.ahrq.gov/products/integrated-pain-management/research

Purpose

This review, commissioned by the Centers for Medicare & Medicaid Services as part of the Todd Graham study, assesses the effectiveness and harms of integrated (i.e., x) and comprehensive (i.e., y) pain management programs that address multiple aspects of pain.

Key Messages

- Integrated pain management programs improved both pain and function in patients with chronic pain at some, but not all, time frames compared with usual care or waitlist.
- Comprehensive pain management programs also improved function at multiple time frames and pain immediately after the program compared with usual care.
- Comprehensive programs also improved function and pain compared with medications alone at multiple timeframes.
- Comprehensive programs were associated with improvement in function in the short term compared with physical activity alone but not in the intermediate or long term. There was no improvement in pain at any time point.
- There were no differences in pain or function between comprehensive programs and psychological support alone at any time.
- Beneficial effects were usually considered small to moderate for both program types.
- Although evidence was limited, serious harms were not reported for either program.
- Formal pain management programs have not been widely implemented in the United States for either general populations or the Medicare population.

Evidence Gaps

Study Population

- Future research is needed to understand how formal programs impact patients with a broader range of pain conditions (e.g., neuropathic pain, nociplastic pain like in fibromyalgia), individuals with complex subacute pain who may be at risk for development of chronic pain, older adults, and Medicare beneficiaries.
- Research on pain management in underserved populations and equity in program delivery.

Interventions

- Research leading to some level of standardization of programs and their delivery may facilitate general understanding of the best combinations of interventions.
- Trials comparing programs with pharmacologic treatments.
- Research into the structure, coordination, and implementation of programs within practices and within systems to understand what may optimize delivery of care and the components and factors that affect adherence and improve outcomes.
- Factors such as program accessibility, acceptability, intensity, and participant cost need further examination as does the relationship of such factors to program adherence and outcomes.

Study Design

- Trials with sufficient sample size designed to evaluate differential effectiveness and safety of treatments in subpopulations of interest to understand how to best tailor programs.

Outcomes

- Studies that reflect understanding of pathophysiological mechanisms and that address multiple domains of pain as well as clinically meaningful outcomes related to change in use of opioids, healthcare utilization, and quality of life.
- Evaluation of the cost-effectiveness of formal pain management programs to understand the balance of benefit and cost.

Interventional Treatments for Acute and Chronic Pain

September 3, 2021

https://effectivehealthcare.ahrq.gov/products/interventional-treatments-pain/research

Purpose

The purpose of this systematic review, commissioned by the Centers for Medicare & Medicaid Services (CMS) as part of the Todd Graham study, was to evaluate the benefits and harms of selected interventional procedures for acute and chronic pain that are not currently covered by CMS but are relevant for and have potential utility for use in the Medicare population, or that are covered by CMS but for which there is important uncertainty or controversy regarding use.

Key Messages

- Vertebroplasty is probably more effective than sham or usual care for vertebral compression fractures for reducing pain and improving function in older (Medicare-eligible) populations, but benefits are small. Benefits are smaller in sham compared with usual care controlled trials and larger in trials of patients with more acute symptoms.
- Kyphoplasty is probably more effective than usual care for vertebral compression fractures for reducing pain and improving function in older (Medicare-eligible) populations, but has not been compared against sham.
- Cooled radiofrequency denervation is probably moderately more effective for reducing pain and improving function than sham for sacroiliac pain in younger populations and similarly effective versus conventional radiofrequency for presumed facet joint pain and piriformis corticosteroid injection for piriformis syndrome may be similarly effective versus sham for pain at 1 week, but more effective for reducing pain at 1 month. These interventions were evaluated in younger (non-Medicare-eligible) populations, but findings can probably be applied to older populations.

Evidence Gaps

Interventions

- Vertebroplasty: additional studies would be helpful to clarify the effectiveness of vertebroplasty, specifically whether some sham interventions have therapeutic effects, whether benefits are greater in patients with hyperacute (e.g., <3 weeks pain), and documentation of long-term outcomes, including harms.
- Intradiscal methylene blue: confirmatory randomized controlled trials (RCTs) are needed.
- Cooled radiofrequency for sacroiliac pain: additional research would be helpful to clarify optimal techniques, given the variability in methods between the two available trials.
- Other procedures addressed in this report: there is a need for rigorous RCTs to clarify benefits and harms.

