Research Prioritization Topic Briefs

PCORI Scientific Program Area:
Assessment of Prevention, Diagnosis and Treatment Options

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Topic 12: Comparative Effectiveness of Strategies for Detecting Mild Cognitive Impairment (MCI)

Criteria	Brief Description
Introduction	
Overview/definition of topic	DESCRIPTION OF CONDITION • Mild cognitive impairment (MCI) is defined as a state of cognitive function below normal, but not severe enough to be classified as dementia, and that does not interfere with daily activities.[1-3] Individuals with MCI are at substantial higher risk to develop dementia.[4-6] The progression rate to dementia is between 6-10% per year in epidemiological studies.[3] • Amnestic MCI (characterized by memory impairment) and non-amnestic MCI (characterized by other cognitive function impairments) are the two clinical subtypes.[7-9] It is hypothesized that because of the different underlying pathogenesis, patients with amnestic MCI are more likely to progress to Alzheimer's disease while patients with non-amnestic MCI are more likely to progress to frontotemporal dementia, dementia with Lewy bodies (Lewy bodies, named after the doctor who first discovered them, are abnormal deposits of protein in nerve cells), and vascular dementia.[3] • Predictors of progression from MCI to dementia include severity of cognitive impairment, apolipoprotein E ε4 carrier status, atrophy on MRI, fluorodeoxyglucose F 18 PET pattern of Alzheimer's disease, cerebrospinal fluid makers compatible with Alzheimer's disease, and positive amyloid imaging scan.[3,10,11] • Diagnosis of MCI is based on clinical and neuropsychological findings, as well as neuroimaging, cerebrospinal fluid and genetic testing.[12] Many screening tools and instruments are available to assess cognitive impairment in older adults; each has its strengths and weakness.[13] The consensus is that changes in cognition are best established with repeated measurements over time.[14] • No drugs have been approved for treatment of MCI to date. The goal of current clinical trials is to slow cognitive deterioration and progression to dementia and Alzheimer's disease.[15]
Relevance to patient-centered outcomes	SYMPTOMS[1] • Neurocognitive decline, with or without memory deficit • Emotional and neuropsychiatric symptoms PATIENT-CENTERED OUTCOMES • Cognition (specific domains or global cognition) • Functional outcomes (e.g., instrumental activities of daily living) • Concerns about progression to dementia and Alzheimer's disease • "Conversion" to dementia and Alzheimer's disease Quality of life

Burden on Society	
Recent prevalence in populations and subpopulations	PREVALENCE[8,12] Prevalence is difficult to establish due to the different diagnostic criteria, definitions, populations' ages, sample type, and methods of diagnosis used in individual studies. The estimated prevalence of MCI in people 70 years and older is between 14-18%.[3] Amnestic MCI affects twice as many people as non-amnestic MCI.[9] The relationship between MCI and sex, race, ethnicity, or education is inconsistent.[16,17]
Effects on patients' quality of life, productivity, functional capacity, mortality, use of health care services	MCI affects patients' quality of life. • QOL (memory loss –disorientation)[18] • Functionality (loss of independence)[18] • Concerns about developing dementia[7] • Emotional burden (anxiety, depression)[10]
How strongly does this overall societal burden suggest that CER on alternative approaches to this problem should be given high priority?	• MCI is a common condition in the elderly, affecting 1 in 6 individuals aged 70 or older. The number of individuals diagnosed with MCI is growing fast due to the aging population as well as increased diagnosis of previously undiagnosed individuals. People with MCI are at substantial higher risk of developing dementia than those without MCI.[4-6] • Early detection of MCI provides the opportunity to manage risk factors (e.g., hypertension, diabetes, chronic renal failure), the underlying disease process, and coping strategies. • The overall societal burden suggests that developing and validating efficient and feasible approaches to detect MCI in different settings is a high priority, if early detection can indeed translate to better management strategies and improved patient-centered outcomes.[7,12]
Options for Addressing the Issue	
Based on recent systematic reviews, what is known about the relative benefits and harms of the available management options?	Based on a recent systematic review conducted in 2013 to inform a United States Preventive Services Task Force recommendation on screening for cognitive impairment in older adults, , many screening tools and instruments are available to assess cognitive impairment in older adults; each has its strengths and weakness. There is no direct trial evidence demonstrating that screening for cognitive impairment improves health outcomes or the outcomes of the family and caregiver.[7] Evidence is also lacking on the adverse psychological effects of screening or harms from false-positive or false negative results. Although many pharmacological and non-pharmacological interventions have been tested and used in individuals with MCI, an effective management strategy for MCI is yet to be established.[7]

	Pharmacological interventions: • There is no FDA-approved drug for MCI. • There is good evidence suggesting that cholinesterase inhibitors (donepezil, galantamine, and rivastigmine) *do not* reduce the risk of incident dementia *nor* provide a clinically meaningful improvement in cognitive test scores.[7,15,19] Cholinesterase inhibitors are associated with increased risk of adverse events, particularly gastrointestinal symptoms.[19] • Donepezil and piribedil, a dopamine agonist may improve global cognition. Galantamine may improve executive functioning and attention. Nicotine patches may improve attention, delayed recall, and self-reported anxiety. Evidence on other pharmacological interventions, including Huannao Yicong, gingko biloba, NSAIDS, vitamins, and omega-3 polyunsaturated fatty acids is inconsistent or equivocal.[15] *Non-pharmacological interventions:* • Cognitive training, long-term and short-term group psychological interventions, family psychological interventions, individual psychological interventions, and exercise programs (group and individual) have been tested in randomized controlled trials.[7,15,20] o Two small studies of group memory training, cognitive stimulation and reminiscence showed improvement in cognition in patients with MCI. There is little evidence demonstrating beneficial effects of other non-pharmacological interventions on dementia onset, cognition (specific domains or global), functional outcomes, or daily activities.[15,21]
What could new research contribute to achieving better patient-centered outcomes?	Research is needed to: • Understand the etiology, natural history, and epidemiology of MCI; identify the molecular, cellular mechanisms, as well as genetic risks for MCI;[22] understand the underlying etiology and subtypes which may be associated with different prognosis and treatment options. • Assess the diagnostic accuracy of the newly proposed *Alzheimer's Association Medicare Annual Wellness Visit Algorithm for Assessment of Cognition* (see description under "Have recent innovations made research on this topic especially compelling?"); assess the feasibility of implementing the algorithm for Medicare beneficiaries in primary care setting; assess the impact, including the harms, of the above-mentioned algorithm on health and patient-centered outcomes, as well as outcomes of family and caregiver. • Evaluate the role of biomarkers and neuroimaging in detecting MCI and early cognitive impairment, and in identifying individuals at high risk for progression to dementia. • Evaluate whether early detection positively impacts important decision-making (e.g., optimize current medical management, coping strategies, decision making autonomy, and planning for the future) that ultimately leads to improved patient outcomes. • Develop effective pharmacological and non-pharmacological interventions for MCI.

