Research Prioritization Topic Briefs

PCORI Scientific Program Area: Addressing Disparities

Minnesota Evidence-Based Practice Center

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Topic 1: Interventions to Avoid Unintentional Overdose and Substance Dependence of Pain Relievers (Opioid and Nonopioid) among Vulnerable Populations

Compare the effectiveness of different opioid and nonopioid pain relievers, in different doses and durations, in avoiding unintentional overdose and substance dependence among Medicaid and/or Medicare beneficiaries belonging to different racial/ethnic/linguistic groups with acute and noncancer chronic pain.

Criteria	Brief Description
Introduction	
Overview/definition of topic	DESCRIPTION OF CONDITION **Chronic Pain** The National Institutes of Health defines chronic pain as any pain lasting more than 12 weeks. Whereas acute pain is a normal sensation that alerts us to possible injury; chronic pain is very different. Chronic pain persists—often for months or even longer.[1] According to a recent Institute of Medicine Report, up to one-third of U.S. adults report chronic pain.[2] Chronic pain is characterized as persistent and difficult to treat. **Analgesic Treatments** There are two classes of prescription medications used to treat chronic pain: narcotic analgesics and non-narcotic analgesics. Narcotic analgesics, also called opioids, include codeine, fentanyl, meperidine, morphine, oxycodone, tramadol, hydrocodone, and hydromorphone. Non-narcotic analgesics, also called nonopioids, include antidepressants, anti-inflammatories, anticonvulsants, and muscle relaxants. **Opioids** **Number of Users** • A movement toward more aggressive management of pain has led to a 10-fold increase in the medical use (prescribed) of opioid painkillers in the last 20 years.[3] **Benefits and Harms** • Opioid analgesics are more effective than non-steroidal anti-inflammatory drugs (NSAIDS) in providing pain relief. They are much stronger and do not seem to have a ceiling effect,[4] in that increasing the dose results in further pain reduction. • Long –term use of opioids can lead to dose escalation, tolerance, and physical dependence.[4] • Potential side effects include: respiratory depression, dizziness, nausea, vomiting, constipation, and mental clouding. **Abuse** • The 2010 National Survey on Drug Use and Health indicated that ~2.4 million people reported using prescription drugs non-

Criteria	Brief Description
	medically (or illicitly/without a prescription) for the first time within the past year. This equates to about 6,600 new users every day.[5] • Among patients who are prescribed opioids, an estimated 80% are prescribed low doses (<100 mg morphine equivalent dose per day) by a single practitioner. These patients account for an estimated 20% of all prescription drug overdoses. Another 10% of patients are prescribed high doses (≥100 mg morphine equivalent dose per day) of opioids by single prescribers and account for an estimated 40% of prescription opioid overdoses. The remaining 10% of patients are of greatest concern. These are patients who seek care from multiple doctors and are prescribed high daily doses, and account for another 40% of opioid overdoses. Persons in this third group not only are at high risk for overdose themselves but are likely diverting or providing drugs to others who are using them without prescriptions. [6] **Nonopioids** **Number of users** • Fewer than 15% of chronic pain patients use nonopioid medications.[7] **Efficacy/Risks/Side Effects** • Nonopioids are effective at relieving slight to moderate pain when prescribed alone.[4] • Nonopioids have an upper limit of pain relief that can be achieved. Once that ceiling has been reached, increasing the dosage will not provide further pain relief.[4] • Potential side effects include: liver damage, kidney damage, and gastrointestinal issues. **Abuse** • Unlike opioid use, nonopioid use seems to have little risk of dependence and abuse. DESCRIPTION OF INTERVENTIONS TO PREVENT ABUSE/DEPENDENCE • The National Prescription Drug Take-Back Day aims to provide a safe, secure, and environmentally responsible means of disposing of prescription drugs, while also educating the general public about the potential for abuse and trafficking of medications. The Drug Enforcement Agency (DEA) launched its first Take-Back event in September 2010, after which the President signed the Secure and Responsible Drug Disposal Act of 2010, which amended the Controlled Substances Act to allow people, including residents of long-term care facilities, to regularly, conveniently, and safely dispose of their controlled substance medications by delivering them to entities authorized by the Attorney General to accept them. DEA is in the process of finalizing regulations to implement the Act, publishing

Criteria	Brief Description
	on December 21, 2012, a Notice of Proposed Rulemaking on the Disposal of Controlled Substances that presented possible disposal options.[8] • Office-based, primary care treatment of opioid addiction with a combination of Buprenorphine and Naloxone was approved in 2002 and has been shown to be effective. Mintzer et al. published positive results of a cohort study in 2008 showing more than half of treated patients were sober at six months.[9] • Urine drug testing compared to patient reporting and prescription monitoring was the most effective identifier of noncompliance.[10] • Opioid Treatment Agreements are documents signed by patients describing their responsibilities (take medications only at the dose and frequency prescribed, not request opioid or any other pain medication from physicians other than from this doctor, obtain all medications from one pharmacy, etc.) outlining an emergency care plan, and providing information on the side effects and risks of opioids. • Opioid Risk Tool The ORT is a five-item survey that uses information related to family history of substance abuse, personal history of substance abuse, age, history of preadolescent sexual abuse, and diagnosis of psychological abuse, along with sex to generate a risk score.[11] • Narcotic Risk Manager The NRM is a survey that uses age, sex, smoking status, history of substance abuse, psychiatric diagnoses, education, race, and insurance to generate a risk score.[12]
Relevance to patient-centered outcomes	Opioid abuse can lead to dependency and potentially death. Those addicted experience an increased dependence on tertiary care,[13] decreased quality of life, and increased mortality.[14]
Burden on Society	
Recent prevalence in populations and subpopulations	• According to the Narcotic Risk Manager, the risk of narcotic misuse (specifically illicit use of prescription narcotics) is elevated in those who are younger, male, smokers, have a history of substance abuse, have multiple psychological problems, are insured by Medicaid or self pay, and are nonwhite.[12] • In the Troup Study, in those prescribed opioid analgesics for chronic pain, younger individuals were more likely to have abuse/dependence, individuals with back pain and headache diagnoses were more likely to have opioid dependence/abuse diagnoses (compared with joint pain, or neck pain). History of mental health and substance use disorders were strongly predictive of opioid abuse/dependence as was the use of sedative/hypnotics.[15] • Nonopioid substance abuse diagnosis was the strongest predictor of opioid abuse/dependence, in a veteran population. Mental health disorders were moderately strong predictors.[16] • Males, younger adults, and individuals with greater days' supply of prescription opioids were more likely to develop abuse/ dependence.[16]

Criteria	Brief Description
	• High-risk populations for prescription drug abuse or overdose include males, middle aged adults (with the highest prescription pain medicine overdose rates), people residing in rural areas (less access to high-cost illicit drugs), whites, Native Americans, and Alaska Natives. Approximately 1 in 10 Native American or Alaska Natives age 12 and older reported using pain medicine for nonmedical reasons in the past year. This compares with 1 in 20 whites and 1 in 30 blacks according to a 2013 publication.[5] <u>Prescribing varies by race.</u> • A cross-sectional survey published in 2005 of 397 black and white patients showed that blacks had significantly higher pain scores (6.7 on a scale of 0 to 10, 95% confidence interval (CI) 6.4 to 7.0) compared with whites (5.6, 95% CI 5.3 to 5.9); however, white patients were more likely to be taking opioid analgesics compared with blacks (45.7% vs. 32.2%, p<.006). Even after controlling for potentially confounding variables, white patients were significantly more likely (odds ratio (OR) 2.67, 95% CI 1.71 to 4.15) to be taking opioid analgesics than black patients. There were no differences by race in the use of other treatment modalities such as physical therapy and nonsteroidal anti-inflammatories or in the use of specialty referral.[17] • Non-Hispanic whites were significantly more likely to speak English, be insured, and suffer nonoccupational injuries. Hispanics were twice as likely as non-Hispanic whites to receive no emergency department pain medication.[18] • We studied if ethnicity influences patient-controlled analgesia (PCA) for the treatment of post-operative pain. Using a retrospective record review, we examined data from all patients treated with PCA for post-operative pain from January to June 1993. We excluded patients who did not have surgery prior to the prescription of PCA or were not prescribed PCA in the immediate post-operative period. The sample consisted of 454 subjects. While there were no differences in the amount of narcotic self-administered, there were significant differences in the amount of narcotic prescribed among Asians, Blacks, Hispanics, and Whites.[19]
Effects on patients' quality of life, productivity, functional capacity, mortality, use of health care services	QUALITY OF LIFE • A 2010 literature review of quality of life among opiate-dependent individuals found that generally, opiate-dependent individuals – at the start of treatment as well as during treatment – report a significantly lower Health-Related Quality of Life compared with the general population or a comparison group. Differences were most obvious in the domains "social functioning," "physical and emotional role limitations," "general health," and "mental health."[20] • Since 2003, more overdose deaths have involved opioid analgesics than heroin and cocaine combined. In addition, for every unintentional overdose death related to an opioid analgesic, nine persons are admitted for substance abuse treatment, 35 visit emergency departments, 161

