



## Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options August 1, 2014 Webinar Summary

### Overview

On August 1, 2014, the 21-member Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options (APDTO) convened for a webinar. The panel includes caregivers, patient-caregiver advocates, clinicians, researchers, organizational providers, and representatives from payers, industry and purchasers.

At the four previous in-person meetings, the APDTO Advisory Panel discussed and prioritized a total of 48 research topics. Ten of these topics were included as high priority topics in PCORI Funding Announcements (PFA) for [large pragmatic studies](#). The remaining 38 topics were reviewed by staff in order to assess whether a potential research opportunities existed. After this review, 23 topics were removed from further consideration due to the volume of research currently being conducted for those topic areas. The 15 topics that remained were discussed and prioritized by the advisory panel during the webinar.

The highest ranked topics include: medical and surgical treatment options for asymptomatic carotid artery stenosis; nonsurgical treatment strategies in delaying or preventing surgery for cervical disc and neck pain; coronary artery bypass surgery (CABG) and percutaneous coronary intervention (PCI) for treatment of adults with coronary artery disease (CAD); surgical options for hip fracture in the elderly; and the assessment of benefits and harms of pelvic floor mesh implants. Three of these high ranked topics were included in the third [PFA](#) for large pragmatic studies.

### Related Information

- [About PCORI's Advisory Panels](#)
- [Advisory Panel on Assessment of Prevention, Diagnosis, and Treatment Options](#)
- [Orientation to PCORI's Research Prioritization](#)
- [Assessment of Prevention, Diagnosis, and Treatment Options Summer Webinar](#)

The Patient-Centered Outcomes Research Institute (PCORI) is an independent organization created to help people make informed healthcare decisions.

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## Prioritization of Topics

After discussion, the panel prioritized 15 rescued topics for the Clinical Effectiveness Research program. Key discussion points are described below each topic.

### **1. Assessment of Benefits and Harms of Pelvic Floor Mesh Implants**

Pelvic floor dysfunction occurs when the muscles in the pelvic floor are excessively weak or tight, or when there are joint problems in the surrounding area. It contributes to urinary incontinence, fecal incontinence, and pelvic organ prolapse. Mesh is sometimes inserted during surgical treatment to provide support. Research could compare treatment outcomes with and without mesh. Because the surgery can be performed by a variety of physicians, future research may need to examine physician training. Surgical outcomes and patient-relevant outcomes that occur when no mesh is inserted need to be measured for comparison. Comparative effectiveness research could focus on the different types of mesh kits and places where mesh can be implanted. There are also differences in outcomes when the implant is inserted by different surgical specialty types. Patient and provider factors may affect patient outcomes in addition to the use of mesh. Panelists also agreed that more research on patient-centered outcomes is needed.

### **2. Coronary artery bypass surgery (CABG) and percutaneous coronary intervention (PCI) for treatment of adults with coronary artery disease (CAD)**

CAD is caused by atherosclerosis, a thickening or hardening of the coronary arteries, which can lead to narrowing and obstruction of blood flow to the heart muscle. CAD may result in chest pain or a heart attack. Some patients require invasive treatments, such as PCI or CABG surgery. CAD is highly prevalent with existing evidence, but there is little research available that looks at subgroup populations. Per a [2010 AHRQ Report](#), research should: enhance patient participation and involve patients in decisions regarding their care; develop performance measures that provide feedback to health care providers; evaluate the ability of tests to predict how well a person will do with different types of revascularization procedures; and evaluate the CE and safety of PCI vs. CABG using existing data. Panelists agree that new comparative effectiveness research should focus on targeted subgroup populations. There is also a possibility for studies that compare different treatment types (i.e. stent vs. surgery, or medical therapy vs. invasive procedures vs. not intervening at all).

### **3. Early vs. late bone marrow treatment for adrenoleukodystrophy (ALD)**

ALD is a rare inherited disorder that affects how cells break down nutrients (very long chain fatty acids). Treatments include replacement of adrenal gland hormones, dietary therapy, hematopoietic stem cell transplantation (HSCT), bone marrow transplant (risky), statins, and gene therapy. Research is needed for a better understanding of the benefits, harms, and costs associated with screening for ALD in newborn males and could facilitate dietary therapy early. There is also a need to define which patient subgroups benefit most from HSCT and examine those outcomes.

Additionally, research comparing less-established therapies to better established therapies in patient subgroups is critical. Panelists noted that potential challenges for research in this area include recruitment and study length.

**4. Medical, surgical and lifestyle treatment options in the prevention and treatment of gestational diabetes**

Normal pregnancy increases the body's need for insulin, resulting in increases in blood sugar. Risk of adverse outcomes for mother and infant increase. There are different definitions for the threshold for distinguishing "gestational diabetes" (GDM) from "normal" elevations in blood sugar. Diet, exercise, medication can lead to improved maternal and child outcomes. Comparative effectiveness research on insulin and oral agents is being conducted by PhRMA, but more evidence is needed to understand the benefits and harms of different behavioral strategies (diet, exercise) and drug treatments on mother and child outcomes. Due to the number of screening approaches and variability in prevention strategies, panelists agreed that there is a need to narrow the research question if PCORI were to pursue this topic. One potential question could be about what is the optimal management of children born to women with GDM and of women diagnosed with GDM after delivery.