Have recent innovations made research on this topic especially compelling?	• The Affordable Care Act added the Annual Wellness Visit as a new Medicare benefit, effective January 1, 2011. The Annual Wellness Visit, which includes an assessment of cognitive function, provides an unprecedented opportunity to identify individuals with MCI (who are previously undiagnosed) and establish a baseline for longitudinal assessment for those without MCI. The Alzheimer's Association, in response to the Annual Wellness Visit requirement, developed *The Alzheimer's Association Medicare Annual Wellness Visit Algorithm for Assessment of Cognition*. The annual assessment and documentation may facilitate detection of gradual cognitive decline over time in individual patients – a key to establish MCI diagnosis.[23] • Biomarkers and neuroimaging for detecting MCI are active fields of research. If proven useful, they may assist in identifying the etiologies underlying MCI and thereby improve accuracy of diagnosis and prognosis, and for monitoring disease progression.[7] • Experimental therapies targeted to alter disease progression and to slow cognitive decline is an active area of research. If proven effective, these will change how MCI is managed. • If improved treatments are found, this will have an impact on the rationale for screening.
How widely does care now vary?	• The diagnostic criteria for MCI have evolved over time. Currently, the approaches for detection of MCI vary widely. Although many screening tools and instruments are available for use in clinical practice such as the Mini Mental State Examination©, Clock Drawing Test, Mini-Cog, Memory Impairment Screen, there is no single tool that satisfies all needs for assessing cognitive impairment. Further, reproducibility of the test performance of these instruments is limited in part because of lack of clarity and standardization of defining MCI in diagnostic accuracy studies.[7] • Currently, there is no standard care for the detection, diagnosis, or management of MCI.
What is the pace of other research on this topic (as indicated by recent publications and ongoing trials)?	We searched *clinicaltrials.gov* for "mild cognitive impairment" on March 3, 2014. • Of the 289 records identified, 230/289 (80%) are registered as "interventional studies"; a majority are "recruiting" (128/289; 44%) or "completed" (97/289; 34%). • Of the 242 records that reported the interventions being examined, "drug" is the most frequently studied intervention (120/242; 50%), followed by "behavioral" (56/242; 23%), "other" (28/242; 12%), and "device" (17/242; 7%) intervention. • Industry funded 84/289 (29%) of these studies, NIH and other federal agencies funded 65/289 (22%), and "Other" funding source is noted in 143/289 (49%) records. A study may have more than one source of funding. We then added "detection OR diagnosis OR screening" to the previous search and identified 34 studies evaluating neuroimaging (mostly using Positron Emission Tomography), six studies evaluating biomarkers, and two studies evaluating both modalities for the detection of MCI. In addition, four studies are evaluating cognitive assessment for detecting MCI.

How likely it is that new CER on this topic would provide better information to guide clinical decision making?	It is very likely that new CER on this topic would provide better information to guide clinical decision making because of the paucity of evidence that directly links the detection of MCI to improved health outcomes of the patients and outcomes of the family and caregiver.
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: • The Annual Wellness Visit provides a unique opportunity to detect MCI and intervene. • Many instruments for detecting cognitive impairment could be reasonably administered in the primary care setting.[7] • Early detection of MCI may provide an opportunity to manage risk factors (such as hypertension or coronary heart disease), modify the underlying disease process, and alter healthcare decision-making and coping strategies. Some patients and families want this, even though effective treatments do not currently exist.[9,11] BARRIERS: • MCI may be misinterpreted as normal aging and some families may not wish for a medical diagnosis and interventions.[12] • There is no single tool that would satisfy all needs for detecting cognitive impairment. Existing cognitive impairment screening tools have differential sensitivity and specificity depending on the prevalence of the condition in the population, the tool(s) used, and the cutoff points chosen. The validity of cognitive assessment tools in low-education or illiterate populations is unclear.[23] • The implications for subsequent workup of individuals with screening-detected MCI are substantial, and are not well understood or researched. • Effective treatment for MCI is currently lacking. Consequently, it is unclear whether early detection can indeed translate to better management strategies and improved patient-centered outcomes.[7]
How likely is it that the results of new research on this topic would be implemented in practice right away?	• Diagnostic strategies that are not technologically intensive or expensive, such as screening instruments in a primary care setting, will be quick to implement. • There is growing effort to build a workforce with the skills to ensure timely and accurate diagnosis, which should facilitate rapid implementation.[22] • Computerized testing may facilitate screening in primary care settings.

Would new information from CER on this topic remain current for several years?	• Given the aging population, MCI is a problem that will remain pressing for years to come. • If treatments for MCI prove useful, it will be a paradigm shift; having the ability to identify patients with MCI will be valuable.

References for Topic 12: Comparative Effectiveness of Strategies for Detecting Mild Cognitive Impairment (MCI)

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Topic 13: Comparative Effectiveness of Management Strategies (e.g., Pharmacologic Treatment, Social/Family Support, Combined Pharmacologic and Social/Family Support) for Community-Dwelling Individuals with Dementia

Criteria	Brief Description
Introduction	
Overview/definition of topic	DESCRIPTION OF CONDITION • Dementia is not a disease but a set of symptoms "associated with decline in memory or other thinking skills severe enough to reduce a person's ability to perform everyday activities."[1] Dementia usually starts with cognitive impairment (most often memory loss) followed with deterioration of other cognitive functions including executive functions, attention, judgment, planning as well as functional declines and emotional control and social behaviors. • Dementia is caused by damage to the brain cells. Depending on the clinical presentation, neuropathology, and underlying etiology, four major types can be defined: Alzheimer's disease, the Parkinson's group (e.g., dementia with Lewy bodies, dementia of Parkinson's), the frontotemporal dementia, and vascular dementia.[2] Alzheimer's disease accounts for 70% of dementia cases and vascular dementia is the second most common type (17%).[3] Recent evidence shows that most individuals may have mixed etiologies.[1,4,5] • Age is the primary risk factor for dementia. Other risk factors include alcohol use, atherosclerosis, diabetes, Down syndrome, genetics, hypertension, mental illness, depression, smoking, and in a small percent, genetic predisposition.[6-8] • Diagnosis of dementia usually includes a careful patient history and physical examination, and neurological evaluation. Brain scans (e.g., computed tomography, magnetic resonance imaging, positron emission tomography), cognitive and neuropsychological tests are also helpful. Clinicians will aim to identify and manage underlying treatable conditions (e.g., depression, abnormal thyroid function). Diagnosis is made based on the absence of other underlying problems. A diagnosis of "probable" is typically made and is only confirmable on autopsy.
Relevance to patient-centered outcomes	SYMPTOMS Symptoms of dementia vary. A diagnosis of dementia is usually made when at least two of the core mental functions are severely impaired:[1] • Memory • Communication and language • Ability to focus and pay attention • Reasoning and judgment • Visual perception Early stages of dementia may be overlooked as simple forgetfulness and absentmindedness of aging. As the condition progresses, patients with dementia may show disorientation, memory and

	communication difficulties, changes in behavior, and deficiency in self-care. During its middle and late stages, behavior changes escalate. Patients may require help with daily activities, and be challenged by "aggressive behaviors, restlessness and wandering, eating problems, incontinence, delusions and hallucinations, and mobility difficulties that can lead to falls and fractures".[9] High levels of dependency and mobility of late-stage dementia challenge the skills and capacity of caregivers. PATIENT-CENTERED OUTCOMES • Changes in symptoms (e.g., cognitive function, behavioral symptoms, and functionality)[10] • Impairment of daily life • Ability to remain independent • Likelihood of institutionalization (e.g., admission to nursing home) • Multiple medications, their interactions, and adverse effects of medications • Quality of life of patients and caregivers[11] • Burden and satisfaction of caregivers[12] • Mortality[13]
Burden on Society	
Recent prevalence in populations and subpopulations	PREVALENCE • In the U.S., it is estimated that between 2.4 and 5.5 million people have dementia and over 1 million new cases develop every year.[5] The prevalence increases substantially with age: 5% in those aged 71-79, 24% in those aged 80-89, and 37% in those aged 90 or above. • Compared to Caucasians, African Americans and Hispanics have higher prevalence and incidence of dementia and Alzheimer's disease.[14] Minority populations tend to have a late diagnosis, when cognitive impairment is more severe.[15,16]
Effects on patients' quality of life, productivity, functional capacity, mortality, use of health care services	• Dementia is a major cause of disability and dependency among older people. As dementia progresses, the increasingly impaired mental, behavioral and neurocognitive functioning makes the patient less aware of his/her surroundings, more dependent for his/her daily activities and self-care, and less mobile. Ultimately, life in all its aspects is affected.[17] • Individuals with dementia live and frequently die in community settings.[18] They are two to four times more likely to die at any given age than those without dementia.[19] One study estimated the median survival time from diagnosis of dementia to death is 4.5 years.[20] • It is estimated that 15.4 million family caregivers devoted 17.5 billion unpaid hours caring for those with Alzheimer's and other dementias in 2012. Of them, nearly 15% of caregivers live more than one hour away from the patient.[21] • Caring for dementia patients can be overwhelming and can exert physical, emotional, and economic pressures on the family and caregivers. Over 60% of caregivers report high or very high levels of emotional stress, and more than one third report symptoms of depression.[21,22]