Criteria	Brief Description
	report drug abuse or dependence, and 461 report nonmedical uses of opioid analgesics. [6] • It has also been illustrated that opioid analgesics are now responsible for more deaths than the number of deaths from both suicide and motor vehicle crashes, or deaths from cocaine and heroin combined. The majority of deaths (60%) occur in patients when they are given prescriptions based on prescribing guidelines by medical boards, with 20% of deaths in low dose opioid therapy of 100 mg of morphine equivalent dose or less per day and 40% in those receiving morphine of over 100 mg per day.[21] PRODUCTIVITY • The societal costs associated with prescription drug abuse are tremendous. In addition to disrupting the health and well-being of individuals, families, and communities, Birnbaum and colleagues estimated the societal cost of prescription drug abuse at $55.7 billion in 2007. This includes costs such as workplace productivity costs ($25.6 billion; 46%), health care costs ($25.0 billion; 45%), and criminal justice costs ($5.1 billion; 9%). These authors concluded that the increasing prevalence of prescription drug abuse will result in higher costs to society. The nonmedical use of prescribed pain medicine alone cost insurers approximately $72.5 billion in direct health care cost annually.[5] MORTALITY • In 2008, drug overdoses in the United States caused 36,450 deaths. Opioid pain relievers were involved in 14,800 deaths (74%) of the 20,044 prescription drug overdose deaths.[14] • In 2008, death rates varied fivefold by state. States with lower death rates had lower rates of nonmedical use of opioid pain relievers and opioid pain reliever sales.[14] HEALTH CARE SERVICE UTILIZATION • More than 15,500 people died in the United States in 2009 after overdosing on narcotic pain relievers, a 300% increase over the last 20 years. And for each death, there are an additional ten treatment admissions, 32 emergency department visits and 825 nonmedical users of these drugs.[22] • Chronic pain is one of the most common reasons for medical visits, affecting 20% to 50% of patients who visit primary care providers.[23]
How strongly does this overall societal burden suggest that CER on alternative approaches to this problem should be	The burden is well established. During the past 2 decades, opioid analgesics have been increasingly prescribed for chronic noncancer pain and are now among the most frequently dispensed medications in the United States. The expansion of opioid prescriptions for chronic pain was initially supported by research from the 1980s and early 1990s, which reported a low risk for opioid addiction. (Research that focused on cancer-related pain.) However, treatment of chronic pain with opioids has continued to increase, despite a lack of

Criteria	Brief Description
given high priority?	rigorous research demonstrating the effectiveness of long-term treatment and a burgeoning public health threat posed by opioid misuse, including abuse, addiction, diversion, and unintentional overdose.[23] A 2012 MMWR estimated that long-term, prescribed opioid analgesics are used by nearly 9 million Americans. Another 5 million use the drugs illicitly.[6] Currently, the primary methods used to prevent opioid abuse include programs that include urine drug testing and opioid treatment agreements. A systematic review by Starrels, et al. found a lack of rigorous evidence to support the use of either intervention.[23]
Options for Addressing the Issue	
Based on recent systematic reviews, what is known about the relative benefits and harms of the available management options?	HARMS OF INTERVENTIONS • Lack of strong evidence base to support efficacy.[23] • For providers: o Agreements and drug testing take limited office time[23] o Some providers may believe it is unethical to require testing and agreements for patients who use analgesic opioids and not those who take other potentially dangerous therapies such as warfarin or insulin.[23] • For patients: o Decreased trust in providers o Urine drug testing false-positives BENEFITS OF INTERVENTIONS • Decrease dependency on tertiary care • Increase in quality of life • Decreased mortality
What could new research contribute to achieving better patient-centered outcomes?	The most commonly suggested prevention interventions for opioid abuse/dependence include urine drug testing and opioid treatment agreements. In three primary care studies of management of patients who were prescribed long-term opioids, only 23% to 44% of physicians completed treatment agreements with these patients, and only 8% to 30% obtained urine drug tests. Among the several reasons for limited use of these approaches by primary care physicians may be the lack of a clear evidence base for their effectiveness in reducing opioid misuse and other adverse outcomes.[23]
Have recent innovations made research on this topic especially compelling?	<u>Abuse Deterrent Formulations</u> The FDA is currently supporting efforts in reducing abuse and misuse is encouraging the development of opioids that are specifically formulated to deter abuse. Abuse-deterrent formulations target the known or expected routes of abuse, such as crushing in order to snort or dissolving in order to inject, for the specific opioid drug substance in that formulation. The science of abuse deterrence is relatively new, and both the formulation technologies and the analytical, clinical, and statistical methods for evaluating those technologies are rapidly evolving. FDA considers the development of abuse-deterrent formulations to be a public health priority and is encouraging their

Criteria	Brief Description
	development.[22] Research into the efficacy of such reformulations would be particularly useful. Packaging/Storage to Prevent Abuse Beyond the printed label, FDA is also interested in exploring whether innovative package/storage designs for opioids can prevent or deter misuse and abuse by patients who receive legitimate opioid prescriptions, and misuse and abuse by others. Examples include a variety of systems designed to dispense medications as scheduled while preventing inappropriate access for abuse.[22] Research into the efficacy of such packaging and storage options would be particularly useful. Products that Treat Abuse and Overdose Naloxone is an injectable medicine that can rapidly reverse the overdose of either prescription (e.g., oxycodone) or illicit (e.g., heroin) opioids. While naloxone is the standard treatment for opioid drug overdoses, it is most commonly used by trained medical personnel in emergency departments and on ambulances. There is widespread interest by prescribers, patients, and advocates in exploring the broader uses of naloxone, including its use in nonmedical settings such as the home.[22] Research into the efficacy and utility of such Naloxone, and similar drugs would be particularly useful.
How widely does care now vary?	Care varies widely by race. Multiple studies have shown that minority populations are less likely to receive prescriptions for analgesic opioids in primary care.[17-19] It is not clear if there are differences in response to the most commonly used management plans.
What is the pace of other research on this topic (as indicated by recent publications and ongoing trials)?	ClinicalTrials.gov: Opioid abuse treatments: 65 open studies Opioid abuse treatments AND race: 0 open studies Opioid abuse treatments AND Medicaid: 0 open studies Opioid abuse treatments AND Medicare: 0 open studies The National Institutes of Health, part of the Department of Health and Human Services, is currently funding an Evidence-based Practice Center to write a systematic review on The Effectiveness and Risks of Long-term Opioid Treatment of Chronic Pain. Their key questions are related to efficacy and comparative effectiveness, harms and adverse events, dosing strategies, and risk assessment and mitigation strategies. This CER will include a look at the differing effects in subpopulations including age, race, ethnicity and sex.
How likely is it that a new CER on this topic would provide better information to guide clinical decisionmaking?	Existing CERs primarily describe treatment agreements and urine drug testing efforts to reduce opioid misuse/dependence. New CERs looking at efficacy of other treatment programs (Naloxone, packaging, abuse-deterrent formulations, etc.) would be very useful to clinicians.