**5. Medical and surgical treatment options for asymptomatic carotid artery stenosis**

Carotid arteries, which carry blood to the brain, are prone to blockage from arteriosclerosis (thickening/hardening of the arteries). Atherosclerotic plaque in the carotid arteries can lead to ischemic strokes or transient ischemic attacks (TIAs). Risk of stroke related to carotid artery disease is higher with higher degrees of stenosis. Neurologic symptoms sometimes last <24 hours. Panelists discussed the difficulty identifying the patients of interest because they often do not have symptoms; could screen all patients as part of a routine exam (but patients at risk may not be going to doctor). Trials comparing CEA or CAS to optimal medical therapy in patients with significant asymptomatic CAD are needed. RCTs are also needed to determine if medical therapy is adequate or better compared to CEA and CAS. Additionally, new research should focus specific subgroups of patients. Panelists agreed that this is an important CER topic, as the existing research leaves a lot of uncertainty in patients and providers.

**6. Surgical and medical options for prevention and care in periodontal disease to increase tooth longevity and reduce systemic secondary effects in other organ systems**

Periodontal disease is a chronic infection of the hard and soft tissue supporting the teeth. It 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. Treatments include medical management (e.g. oral hygiene at home, root planning) and surgery (e.g. flap/pocket reduction, bone grafts). However, few studies have provided evidence on the treatment options. Panelists noted that prevention (improving oral hygiene) might be good focus of new research. There is a

need for longitudinal studies adjusting for relevant confounding factors, such as smoking and diet, especially for highest risk populations. Additionally, high quality reviews of single intervention trials and non-randomized studies, or original research directly comparing medical with surgical treatments for periodontal disease is needed. The outcomes are very patient-centered, but research should also consider patient-centeredness. Insurance coverage may also pose challenges for future research, as dental coverage is inconsistent and presents an access issue for some patients.

#### **7. Surgical options for hip fracture in the elderly**

Hip fracture refers to a break of the upper part of the femur (large bone of the upper thigh). It can result in pain, functional impairment, prolonged rehabilitation, loss of ability to live independently, and premature death. There is high variability in care. Per a [2010 AHRQ Report](#), research gaps include predictors of short time-to-recovery and functional outcomes; impact of suboptimal surgical quality on functional outcomes; optimal treatment for different types of fractures or defined populations; and between-class and within-class comparisons. There could be implementation issues regarding the availability of surgical intervention. There is also uncertainty regarding technical issues in surgical management, such as the type of equipment to use. Panelists noted that new research in this area could overlap with PCORI targeted PFAs and AHRQ, but should still be considered because there is little information on patient preferences and patient-centered outcomes. New research could also look at the methods to ascertain provider practice and patient match.

#### **8. Treatment options for topical or systemic eczema in children and adults**

Eczema is a chronic inflammatory skin condition and is often the first sign of an allergic disease. It is increasing in prevalence. It poses a significant impact on quality of life, costs, and use of health care services. Standard therapy includes skin hydration, topical corticosteroids, and antihistamines. Better diagnostic methods needed, as well as how to evaluate debilitating/frequent conditions (such as missed school or work). There is a need for identifying the allergen causing the eczema and/or for identifying a medication that will treat the reaction. Care varies widely and many patients self-treat, especially because information on treatment options is so accessible via the internet. Research is needed on the development and efficacy of current treatments, such as topical therapies to control itching, is needed. Larger trials of fish oil and/or omega-3s are also needed. Panelists agreed that this is an important topic that addresses a common and bothersome condition, particularly in terms of patient QOL, but that it is very broad and doesn't narrow to particular severity or stage of eczema.

#### **9. Concussion Management**

Concussion management is a form of traumatic brain injury that may occur when the head hits an object, or a moving object strikes the head; can lead to a bad headache, changes in alertness, or loss

of consciousness. Recovery occurs over a period of days or weeks. In 2009, 250,000 US children were treated for sports and recreation-related injuries that included a diagnosis of concussion or TBI. One preventative possibility may include the requirement of helmets for all sports. There is a lack of well accepted methods for classifying the severity of the injury and treatment options need to be better defined before comparative research can be done. Panelists agreed that comparative effectiveness research should be able to compare types of concussions. Research on neural activities as opposed to signs or symptoms might be good approach. The evidence gaps are related to prevention and diagnostic options are not addressed. Therefore, panelists determined that prevention research is needed to clarify how to pursue and clarify treatment options by characterizing people via valid diagnostic options.