	• In the U.S. in 2010, the estimated yearly cost for care of a patient with dementia was between $41,000 to $56,000 in 2010, leading to a total cost between $157 billion and $215 billion. This cost calculation includes care purchased in marketplace (i.e., total out-of-pocket spending, total Medicare spending, net formal home care, nursing home care) and informal home care. Medicare paid approximately $11 billion of this cost.[23] • Compared to those without dementia, dementia patients have more Medicare and Medicaid nursing facilities use, greater hospital and home health use, and more transitions in care.[18] The Medicare costs per person are three times higher and the Medicaid costs are 19 times higher than those without dementia.
How strongly does this overall societal burden suggest that CER on alternative approaches to this problem should be given high priority?	• Dementia is a highly prevalent condition among older Americans. About 70% of the individuals with dementia live in the community. • Caring for dementia patients puts enormous physical, emotional, and economic stress on the family and caregivers. • The overall societal burden of the condition, given the prevalence of the condition and the dependency and behavioral challenges of the affected individuals, suggests that developing effective management strategies for community-dwelling individuals with dementia is a high priority. Development of new paradigm for dementia caregiving should be given high priority.
Options for Addressing the Issue	
Based on recent systematic reviews, what is known about the relative benefits and harms of the available management options?	There is no effective treatment (yet) to slow or halt the progression of dementia caused by neurodegeneration, including Alzheimer's disease, frontotemporal disorders, and Lewy body dementia. *Pharmacologic interventions:* *For the cognitive symptoms of Alzheimer's disease:* • Mild to moderate Alzheimer's disease: There is good quality evidence suggesting that the acetylcholinesterase (AChE) inhibitors, donepezil, galantamine, and rivastigmine are effective in improving cognition (e.g., assessed by Alzheimer's Disease Assessment Scale – cognitive subscale, Mini Mental State Examination©) but results for other outcomes including functional outcomes (e.g., assessed by activities of daily living), behavioral symptoms, and global outcomes (e.g., assessed by clinical dementia rating, global deterioration scale) are mixed.[24] There is little information on quality of life, time to institutionalization, and mortality. • Moderate to severe Alzheimer's disease: Memantine is effective in improving cognition at 12 weeks and in function at 24-28 weeks.[24] *For the cognitive symptoms of non-Alzheimer dementias:* • AChE and memantine are *not* effective for the treatment of cognitive decline in non-Alzheimer dementias.[24]

	For the behavioral and psychiatric symptoms of dementia: • No drug has been approved by the FDA to treat behavioral and psychiatric symptoms of dementia. In managing these symptoms, antidepressants (for mood), anxiolytics (for anxiety/restlessness), and antipsychotic medications (for hallucinations) are used "off label". • Both first- and second-generation antipsychotics are associated with increased risk of stroke and death in dementia patients.[25] • The decision to use an antipsychotic drug needs to take into account expected therapeutic benefits and potential harms. *Other pharmacologic interventions:* • The effectiveness and safety of dietary supplements (e.g., ginkgo biloba, omega-3 fatty acids, vitamin E, caprylic acid and coconut oil, coenzyme Q10, coral calcium, phosphatidylserine, tramiprosate) and other agents (e.g., anti-inflammatory drugs, nootropics, selegiline, oestrogens, pentoxifylline, or statins) in the treatment of dementia are unknown. The evidence for EGb 761 and cerebrolysin is inconsistent.[26] *Non-pharmacologic interventions:* Non-pharmacologic approaches are recommended as a first-line alternative to pharmacologic therapy given the observed side effects of the later.[24,27,28] *Delivered to patients directly:* • Based on a systematic review of 11 randomized controlled trials, cognitive training was not effective for any cognitive or non-cognitive outcomes for patients with *mild Alzheimer's disease or vascular dementia*. The overall quality of the trials was low to moderate.[29] • Non-pharmacologic interventions for the *behavioral symptoms of dementia* encompass a wide range of approaches such as emotional oriented approaches (e.g., reminiscence therapy, simulated presence therapy, validation therapy), stimulation oriented approaches (e.g., acupuncture, aromatherapy, light therapy, massage and touch, music therapy, snoezelen multisensory therapy, transcutaneous electrical nerve stimulation), behavior management techniques, other psychosocial interventions (e.g., animal-assisted therapy, exercise), therapies targeted at behavioral symptoms (e.g., wandering in the domestic setting).[28] Currently, the evidence on the effectiveness of non-pharmacologic approaches for treating *behavioral and psychiatric symptoms of dementia* is mixed. *Delivered through family and caregivers:* • Based on a recent systematic review of 23 studies, community-based non-pharmacologic interventions delivered through family caregivers were effective in reducing behavioral and psychological symptoms, as well as in ameliorating caregiver reactions to these behaviors.[30,31] Other studies also support these findings.[32]
What could new research contribute to	The National Alzheimer's Project Act, signed into law in January 2011, offers a historic opportunity to address the many challenges facing patients with Alzheimer's disease and their families. The 2013 update of the National Plan to Address Alzheimer's Disease includes a comprehensive list of

achieving better patient-centered outcomes?	research priorities.[33] In our view, the following topics are also applicable to other dementias: • Expand research aimed at preventing and treating Alzheimer's disease (and dementia). • Accelerate efforts to identify early and pre-symptomatic stages of Alzheimer's disease (and dementia). • Facilitate translation of findings into medical practice and public health programs. • Build a workforce with the skills to provide high-quality care. • Ensure timely and accurate diagnosis. • Educate and support people with Alzheimer's disease (and dementia) and their families upon diagnosis. • Identify high-quality dementia care guidelines and measures across care settings. • Explore the effectiveness of new models of care for people with Alzheimer's disease (and dementia). • Ensure that people with Alzheimer's disease (and dementia) experience safe and effective transitions between care setting and systems. • Advance coordinated and integrated health and long-term services and supports for individuals living with Alzheimer's disease (and dementia). • Improve care for populations disproportionately affected by Alzheimer's disease (and dementia) and for populations facing care challenges. • Ensure receipt of culturally sensitive education, training, and support materials. • Enable family caregivers to continue to provide care while maintain their own health and well-being. • Assist families in planning for future care needs • Maintain the dignity, safety, and rights of people with Alzheimer's disease (and dementia). • Assess and addressing the housing needs of people with Alzheimer's disease (and dementia). We also identified the following research gaps based on our review of the literature and consultation with the clinician expert. There is a need to: • Develop and validate instruments to measure patient-centered outcomes and quality of life in patients with *late stage* dementia. • Provide better understanding of the prognosis and care needs of dementia patients who live alone in the community. • Assess the comparative effectiveness of pharmacologic interventions vs. non-pharmacologic interventions for different types of dementia at various stages. • Evaluate management strategies for co-occurring conditions in patients with dementia. • Develop and evaluate non-pharmacologic interventions, delivered through family caregivers, for patients with mild and early stage dementia. • Evaluate AChE and memantine for the treatment of psychotic symptoms in dementia.