Criteria	Brief Description
Potential for New Information to Improve Care and Patient-Centered Outcomes	
What are the facilitators and barriers that would affect the implementation of new findings in practice?	FACILITATORS: Urine drug testing and treatment agreements: • Though little evidence exists to support the use of either intervention, primary care providers who use opioid treatment agreements report improved satisfaction, comfort, and sense of mastery in managing chronic pain.[23] Management strategies that include treatment agreements have been associated with reductions in emergency department visits.[23] Urine drug testing is a valuable tool to detect use of nonprescribed drugs and confirm adherence to prescribed medications beyond that identified by patient self-report or impression of the treating physician.[23] Implementing routine urine drug testing may improve the provider–patient relationship and clinic morale.[23] BARRIERS: • Clinicians may be concerned about the time required to complete a treatment agreement with the patient or that committing to a treatment agreement will restrict their clinical decisionmaking.[23] • Some clinicians may regard it as unethical to require treatment agreements for patients who take opioid analgesics but not for patients who take other potentially dangerous therapies, such as warfarin or insulin.[23] • Barriers to conducting urine drug testing in primary care practices include discomfort with discussing testing with patients, lack of access to appropriate tests, confusion about how to interpret or respond to test results, and belief that one's patients are not at risk for opioid misuse and urine drug testing would be unnecessary.[23] • Misinterpretation of test results can lead to falsely accusing patients of opioid misuse and consequently harming the provider-patient relationship.[23]
How likely is it that the results of new research on this topic would be implemented in practice right away?	Treatment of chronic pain with opioids has continued to increase, despite a lack of rigorous research demonstrating the effectiveness of long-term treatment and a burgeoning public health threat posed by opioid misuse, including abuse, addiction, diversion, and unintentional overdose.[23] Results from any new research into the area would most assuredly be implemented immediately.
Would new information from a CER on this topic remain current for several years, or would it be rendered obsolete quickly by subsequent studies?	• Interventions primarily addressed by the literature thus far include urine drug testing and opioid treatment agreements. This research and these interventions remain current today. • While durability will be specific to the intervention, specific population, mental health and or substance abuse comorbidities, new research is likely to remain relevant for several years as use and abuse of analgesic opioids increases.

References for Topic 1: Interventions to Avoid Unintentional Overdose and Substance Dependence of Pain Relievers (Opioid and Nonopioid) among Vulnerable Populations

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Topic 2: Compare the Effectiveness of Disease Identification/Risk Assessment for Autism Spectrum Disorders and Therapeutic Strategies (e.g., Behavioral or Pharmacologic Interventions, the Combination of the Two) for Different Autism Spectrum Disorders among Populations Likely to Experience Disparities (i.e., Racial/Ethnic Minorities, Rural Populations, Low SES Populations). For Therapeutic Strategies, Examine Effectiveness across Different Levels of Severity and Stages of Intervention.

Criteria	Brief Description
Introduction	
Overview/definition of topic	• The Centers for Disease Control and Prevention (CDC) estimate approximately 1 in 68 children over 8 years old will meet the diagnostic criteria for an autism spectrum disorder (ASD), the hallmarks of which include difficulty interacting and communicating socially, and the presence of restricted, repetitive behaviors and interests.[1] • To the extent therapies are effective with any populations, there is no evidence that treatments are differentially effective in populations likely to experience disparities. However, racial and ethnic minorities and populations with low socio-economic status (SES) experience differential access to services, time to diagnosis, and utilization of therapies; this topic brief will focus on those disparities. • A growing body of literature suggests ASDs may be accurately diagnosed in toddlers,[2, 3] with more severe ASD symptomology leading to greater diagnostic sensitivity and stability.[4, 5] Early diagnosis and detection is important because EIBI programs for children with autism have been associated with significant improvements in adaptive behavior, IQ, and language.[6-9] • Disparities exist in the diagnosis and treatment of ASDs. African Americans, Hispanics, other nonwhite racial and ethnic populations (excluding Asian Americans), and children from poor families are less likely to have an ASD identified.[10, 11] African Americans experience more time in treatment before receiving an ASD diagnosis and enter treatment at a later age than white children (7.9 vs. 6.3 years).[12] Part of this gap in diagnosis post-treatment engagement can be explained by differential diagnosis. African Americans are almost three times more likely than white children to receive a different diagnosis before an ASD is detected. African Americans are more likely to receive an incorrect diagnosis of conduct or adjustment disorder.[13] • In addition to provider diagnostic bias, there are multiple mechanisms that may lead to differential care for nonwhite and low-income populations[14]

Criteria	Brief Description
	including, but not limited to: o Differential access to primary diagnosis and specialty care.[15] o Cultural differences in care seeking behaviors, perceptions of disability, and interpretation of ASD symptomatology.[16-19] o Differential maternal education and knowledge regarding treatment options for ASDs.[20-22]
Relevance to patient-centered outcomes	PATIENT-CENTERED OUTCOMES • In addition to the definitional symptoms described in the overview, persons with ASDs may face several comorbidities, including: o Intellectual disability[23] o Language delays[24] o Epilepsy and seizure disorders[25-27] o Other psychopathology including attention-deficit/hyperactivity disorder (AD/HD), depression, phobias, obsessive compulsive disorder (OCD), sleep disorders, bipolar disorder, schizophrenia, and psychosis[28, 29] • People with ASDs can live well into adulthood;[30] almost half of whom do not continue to meet the diagnostic criteria for Autistic Disorder diagnosed in childhood.[31] This life course perspective has refocused attention on early intervention programs, assuming that symptomology is somewhat malleable. • Early intervention programs, primarily based on the University of California Los Angeles (UCLA) Lovaas Model or the Early Start Denver Model (ESDM), have demonstrated some improvements in cognitive performance, adaptive behavior skills, and language skills.[6, 32] The effectiveness of these programs likely varies by severity of ASD symptoms and parental education, but age of treatment initiation may also be a factor.[33]
Burden on Society	
Recent prevalence in populations and subpopulations	PREVALENCE • Non-Hispanic white children are 30% more likely to be identified than African American children; non-Hispanic white children are 50% more likely to be identified than Hispanic children.[1] African American and Hispanics are more likely than non-Hispanic white children to have a comorbid intellectual disability.[1] Clinicians may be less likely to assess and diagnosis ASDs in the presence of cognitive impairment, which would compound disparities.[10] • Rural and near-poor children also had a delay in diagnosis of .4 and .9 years respectively.[34] Wealthier children are more likely to have an ASD diagnosed; there is a dose-response relationship between SES and ASD prevalence.[35] It is supposed that this difference is due to the diagnostic, cultural and access disparities discussed in the introduction.

Criteria	Brief Description
Effects on patients' quality of life, productivity, functional capacity, mortality, use of health care services	QUALITY OF LIFE / PRODUCTIVITY • While some adults with ASDs see a lessening of symptoms and relative independence, the majority of people with ASDs have difficulty maintaining close friendships and permanent employment throughout their lives and rely heavily on families or support services.[36] This is particularly true for persons with comorbid intellectual disability (a group in which African Americans and Hispanics are disproportionally represented). HEALTH CARE SERVICE UTILIZATION • Partially because of the complexity and comorbidity described above, persons with ASDs have more dissatisfaction and unmet healthcare needs than the general public, including:[37] o Lower satisfaction with provider communication. o Less chronic disease self-efficacy. o More unmet physical, mental health, and prescription needs. o Lower rates of preventive care. o Higher odds of using the emergency department for care. • Race and SES drives utilization; parental education is associated with increased use of conventional and alternative treatments for ASD.[38] Caucasian children may also be more likely to be prescribed psychotropic medications.[39]
How strongly does this overall societal burden suggest that CER on alternative approaches to this problem should be given high priority?	• On average, a child with an ASD has annual healthcare expenditures of $6,132 (typical child, $860).[40] The estimates vary based on symptom severity. • Over the life course, the per capita cost of care for a person with an ASD is approximately $3.2 million, with lost productivity and adult care comprising most of these costs.[41] • Persons with ASDs are the most costly population receiving vocational rehabilitation and tend to work fewer hours for less money than other groups with disabilities.[42] • In addition to the potential symptom improvements, early intervention programs are credited with savings over the 18 educational years of approximately $200,000.[43] This is particularly significant as children with ASDs are the most costly population in special education.[44] • To the extent racially, ethnically, and socio-economically disadvantaged populations are able to access early intervention and treatment services, downstream costs may be lessened.

