

AHRQ EVIDENCE-BASED PRACTICE CENTER PROGRAM

RESEARCH GAPS SUMMARY:

PRIMARY CARE

An EPC publication summarizing evidence gaps identified across recent EPC reviews for select healthcare topics

Prepared by:

Angela Carr, R.N., M.H.A.

David Niebuhr, M.D., M.P.H., M.S.

Cleothia Alford, M.P.S., M.Sc.

Christine Chang, M.D., M.P.H.

Lionel Banez, M.D.

Suchitra Iyer, Ph.D.

Kim Wittenberg, M.A.

Chunliu Zhan, M.D., Ph.D.

Patrick O'Malley, M.D., M.P.H., M.A.C.P.

Craig A. Umscheid, M.D., M.S.

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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.

Robert “Bob” Otto Valdez, Ph.D., M.H.S.A.
Director
Agency for Healthcare Research and Quality

Craig A. Umscheid, M.D., M.S.
Director
Evidence-based Practice Center Program
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality

Arlene S. Bierman M.D., M.S.
Director
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality

Angela Carr, R.N., M.H.A.
Stakeholder Engagement Coordinator for the USPSTF
and EPC Programs
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality

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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. Primary care research 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. Identifying gaps in primary care research can inform future studies and outline areas that need to be addressed to inform clinical practice to improve the Nation's overall health and well-being.

To identify primary care gaps, the EPC Program examined all reviews conducted by an EPC in calendar years 2019–2021 that addressed a research topic in primary care. AHRQ defines primary care research as:

- Research conducted in a primary care setting
- Research conducted by or about primary care clinicians
- Research on a topic integral to the primary care setting

Identified reports are presented in this report in descending order, by date. The purpose, key messages, and evidence gaps identified in each review are summarized. Evidence gaps are organized by population, intervention, study design, and outcomes 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 the identified primary care research gaps revealed the following:

- **Study 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).
- **Study design.** In general, longer followup periods, study expansion to multiple sites, and the recruitment of larger sample sizes can help address evidence gaps.
- **Outcomes.** More research should examine outcomes assessing quality of life, functionality, and others which are patient-centered (e.g., patient engagement).

The primary care gaps identified in this report (Table 1) are provided to inform research funders, researchers, and policymakers about the types of questions 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 Disease Category	Acute & Chronic Pain Management	8
	Mental Health Conditions and Substance Abuse	5
	Dementia	2
	Respiratory – COPD/Asthma	2
	Technology/Telehealth	2
	Gastrointestinal/Genitourinary	1
	Musculoskeletal Disorders	1
	Patient Engagement	1
	Other	3
Reports by Year	2021	5
	2020	13
	2019	7
Reports by Intervention Type	Pharmacologic	16
	Behavioral	8
	Other	7
Reports by Target Audience	Professional Societies (Guideline panels)	24
	Clinicians	19
	Health Systems or Health Plans	6
	Other	1

Total Number of Reports = 25

Management of High-Need, High-Cost Patients: A “Best Fit” Framework Synthesis, Realist Review, and Systematic Review

October 29, 2021

<https://effectivehealthcare.ahrq.gov/products/high-utilizers-health-care/research>

Purpose

The goal of this review is to provide evidence to help identify high-need, high-cost patients and determine the causal mechanisms and effectiveness of complex interventions that intend to improve high-need, high-cost patient and healthcare system outcomes.

Key Messages

- Data from claims and health records can identify characteristics associated with high-need, high-cost (HNHC) patients but are limited in selecting specific patients who are most appropriate for care management interventions.
- Identifying and targeting HNHC patients for interventions to change their healthcare use requires capturing their medical and social complexities. Building and maintaining trusting, caring relationships between HNHC patients and care providers underpins successful patient interventions. Both patients and care providers require support and practical resources to foster an effective relationship. We found—
 - moderate to low strength of evidence (SOE) that emergency department (ED)–based, primary care–based, and home-based care interventions are associated with reduced use of healthcare services;
 - low SOE that ED, ambulatory intensive caring unit (aICU), and other primary care models are associated with reduced costs; and
 - low SOE that system-level transformation and telephonic/mail models are not associated with use or cost differences.

Evidence Gaps

Study Populations

- More work is needed to support an understanding of targetable patient characteristics associated with modifiable and preventable high use.
- Studies to understand the role of patient health behaviors, such as self-efficacy, health literacy, and activation.
- Research to better understand the impact of behavioral health conditions on use of potentially preventable or modifiable high-cost medical care. The research should focus on clearly delineating behavioral health diagnosis or diagnoses, co-occurring chronic clinical conditions, the severity of the behavioral health condition, and whether the patient is actively engaged in treatment for their behavioral health problems.

Interventions

- Comparative effectiveness research that directly compared individual interventions or types of interventions.
- Intervention studies to evaluate the impact on changes in patients’ clinical and social risk outcomes, quality of care, or experience with care.

Outcomes

- The limited understanding of how and why interventions help HNHC patients speaks to the need for more qualitative and implementation research describing the process of care and patients’ experiences.
- Research focused on developing tools to help measure patient trust in the healthcare system and in their care providers.
- Studies that address multiple and potentially correlational factors, including the dynamic nature of high-cost service use among chronic, high-need patients, and distinguishing between the individual level between preventable or modifiable care and unavoidable service use.