Have recent innovations made research on this topic especially compelling?	Dementia is an extremely active area of research. Although new pharmacologic interventions might be promising, they are not on the immediate horizon. Targets for future Alzheimer's disease drugs include beta-amyloid, tau protein, inflammation, and insulin resistance. Many non-pharmacologic interventions that aim at enhancing care quality and efficiency, and expanding supports for people with dementia and their families are being tested in clinical trials. If beneficial effects are established, non-pharmacologic interventions would have an impact on dementia care.
How widely does care now vary?	• We did not identify any practice guidelines recommending management strategies for community-dwelling individuals with dementia. There are limited data on their care needs, the care model, and effective interventions designed specifically for them. Presumably care varies widely given the lack of recommended approaches. • We identified one set of dementia management quality measures developed by the Dementia Measures Work Group representing the major national organizations and advocacy organizations.[34]
What is the pace of other research on this topic (as indicated by recent publications and ongoing trials)?	We searched *clinicaltrials.gov* using "dementia" on March 10, 2014 and identified 2353 records. • A majority of the studies are registered as "interventional" (1860/2353; 79%); about half of them are "completed" (1060/2453; 45%) and one third are recruiting (748/2453; 32%). • Of those, 1974 records reported the intervention under study; most are evaluating "drug" (1215/1974; 62%), followed by "behavioral" (275/1974; 14%), "other" (187/1974; 7%), "device" (98/1974; 5%), "procedure" (75/1974; 4%), "dietary supplement" (53/1974; 3%), and "biological" (52/1974; 3%). "Radiation" (13/1974; 0.7%) and "genetic" (6/1974; 0.3%) are the least studied. • Industry funded 838/2353 (36%) of these studies, NIH and other federal agencies funded 420/2353 (18%), and "Other" funding source is noted in 1532/2353 (65%) records. A study may have more than one source of funding. • The median target enrollment sample size is 90 (IQR: 38 to 242).
How likely it is that new CER on this topic would provide better information to guide clinical decision making?	• There is no pharmacologic or other interventions that definitely prevent, treat, or cure dementia. Little is known about the optimal management of the community dwelling adults with dementia. Therefore, it is very likely that new, high quality CER on this topic would provide better information to guide clinical decision-making. • For the new CER to be useful, future research must be planned and carried out carefully to address the quality deficiencies observed in the literature. The quality of existing evidence on treatment alternatives for dementia is mixed at best. No firm conclusions could be drawn on the benefits and harms of non-pharmacologic interventions. Future research should address caregivers as well, and the impact of interventions on their quality of life.

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:[33,35] • There is an increasing awareness on the rise in the prevalence of dementia and its growing burden on older adults, their families, the society and the health care system. • The majority of people with dementia live in the community and their families provide most of their care. Family members and caregivers need a continued support and a coordinated effort alongside the primary care physician, who provide the daily care. • The National Alzheimer's Project Act and the National Alzheimer's Project provide an unprecedented opportunity to tackle the challenges that Alzheimer's disease and dementia pose. The well-established national plan (including research priorities), infrastructures, research communities, and research supports will accelerate the research. • The American Association of Retired Persons as well as many other non-governmental and governmental organizations that are interested in caregiving and dementia are valuable stakeholders who might help with disseminating research findings. BARRIERS: • There are no well-established quality measures to assess dementia care. • There are presently no practice guidelines into which new findings could be incorporated. • Bringing pharmacologic treatments to market takes time. • Currently, research on dementia, although extremely active, is poorly coordinated which may impair dissemination for research results.
How likely is it that the results of new research on this topic would be implemented in practice right away?	• New pharmacologic agents will not come quickly into practice given the need for regulatory approval. • Newly proven effectiveness of existing medications would be quickly implemented. • Non-pharmacologic treatments with well-established effectiveness and feasibility could be implemented quickly in practice if a trained workforce is available to deliver these interventions.
Would new information from CER on this topic remain current for several years?	• Dementia is a problem that will remain pressing for years to come. There are many trials presently underway. • CER on this topic could potentially be made irrelevant by the results of trials underway, although we are not aware of any that are expected to result in major changes to the dementia management paradigm. The impact of studies presently being conducted will depend largely on the effect size, applicability to community dwelling individuals with dementia, and the ease of implementation of the intervention. This is difficult to foresee.

References for Topic 13: Comparative Effectiveness of Management Strategies (e.g., Pharmacologic Treatment, Social/Family Support, Combined Pharmacologic and Social/Family Support) for Community-Dwelling Individuals with Dementia

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Topic 14: Comparative Effectiveness of Treatment Strategies for Primary Open-Angle Glaucoma (e.g., Initial Laser Surgery, New Surgical Techniques, New Medical Treatments), Particularly in minority populations on clinical and patient-reported outcomes

Criteria	Brief Description
Introduction	
Overview/definition of topic	DESCRIPTION OF CONDITION • Glaucoma is an acquired disease of the optic nerve, a form of neuropathy, characterized by a particular appearance of the optic nerve and associated visual field defects. Open-angle glaucoma (OAG; the subject of this report) is a subtype of glaucoma in which the drainage channels for aqueous humor in the front of the eye are open.[1] • The cause for OAG is unknown; the risk of developing OAG increases with increased intraocular pressure (IOP), age, a family history of glaucoma, use of steroids, and being African American over age 40.[1,2] • Because intraocular pressure (IOP) is the only known, modifiable risk factor, treatment for OAG has focused on lowering IOP, which secondarily slows its progression, prevents the worsening of visual field loss, and may have protective effects on visual impairment and blindness.[1]
Relevance to patient-centered outcomes	SYMPTOMS • The initial damage to the optic nerve caused by glaucoma is usually asymptomatic. As glaucoma progresses, patients may experience difficulty with peripheral vision, contrast sensitivity, adjustment between light and dark, and central vision, all of which affect daily function and quality of life. In its most severe form, glaucoma results in total and irreversible blindness.[1,3] PATIENT-CENTERED OUTCOMES [4,5] • Visual impairment • Functional outcomes such as ability to read, walk, and drive • Falling and fear of falling • Concerns about future vision loss and blindness • Satisfaction with therapy • Vision- and health- related quality of life • Blindness

Burden on Society	
Recent prevalence in populations and subpopulations	PREVALENCE • It is estimated that 2.7 million Americans aged 40 and older have glaucoma, and another 2 million Americans have glaucoma without knowing it.[2,6] A major problem of OAG is the high prevalence of persons with undetected disease, being higher in Hispanics (75%) and African Americans (58%), compared to 50% in whites.[6,7] Many more Americans will be diagnosed with glaucoma in the coming years given the aging population.[2] • OAG is the most common form of glaucoma and accounts for about 74% of the cases.[7] It is estimated that 2.29 million Americans aged 40 and older had OAG in 2008: 60% were female, 69% were white, 20% were Black, and 6% were Hispanic.[8] The prevalence is higher in African Americans over age 40 and might be lower in Hispanics of Mexican descent. • Glaucoma of all types is the second leading cause of blindness worldwide.[9] Glaucoma of all types causes 9-12% of cases of blindness in the United States (120,000 cases).[6] • Glaucoma is the leading cause of blindness in African-Americans and Hispanics.[6,10] • OAG accounts for 19% and 6% of all blindness among African Americans and Caucasians respectively.[6] Compared to Caucasians, African American are 6 to 8 times more likely to become blind from glaucoma.[6]
Effects on patients' quality of life, productivity, functional capacity, mortality, use of health care services	• More than 30 instruments have been used to measure visual function, visual disabilities, and vision-related quality of life in glaucoma patients, with the National Eye Institute Visual Function Questionnaire 25 (NEI-VFQ-25) being the most commonly used.[11,12] • Decreased vision-related QOL and visual function directly correlate with the severity of glaucoma.[13] Difficulty with extreme lighting is the most frequent complaint in individuals with glaucoma. Those with bilateral glaucoma report worse visual abilities such as reading, walking, driving, and a decline in mobility.[4,12-15] • The total Medicare cost of the visits, tests, and procedures for managing patients with OAG and OAG suspects was estimated to be $1.25 billion in 2009 (about $228 per glaucoma patient, excluding medications). The total cost and cost per patient increased at a rate less than other medical costs and less than the consumer price index from 2002 to 2009. Of the total OAG expenditures, 50% are for office visits, 30% for diagnostic procedures, and 10% for surgical procedures. The total cost for providing other eye care such as cataract surgery and care of retinal disease to patients with glaucoma was substantially higher than glaucoma care costs.[16]
How strongly does this overall societal burden suggest that CER on alternative approaches to this problem should be	• The non-economic burden of OAG is high. OAG is a highly prevalent eye condition. Under-diagnosis and under-care are common, especially among minority populations. If left untreated, OAG can lead to irreversible visual damage and blindness. The negative impact of OAG on patient reported outcomes and vision-related quality of life is well established. [17] • The cost to Medicare (excluding medications) of care for OAG is modest (about $228 per glaucoma patient in 2009). About half of the total cost is for office visits because glaucoma is