Study Design

- Vertebroplasty: possible study designs include sham controlled RCTs and individual patient data meta-analysis of existing trials. Comparator treatments, including the components of usual care, should be described with sufficient detail to determine applicability to practice.
- Other procedures addressed in this report: future RCTs should attempt to minimize placebo effects by utilizing appropriate sham interventions and include rigorous assessment of harms and longer term outcomes.

Outcomes

- Prospective clinical registries designed to evaluate uncommon and serious harms would be a useful supplement to RCTs, given likely sample size limitations.

Management of Primary Headaches in Pregnancy

November 12, 2020

https://effectivehealthcare.ahrq.gov/products/headaches-pregnancy/research

Purpose

This review, nominated by the American College of Obstetrics and Gynecology, evaluates the literature on pharmacologic and nonpharmacologic interventions to prevent or treat attacks of primary headaches (migraine, tension headache, cluster headache, and other trigeminal autonomic cephalgias) in women who are pregnant (or attempting to become pregnant), postpartum, or breastfeeding.

Key Messages

- Prevention of primary headache – venlafaxine, tricyclic antidepressants (any), benzodiazepines (any), beta blockers (any), prednisolone, and oral magnesium use during pregnancy may have increased risk of fetal/child adverse effects, but calcium channel blockers (any, but nifedipine in particular) and antihistamines (any) may have a low risk of adverse effects (indirect evidence).
- Pharmacologic treatment of acute attacks of primary headache – use of triptans for migraine during pregnancy may not be more harmful than their use before pregnancy. Compared with nonuse, triptan use may not be associated with spontaneous abortions or congenital anomalies, but may be associated with worse child emotionality and activity outcomes at 3 years of age.
- Systematic reviews of harms (regardless of indication) report that acetaminophen, prednisolone, indomethacin, ondansetron, antipsychotics (any), and intravenous magnesium use during pregnancy may be associated with fetal/child adverse effects, but low-dose aspirin use may not be associated with increased risk of adverse effects.

Evidence Gaps

Interventions

- Studies addressing prevention or treatment of cluster headache and other primary headache disorders in pregnant women.

Study Design

- Given the concern regarding exposing the fetus to potentially harmful pharmacologic interventions, when observational studies using patient registries are conducted, they should be adequately designed and analyzed to compare treatments and measure fetal/neonatal outcomes.
- Future studies should either randomize patients (after considering the ethical issues in this population) to minimize selection bias, or report between-arm estimates of treatment effect that adequately account for important confounders, such as age and severity of headache attack (or of history of headaches). Studies should also, where feasible, conduct blinding of participants, care providers, and outcome assessors to minimize the likelihood of performance and detection biases.

Outcomes

- Since registry data will likely continue to be important in identifying harms, researchers should report more details about disease severity, intervention doses, durations, and frequencies.
- Evaluate maternal outcomes, such as headache related symptoms (e.g., photosensitivity), quality of life, functional outcomes (e.g., impact on employment/school attendance), and patient satisfaction with intervention; adverse effects on breastfeeding, such as decreased milk supply; and fetal/child adverse outcome.

Treatment for Acute Pain: An Evidence Map

October 22, 2019

https://effectivehealthcare.ahrq.gov/products/acute-pain-treatment/technical-brief

Purpose

The purpose of this evidence map, nominated by various U.S. Department of Health and Human Services agencies, is to provide a high-level overview of the current guidelines and systematic reviews on pharmacologic and nonpharmacologic treatments for acute pain. We map the evidence for several acute pain conditions including postoperative pain, dental pain, neck pain, back pain, renal colic, acute migraine, and sickle cell crisis.