Integrated and Comprehensive Pain Management Programs: Effectiveness and Harms

October 29, 2021

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

Purpose

Our review 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, timeframes compared with usual care or waitlist.
- Comprehensive pain management programs also improved function at multiple timeframes 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.

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

October 27, 2021

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

Purpose

The purpose of this systematic review 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 moderate increased risk of nausea.
- Synthetic THC may be associated with moderate improvement in pain severity, no effect on overall function, and 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 (cannabidiol), 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 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, non-opioid 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).

Safety of Vaccines Used for Routine Immunization in the United States: An Update

May 25, 2021

<https://effectivehealthcare.ahrq.gov/products/safety-vaccines/research>

Purpose

The scope of this systematic review of the evidence was to assess the safety of vaccines in the immunization schedule recommended for children and adolescents (hereafter, we refer to children and adolescents simply as “children”), adults, and pregnant women.

Key Messages

- Since the prior 2014 AHRQ report on vaccine safety, we found no new evidence of increased risk for key adverse events following administration of vaccines that are routinely recommended for adults, children, and pregnant women.
- Signals from the prior report remain unchanged for adverse events that include anaphylaxis in adults and children, and febrile seizures and idiopathic thrombocytopenic purpura in children. There continues to be no evidence of increased risk of adverse events for vaccines currently recommended in pregnant women.
- There remains insufficient evidence to draw conclusions about some rare potential adverse events.

Evidence Gaps

Study Populations

- As HPV9 is now approved for adults up to age 45, epidemiological studies should track and report any adverse events in adults over age 26 as a subgroup.
- Further study of the risk of spontaneous abortion among women who become pregnant shortly after vaccination.

Outcomes

- Studies are needed to assess and report on serious adverse events of the measles, mumps, and rubella vaccine in adults.
- The potentially increased risk of herpes zoster and myocardial infarction following HEPLISAV-B as identified by the U.S. Food and Drug Administration warrants further research and ongoing post marketing surveillance.
- The increased rate of local reactions could potentially lead to increased rate of injury (e.g., from falls) due to functional limitations; this warrants further research.

Automated-Entry Patient-Generated Health Data for Chronic Conditions: The Evidence on Health Outcomes

March 1, 2021

<https://effectivehealthcare.ahrq.gov/products/health-data-mapping/report>

Purpose

To summarize the research related to automated-entry consumer health technologies that provide patient-generated health data (PGHD) for the prevention or management of 11 chronic diseases.

Key Messages

- For three chronic conditions (coronary artery disease [CAD], heart failure, and asthma), we found a possible positive effect of PGHD technologies on health outcomes.
- For obesity, we classified the health outcome data as unclear, and we found consistent evidence of a lack of effect of PGHD interventions on body mass index/weight.
- For hypertension, we classified the health outcome data as unclear, and we found evidence of a possible positive effect of PGHD interventions on blood pressure.
- For cardiac arrhythmias, we classified the health outcome data as unclear but found consistent evidence of a beneficial effect of PGHD interventions on time to arrhythmia detection.
- The evidence on both health outcomes and surrogate outcomes was unclear for the other five conditions (chronic obstructive pulmonary disease, diabetes prevention, sleep apnea, stroke, and Parkinson's disease).

Evidence Gaps

Study Populations

- Randomized controlled trials (RCT) with females and other underrepresented populations evaluating PGHD interventions for patients with CAD.

Interventions

- Research to address the primary barriers to good adherence and how much device adherence is necessary to improve health.
- As a prevention strategy to prevent progression to diabetes, studies exploring the use a glucose meter to educate patients about the relationship between eating/exercise behavior and their glucose level.
- Studies should explore the role of devices, such as the Apple Watch, in accelerating the diagnosis of sleep apnea by providing information to signal that a patient has a high probability of having the condition.

Study Design

- Longer term RCTs that isolate PGHD's effects to clarify impacts on both surrogate and health outcomes.

Outcomes

- Since these conditions require long-term management, trials with longer term followup are needed to determine the efficacy of PGHD interventions for chronic conditions.
- Studies to measure health outcomes in obese patients, rather than merely body mass index or weight.

Acute Treatments for Episodic Migraine

December 29, 2020

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

Purpose

This systematic review 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-HT_{1F} receptor agonist) probably improve pain relief at 2 hours and increase the likelihood of being pain-free at 2 hours, 1 day, and at 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 sulfate octreotide, 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 amongst 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

December 29, 2020

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

Purpose

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, 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 follow up 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.

Pharmacologic and Nonpharmacologic Treatments for Posttraumatic Stress Disorder

November 4, 2020

<https://effectivehealthcare.ahrq.gov/products/ptsd-repository-expanded/research>

Purpose

Identify and abstract data from posttraumatic stress disorder (PTSD) treatment randomized controlled trials (RCTs) to update the PTSD Trials Standardized Data Repository (PTSD-Repository) with data on PTSD and mental health, including suicide-related outcomes and substance use.

Key Messages

- Reporting was incomplete for many data elements in published studies: less than half of studies reported on the loss of PTSD diagnosis (i.e., no longer meeting criteria for PTSD) or clinically meaningful response/remission of symptoms.
- Risk of bias (ROB) was assessed for all included studies; most were rated as having a medium ROB (57%), and only 6 percent were rated as having a low ROB.
- An exploration of an expanded ROB system was developed and pilot tested.