## **10. Management of Arrhythmogenic Right Ventricular Dysplasia (ARVD)**

ARVD is a rare familial disorder in which heart muscle of right ventricle is replaced by fibro fatty tissues. It is caused by mutation in genes and usually inherited. ARVD is present in up to 20% of patients who die of sudden cardiac death, especially in young athletes. Research is needed on improved diagnosis of ARVD in primary care and local settings. The topic briefs could not identify any systematic reviews or completed RCTs that assessed different treatment options for ARVD. Additionally, the benefits of existing treatment options for ARVD are largely unclear due to a lack of RCT evidence. Panelists agreed that potential research questions could focus on screening and diagnosis, such as identifying those with dysplasia and the best diagnostic methods. There was some concern with potential recruitment barriers and how long it would take for study results to be gathered. Another common concern is sudden cardiac death. Systematic reviews are also needed in this area.

## **11. Nonsurgical Treatment for Cervical Disc and Neck Pain**

Cervical disc and neck pain is a common, bothersome, and potentially debilitating problem that results from degeneration of the structures of the cervical spine. Options for addressing neck pain depend greatly on its cause and chronicity. There is a lack of a concise definition of neck pain, and no clear correlation between pain and why patients decide to seek care. Additionally, better definition of patient sub-groups is needed in this area. Providers tend to choose treatments within their specialty areas. In terms of treatment options, there are many high cost therapy options; these may be efficacious to study if low cost options are just as beneficial. Panelists agreed that nonsurgical treatment options in this area are an important subject in general, particularly relating to improving understanding of the benefits and risks of alternatives (to prevent surgery but also to ameliorate pain). There may be an opportunity for PCORI to conduct new systematic reviews to inform public on this topic. Well-structured large clinical trials are also needed.

## **12. Treatment options for hypercholesterolemia among patients who do not tolerate statin therapy**

Statins are effective in reducing low-density lipoprotein cholesterol (LDL-c) and preventing cardiovascular events. However, some people cannot tolerate statin therapy due to its adverse effects and care varies for this patient population. Muscle toxicity, including myopathy and rhabdomyolysis, is statin-related. Patient-centered outcomes include mortality, cardiovascular events, and muscle pain. A review of the current research did not identify any US-based clinical practice guidelines recommending approaches to manage patients who are truly statin intolerant. Additionally, the topic brief identified zero systematic reviews and six RCTs. Future comparative effectiveness research could explore alternative agents for treating patients who are truly intolerant to statins. However, panelists agreed that statin intolerance and patient population should be better defined and that better identification of risk factors for statin intolerance is needed before PCORI can pursue this topic.

### **13. Treatment Options for Pemphigus Vulgaris**

Pemphigus Vulgaris is a rare autoimmune disease that causes blisters in the mouth and/or widespread erosions on the skin. Oral, topical, intravenous, and intramuscular delivery systems are used to deliver medications. Existing trials used time to no new lesions, serum antibody levels and steroid dose as primary outcome measures, but there are few trials because it is difficult to recruit patients. Of those trials, most reported adverse effects but it is unclear if any were designed to measure differences in adverse effects between treatment groups. Understanding the patient-centered outcomes and designing studies to measure meaningful differences in outcomes is needed. Additionally, research on the benefits of therapies alone and in combination, as well as timing of therapies, is needed.

### **14. Treatment Options Involving Mesh for Management of Inguinal and Abdominal Hernias**

Hernias are caused by weakness in the abdominal fascia, allowing abdominal contents to bulge out. Treatment options include watchful waiting, supportive garment, or laparoscopic or open surgery. During surgery, a layer of mesh is often used to provide support; hernia recurrence is less likely to occur if mesh is used. Complications after surgery depends on patient factors, type of mesh used, and surgical technique; may increase with age, obesity, and other patient comorbidities. However, comprehensive study of the different combinations in U.S. populations is lacking and studies using existing data often do not include info on type of mesh used. Panelists agreed that numerous different options may limit the feasibility of randomized clinical trials, and that primary data collection for a prospective cohort study or registry may be required but would be feasible since hernias are common.

### **15. Treatment Strategies for Intermittent Claudication**

Intermittent claudication is leg pain that occurs with exertion, caused by peripheral arterial disease (PAD). It can result in poorer functional capacity, worse quality of life, and higher morbidity and mortality, and its prevalence is on the rise. The IOM identified this area as top priority for CER, as



few studies have compared current treatment options. Panelists agreed that more head to head comparisons and evaluations of non-pharmacologic treatments are needed. Few existing studies focus on patient-centeredness or patient-centered outcomes, so panelists also noted the opportunity for PCORI to focus on this area. However, IC is often associated with comorbid conditions (such as diabetes or smoking), so a multifactorial approach may be needed and may require stratification of study participants. Because many different practitioners manage PAD, there are also potential barriers to standardization and dissemination of treatment strategies.

## Next Steps

The next Advisory Panel meeting will be an in-person meeting held in September 2014 in Washington, DC.