Criteria	Brief Description
Options for Addressing the Issue	
Based on recent systematic reviews, what is known about the relative benefits and harms of the available management options?	• In 2011, the Vanderbilt Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ) prepared a comparative effectiveness review of autism treatments for children.[45] At that time, there was not enough evidence to support the effectiveness of behavioral and educational interventions, although Early Intensive Behavioral Interventions (EIBI) for toddlers showed promise.[45] The EIBI literature has grown rapidly in the past few years, and an update of this review is forthcoming. This systematic review was not specific to racial and ethnic minorities, rural, or low-income children with ASDs. More rigorous research on behavioral and educational interventions is needed in general, and specific to these populations.
What could new research contribute to achieving better patient-centered outcomes?	• While there is adequate documentation of gaps in diagnosis and treatment by race, ethnicity, and income, there is little research on what can be done to close these gaps. • Standardized screening of toddlers using the Modified Checklist for Autism in Toddlers (M-CHAT) with a followup interview to reduce false positives may reduce disparities in diagnosis age.[46] • Greater maternal education is associated with an increased probability of a child receiving a ASD diagnosis.[10] There are likely several mechanisms underlying this association, including education leading to increased knowledge of developmental milestones or greater ability to advocate for the proper diagnosis.[10] Targeted education of mothers is an area for further research. • Targeting physician bias may also be part of improving diagnosis across income and racial strata.
Have recent innovations made research on this topic especially compelling?	• The potential for long-term mediation of symptoms and costs associated with early intervention, and the established delay in care acquisition among minority and poor populations makes this an important topic for further research.
How widely does care now vary?	• Care disparities begin at diagnosis. Compared to white children: • African Americans were almost 20% less likely to have an ASD documented. • Hispanics were approximately 25% less likely to have an ASD documented, and persons from other race/ethnicities were 35% less likely to have an ASD documented.[10] • Once diagnosed, disparities in access to services exist for low-income populations (among which racial minorities are overly represented) based on state variation in Medicaid coverage.[47] • Among Medicaid recipients, African Americans were more than 20% less likely to be prescribed psychotropic medications.[39]

Criteria	Brief Description
What is the pace of other research on this topic (as indicated by recent publications and ongoing trials)?	ONGOING TRIALS Clinicaltrials.gov: (search for "autism" and phases 2–4) o Total ongoing trials: o Recruiting: 60 o Not yet recruiting: 13 o Active, not recruiting: 16 o Total Completed trials: 95 • No clinical trials were found specific to combinations of autism and race, ethnicity, or income key words.
How likely is it that a new CER on this topic would provide better information to guide clinical decisionmaking?	• Based on the recent AHRQ-funded comparative effectiveness review, more well-designed studies are needed in this area.[45] Further, comparative effectiveness research powered to detect differences, if any, in racial, ethnic, or socio-economic sub-populations would be important for political and clinical decisionmaking.
Potential for New Information to Improve Care and Patient-Centered Outcomes	
What are the facilitators and barriers that would affect the implementation of new findings in practice?	FACILITATORS: • Evidence based changes to Medicaid reimbursement for early detection and intervention services. BARRIERS: • Cultural perception of symptoms. • Provider bias in diagnosis. • Knowledge of available services in low-income, racially, and ethnically diverse populations. • Lack of time to participate in intensive treatments in low-income populations.
How likely is it that the results of new research on this topic would be implemented in practice right away?	• It is likely that relatively minor modifications, for example making existing screening tools more cross-cultural, could be implemented right away. However, system level recommendations for reducing disparities that involve changes to reimbursement may be harder to implement in a timely manner.
Would new information from a CER on this topic remain current for several years, or would it be rendered obsolete quickly by subsequent studies?	• It is likely well-designed CER studies will remain current for several years. In particular, CER targeting parent and physician education and outreach, universal screening and early intervention is needed.

References for Topic 2: Compare the Effectiveness of Disease Identification/Risk Assessment for Autism Spectrum Disorders and Therapeutic Strategies (e.g., Behavioral or Pharmacologic Interventions, the Combination of the Two) for Different Autism Spectrum Disorders among Populations Likely to Experience Disparities (i.e., Racial/Ethnic Minorities, Rural Populations, Low SES Populations). For Therapeutic Strategies, Examine Effectiveness across Different Levels of Severity and Stages of Intervention.

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Topic 3: Compare the Relative Effectiveness of Different Treatment Strategies for Osteoarthritis in Populations Likely to Experience Disparities

Criteria	Brief Description
Introduction	
Overview/definition of topic	DESCRIPTION OF CONDITION OVERALL: • Osteoarthritis (OA), also called degenerative joint disease (DJD), is the most common form of arthritis in the U.S. and is a leading cause of chronic musculoskeletal pain and disability worldwide.[1] OA is a major cause of physical disability, decreased quality of life, and increased health care costs in the U.S. • OA is characterized by a progressive loss of the cartilage that covers the ends of bones within joints. The normally smooth cartilage gradually wears away, leaving a rough, eroded cartilage surface.[2] Normal joint movements over eroded cartilage result in localized pain and swelling in and around joints.[2] Joint space narrowing and adjacent bony changes eventually occur (bony spurring and erosion).[1] • One or multiple joints can be affected. If multiple joints are affected (such as both knees), the degree of OA changes (on x-ray, motion restrictions) and symptoms are generally not symmetric. • OA is believed to occur due to anatomical, biomechanical, genetic and/or environmental factors.[3] Obesity, prior joint injury and family history of OA are known risk factors for the development and progression of OA. • The burden of OA is expected to grow substantially due to dramatic increases in rates of adult obesity and due to the aging of the U.S. population. • There is no known cure for OA; treatment is aimed at relieving symptoms and improving function.[1] • Diagnosis is made by symptoms and/or by objective signs of OA: o Symptoms: joint pain, stiffness, or swelling o Objective signs: Physical exam (i.e., range of motion, joint deformity, and swelling) and x-ray changes (i.e., joint space narrowing, bony spurring or thickening, or other bony changes beneath the defective cartilage). Symptoms and x-ray changes are poorly correlated in OA[4]; only 7-17% of those with x-ray evidence of OA report having symptoms.[5] Generally, when x-ray changes are severe (bone on bone with advanced joint space narrowing), there is greater consistency between subjective symptoms and objective findings. • Treatments: Treatment initiation is typically triggered by pain and functional problems. Initial treatments are conservative (i.e., noninvasive, nonoperative) and involve weight loss, exercise, nonsteroidal anti-inflammatory drugs (NSAIDs), physical therapy, and/or other interventions.

Criteria	Brief Description
	Conservative: o Combinations of conservative approaches are common. o There is strong literature support for aerobic and strengthening exercise (land and water based) to mitigate pain and improve function in adults with mild-moderate OA of the hip or knee.[6] o Low impact or nonweightbearing aerobic exercises are typically recommended. Patients with high compliance to exercise tend to have better treatment responses overall,[7] subgroup differences are largely unknown. o Intermediate, more invasive conservative treatments include cortisone or hyaluronic acid injections into the joint, both of which are utilized in moderation and in attempt to delay the need for joint replacement surgery. *Surgical*: o Surgical options include (1) arthroscopy to remove small pieces of bone or small loose/damaged structures; (2) osteotomy to realign an arthritic joint; (3) joint fusion (such as wrist or hand bones); or (4) joint replacement surgery. o Elective joint replacement surgery (arthroplasty) is undertaken when all conservative treatments have failed and OA-related pain and increasing mobility impairment is intolerable. There is robust clinical trial evidence that joint replacement improves pain, mobility, and quality of life, and is the treatment of choice for end-stage (severe) OA.[1, 2] However, joint replacement is major surgery; adults with high comorbidity burden, the frail, and those with unstable medical conditions may be offered joint replacement less often than among healthier adults due to substantially higher risks of complications and mortality after arthroplasty in sicker adults.[8-12,13] More than 700,000 patients undergo elective joint replacement annually in the U.S.[9, 14] Total knee replacement is the most common major joint replacement surgery in the U.S. DISPARITIES: • Health care disparities, or differences in the utilization of indicated treatments or procedures, may occur in health care access and/or health care quality, and utilization and access are the common topic of disparities research. But for many reasons, subgroups prone to health care use disparities may also be prone to negative health care outcomes.[12, 13, 15-19] (See Patient-Centered Outcomes, Adverse Effects below). The risk of adverse events is particularly important to consider for OA when examining differences in elective ("preference-sensitive"[20]) health care utilization, especially major joint replacement procedures, since preference for and utilization of joint replacement may not be separately identifiable.[21] In addition to procedure utilization, greater disparities may exist in differential (worse) outcomes, such as in procedure complication