Evidence Gaps

Interventions

- Comparative studies on the response to antibiotic therapy as well as corticosteroid therapy based on the phenotype of the exacerbation episode. These studies should explore systemic corticosteroid treatment of chronic obstructive pulmonary disease (COPD) exacerbation based on blood eosinophils.
- Studies exploring systemic corticosteroids in COPD exacerbation to assess the benefits and treatment effect stratified by blood eosinophil count, chest physiotherapy using breathing technique and/or vibration/percussions and/or positive expiratory pressure.
- Studies to determine whether pulmonary rehabilitation commenced during hospitalization for COPD exacerbation is associated with increased mortality.
- High quality randomized controlled trials exploring the potential benefit of pulmonary rehabilitation to counteract the deconditioning associated with COPD exacerbation.
- Large high-quality randomized controlled trials to evaluate new treatment options of whole-body vibration and transcutaneous electrical nerve stimulation (TENS) and dietary interventions with caloric supplements and vitamin D.
- Studies to identify the optimal route of administration for systemic corticosteroids, i.e., oral, inhaled, or intravenous corticosteroids.
- More studies assessing the effectiveness of interventions to reduce the risk of adverse outcomes following hospital discharge. Outcomes should include with final health outcomes such as quality of life, mortality, and repeat hospitalizations.

Outcomes

- Studies in exacerbation of COPD that focus on final health outcomes such as dyspnea and quality of life and include clinical resolution and risk of repeat exacerbation (with or without hospital admission).

Prevention, Diagnosis, and Management of Opioids, Opioid Misuse, and Opioid Use Disorder in Older Adults

November 3, 2020

<https://effectivehealthcare.ahrq.gov/products/opioids-older-adults/report>

Purpose

To provide a framework for understanding how to reduce adverse outcomes of opioid use among older adults, and to describe the evidence available for different factors associated with and interventions to reduce adverse outcomes related to opioid use in this population.

Key Message

- All studies that looked at prior or early postoperative opioid use found mostly strong associations (e.g., relative risk [RR] >2.0) with long-term opioid use.
- All studies that examined greater amounts of prescribed opioids (higher number of opioid prescriptions or higher opioid dose) found mostly strong associations with long-term opioid use.
- Studies consistently (≥75% agreement) reported that concomitant benzodiazepine use, higher comorbidity score, (generally undefined) substance misuse, tobacco use, and low income were each associated with long-term opioid use, but the associations were mostly weak.
- Studies were mostly consistent in finding that alcohol "abuse" and healthcare utilization were not associated with long-term opioid use.
- Studies found no consistent associations between alcohol misuse or gender and opioid misuse.
- Two studies found that prescription drug monitoring programs have been associated with less opioid use, at the State level.
- Studied interventions included multidisciplinary pain education for patients, an educational pamphlet for patients, implementation of an opioid safety initiative, provision of patient information and pain management training for clinicians, a bundle of educational modalities for clinicians, clinician education, free prescription acetaminophen, a nationally mandated tamper-resistant opioid formulation, and motivational interview training for nursing students.

Evidence Gaps

Study Populations

- Need more studies specifically for or evaluated in older adults.
- Studies in older adults should emphasize the adaptation of existing interventions to account for the heterogeneity in characteristics of the older adult population, incorporate outcomes of greatest importance to seniors, and determine how caregivers can help to actively implement interventions.

Interventions

- Studies exploring how to deprescribe opioids safely in older adults, especially when individuals are dependent on opioids and experiencing pain.
- The development, validation, and evaluation of new interventions tailored to the needs of older adults to manage opioid misuse and opioid misuse disorder in older adults.
- Factors associated with opioid use disorder (high-risk obtainment of prescription opioids, procuring multiple opioid prescribers, mental health outcomes, physical health outcomes, all-cause hospitalization, opioid-related hospitalization, nonopioid-specific hospitalization, emergency department visits, opioid overdose, all-cause death, opioid-related death, and nonopioid-related death).

Study Design

- Studies among older adults to confirm the reliability, validity, and factor structure of screening tools for detecting opioid misuse.

Outcomes

- Studies exploring opioid related outcomes and of the effectiveness of interventions for older adults. These studies should parse out benefits and harms among the older adult subgroups (e.g., by age within the category of "older adults," by generational cohort, or by underlying condition).

Management of Colonic Diverticulitis

October 12, 2020

<https://effectivehealthcare.ahrq.gov/products/diverticulitis/research>

Purpose

This systematic review evaluates: (1) imaging for diagnosis of diverticulitis; (2) effectiveness of hospitalization for acute uncomplicated diverticulitis, antibiotics for acute diverticulitis, and interventional radiology for acute complicated diverticulitis; (3) need for colonoscopy in people with a history of diverticulitis; and (4) the effectiveness of pharmacologic prevention of recurrent diverticulitis.