given high priority?	a chronic condition (new patient visits made up only 5% of total office visits every year).[16]
Options for Addressing the Issue	
Based on recent systematic reviews, what is known about the relative benefits and harms of the available management options?	Evidence on the comparative effectiveness of medications, laser, and incisional surgeries was thoroughly reviewed in a systematic review conducted in 2012 as part of AHRQ's Effective Health Care Program.[1] This review summarized data from 73 randomized controlled trials (RCTs), 13 observational studies, and 23 systematic reviews published before October 2011, and concluded the following: *Effectiveness* • Medications, laser, and incisional surgeries are all effective in lowering IOP. • Among medications, the prostaglandin analogs seem to lower IOP more than other classes and have a better safety profile. • Laser trabeculoplasty, a technique that uses a focused beam of light to help fluid leave the eye, lowers IOP. • Trabeculectomy, a surgical procedure that creates new drainage pathways, lowers IOP more than nonpenetrating surgical procedures such as viscocanalostomy and deep sclerectomy. Mitomycin-C used during the surgery improves the IOP reduction effect of trabeculectomy (but not other surgical methods). • Patients treated with medications, laser trabeculoplasty, or trabeculectomy were less likely to experience worsening of visual field loss and optic disc damage than patients who did not receive treatment. *Harms* • Medications may cause side effects such as conjunctival hyperemia and ocular irritation; but in general, the harms of medications do not threaten vision. • Surgeries come with risk of infection, bleeding, cataract formation, choroidal effusions (abnormal accumulation of fluid between the choroid and the sclera of the eye), hyphema (blood in the front chamber of the eye), and flattening of the anterior chamber; and these complications are more severe than those caused by medications. • Trabeculectomy seems to cause more complications than nonpenetrating surgeries and the risk may be increased in the presence of mitomycin-C. We did not find evidence suggesting that the effectiveness and harms of glaucoma interventions are different in minority populations.
What could new research contribute to achieving better patient-centered	• Although OAG reduces vision-related quality of life, a direct link between treatment for OAG and improvement in patient-centered outcomes is lacking.[1] Almost all treatment studies have focused on IOP and other intermediate outcomes. Demonstration of impact on patient-centered outcomes may require large numbers of participants who are followed for a long time (e.g. more than 10 years).

outcomes?	• New research on glaucoma treatment could provide information on the comparative effectiveness of: o one treatment versus another on patient-centered outcomes o medical and surgical treatments not covered in the above mentioned EPC review o therapies in relevant subgroups such as minority populations. • Design future glaucoma treatment studies to allow complete stratification by risk. • New research might allow development and evaluation of improved identification of high-risk population and care delivery to underserved patients with OAG.
Have recent innovations made research on this topic especially compelling?	• Newer medications including Tafluprost (approved by FDA in 2012) and Simbrinza (approved by FDA in 2013) have not been compared against existing treatment options. • A variety of new techniques, referred to collectively as "minimally invasive glaucoma surgery" are emerging for managing glaucoma. Minimally invasive glaucoma surgery has the potential to reduce the occurrence of major complications of traditional filtration surgeries related to blebs, tubes, and hypotony. However, to date, these procedures appear to reduce IOP less than traditional operations. • Minimally invasive glaucoma surgery can be classified by their surgical approach as ab externo (outside in) or ab interno (inside out). Examples include iStent trabecular micro-bypass (Glaukos; approved by FDA in 2012), CyPass (Trascend Medical; approved by FDA in 2012), and trabectome (NeoMedix; approved by FDA in 2004).[18]
How widely does care now vary?	• The Preferred Practice Patterns, developed by the American Academy of Ophthalmology, provide guidance regarding how to manage patients with OAG.[19,20] In general, the management approaches for minorities are the same as for others. That said, published studies indicate that minorities are less likely to seek comprehensive eye exams to have OAG diagnosed.[6,21,22] • Practice variations exist among individual ophthalmologists caring for OAG patients. One contributing factor is that ophthalmology is a highly innovative specialty area and innovations in drugs, devices, and technologies are often included into practice at variable rates.

What is the pace of other research on this topic (as indicated by recent publications and ongoing trials)?	• Research on OAG is active, but focused research on minority populations is less common. We searched *clinicaltrials.gov* using term "open angle glaucoma" on February 15, 2014. Of the 534 records identified, 413 are registered as "interventional studies". • More than half of the interventional studies (256/413; 62%) are registered as "completed", followed by 77/413 (19%) records registered as "recruiting". • A large proportion of the interventional studies (287/413; 69%) examined "drug", followed by "device" (74/413; 18%) and "procedures" (27/413; 11%). • IOP is the most frequently studied outcome and very few studies (n=6) examined QOL. • Alcon Research sponsored about a quarter of all interventional studies (97/413; 23%), followed by Allergan (25/413; 6%), Glaukos Corporation (22/413; 5%), and Pfizer (18/413; 4%). Pharmaceutical companies also sponsor most of the remaining studies.
How likely it is that new CER on this topic would provide better information to guide clinical decision making?	• It is very likely that new CER addressing the evidence gaps identified above would provide better information to guide clinical decision-making given the observed paucity of research (1) evaluating the comparative effectiveness of new medications and surgical procedures against the most appropriate "standard of care"; (2) demonstrating a direct link between treatments and patient-centered outcomes; (3) identifying high-risk population and under-cared population; (4) providing risk-stratified care.
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: • OAG is a common condition. The number of people affected by OAG will increase enormously given the aging population. • Glaucoma drugs are recommended as the first line treatment,[19,20] however, patients do not always adhere to their medical therapy[6,22] and adherence is less in the minorities.[23] • Other non-medical treatments, especially newer surgical techniques may play a role as the first line treatment. • There exist active research communities and patient groups. Ophthalmologists adopt new information quickly. • Implementation of EMRs across the United States offers the possibility of collecting outcomes on large number of OAG patients. • The Preferred Practice Patterns are well known and have a role in guiding practice. BARRIERS: • Need large cohorts and a long follow-up time (greater than 10 years) to establish a direct link between treatment for OAG and visual impairment and/or patient-reported outcome. • An efficient real-world approach to identify high-risk population is lacking. • Many OAG patients are not diagnosed and may not be receiving all treatments indicated for their severity of disease according to practice guidelines. • New drugs and devices are generally approved by the FDA to decrease IOP; the impact of these drugs on visual impairment or patient centered outcomes remains unknown.

How likely is it that the results of new research on this topic would be implemented in practice right away?	• Findings from new CER are likely to be implemented in practice right away because the research gaps outlines above are well established in the literature and shared by the community. However, treatments will not be effective in patients including the minorities who do not seek diagnosis and that are less adherent when prescribed treatments. New evidence is likely to be incorporated into systematic reviews and practice guidelines to influence practice.
Would new information from CER on this topic remain current for several years?	• New information from CER is likely to remain current for several years given the observed evidence gaps. • Minimally invasive glaucoma surgery might be a "game changer" if comparative effectiveness and safety can be demonstrated. • Establishing a direct link between *treatment* for OAG and visual impairment and/or patient-centered outcomes is critical for future glaucoma research.