Criteria	Brief Description
	rates, hospital readmission rates, functional gains, pain reduction, and treatment-associated mortality.[12, 13, 15, 18, 19] • Among OA treatments, the main focus is on total joint replacement. Reasons for differences in utilization rates of joint replacement surgery by race or ethnicity have been studied the most and are complex.[20, 22-24] Reasons may include patient factors[22] (such as health status, familiarity with and perception of joint replacement procedures, lifestyle choices, treatment preferences, social context and employment factors), physician/provider factors[22] (communication, willingness to refer) and system level factors[22] such as access and specialist wait times. Studies that assess procedure utilization rates in subgroups have under-assessed or not considered, highly pertinent factors simultaneously. For example, for patient factors alone, it is common to find database studies that report controlling for multiple patient factors but lack sufficient detail about actual (versus claims-based) number and type of comorbidities (from single hospital admission claims), severity of comorbidities, smoking status, substance abuse, degree and type of employment (including insurance, sick leave and disability benefits), and living situation/social support information that would better explain reasons for differential use of major joint procedures and physician recommendations thereof within racial and other subgroups. Thus, the choice to receive total joint replacement depends on patient willingness,[25] ability (insurance, finances, rehabilitation coverage, sick leave, work time off, social support) and fitness/health status for major surgery, in addition to access to services, surgeon recommendation, and health system factors. • The goal of elective joint replacement is to render patients better off than they were prior to surgery. While joint replacement surgery is known to provide substantial improvements in pain, function, and quality of life for most patients, the rate of adverse events and mortality from joint replacement surgery increases considerably in individuals with poor underlying health status, especially cardiovascular disease and increasing age. With increasing obesity and comorbidity burden (in number and severity) in the U.S. adult population, and better durability of arthroplasty implants, surgeons are performing arthroplasty operations not only on sicker, middle-aged to retiring adults, but also on older mobile adults with OA, both of which have higher risks of complications than among healthier middle-aged adults.
Relevance to patient-centered outcomes	PATIENT-CENTERED OUTCOMES Patient-centered outcomes for adults and adult subgroups with OA may include: • Pain • Physical function and mobility • Quality of Life (QoL)

Criteria	Brief Description
	• Socialization (affected by pain, impaired mobility) • Fatigue • Impaired sleep/altered sleep quality • Depression, anxiety • Work limitations (limits type and duration of work) The main outcomes for OA are pain, function and quality of life. Other outcomes may be included but those often result from issues related to pain, function, and quality of life. Benefits of treatments positively affect any/all of the outcomes above. Joint replacement surgery is known to substantially improve pain, mobility and quality of life. Additional outcomes include adverse effects (harms) of treatments for OA: • Long-term NSAID use: peptic ulcer disease, impaired renal function, kidney disease, mortality. • Exercise and physical therapy: muscle aches, transient pain, stiffness, swelling, falls. Such adverse events are uncommon and do not deter participants from continuing treatment.[26] • Cortisone injections: enhanced cartilage erosion over time. • Joint replacement surgery: infection, pulmonary embolism, myocardial infarction, pneumonia, bleeding, stroke, mortality, dislocation of the new joint, need for revision surgery, and impaired mobility.[8-11] o 30-day hospital readmission rates after primary (initial) total knee replacement were 24% higher for African-Americans than Caucasians in 2008; the readmission rate gap by race *widened* over time (6% in 1991 vs. 24% in 2008).[15] Black patients were at increased risk for needing revision surgery within 10 years of initial joint replacement, after adjustment for insurance type, poverty level, and education.[27] o Data from the Veterans Affairs found no differences in 30-day mortality after hip or knee arthroplasty by race/ethnicity, [17] but the risk of infection and other complications was 40-50% higher in African-American compared with Caucasian Veterans following knee arthroplasty.[17] o Patients, including subgroups,[28] who undergo arthroplasty at mid- to high volume hospitals by higher volume surgeons have fewer complications,[29, 30] yet most rural hospitals are small, lower-volume facilities. o In general, patients who underwent joint replacement in low-volume hospitals by low-volume surgeons had worse functional outcomes two years after surgery.[31] Early revision surgery is strongly associated with low surgeon arthroplasty case volume.[32] Race and poverty are associated with the choice to undergo joint replacement at lower-volume urban hospitals.[33] o Although a recent Medicare fee-for-service study using 2008-2010

Criteria	Brief Description
	data found that hospitals with higher proportions of Medicaid and black patients had complication rates similar to those of hospitals with lower proportions, there is a continued need to monitor for disparities in outcomes after hip and knee replacement.[34] Most fee-for-service Medicare patients are white. o The odds of willingness to undergo total knee replacement were lower in African American men and women (relative to white males) when sociodemographic, clinical, and social support measures were controlled. African American patients reported less structural and functional social support than whites.[35]
Burden on Society	
Recent prevalence in populations and subpopulations	INCIDENCE • OA increases with age, most often occurring in people over age 45.[3] • The incidence of OA is increasing with high rates of adult obesity and population aging.[1] • The incidence of OA is difficult to determine because OA develops gradually. Incidence estimates for OA depend on the diagnostic criteria used (symptoms and/or imaging) and the timing of OA diagnosis, which is dependent upon a physician or clinic visit[36]). Also, interobserver variation exists in assessing the extent of OA from radiographs, depending upon physician assessment and the grading scale used.[37] PREVALENCE • Studies of discrepancies in the rate of joint replacement within subgroups need to account for differences in the prevalence (and severity) of OA in subgroups; most studies do not. • There is very limited information on subgroups. Most prevalence estimates are overall, and by sex and age. o Overall in U.S. adults: millions of Americans are affected o In 2005, OA affected 13.9% of adults aged 25 years and older in the U.S., and 34% (12.4 million) of adults age 65 or older. An estimated 27 million U.S. adults had OA in 2005 (up from 21 million in 1990).[38, 39] o The distribution of sites of OA (i.e., knee, hip, hand, shoulder) varies to some degree by sex and race/ethnicity among other factors o Obesity, a risk factor for OA, is differentially distributed in adults: - Non-Hispanic blacks have the highest age-adjusted obesity rates • OA prevalence estimates vary by OA definition, location of OA (hip, knee, hand, etc.), and populations studied:[5] o 19% of people aged 45 or older and 37% of people aged 60 or older had knee OA on x-ray.[5] o In populations with higher proportions of African American, rural, and obese residents, 28% of people aged 45 or older and 50% of those age 75 or older had knee OA on x-ray;[5] the prevalence of hip OA was similar.