Key Messages

- Computed tomography (CT) accurately diagnoses acute diverticulitis and may contribute to appropriate management in addition to clinical diagnosis. There is insufficient evidence about CT accuracy to stage acute diverticulitis.
- For patients with uncomplicated acute diverticulitis, outpatient management may be as effective as inpatient care.
- For patients with uncomplicated diverticulitis, antibiotic treatment may not affect pain symptoms, length of hospital stay, recurrence risk, quality of life, or need for surgery compared to no antibiotic treatment.
- Evidence is insufficient regarding the benefits or harms of percutaneous drainage for patients with complicated acute diverticulitis.
- Patients who are 50 or older or who had complicated diverticulitis (with abscess, peritonitis, etc.) are at increased risk of having colorectal cancer, advanced colonic neoplasia, or advanced adenoma.
- Colonoscopies conducted within 1.5 to 12 months after acute diverticulitis rarely have complications or incomplete tests.
- 5-aminosalicylic acid (5-ASA) offers no benefit to patients to reduce the risk of recurrence of diverticulitis.

Evidence Gaps

Interventions

- Evaluations of heterogeneity of treatment effect to better understand which patients may most benefit from (or may be most harmed by) a given intervention.

Study Design

- Studies that review and analyze large databases to compare interventions.
- Large-scale, multicenter RCTs should be conducted in unrestricted populations with appropriate subgroup analyses.

Outcomes

- Large RCTs to evaluate potential clinically important differences in rates of the most important outcomes to patients (e.g., death, treatment failure, emergency surgery, and time to recurrence) and important harms, adverse events, and complications (e.g., risk of *C. difficile* infection from antibiotics, which can be devastating for patients who already have diverticulitis; postoperative death; and permanent stomas).

Care Interventions for People Living With Dementia and Their Caregivers

August 31, 2020

<https://effectivehealthcare.ahrq.gov/products/care-interventions-pwd/report>

Purpose

To understand the evidence base for care interventions for people living with dementia and their caregivers, and to assess the potential for broad dissemination and implementation of that evidence.

Key Messages

- An intensive multicomponent intervention with education, group discussion, in-home and phone support sessions, and caregiver feedback for informal caregiver support (i.e., discrete adaptations of REACH II), may improve informal caregiver depression at 6 months. (low-strength evidence)
- Collaborative care models (i.e., care ecosystems or discrete adaptations of the ACCESS models) may improve quality of life for people living with dementia (PLWD). (low-strength evidence) The literature does not allow for further determination of whether the very small to small average effects apply to all enrolled PLWD or if larger effects were concentrated in an unidentified subgroup.
- Collaborative care models (i.e., discrete adaptations of the ACCESS model) may improve system-level markers, including guideline-based quality indicators and reduction in emergency department visits. (low-strength evidence)
- For all other outcomes and interventions, we found the evidence was insufficient because the uncertainty of the evidence was too high to draw conclusions.

Evidence Gaps

Interventions

- Research exploring questions of “what works” in dementia care and how to deliver that care greatly interests researchers, funders, care providers, healthcare systems, people living with dementia, and their families.
- Effectiveness studies on practices regarding how persons living with dementia are diagnosed, treated, and supported throughout the disease trajectory, including identifying key support needs of family caregivers.

Strategies for Patient, Family, and Caregiver Engagement

August 26, 2020

<https://effectivehealthcare.ahrq.gov/products/family-engagement/research>

Purpose

This Technical Brief applies a framework to create a map of the currently available evidence on patient and family engagement strategies that helps people manage chronic conditions. Direct patient care strategies are those that directly inform the patients' own treatment decisions, health behaviors, or outcomes (e.g., self-management support, shared decision making, and communication strategies). A health system level strategy has an impact beyond the individual patient's care (e.g., informing changes to the services of the clinic and health care system). A community or policy strategy engages patients, consumers, or citizens in policymaking or that engages communities in healthcare policies.

Key Messages

- The majority of systematic reviews focused on direct patient care engagement strategies
- Strategies most commonly included team-based care to support patient self-management, patient-provider communication using shared decision making, and mobile health and electronic health record tools to improve engagement.
- The direct patient care engagement strategies with the highest volume of evidence (i.e., several large randomized controlled trials [RCTs]) included group-based educational programs to promote chronic disease self-management by peers and other healthcare professionals; web-based and short message service interventions for cancer survivors; promising telehealth programs to promote communication, self-monitoring, and counseling; and mobile health to promote weight loss.
- Health system-level patient engagement strategies demonstrated some benefits, such as improvements in healthcare processes, development of organizational plans and policies, and education.
- The single article addressing a community level patient engagement strategy described a neighborhood-clinic partnership in the Navajo Nation aimed at improving care for people living with diabetes.

Evidence Gaps

Study Populations

- Studies that examine subpopulations including older adults and people with impaired decision-making capacity.
- Studies on families with children with medically complex health conditions.
- Adult and pediatric studies that include family caregivers.

Interventions

- Research that assesses direct patient care strategies on shared decision making and patient-provider communications on clinical outcomes.
- Studies focused on advanced care planning for patients with chronic conditions.
- Studies that examine the effect of technology among children and adolescents living with chronic disease.
- Studies on strategies at the health system level.

Study Design

- Studies evaluating health system interventions using health services design methods that include a comparison group.
- Design and analysis methods should include interrupted time series and propensity score approaches.

Outcomes

- Studies to assess risks and benefits including patient anxiety and disproportionate access to engagement methods, which could worsen health disparities.
- Studies focused on the development of a validated measures to assess the extent health systems are supporting the engagement of patients and caregivers.
- Studies with patient and organizational level outcomes.
- Adult and pediatric studies that measured caregiver-related outcomes and the effectiveness of strategies on clinical outcomes.