References for Topic 14: Comparative Effectiveness of Treatment Strategies for Primary Open-Angle Glaucoma (e.g.,Iinitial Laser Surgery, New Surgical Techniques, New Medical Treatments) Particularly in Minority Populations on Clinical and Patient-Reported Outcomes

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Topic 15: Comparative Effectiveness of Surgical and Medical Options for Prevention and Care in Periodontal Disease to Increase Tooth Longevity and Reduce Systemic Secondary Effects in Other Organ Systems

Criteria	Brief Description
Introduction	
Overview/definition of topic	DESCRIPTION OF CONDITION[1] • Periodontal disease is a chronic infection of the hard and soft tissue supporting the teeth. Periodontal disease is the leading cause of tooth loss in older adults and contributes to the pathogenesis of chronic inflammation and other chronic conditions that affect general health including diabetes, rheumatoid arthritis and pregnancy outcomes. • Periodontal disease is classified as mild, moderate and severe depending on the depth of the inflammation and loss of tissue. • Treatments for periodontal disease include medical management and surgery. • Medical treatments include o Oral hygiene performed at home (*i.e.,* brushing and flossing) o Professional dental cleaning o Scaling: tartar and build up above and below the gum line are scraped away after the patient receives a local anesthetic o Root planning: rough spots on the tooth root are smoothed after the patient receives a local anesthetic) • Surgical treatments include o Flap surgery/pocket reduction surgery: gums are lifted back, cleaned and replaced to decrease the space between the gum and the teeth ▪ Tissue engineering is sometimes used in combination with flap surgery. [2] A piece of mesh with growth factors is inserted between the bone and the gum to regenerate tissue and decrease the gap between the bone and the gums. ▪ Bone surgery is sometimes used in combination with flap surgery to reshape damaged bone. o Bone grafts use the patient's own bone, synthetic bone or donor bone to replace damaged bone. o Soft tissue grafts: tissue from the root of the mouth is removed and stitched in to replace gaps in the gum line. Dental lasers can be used during surgical and non-surgical procedures.[3] There are over 20 indications for the use of lasers in dental care in the United States.[4]

Relevance to patient-centered outcomes	SYMPTOMS • Gingivitis or swelling and reddening of the gums • Tenderness and/or bleeding gums • Receding gums • Sensitive teeth and pain when chewing food • Halitosis or bad breath PATIENT-CENTERED OUTCOMES • Pain • Tooth loss • Impaired nutrition (reduction of ingestion due to pain when eating, or difficulties due to missing teeth) • Aesthetics • Decreased quality of life • Risk of systematic diseases
Burden on Society	
Recent prevalence in populations and subpopulations	PREVALENCE[5] • Approximately 47% of the Americans older than 30 years, have periodontal disease equaling 65 million adults: o 8.7% mild o 30% moderate o 8.5% severe • Periodontitis increases with age. Over 70% of those older than 65 have periodontal disease • Prevalence is higher in populations with greater poverty levels and less education. 65% of individuals with incomes greater than 100% below the federal poverty level compared with 35% of individuals greater than 400% above the federal poverty level. Similarly, 67% of individuals with less than a high school education have periodontitis compared with 39% among those with a greater than high school education. • Smokers (64%) and former smokers (53%) have higher rates of periodontal disease than non-smokers (40%). • All stages of periodontal disease are more frequent in men (56%) than women (38%). • Periodontal disease is more prevalent among non-Hispanic blacks (59%) and Mexican-Americans (60%) than whites (43%). • Women are at risk of developing pregnancy-associated gingivitis and other hormone-related conditions.
Effects on patients' quality of life, productivity, functional	• Periodontal disease affects quality of life due to pain, painful chewing, reduced food intake and aesthetic concerns including damaged gum lines, missing teeth and bad breath. • Since periodontal disease is the product of a continual inflammatory process and infection (or persistent bacteremia), this continued systemic inflammatory/immune process may initiate or

capacity, mortality, use of health care services	mediate a wide range of systemic diseases such as cardiovascular disease, diabetes mellitus and rheumatoid arthritis. [6] • Periodontal disease has been associated with multiple systemic conditions that affect mortality and use of health care services, although the percent of mortality and health care utilization attributable to periodontal disease for any specific condition has not been estimated.[7] • Research has linked periodontal disease with the following systemic conditions[6] o Cardiovascular disease o Diabetes o Metabolic syndrome o Obesity o Cancer o Respiratory diseases such as chronic obstructive pulmonary disease and pneumonia o Chronic kidney disease o Rheumatoid arthritis o Osteoporosis o Cognitive impairment o Preterm birth and low birth weight babies
How strongly does this overall societal burden suggest that CER on alternative approaches to this problem should be given high priority?	• Nearly half of adults over age 30 have some form of periodontal disease. Periodontal disease is one of the most common chronic conditions affecting Americans. • Periodontal disease is associated with conditions that contribute to the leading causes of death such as cardiovascular disease and cancer. • Understanding the best treatments for periodontal disease will affect the burden of disease for multiple chronic conditions.
Options for Addressing the Issue	
Based on recent systematic reviews, what is known about the relative benefits and harms of the available management options?	There are 20 Cochrane Collaboration reviews related to periodontal disease. • None directly compared medical with surgical management for periodontal disease. • A 2010 review was focused on the relationship between periodontal disease and another condition, diabetes. Seven trials were identified that included individuals with periodontitis and type 1 or 2 diabetes mellitus. The review concluded that there were few studies available and no individual study had sufficient power to detect a meaningful effect.[8] No AHRQ Effective Health Care Program reviews related to periodontal disease or oral health were identified. There are no systematic reviews aimed at comparing surgical with non-surgical or medical treatments for periodontal disease, although there are numerous reviews comparing either surgical or non-surgical treatments.

	Several reviews on periodontal disease and systemic disease were published in 2013 in association with a workshop of the European Federation of Periodontology and the American Academy of Periodontology.[6] • Overall, there was heterogeneity in the definition of periodontitis in the identified studies.[7] The majority of the literature used a cross-sectional study design rather than prospective studies. • The strongest evidence existed for a relationship between periodontal disease and pneumonia. Associations with other systemic diseases were found (such as obesity, chronic kidney disease and rheumatoid arthritis), although the studies were limited and many failed to control for confounding factors such as smoking and diet.
What could new research contribute to achieving better patient-centered outcomes?	• High quality reviews of the single intervention trials and non-randomized studies (*i.e.,* studies that compare either medical or surgical interventions to no treatment) or original research directly comparing medical with surgical treatments for periodontal disease can provide additional information for patients and their providers to make treatment decisions. Including populations at highest risk for periodontal disease such as the elderly, non-white and less wealthy individuals will be important. • Longitudinal studies adjusting for relevant confounding factors, such as cigarette smoking and diet, to understand the relationship between periodontal disease and chronic conditions are needed. These studies should also include populations at highest risk for periodontal disease.
Have recent innovations made research on this topic especially compelling?	• The use of lasers in the treatment of periodontal disease remains controversial despite their initial introduction in the 1990s. Designing and implementing high quality studies to understand the effectiveness of lasers compared with other surgical and non-surgical treatments is needed. • Treatments involving tissue engineering are an active area of research although its use in clinical practice is not routine.
How widely does care now vary?	• Estimates of practice variation in treatments for periodontal disease are difficult to estimate. Because dental care is covered under different insurance plans than medical care, common sources of estimating national variation in treatment are not available. • The independence of dental and medical insurance and care also limits the ability to understand the variation in care to prevent chronic diseases among those with periodontal disease. Most medical providers do not record periodontal disease in their records and do not routinely receive dental records related to their patients. • Variation in care is also likely related to the primary oral health care provider. Many individuals receive care from a dentist and may not have access to a periodontist.