Criteria	Brief Description
	○ Higher prevalence of OA in rural residents, African Americans, and Hispanics (relative to whites), among unemployed and blue-collar workers and in adults with lower incomes per the findings of one systematic review on disadvantaged populations.[40] ○ A one-county study from North Carolina found that African Americans had slightly higher prevalence of knee symptoms, radiographic, and symptomatic knee OA, but significantly higher prevalence of severe radiographic knee OA compared to Caucasians.[41] • The prevalence and associated activity limitations are higher in older women than men of similar ages.
Effects on patients' quality of life, productivity, functional capacity, mortality, use of health care services	Overall: • OA, especially advanced OA, is associated with pain and significant physical disability.[1] • Knee OA was associated with dependence in four important tasks: stair climbing, walking ability, housekeeping, and carrying bundles (Framingham Study data).[42] 25% of affected adults with knee OA could not perform major activities of daily living (ADLs).[42] • 45% of affected individuals had pain, aching, or stiffness in a knee joint on most days among individuals with knee OA.[41] Subgroups: Most information to date is by race/ethnicity. Individual adults may fit within several subgroups (e.g., race, SES) although the literature tends to describe subgroups as isolated entities, if identified. • OA symptom severity reported by African Americans is greater than that among Caucasians. • African American adults who were candidates for joint replacement surgery differed from whites with similar age and clinical factors in that black patients were less likely to be employed or married, more likely to report very low household incomes and less than a high school education, and more likely to expect longer hospital stays, more pain, and extreme difficulty walking after surgery than whites, indicating less familiarity with the procedures.[23] • African Americans with OA had significantly lower expectations for joint replacement surgery outcomes than white patients; the difference was not entirely explained by racial differences in demographics, disease severity, education, income, social support, or trust.[43] • Lower disease-specific pain scores and better functioning (WOMAC) were predicted by higher educational level.[44] • Obesity, alcohol and drug abuse, depression, renal disease and hemiplegia and paraplegia were associated with early revision of joint replacement surgery.[12] • Depending on the disability, adults with disabilities may be less likely to undergo joint replacement surgeries unless the affected joint(s) markedly

Criteria	Brief Description
	interfere with mobility and ADLs.
How strongly does this overall societal burden suggest that a CER on alternative approaches to this problem should be given high priority?	• While the main research focus has been on utilization rates and treatment preferences by race, the occurrence of and potential for suboptimal outcomes in disadvantaged populations from OA treatments, especially joint replacement, is understudied. Disadvantaged individuals are more likely to experience poor health that renders them at higher risk for complications from elective surgical and pharmacologic treatments. Therefore, quantifying outcomes differences in subgroups that can be supported by comprehensive baseline health and social context information, as well as preferences, would advance knowledge of the reasons for and extent of outcomes differences in disadvantaged subgroups. Recent research has begun to focus on factors associated with poor outcomes after elective arthroplasty in general, which is beginning to highlight higher complications in some subgroups. However, factors driving worse outcomes in subgroups, given baseline comorbidities, have been only marginally explored. • More information is needed on potential differences in the prevalence of severe OA in subgroups (not just African Americans), which is an indication for surgery. Pain alone without evidence of severe OA (criteria vary) is typically not an indication for surgery. Robust evidence on potentially differential prevalence of severe OA in subgroups would help to better gauge arthroplasty utilization differences in subgroups as disparities. • The extent to which existing studies provide sufficient information on subgroups that would be required for a CER of alternative treatments may be limited by low subgroup utilization rates for certain treatments (surgical) and sparse subgroup information[40] beyond age and sex. • All cause 30-day hospital readmission rates after initial (primary) and revision total knee replacement in the U.S. are increasing, including increased readmission for wound infections.[14] Factors driving these trends warrant further investigation as the use of joint replacement continues to increase rapidly.[14] Recent national insurance coverage changes may impact treatment choices.
Options for Addressing the Issue	
Based on recent systematic reviews, what is known about the relative benefits and harms of the available management options?	Most systematic reviews cover general treatment effects for OA and do not specifically address subgroup outcomes. • Only one systematic review examined the evidence for interventions to improve health care quality in disadvantaged populations with OA.[40] Of the 10 studies that met inclusion criteria, only 4 studies were randomized clinical trials. Nine of 10 studies examined arthritis self-management programs (ASMP) and all nine reported positive results that supported the use of arthritis self-management programs. Only two studies also targeted health care provider behaviors. ASMPs improved knowledge (treatment options, OA), exercise behavior, self-care behavior, perceived helplessness

Criteria	Brief Description
	and pain; other clinical outcomes varied. • No systematic reviews specifically examined OA treatment outcomes by race/ethnicity, low socioeconomic status, rural residence, low literacy or among those with disabilities o Individual studies sometimes provide subgroup outcomes related to provider volume, attributes of individuals with hospital readmissions, or early revisions after joint replacement, but those were not specifically sought for this topic brief (but are noted if identified) • General literature: o Surgical: Little information exists outside of the total joint replacement literature and subgroup outcomes are rarely reported. When subgroup outcomes were reported, they were typically in terms of adverse event rates, such as 30-day hospital readmissions, mortality or other complications of primary and revision joint replacement. Adverse event outcomes reporting by age, sex and comorbidities are by far the most common. Few studies reported differences by race/ethnicity but not by other subgroups identified by PCORI. We found no systematic reviews on subgroup effects of newer, less utilized procedures such as joint resurfacing. Common issues that limit subgroup analyses include the small proportion of nonwhites who underwent joint replacement in existing Medicare data files and limited ability to ascertain non-claims information (SES, literacy, and until recently, race). o Nonsurgical: We found no systematic reviews that reported outcomes from nonsurgical treatments specifically by pre-specified subgroups, including newer injectable treatments or CAM therapies.
What could new research contribute to achieving better patient-centered outcomes?	<u>Prevention, education, and self-management</u>: • Intervention literature has focused mainly on treatments for OA rather than on prevention efforts that target modifiable risk factors for OA, OA-related disability, and OA progression. Prevention and self-management interventions were recently identified as top priorities for osteoarthritis systematic reviews, including disadvantaged populations.[45] Research on prevention, overall and in subgroups, could have profound positive effects in the long run,[46] including optimal weight management,[11] and the prevention of joint injury that predisposed individuals to early OA.[5] • Obesity is a strong risk factor in OA development and progression that is both modifiable and has the potential for substantial impact on OA at a population level.[5] Research on ways to improve weight loss in adults with OA overall, and specifically interventions that are tailored to subgroup needs, could lessen the future burden of OA in the U,S. Weight loss alone may reduce knee OA pain even if the OA symptoms are not otherwise treated. Adults with higher body mass index (BMI) have greater pain than those with lower BMI after controlling for OA severity, and increasing BMI/obesity is associated with a significantly higher risk of wound

Criteria	Brief Description
	infections, pulmonary embolism, and deep vein thrombosis after joint replacement surgery.[10] • Educational interventions regarding joint replacement procedures improve willingness to undergo joint replacement surgery in African Americans.[25] <u>Treatments: utilization and outcomes (benefits and harms)</u> • While some racial differences in OA prevalence and severity have been identified, more research is needed on the prevalence and severity of OA in under-studied racial and ethnic groups, and for other affected joints (e.g., foot, spine).[3] It is necessary to use data on the prevalence and severity of OA in subgroups to better understand disparities in total joint replacement utilization. • More information on differences in baseline health status in subgroups versus other patients for groups that typically utilize fewer of specific procedures and services could broaden the depth of subgroup disparities research. Research to date has largely focused on subgroup differences in OA prevalence (defined by various metrics), patient preferences and knowledge of procedures, or the frequency to which physicians offer joint replacement surgeries. Less information exists on the presence and severity of baseline health status (medical comorbidities, obesity, mental health conditions) and lifestyle choices (smoking, alcohol/drug abuse, oral health) in subgroups that appear to underutilize treatments. Such factors have a profound impact on surgical decisionmaking and the risk of death and serious medical complications from arthroplasty surgery. Reasons for higher readmission rates in nonwhites have been understudied and merit closer attention. Greater attention to factors that influence fitness for surgery (baseline health status risks for complications and mortality) and ability to recover from surgery (social context and role, social support, caregiving demands, work (sick leave, paid time off), finances (copayments) and similar factors would advance OA knowledge in disadvantaged populations. • Once health status differences are better delineated in OA subgroups at risk for disparities, interventions to routinely assess, treat medical conditions, and/or support lifestyle modifications (such as smoking cessation and weight reduction prior to considering surgery) may best optimize higher-risk adults to improve joint replacement outcomes. • The impact of increasing obesity, diabetes, and cardiovascular disease on the risk of adverse events during and after major joint replacement surgery is understudied in the population overall and even less studies among subgroups known to be differentially affected by these and other comorbid conditions. • Areas that require further research include examination of the long-term effects of exercise programs for OA, exercise programs for severe OA, the effect of exercise programs on progression of OA, the effectiveness of exercise for joint sites other than the knee or hip, and the effectiveness of