Interventions for Substance Use Disorders in Adolescents: A Systematic Review

May 21, 2020

<https://effectivehealthcare.ahrq.gov/products/substance-use-disorders-adolescents/research>

Purpose

This systematic review synthesizes the literature on behavioral, pharmacologic, and combined interventions for adolescents ages 12 to 20 years with problematic substance use or substance use disorder. We included interventions designed to achieve abstinence, reduce use quantity and frequency, improve functional outcomes, and reduce substance-related harms.

Key Messages

- Adolescents, 12 to 20 years, with problematic alcohol and/or cannabis use or use disorder:
 - Brief behavioral interventions (1–2 encounters):
 - Motivational interviewing decreases days of heavy alcohol use and overall alcohol use.
 - Motivational interviewing decreases problems associated with substance use.
 - Intensive behavioral interventions (> 2 encounters):
 - Family-focused therapies reduce alcohol use.
 - Motivational interviewing decreases combined alcohol and other drug use.
 - Combined cognitive behavioral therapy and motivational interviewing decrease illicit drug use.
- Adolescents, 12 to 25 years of age, with substance use disorders:
 - Pharmacological interventions:
 - In opioid use disorder, longer courses (2–3 months) of buprenorphine/buprenorphine-naloxone are more effective than shorter courses (14–28 days) to reduce days of opioid use and achieve abstinence.

- College students with problematic alcohol use:
 - Behavioral interventions:
 - Mandated alcohol programs decrease alcohol use in the medium term, regardless of intervention. Four commercially available interventions are more effective in the short term than no intervention.
 - Brief behavioral interventions, particularly those based on motivational interviewing, reduce alcohol use compared to no intervention in college students with heavy or hazardous alcohol use.

Evidence Gaps

Study Populations

- Large “adult” trials that enroll older adolescents (age 18 to 20) and report outcomes for this subgroup.
- Research should also seek to clarify whether specific subpopulations may benefit from specific intervention components (e.g., identifying which interventions are most effective for a given primary substance of misuse, severity of use, and how effectiveness is moderated by the presence of co-occurring psychiatric disorders).

Outcomes

- There is a need to adopt a set of core outcome measures and standard approaches to reporting of these outcomes. Consistently reported core outcomes utilizing common measures facilitates better comparative analysis.

Diagnosis and Treatment of Clinical Alzheimer's-Type Dementia

April 28, 2020

<https://effectivehealthcare.ahrq.gov/products/alzheimers-type-dementia/research>

Purpose

To summarize evidence on cognitive test accuracy for clinical Alzheimer's-type dementia (CATD) in suspected cognitive impairment; biomarker accuracy for Alzheimer's disease (AD) in dementia; and effects of CATD drug treatment.

Key Messages

- Many brief cognitive tests were highly (>0.8) sensitive and specific distinguishing CATD from normal cognition, but less from mild cognitive impairment.
- Amyloid positron emission tomography (PET) and magnetic resonance imaging were highly sensitive and specific distinguishing autopsy-confirmed AD from non-AD dementia; fluorodeoxyglucose (FDG)-PET was highly sensitive and moderately (>0.5 to <0.8) specific; cerebrospinal fluid (CSF) tests were moderately sensitive and specific. Data were limited on biomarkers added to clinical evaluation.
- Cholinesterase inhibitors (ChI) were slightly better than placebo for cognition and function, but increased withdrawals due to adverse effects; evidence was insufficient for supplements. In moderate to severe CATD, memantine plus ChI slightly improved cognition versus ChI, but not function.
- Donepezil and antidepressants appeared similar to placebo for agitation and depression, respectively; for other prescription drugs and all supplements, evidence was insufficient on behavioral and psychological symptoms.

Evidence Gaps

Study Populations

- CATD trials that enroll more diverse participants, including non-Whites, and prespecify analyses with sufficient statistical power to examine whether treatment effects are modified by patient characteristics, including age, sex, race/ethnicity, baseline CATD severity, baseline severity of behavioral and psychological symptoms of dementia, and living setting.

Interventions

- Studies comparing the accuracy of individual and combined accuracy of cognitive tests (including the MoCA, Mini-Cog, SLUMS, TICS, CANTAB, and other web-based tests), to help identify the best test or combination of tests for maximizing classification accuracy and feasibility in typical clinical settings. These studies should prespecify analyses to examine whether results differ as a function of characteristics like age, race/ethnicity, sex, and education. They should also collect data on psychological and other harms of cognitive testing.
- Trials that evaluate the long-term efficacy and safety using various doses of antipsychotics and antidepressants for agitation, psychosis, and other behavioral and psychological symptoms.

Study Design

- Studies exploring the accuracy of biomarkers for distinguishing AD from non-AD dementias in patients with CATD and that compare brain imaging, CSF, and blood biomarker accuracy with autopsy-confirmed AD.

Outcomes

- Large, longitudinal trials investigating drug treatment for CATD to detect response to treatment based on cognitive, functional, global outcome measures, patient quality of life, and caregiver outcomes, and investigate treatment efficacy and harms outcomes.