What is the pace of other research on this topic (as indicated by recent publications and ongoing trials)?	There are 403 studies registered in ClinicalTrials.gov associated with periodontal disease. 124 were open studies and 279 were closed (27 with results). • 64 of 92 open studies are active interventional studies o 4 are relevant Phase 0 or 1 studies including stem cells for tissue regeneration, non-surgical treatment for individuals with periodontal disease and metabolic syndrome, anti-plaque chewing gum for gingivitis and an amnion-derived Cellular Cytokine Solution (ACCS) for gingivitis. o 12 are relevant Phase 2 or 3 studies including comparisons of ▪ Randomized trial of systemic doxycycline + photodynamic therapy versus doxycycline and standard non-surgical treatment in patients with Type 2 diabetes mellitus ▪ 4 trials related to dental implants and peri-implantitis, when inflammation affects a dental implant. The treatments included laser therapy, arestin, a chlorhexidine gluconate chip and synthetic bone substitutes ▪ 7 studies among patients with periodontal disease including • Manual versus automated periodontal probes • Randomized trial of probiotic lozenges versus placebo • Randomized trial of anti-plaque chewing gum • Randomized trial of mouthwashes containing propolis or chlorhexidine • Randomized trial of a mouthwash containing iodide or placebo • Randomized trial of a probiotic versus placebo for pediatric gingivitis • Randomized trial of 2 surgical and 1 non-surgical treatments including non-surgical subgingival debridement, simplified papilla preservation flap and resective periodontal flap with osseous recontouring (NCT01642641) o 18 are relevant Phase 4 studies • Anti-IL-6 for periodontitis among individuals with rheumatoid arthritis • Scaling and planing for individuals with coronary artery disease • 6 studies related to dental implants including 4 for guided bone regeneration, 1 for surgical treatment and 1 for ultrasonic debridement • 5 studies among patients with periodontal disease including ✓ Minocycline ✓ Photodynamic therapy ✓ Erythritol powder and metronidazole gel ✓ Mouth rinse ✓ Probiotic • 243 projects in NIH Reporter include the term periodontal. 30 of these include the term surgical of which none aim to directly compare surgical with non-surgical treatments for periodontal disease.

How likely it is that new CER on this topic would provide better information to guide clinical decision making?	• There is little existing information to guide clinical decision makers when deciding between medical and surgical treatments for periodontal disease. One expert consensus concluded treatment should be chosen by each practitioner according to individual patient's needs.[9] • There is only 1 ongoing trial of medical versus surgical treatments for periodontal disease (NCT01642641). Additional trials comparing medical versus surgical treatments for periodontal disease are needed. • There are several trials and projects aimed to examining periodontal disease among individuals with type 2 diabetes mellitus and rheumatoid arthritis. Longitudinal studies of other chronic diseases and pregnancy are needed based on the results of the European Federation of Periodontology and the American Academy of Periodontology workshop. [6]
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: • The European Federation of Periodontology and the American Academy of Periodontology are invested in examining relationships between periodontal disease and other systemic diseases. Both the American Academy of Periodontology and American Dental Association have websites with information for their members. Information could be shared with these associations. BARRIERS: • Dental care is not covered under most health care plans. • Not all dentists perform the surgical procedures under consideration and may be limited to choosing medical options for therapy, especially if a periodontist who does perform the surgical procedures is not part of their practice. • Dental and medical providers do not routinely share clinical information. • Medical providers may not ask patients about their oral health and dentists may not ask patients about their predispositions to medical conditions. • Future evidence examining the relationship between periodontal disease and chronic diseases may not be fully utilized unless there is better communication between dental and medical providers.
How likely is it that the results of new research on this topic would be implemented in practice right away?	• The latest innovations include FDA-approved lasers and tissue regeneration are unlikely to quickly replace existing medical and surgical techniques. • The major barrier to rapid implementation is access to care due to lack of dental health coverage and poor communication between dentists and other health care providers. The Affordable Care Act is expected to greatly improve dental care coverage, particularly for children, which should help with implementation of results in practice.
Would new information from CER on this topic remain current for several years?	• New information is likely to remain relevant for several years. Examining the roles of lasers in medical and surgical treatments will help ensure that the results remain current.

References for Topic 15: Comparative Effectiveness of Surgical and Medical Options for Prevention and Care in Periodontal Disease to Increase Tooth Longevity and Reduce Systemic Secondary Effects in Other Organ Systems

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Topic 16: Comparative Effectiveness of Wraparound Home and Community-Based Services and Residential Treatment in Managing Serious Emotional Disorders in Children and Teens

Criteria	Brief Description
Introduction	
Overview/definition of topic	• Serious emotional disorders are a group of psychiatric disorders that cause severe disturbances in behavior, thinking and feeling. • Serious emotional disorders may occur independently, and may also be associated with medical conditions (*i.e.,* autism, cerebral palsy, epilepsy, genetic syndromes, serious somatic illness) and/or have environmental roots (*i.e.,* economic or social factors, substance abuse). Many children with serious emotional disorders are identified from the juvenile justice system or after a parent or guardian has an encounter with the criminal justice system. Others are identified after causing physical harm to themselves or others, after treatment in community mental health centers, at-risk school programs or somatic care settings. • Children and teenagers with serious emotional disorders require extra help to learn behaviors to help them participate in society fully. Interventions that allow the child or teenager (if he or she has the intellectual capacity), with support, to incorporate productive behaviors into his or her daily routine may result in better long-term outcomes for the child and his or her community. • School-age children and teenagers with serious emotional disorders are eligible for special education as part of the Individuals with Disabilities Education. [1] Special education services can be one component of the wraparound services. • The wraparound system or philosophy was conceived to provide children and teenagers with complex behavioral problems, arising from emotional disorders, with individualized and community-based care. The goal is to use value-based principles to improve mental health, avoid institutionalization and prepare them for life as adults.[2] • The wraparound system implies a coordinated and collaborative effort between the child or teenager and his or her family and important resources such as the school system and other community services such as care managers, psychiatrists, pediatricians, psychologists, speech therapists, and others, depending on the specific case.[2] • Wraparound services differ based on the cause of the serious emotional disorder. For example, children with autism will receive different services than a child identified from the juvenile justice system or child protective services but the general concept of coordinated, personalized care individually tailored to each child's unique needs are consistent across all forms of wraparound interventions.
Relevance to	The outcomes that matter most depend on the child or teenager and his or her specific needs.

patient-centered outcomes	Common outcomes include: • Ability to participate fully in society • Ability to participate in school and extracurricular functions • Ability to live at home or supervised residence instead of in a long-term care facility • Employment preparedness for adulthood • Prevention of injury to self or others • Family burden (financial and otherwise) • Avoidance of hospitalizations • Ability to perform activities of daily living and demonstrate at least partial independence in self-care
Burden on Society	
Recent prevalence in populations and subpopulations	• Estimates of serious emotional problems vary from 5% to 26% of children and teenagers.[3] • According to a 2011 National Health Interview Survey of parents, parent-reported serious difficulties with emotions, concentration, behavior, or being able to get along with other people[4] among children aged 4 to 17 years old were more common in: o Males (7%) than females (4%) o Children living below the federal poverty level (8%) than children 200% above the federal poverty level (4%) o Children from single-mother families (8%) than two-parent families (4%) o Non-Hispanic whites (6%) and non-Hispanic blacks (6%) than Hispanic children (4%) • Less than 50% of the children and teenagers with emotional disorders get professional help. From those approximately 50% receive adequate treatment.[5]
Effects on patients' quality of life, productivity, functional capacity, mortality, use of health care services	• Exact estimates on the quality of life of the child and teenager with a serious emotional disorder and their family are difficult to estimate and likely vary with the severity of the condition. • Hospitalizations related to serious emotional disorders directly are difficult to estimate. The National Statistics for Mental Health reported 8 million hospital discharges due to mental health and substance abuse in 2011. For the age group 1-17 years, discharges were classified:[6] o 161,070 as mood disorders o 109,146 as attention-deficit, conduct or disruptive behavior disorders o 60,487 as anxiety disorders o 58,928 as suicide and intentional self-inflicted injury o 36,988 as substance related disorders o 13,116 as alcohol related disorders
How strongly does	Up to one in four families include a child or teenager with a serious emotional disorder. Most of