Criteria	Brief Description
	exercise for OA by such factors as age, sex, and obesity. Efforts to improve adherence to evidence-based exercise programs for OA and to promote the dissemination and implementation of these programs are crucial.[6] • Many studies focused on a single therapy modality rather than the combinations typically used in practice.[7] Assessing effects of nonoperative treatment combinations, particularly if used more often in subgroups, could advance knowledge and improve care. • Impact of occupational tasks on OA and OA-related outcomes and the ability to return to work after arthroplasty in subgroups has been understudied. Type of work predisposes individuals to injury and repetitive use conditions. Subgroups at risk for health care and health outcomes disparities may be employed in more physically demanding jobs[47] that can contribute to subgroup differences in reports of OA pain[47] and functional limitations, and the ability to return to work post-surgery. • Design of evidence-based, targeted interventions to eliminate or reduce any inequities in treatment use have been recommended.[24]
Have recent innovations made research on this topic especially compelling?	No recent innovations were identified for subgroups that make the OA treatment topic especially compelling. • Since arthroplasty implants have an average lifespan of 10-15 years, surgeons continue to focus on joint replacement surgery and less-invasive newer treatments to delay the use of total joint replacement. • Long-term benefits and harms of newer, less-utilized treatments for middle-aged adults, such as joint resurfacing, hyaluronic acid injections, and biosubstances injected to stimulate cartilage regrowth, are only starting to emerge; subgroup information does not exist. Joint replacement procedures are substantially more common. • The affordable care act may enhance access to OA interventions, particularly total joint replacement surgeries for adults who did not previously select joint replacement due to financial constraints.
How widely does care now vary?	• Unable to determine how widely care varies for subgroups. • Overall care for OA varies widely. The timing of OA diagnosis is highly varied. Most providers try conservative interventions and medications first before moving to more invasive options. • Variation is driven by patient, physician, and health system factors.[20]
What is the pace of other research on this topic (as indicated by recent publications and ongoing trials)?	Disparities research started with utilization counts by race/ethnicity, followed by variation in physician recommendations for joint procedures and patient preferences and familiarity with procedures. Differences in subgroup complication rates, other than by age and sex, are starting to emerge. Relatively low adverse event rates and small proportions of subgroups in clinical studies make investigating subgroup effects more difficult. The overall pace is slow but has been increasing recently given the Medicare focus on reducing all cause 30-day hospital readmissions. ClinicalTrials.gov:

Criteria	Brief Description
	o Ongoing trials: disparities (2), race (0), ethnicity (0), low socioeconomic/SES (0), disabled (2), rural (0). o Completed trials: disparities (3), race (1), ethnicity (5), low socioeconomic/SES (0), disabled (2). o Unknown status trials: disparities (1), race (1). NIH reporter: 5 trials
How likely is it that a new CER on this topic would provide better information to guide clinical decisionmaking?	• Better information on differential outcomes in subgroups, and more refined baseline health status and social factors in subgroups prone to disparities could improve treatment choices for both patients and physicians, particularly for major elective joint replacement procedures
Potential for New Information to Improve Care and Patient-Centered Outcomes	
What are the facilitators and barriers that would affect the implementation of new findings in practice?	FACILITATORS: • Excellent physician communication with subgroup patients appropriate to education, literacy, and culture enhances familiarity with arthroplasty procedures and perioperative expectations. • Health system and provider support for educational programs on OA, OA self-management and treatment options improves patient treatment knowledge and better aligns treatment expectations. • Subgroups may require closer monitoring of self-directed treatments to enhance compliance. • Multiple: insurance coverage, access and proximity to treatment options, social support, job benefits to allow for recovery. BARRIERS: • Barriers are dependent upon the type of program or intervention to be implemented but may include costs, time, training, communication barriers (patient, provider, and health system), and ease of implementation around existing programs and demands
How likely is it that the results of new research on this topic would be implemented in practice right away?	• Unable to determine; varies by a multitude of factors

Criteria	Brief Description
Would new information from a CER on this topic remain current for several years, or would it be rendered obsolete quickly by subsequent studies?	• For joint replacement: information would likely remain current since subgroup utilization of joint replacement is increasing, and is expected to further increase given the ongoing demographic changes in the U.S. population.

References for Topic 3: Compare the Relative Effectiveness of Different Treatment Strategies for Osteoarthritis in Populations Likely to Experience Disparities

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Topic 4: Compare the Effectiveness of Pharmacologic and Nonpharmacologic Treatments (e.g., Social/Family Support) in Managing Behavioral Disorders for Populations Likely to Experience Disparities (i.e., Racial/Ethnic Minorities, Rural Populations, Low SES Populations) with Alzheimer's Disease and Other Dementias in Home and Institutional Settings

Criteria	Brief Description
Introduction	
Overview/definition of topic	DESCRIPTION OF CONDITION • Dementia, a neurodegenerative disease, refers to impairments in cognitive and intellectual ability, memory, language, reasoning, and judgment to an extent interfering with everyday functioning.[1] Dementia is one of the most costly diseases in the United States. The most costly aspects of the disease are for caregiving, including informal care (i.e., unpaid care provided by family and friends) and formal caregiving (e.g., long-term care).[2, 3] Caregiving is driven by the need for assistance with functional activities (i.e., activities of daily living). • Patients with behavioral or psychological symptoms may challenge caregivers, increase difficulties associated with caregiving, and in turn increase the cost of care. Symptoms can include depression, psychosis, aggression, agitation, anxiety, and wandering, and often occur in clusters.[4, 5 6] • The management of challenging behaviors has historically relied on pharmacological approaches, namely antipsychotics. Antipsychotic medications have limited evidence for efficacy and high risk for adverse effects including Parkinsonism or extrapyramidal signs, sedation, confusion, mental status change, cardiovascular events, seizures, cognitive disturbance, and mortality and their use is associated with reduced quality of life.[10] • Concern about these issues has led to clinical guidelines recommending nonpharmacologic interventions as first choice therapies for agitation and aggression in patients with dementia.[11-14] • A wide variety of nonpharmacological interventions are used to manage behavioral symptoms in dementia patients. Nonpharmacologic interventions may be patient focused and directly intervene on patients (e.g., sensory based interventions and structured activities) or may be caregiver focused and intervene on patients indirectly through caregivers and the environment (e.g., caregiver training).[15] • Nonpharmacological interventions can be general strategies for managing behavioral symptoms or interventions that target patient-specific behaviors.[16] o General approaches can be implemented, often at the setting level.

Criteria	Brief Description
	Examples include staff/caregiver education and training, structured activities, and sensory interventions (e.g., light therapy).[16] o Certain environmental interventions, such as environmental design and enhanced environment,[15] would also be considered general approaches. o Targeted approaches are interventions directed at single behaviors (e.g., agitation).[16] These approaches typically involve a comprehensive assessment of the behavior to identify triggers and devise a plan to address the behavior by modifying exposures to triggers or and/or offering stimulating environmental distractions.[16] Nonwhites in the U.S. are less likely to receive special dementia care services[17] perhaps because they reside in facilities without these services, especially in the South. Nonwhite Hispanics exhibit less biomedical understanding of these behavioral symptoms. • Comprehensive literature review aiming to identify literature comparing two or more racial, cultural, or national groups on aspects of the dementia caregiving experience found 18 studies and reported that white caregivers are more likely spouses; more likely to report stress and depression than African Americans.[18]
Relevance to patient-centered outcomes	PATIENT-CENTERED OUTCOMES • Behavioral and psychological symptoms cause considerable patient and caregiver distress; are associated with accelerated functional and cognitive decline; and are leading predictors of institutionalization.[19] These symptoms also challenge staff in long-term care (LTC) facilities where an estimated 80% of the residents with dementia experience some degree of behavioral and psychological symptoms.
Burden on Society	
Recent prevalence in populations and subpopulations	PREVALENCE • An estimated five million Americans suffer from dementia.[3] Dementia primarily affects older adults with approximately 14 percent of those 70 and older suffering from dementia.[20] • More than 15 million Americans provide care to someone with Alzheimer's disease and other dementias.[3] o There is no statistical difference of the proportion of caregivers within race. o Black and Hispanic caregivers typically provided more hours of care per week (approximately 30) than white (approximately 20) or Asian caregivers (approximately 16). o Black and nonwhite Hispanic caregivers are more likely to report stress or burden. • Behavioral or psychological symptoms affect up to 90 percent of persons with dementia at some stage, but they are more prevalent in advanced