Characteristics of Existing Asthma Self-Management Education Packages

April 27, 2020

<https://effectivehealthcare.ahrq.gov/products/asthma-education/technical-brief>

Purpose

To identify the components that comprise asthma self-management education (AS-ME) packages used in the United States, and examine, compare, and organize their key characteristics and available research to enable a better understanding of current practice and future needs.

Key Messages

- Most packages rely on in-person instruction with paper-based materials.
- Packages are often tailored to local settings, but little is known about how they are modified.
- Numerous studies found that packages are associated with improved asthma control, reduced symptom frequency, increased asthma knowledge, and fewer school absences; results are mixed for outcomes such as hospitalizations, emergency department visits, and quality of life.

Evidence Gaps

Interventions

- Studies that address patient population needs by evaluating (AS-ME) packages designed for adult asthma patients, including study of home-based, community-based, and self-directed packages.

Study Design

- Strengthen the body of evidence for asthma self-management education packages by researching packages that have not been widely studied, and conducting head-to-head studies that compare packages to other packages and to other widely used interventions.

Outcomes

- Studies should report asthma severity, comorbidity, and socioeconomic factors and examine how patient literacy/health literacy, cultural competence of (AS-ME) educators/providers, and social determinants of health influence the use and effectiveness of asthma self-management education packages.
- Studies with improved rigor of outcome that include standard measures of asthma control and absenteeism, and methods to more effectively assess and report medication use and trigger avoidance.

Opioid Treatments for Chronic Pain

April 16, 2020

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

Purpose

To assess 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 such as rates of overdose, abuse, addiction, and misuse.
- Comparative effectiveness studies on alternative tapering strategies and concomitant use of cannabis or gabapentinoids with opioids.
- Studies to develop and validate instruments for accurately predicting risk of opioid use and determine how using 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).

Nonopioid Pharmacologic Treatments for Chronic Pain

April 16, 2020

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

Purpose

Evaluate 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)

Noninvasive Nonpharmacological Treatment for Chronic Pain

April 16, 2020

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

Purpose

To assess noninvasive nonpharmacological treatments for common chronic pain conditions.

Key Messages

- Interventions that improved function and/or pain for ≥ 1 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 outcomes 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.

Achieving Health Equity in Preventive Services

December 3, 2019

<https://effectivehealthcare.ahrq.gov/products/health-equity-preventive/research>

Purpose

To summarize research on achieving health equity in 10 preventive services for cancer, cardiovascular disease, and diabetes in adults by identifying effects of impediments and barriers that create disparities and effectiveness of interventions to reduce them.

Key Messages

- No eligible studies evaluated effects of provider barriers.
- Evidence is low or insufficient for effects of population barriers, including insurance, access, age, rural location, income, language, health literacy, country of origin, and attitudes.
- Screening rates are higher with patient navigation for colorectal, breast, and cervical cancer; telephone calls and prompts for colorectal cancer; and reminders with lay health workers for breast cancer.
- Evidence is low or insufficient for other interventions due to lack of studies or their limitations.

Evidence Gaps

Study Populations

- Studies on broader populations to understand their experiences and adverse effects of healthcare disparities, including racial and ethnic populations, socioeconomically disadvantaged populations, underserved rural populations, sexual and gender minority populations, non-English speakers, and others subject to discrimination.
- Studies evaluating interventions found to be successful (i.e., patient navigators or clinician-linked outreach and education), should be extended to additional populations and settings.

Interventions

- Studies evaluating the effectiveness of telemedicine, electronic health records, and quality-based care using clinical quality measures in improving preventive care in patient populations

Study Design

- Studies to understand the impact of barriers and impediments related to providers and health systems on disparities in preventive service use.
- Studies that explore race bias among healthcare providers and its influence on decision making. Similarly, exploring group-level differences in availability of services (e.g., after-hours clinics) and the degree to which they contribute to disparities in preventive care.
- Future studies should collect sexual orientation or gender identity data so it can be included as a standard demographic data.
- Studies should expand to include more than one site or geographic region to improve statistical power for subgroup comparisons and improve understanding of similarities and differences across defined groups.

Outcomes

- Studies to identify the most effective and efficient methods to implement patient navigation and reminders in different healthcare settings as a strategy to reduce disparities

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 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.

Pharmacologic and Nonpharmacologic Therapies in Adult Patients With Exacerbation of COPD

October 11, 2019

<https://effectivehealthcare.ahrq.gov/products/copd/research>

Purpose

To evaluate the effectiveness and harms of pharmacologic and nonpharmacologic treatments for exacerbations of chronic obstructive pulmonary disease (COPD).

Key Messages

- Antibiotic therapy increases the clinical cure rate and reduces the clinical failure rate.
- Oral and intravenous corticosteroids improve dyspnea and reduce the clinical failure rate.
- Antibiotics and corticosteroids are not associated with increase in serious adverse events.
- The evidence is insufficient to support the effect of aminophyllines, magnesium sulfate, mucolytics, inhaled corticosteroids, inhaled antibiotics, 5-lipoxygenase inhibitor, and statins on mortality, dyspnea, need for intubation, clinical failure, or hospital admission.
- Titrated oxygen reduces mortality compared with high flow oxygen.
- The evidence suggests benefits of some nonpharmacologic interventions such as chest physiotherapy using vibration/percussion/massage or using breathing technique (on dyspnea), resistance training (on dyspnea and quality of life), early pulmonary rehabilitation commenced before hospital discharge during the initial most acute phase of exacerbation rather than the convalescence period (on dyspnea), and whole-body vibration training (on quality of life).
- Vitamin D supplementation may improve quality of life.
- The evidence is insufficient for comparative effectiveness of different regimens of antibiotics and corticosteroids based on type of agents, delivery modes, and duration of treatments.
- The evidence is insufficient for effectiveness of combinations of treatments that are each individually effective.
- Serious adverse events were not found to be different between most evaluated interventions.