Key Messages

- Few systematic reviews provide a comprehensive rigorous assessment of all potential interventions, including nondrug interventions, to treat pain attributable to each acute pain condition. Acute pain conditions that may need a comprehensive systematic review or overview of systematic reviews include postoperative postdischarge pain, acute back pain, acute neck pain, renal colic, and acute migraine.
- Certain acute pain conditions have many published systematic reviews: postoperative pain, pain associated with dental procedures and oral surgery, low back pain, acute migraine. Several acute pain conditions have sufficient new data to warrant a new systematic review: pain associated with dental procedures and oral surgery, low back pain, renal colic, acute migraine.
- Few systematic reviews of acute pain treatments examine outcomes other than very short-term outcomes. Pain during the week or month following the inciting event and persistent opioid use were rarely reported.
- Most systematic reviews report pain outcomes using scales that measure only pain intensity, while few assess function or other pain characteristics.
- Few reviews focused on specific settings or populations other than general adults or children and adolescents.

Evidence Gaps

Study Populations

- Updated comprehensive assessment of the evidence related to renal colic, acute migraine in primary care and specialty clinics in individuals with chronic or episodic migraine, and dental pain associated with dental procedures and oral surgery.
- Studies that address subpopulations, including, individuals with a history of substance use disorder.
- Future studies should continue to examine how patient baseline characteristics (history of substance abuse disorder, fear avoidance, pain catastrophizing, mental health issues) and condition characteristics (trauma, abuse) modify response to treatment and lead to chronic pain or persistent opioid use.

Interventions

- Studies to comprehensively address acute pain, which is a critical focus for these conditions, because effectively treating acute and episodic musculoskeletal pain can prevent transition to chronic pain.
- Systematic reviews and trials should expand the set of interventions addressed in research on treatments for acute pain including nondrug interventions, multicomponent interventions, and drugs prescribed at postoperative discharge.

Study Design

- Systematic reviews and trials that increase followup time and pain assessment beyond 48 hours, and measure analgesic use in the days following discharge.

Outcomes

- Studies that expand on outcomes reporting, including pain and its impact on function and recovery as measured by multidomain scales that assess more than just pain intensity.

Comparative Effectiveness of Analgesics To Reduce Acute Pain in the Prehospital Setting

September 3, 2019
https://effectivehealthcare.ahrq.gov/products/acute-pain-ems/research

Purpose

This report, nominated by the National Highway Traffic Safety Administration in the Department of Transportation, evaluates the effectiveness and harms of opioids compared to nonopioid analgesics as treatment of moderate to severe acute pain in the prehospital setting.

Key Messages

As initial therapy in the prehospital setting:

- Nonsteroidal anti-inflammatory drugs provide similar pain relief to opioids and may cause fewer overall side effects and less drowsiness.
- Acetaminophen may provide similar pain relief to opioids, and may cause fewer side effects overall and less dizziness.
- Ketamine may provide similar pain relief to opioids. Ketamine may cause more dizziness or overall side effects, while opioids may cause more respiratory depression.
- Combining an opioid with ketamine may be more effective in reducing pain compared with opioids alone.
- If morphine does not adequately relieve pain, changing to ketamine may be more effective and more quickly reduce pain than giving additional morphine.

Evidence Gaps

Study Populations

- Studies to understand how formal programs impact patients with a broader range of pain conditions, including individuals with complex subacute pain, those at risk for developing chronic pain, older adults, and Medicare beneficiaries.
- Studies in underserved populations and equity in program delivery.
- Studies with sufficient size to evaluate differential effectiveness and safety of treatments in subpopulations of interest to understand how to tailor programs.

Interventions

- Studies on effectiveness of formal pain management programs, particularly those based in primary care.
- Studies comparing programs with pharmacologic treatments.

Study Design

- Evaluation of the cost-effectiveness of formal pain management programs to understand the balance of benefit and cost.

Outcomes

- Studies to understand how factors such as program accessibility, acceptability, intensity, and participant cost impact adherence and outcomes.
- Studies into the structure, coordination, and implementation of programs within practices and systems to understand how to optimize the delivery of care and the components and factors that affect adherence and improve outcomes.
- Studies that report clinically meaningful outcomes, including improvement in pain, function, quality of life, change in use of opioids, and healthcare utilization.