Criteria	Brief Description
	stages.[5] • Over fifteen million people provide unpaid caregiving for adults who have dementia.[3] • Hispanics provide more informal[21] caregiving than other groups. • 22% of the general older population lives in rural communities according to the 2000 U.S. Census.[22] These communities are less likely to have specialized dementia services.
Effects on patients' quality of life, productivity, functional capacity, mortality, use of health care services	• Improvements in behavior and mood have been reported in studies of stimulation-oriented treatments such as recreational activities; therapies involving music, art, and pets; and other programs that increase the number of pleasurable activities.[23] • Family caregivers of patients with dementia can suffer from emotional stress, depression, impaired immune function, lost wages, and depleted financial standing.[3] • Antipsychotic medications are associated with higher mortality rates. • Agitation and aggression lead to increased admission to long-term care facilities.
How strongly does this overall societal burden suggest that a CER on alternative approaches to this problem should be given high priority?	• A systematic review of literature published between 1980 and 2009 to identify ethnic group differences in caregiving and the extent to which culturally appropriate nonpharmacologic interventions for caregivers in ethnic groups are evidence-based.[24] o The review identified 18 studies that addressed cultural tailoring of caregiver support interventions: ▪ 10 included African Americans, 11 addressed Latinos, and 1 included Chinese Americans. ▪ 11 of 18 considered cultural factors in designing intervention. 8 of these were studies from the Resources for Enhancing Alzheimer's Caregiver Health (REACH) program. "Cultural tailoring addressed familism, language, bilingual-bicultural staff, literacy, need for advocacy, protecting elders, and logistical barriers." ▪ Among African Americans, multicomponent skills training or social support interventions led to improved affect, decreased burden, decreased upset with individual with dementia, more positive caregiving, and greater self-efficacy. Specific cultural tailoring was rarely described in these studies. ▪ Among Hispanics, psychoeducation and skills training lead to better anger control, decreased bother with individual with dementia, and better self-efficacy. These studies often described substantial cultural tailoring. ▪ This systematic review described the lack of research on cultural tailoring of caregiver interventions is concerning given the growing increase of dementia in African Americans and Hispanics as they age. They specifically recommend theory-driven multidimensional

Criteria	Brief Description
	models of caregiver experiences that incorporate cultural roles and structural inequality. Research on caregiver interventions should also measure positive outcomes such as gratitude and self-efficacy.
Options for Addressing the Issue	
Based on recent systematic reviews, what is known about the relative benefits and harms of the available management options?	• A systematic review of nonpharmacologic interventions to address behavioral symptoms in dementia is underway at the Minnesota EPC. • Previous systematic reviews demonstrate promising results of many interventions. One recent review identified 40 studies and 40% of those reported statistically significant improvements from nonpharmacologic interventions for behavioral symptoms in dementia in long term care facilities.[25] Among these were staff training, mental health consultation and treatment planning, recreational activities, and sensory therapies. Benefits from the interventions can include reduced frequency and severity of challenging behaviors, reduced caregiver stress, improved patient, and caregiver quality of life. • Differences in efficacy of particular strategies by particular subgroups have not been studied. Most of the studied included in previous systematic reviews were efficacy studies; there is little evidence on the comparative effectiveness of various treatments for behavioral symptoms of dementia.
What could new research contribute to achieving better patient-centered outcomes?	• Research suggests that differences in dementia care for populations likely to experience disparities are associated with access, education, cultural views, and understanding of the disease. • While head-to-head trials comparing various interventions may be premature, efficacy and comparative effectiveness research that aims to enhance family caregivers' understanding of the disease and approaches that can improve patient and caregiver outcomes within specific cultural or geographic contexts would provide valuable information about the types of interventions necessary to improve the care of persons with dementia and the types of cultural/geographic adaptations necessary to achieve results similar to those of previous studies..
Have recent innovations made research on this topic especially compelling?	• The Affordable Care Act may enhance access to special dementia care to those individuals that did not have access due to financial reasons.
How widely does care now vary?	• A meta-analysis of 33 studies reported:[26] o Persons with dementia from minority ethnic groups in western countries were more cognitively impaired when referred for diagnostic testing. o Hispanic persons with dementia had suffered longer duration of memory loss before referral for diagnostic testing. o African Americans were 30% less likely to be prescribed cholinesterase inhibitors [OR=.7; CI=0.6 to 0.9].

Criteria	Brief Description
	o Minority ethnic groups are underrepresented in U.S. dementia research. o Persons with dementia from minority ethnic groups in western countries are 40% less likely to enter 24-hour care. • African Americans may be at more risk of Alzheimer's disease; differ from nonwhite Hispanic population in risk factors and disease manifestation.[27] • Racial and ethnic disparities exist in utilization of antidementia drugs among Medicaid beneficiaries that are not accounted for by demographic, economic, [21]health status, or health utilization factors.[28] • A systematic review of literature published between 1980 and 2009 to identify ethnic group differences in caregiving and the extent to which culturally appropriate evidence-based nonpharmacologic interventions for caregivers in ethnic groups are identified:[24] o 78 studies reported a significant difference in caregiving experiences of African Americans, Latinos, or Chinese Americans (they do not report the number of studies that address this research question). ▪ Whites were more likely than other races to use residential long-term care. Other racial/ethnic groups were more likely to rely on family caregivers. ▪ African American caregivers report lower levels of stress [contradictory to other reports]. ▪ Latino and Asian caregivers are more likely to become depressed.
What is the pace of other research on this topic (as indicated by recent publications and ongoing trials)?	We identified very few ongoing studies evaluating effectiveness of interventions in specific subpopulations. However, searching funded research and clinical trials registries for subgroup analysis is fairly limited. The pace of research in this area appears to be slow. ClinicalTrials.gov: o Ongoing trials: 3 (Preventing aggression in Veterans with Dementia' Northern Manhattan Hispanic Caregiver Intervention Effectiveness Study; Memantine on aggression and agitation in dementia) o Completed trials: 0 NIH reporter: 1 (New York City Hispanic Dementia Caregiver Research Project)
How likely is it that a new CER on this topic would provide better information to guide clinical decision making?	• New comparative effectiveness research would provide valuable information that could guide decisionmaking. However, CERs comparing various interventions in relation to each other may be premature for these subpopulations. Alternatively, studying the cultural adaptation of interventions with an evidence base in the general population would provide valuable insight. • Disparities are likely at least partially due to access and health literacy and cultural beliefs about dementia within vulnerable subgroups. Therefore, research on effective outreach and education models for specific populations may improve decision-making.

Criteria	Brief Description
Potential for New Information to Improve Care and Patient-Centered Outcomes	
What are the facilitators and barriers that would affect the implementation of new findings in practice?	FACILITATORS: • Trends towards patient-centered care and tailored approaches to prevent and/or manage behavioral symptoms in dementia. • Growing evidence-base and available guidelines on effective non-pharmacologic interventions for behavioral symptoms in dementia. BARRIERS: • Cost and appropriate staff to implement interventions. • Understanding regarding cultural appropriateness and feasibility.
How likely is it that the results of new research on this topic would be implemented in practice right away?	• It seems likely that results of comparative effectiveness research on this topic could be implemented in a timely manner.
Would new information from a CER on this topic remain current for several years, or would it be rendered obsolete quickly by subsequent studies?	• Research on this topic is likely to remain current. It is not dependent on technology; family caregiver and staff issues are likely to remain major issues for years to come.

References for Topic 4: Compare the Effectiveness of Pharmacologic and Non-pharmacologic Treatments (e.g., Social/Family Support) in Managing Behavioral Disorders for Populations Likely to Experience Disparities (i.e., Racial/Ethnic Minorities, Rural Populations, Low SES Populations) with Alzheimer's Disease and Other Dementias in Home and Institutional Settings

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