Evidence Gaps

Interventions

- Comparative studies on the response to antibiotic therapy as well as corticosteroid therapy based on the phenotype of the exacerbation episode. These studies should explore systemic corticosteroid treatment of COPD exacerbation based on blood eosinophils.
- Studies exploring systemic corticosteroids in COPD exacerbation to assess the benefits and treatment effect stratified by blood eosinophil count, and chest physiotherapy using breathing technique and/or vibration/percussions and/or positive expiratory pressure.
- Studies to determine whether pulmonary rehabilitation commenced during hospitalization for COPD exacerbation is associated with increased mortality.
- High quality randomized controlled trials exploring the potential benefit of pulmonary rehabilitation to counteract the deconditioning associated with COPD exacerbation.
- Large high-quality randomized controlled trials to evaluate new treatment options of whole-body vibration and transcutaneous electrical nerve stimulation (TENS) and dietary interventions with caloric supplements and vitamin D.
- Studies to identify the optimal route of administration for systemic corticosteroids, i.e., oral, inhaled, or intravenous corticosteroids.
- More studies assessing the effectiveness of interventions to reduce the risk of adverse outcomes following hospital discharge. Outcomes should include with final health outcomes such as quality of life, mortality, and repeat hospitalizations.

Outcomes

- Studies in exacerbation of COPD that focus on final health outcomes such as dyspnea and quality of life and include clinical resolution and risk of repeat exacerbation (with or without hospital admission).

Antipsychotics for the Prevention and Treatment of Delirium

September 3, 2019

<https://effectivehealthcare.ahrq.gov/products/antipsychotics/research>

Purpose

To assess the benefits and harms of antipsychotics for the prevention and treatment of delirium among adult patients.

Key Messages

- Haloperidol or second-generation antipsychotics used to prevent or treat delirium did not decrease length of stay in hospital.
- There was little or no evidence to determine the effect of antipsychotics on cognitive function, delirium severity, or caregiver burden, or for sedation when used for prevention.
- Second-generation antipsychotics may lower the occurrence of delirium in postoperative patients.
- Haloperidol or second-generation antipsychotics used to prevent or treat delirium may lead to little or no difference in sedation or extrapyramidal side effects (problems with muscles such as spasms or restlessness). Heart-related side effects tended to occur more frequently with the use of antipsychotics, in particular QT interval prolongation in second-generation antipsychotics.

Evidence Gaps

Study Populations

- With the exception of critically ill patients, studies of patient subpopulations including postoperative patient populations, where larger, well-controlled trials of second-generation antipsychotics in the prevention of delirium are needed to clarify whether there is any beneficial role for the perioperative setting.

Interventions

- Studies evaluating pharmacologic prevention and treatment strategies in patient groups that are anticipated to have similar delirium risk factor(s) and associated pathophysiology, including anticholinergic agents and other medications taken before delirium occurs.
- Studies comparing pharmacologic and nonpharmacologic approaches, quality of life outcomes, and best treatment approaches in populations of patients such as those with pre-existing dementia.

Study Design

- The field would benefit from the development of standardized, clinically meaningful measures of the following outcomes: patient agitation and distress, subsequent memories of delirium, caregiver burden and distress, inappropriate continuation of antipsychotics, and long-term cognitive and functional outcomes.
- Additionally, better phenotyping of delirium subtypes, through adoption and development of more detailed standardized measurement tools.

Outcomes

- Outcome should include delirium severity, impact on cognitive functioning, caregiver burden, inappropriate continuation of medications, patient agitation and distress, and subsequent memories of delirium.

Telehealth for Acute and Chronic Care Consultations

April 24, 2019

<https://effectivehealthcare.ahrq.gov/products/telehealth-acute-chronic/research>

Purpose

To assess the effectiveness of telehealth consultations and explore supplemental decision analysis.

Key Messages

- Results vary by setting and condition, with telehealth consultations producing generally either better outcomes or no difference from comparators in settings and clinical indications studied.
- Remote intensive care unit consultations likely reduce mortality.
- Specialty telehealth consultations likely reduce patient time in the emergency department.
- Telehealth consultations in emergency services likely reduce heart attack mortality.
- Remote consultations for outpatient care likely improve access and clinical outcomes.
- More detailed telehealth consultation costs and outcomes data would improve modeling assumptions.

Evidence Gaps

Study Population

- Studies should include patient characteristics and context of care delivery to understand how telehealth impacts outcomes.

Interventions

- Studies evaluating the use of remote specialist guiding the use of technology such as echocardiograms, ultrasound, or endoscopy by an appropriate technician. These studies need to evaluate if this technology increases access to critical services, improves patient outcomes, satisfaction, and cost effectiveness.