this overall societal burden suggest that CER on alternative approaches to this problem should be given high priority?	these children, teenagers and their families do not receive adequate care. Identifying the most effective care, and how to make that care available to all, is a high priority in our country. Providing adequate care will not only assist the affected child or teenager, but will have implications on the quality of life for the siblings, parents, other family members, the immediate community and society at large.
Options for Addressing the Issue	
Based on recent systematic reviews, what is known about the relative benefits and harms of the available management options?	• There are no systematic reviews on wraparound services for children and teenagers by the Cochrane Collaboration or by AHRQ's Effective Health Care (EHC) Program. There is an EHC review on interventions addressing maltreatment in children, although wraparound services are not specifically mentioned.[7] • A 2011 review searched numerous databases, focusing on books, monographs and articles identified 118 items published between 1987 and 2008.[8] Five of the studies compared wraparound services with traditional services including family-centered intensive case management services, traditional foster care, drug abuse treatment services, multisystemic therapy (MST), other forms of case management, and traditional mental health services. • The authors conclude that future funding should examine the populations best suited for wraparound services; the services that are most effective in the populations suited for wraparound services; and characteristics of the service delivery. Service delivery components include the characteristics of the wraparound team, characteristics of the intervention program, and methods of assessing program effectiveness at the patient, team and program levels. The National Wraparound Initiative *Resource Guide to Wraparound*[9] includes a chapter regarding outcomes (Section 3). In that review (based on 4 publications) the following outcomes were identified as essential targets of care:[10] stabilization in the community, ability to reside with family, physical aggression control, problem behaviors reduction, abuse, neglect, peer interaction, substance or alcohol abuse control, and compliance with the wraparound program.
What could new research contribute to achieving better patient-centered outcomes?	• The wraparound literature has not been extensively or systematically reviewed from perspectives outside of the mental health community. The majority of the literature has focused on the structure of the wraparound model and how to provide appropriate training and retention of providers. Comparing wraparound models to alternative care delivery systems and different formats of wraparound with regards to patient and family outcomes, including costs of care covered and not covered by traditional medical insurance, may provide a fresh perspective. • Secondary data analysis may also be possible given the large number of states with wraparound initiatives and publication of their characteristics in the State Wraparound Survey.[11] These analyses might inform how different statewide approaches lead to different

	outcomes measured at the state level. State-level information can be identified from other resource such as the Kids' Inpatient Database (KID)[12] the Behavioral Risk Factor and Surveillance System (BRFSS)[13] and National Survey on Drug Use and Health (NSDUH).[14] • Outcome studies involving school wraparound initiatives are needed, given the potential role that schools play in addressing the emotional and mental health needs of children and adolescents. [15]
Have recent innovations made research on this topic especially compelling?	• The Affordable Care Act's interest in delivering care through Patient-Centered Medical Homes [16] provides a unique opportunity to examine the patient and family-centered outcomes of wraparound homes including their impact on health care utilization. • The Affordable Care Act is also expanding mental health care coverage to include behavioral assessments of children and additional funding for state-based programs and training of mental health providers.[17]
How widely does care now vary?	National Wraparound Initiative was founded in 2003 to standardize care.[8] In 2007 advisors to the National Wraparound Initiative recommended a review of the research base because of the variation in care. Despite detailed guides on the topic, variation in the structure of the wraparound delivery exists.[9]
What is the pace of other research on this topic (as indicated by recent publications and ongoing trials)?	• There is little research evaluating wraparound delivery in terms of patient and family centered outcomes or in health care utilization. • There are 4 relevant studies identified in ClinicalTrials.gov when searching for the term "wraparound" • Recruiting: o NCT01895738: *WrapAround Care for Youth Injured by Violence* is a randomized control trial conducted in Canada comparing a wraparound model initiated at the time a youth visits an emergency room for a violence related injury with standard of care which is usually a list of resources. The outcomes of interest are fidelity to the treatment protocol, participant adherence, serious adverse events including retaliatory gang-related violence, repeat visits to the emergency room and the severity of the injuries, substance abuse and mental health related hospital visits, enrollment in high school or other educational setting, presence of stable housing, criminal behavior, injuries not treated in an emergency room and involvement in structured activities such as work or school. The trial was initiated in 2013 and is estimated to last 2 years. o NCT01665872: *New Haven MOMS Partnership* focuses on conducting a needs assessment of mothers residing in public housing in New Haven, CT and trial of the Wraparound Milwaukee Model of Case Management compared with group cognitive behavioral therapy. Although the unit of intervention is the mother, the program will likely affect the children as well. The outcomes of interest are attitude towards seeking mental health treatment, depressive and anxiety symptoms, parenting stress, gainful employment and cost. • Completed:

	○ NCT01751464: *A WrapAround Case Management Program for Youth Injured by Violence* was a pilot for the recruiting project described above. No publication or study results posted. ○ NCT00559208: *Children's Aid Societies: Differential Response and Wraparound Prevention Trial* was a trial started in 2006 and completed in 2009 taking place in Canada to prevent children who were maltreated from further maltreatment and need for out of home and out of community placement. No publications or study results posted. • There are 2 active studies listed in NIH Reporter relevant to wraparound care ○ 2R42MH095516: *Development, Usability Testing, And Effectiveness Evaluation of The Wraparound* will create a web-based system to track and develop wraparound care delivered to children and evaluate the usability and effectiveness of the system. Once the system is developed and usability is acceptable, a randomized trial will be conducted to compare "practitioner, implementation, and youth/family outcomes" among a set of practitioners using the system and those providing wraparound services but that do not use the system. ○ 5R21MH096061-02: *Effects of the Wraparound Service Model for Maltreated Youth in a System of Care* will examine outcomes of children monitored by one state's Child Protective Services who received wraparound or non-wraparound services with regards to "child and family clinical, behavioral, and functional outcomes."
How likely it is that new CER on this topic would provide better information to guide clinical decision making?	There is little existing or ongoing research to identify patient, family or health service utilization outcomes related to wraparound care. Therefore, new CER is likely to be informative to decision makers.
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: • The implementation of Patient-Centered Medical Homes and expanded mental health coverage under the Affordable Care Act may facilitate the implementation of wraparound services. • Each state is required to have a Department of Mental Health and Hygiene that could incorporate the new findings into care models. BARRIERS: • Access and coverage is variable from state to state and for the conditions covered. • Individuals with sufficient training in wraparound care may not be available to implement the findings. Retaining the sufficiently trained workforce is also an issue. • Many wraparound services are provided by state or federal funds which may not have

	flexibility to incorporate all new findings immediately. Private insurance may not cover this model of care.
How likely is it that the results of new research on this topic would be implemented in practice right away?	Coordinating the research with the National Wraparound Initiative so that the results are incorporated into their practice guides will likely facilitate implementation.
Would new information from CER on this topic remain current for several years?	Given the paucity of research examining the patient, family and health services utilization associated with wraparound homes compared with other approaches, the new information will likely remain current for several years.

References for Topic 16: Comparative Effectiveness of Wraparound Home and Community-Based Services and Residential Treatment in Managing Serious Emotional Disorders in Children and Teens

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