Study Design

- Studies that include contemporary comparison groups, either groups of patients or other organizations, so that the effect of the telehealth consultations could be more successfully isolated from historical changes or the idiosyncrasies of a specific organization.
- Multisite trial-based studies, where patients are randomized to standard management, telehealth consultation or a hybrid approach and explore costs, access, and outcomes data.
- Studies exploring the use of telehealth consultations across several specialties, including systems level implementation that would facilitate consultations throughout an organization and spread the cost of the technology, the workflow changes, and any needed training or new skills more broadly across a system.

Outcomes

- Studies exploring outcomes from the perspective of a payer, a health system, a hospital, a practice group, or an individual provider.
- Telehealth and telehealth consultations studies in multisite, rural, or undersourced healthcare settings using standardized outcomes for consistent measurement of effectiveness.

Long-Term Drug Therapy and Drug Holidays for Osteoporosis Fracture Prevention: A Systematic Review

April 23, 2019

<https://effectivehealthcare.ahrq.gov/products/osteoporosis-fracture-prevention/research>

Purpose

To summarize the effects of long-term osteoporosis drug treatment and of osteoporosis drug treatment discontinuation and holidays.

Key Messages

- Evidence on the effects of long-term osteoporosis drug treatment and drug continuation versus discontinuation is mostly limited to white, healthy, postmenopausal women.
- Long-term alendronate reduces radiographic vertebral and nonvertebral fractures in women with osteoporosis; long-term zoledronate reduces vertebral and nonvertebral fractures in women with osteopenia or osteoporosis.
- Long-term bisphosphonates may increase atypical femoral fractures and osteonecrosis of the jaw, although both are rare.
- In women with osteoporosis, long-term raloxifene reduces vertebral fractures, but not hip or nonvertebral fractures, and increases venous thromboembolism.
- Long-term oral hormone therapies reduce hip and clinical fractures but increase multiple serious harms.
- Evidence is insufficient about the effects of long-term denosumab, risedronate, ibandronate, teriparatide, and abaloparatide on fractures and harms.
- Continuing bisphosphonates after 3–5 years versus discontinuation reduces some measures of vertebral fractures, but not nonvertebral fractures

Evidence Gaps

Study Populations

- Randomized controlled trials of long-term osteoporosis drug treatment and of osteoporosis drug continuation versus discontinuation with sub population focus that includes men, non-White women, and the oldest old, diverse populations, those with multiple comorbidities, and in a variety of geographic regions.

Interventions

- Randomized controlled trials with adequate power to compare risk of clinical fracture endpoints for osteoporosis drugs that don't yet have established long-term fracture prevention efficacy, including ibandronate, risedronate, and denosumab.
- Randomized controlled trials with adequate power to compare risk of clinical fracture endpoints to compare sequential therapy, including denosumab followed by bisphosphonate therapy, and anabolic therapy (e.g., teriparatide or abaloparatide). Studies should include a continuous long-term antiresorptive treatment control group.
- Randomized controlled trials with adequate power to compare risk of clinical fracture endpoints to anabolic therapy (e.g., teriparatide or abaloparatide) followed by antiresorptive therapy versus antiresorptive therapy alone.

Outcomes

- Retrospective and prospective cohort studies to estimate the risk of rare harms associated with antiresorptive osteoporosis drug treatment to best place these risks in the context of the effects of these treatments on other potentially beneficial and harmful outcomes.
- Trials and prospective cohort studies that compare long-term osteoporosis drug treatment versus placebo and systematically collect harms outcomes; should plan a priori to examine possible effect modifiers of harms outcomes.

Adverse Effects of Pharmacological Treatments of Major Depression in Older Adults

March 28, 2019

<https://effectivehealthcare.ahrq.gov/products/depression-harms/research>

Purpose

To assess adverse events of antidepressants in the treatment of major depressive disorder in adults 65 years of age or older.

Key Messages

- Serotonin norepinephrine reuptake inhibitors (SNRIs) (duloxetine and venlafaxine) cause adverse events more often than placebo and most likely lead to discontinuation of therapy during treatment of up to 12 weeks.
- Selective serotonin reuptake inhibitors (SSRIs) (escitalopram and fluoxetine) most likely cause adverse events at a similar frequency to placebo therapy but still may lead to discontinuation of therapy during treatment of up to 12 weeks.
- Duloxetine most likely increases the risk of falls over longer treatment (<24 weeks)
- Adverse events contributing to discontinuation of therapy were rarely reported in a way that allowed clear characterization of what adverse events to expect.
Few studies compared other antidepressants to placebo or to each other, or reported other outcomes. Trial data were sparse, and trials were short in duration, underpowered, and studied low

doses of antidepressants. Observational studies had limitations related to their design.

Evidence Gaps

Study Populations

- Studies that focus on outcomes specific to subgroups important to the care of older adults and also account for other important factors such as nursing facility residence.

Interventions

- Comparative studies exploring the use of several therapies within the classes of SSRIs and SNRIs and other treatment options other than SSRIs and SNRIs.
- Randomized controlled trials with a placebo group to provide a direct comparison among antidepressants requiring assessment of comparative harms and comparative efficacy.

Outcomes

- Long-term, rigorous comparative studies are needed.
- Studies should include outcomes of interest (e.g., syndrome of inappropriate antidiuretic hormone).